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Reinventing Sample Management: Integrating New Technologies to Develop a Complete Store-to-Assay Solution Utilizing Acoustic Liquid Handling

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Introduction

In collaboration with AstraZeneca, Brooks Life Sciences and Titian Software, Labcyte has developed a fully automated system that combines new acoustic tube and acoustic liquid handling technologies with industry leading devices to improve the overall efficiency of assay-ready plate production for screening. The system is optimized to provide a high level of processing throughput and is equipped with a unique integrated environment design to preserve sample integrity. Additionally, the system implements an advanced LIMS integration to track samples from order creation to scientific assay data. This poster highlights each new technology and describes how they come together to deliver the ultimate sample management platform.

Acoustic Tube Benefits:

1. **Increased sample storage capacity:** High Density Racks vs. Storage in traditional tubes and microplates
2. **Avoid unecessary freeze-thaw cycles or hydration/ evaporation of samples stored in intermediate plates containing samples of interest**:
   - Pick and sort tubes of interest versus unsealing an entire library plate
3. **Increased life cycle for sample source storage**
   - Increased tube capping cycle limit from 15 to over 300
   - Eliminate library source plate disposal due to seal/ unseal cycles
4. **Overall reduction in sample consumption and requirements**
   - Reduce overall volume and dead volume used in processing
   - Use 1536w intermediate plate for better efficiency/ formats or can go direct from tube to assay plate
5. **Eliminate need for tip-based liquid handling to perform serial dilutions or transfer samples from tubes to intermediate Echo® Qualified plates.**
   - Reduction in consumable waste, steps, and robot movements = faster processing
6. **Overall improvement in data quality**
   - Avoid risk of sample carryover from tips that can affect assay results by performing direct dilution or acoustically dispensing directly to assay plates

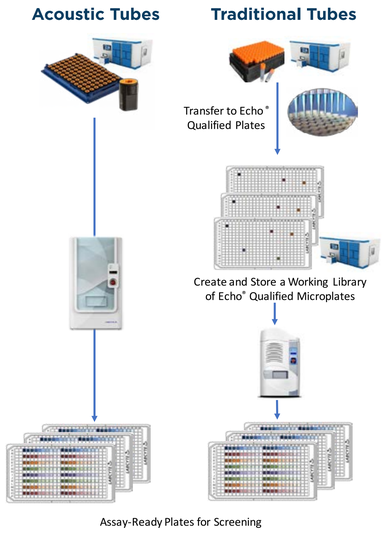


FIGURE 1: Overview of new acoustic tube workflow as compared to the traditional approach. The adoption of the acoustic tube reduces processing steps and increases storage capacity by eliminating the need to store multiple copies of sample libraries in Echo® Qualified Microplates.

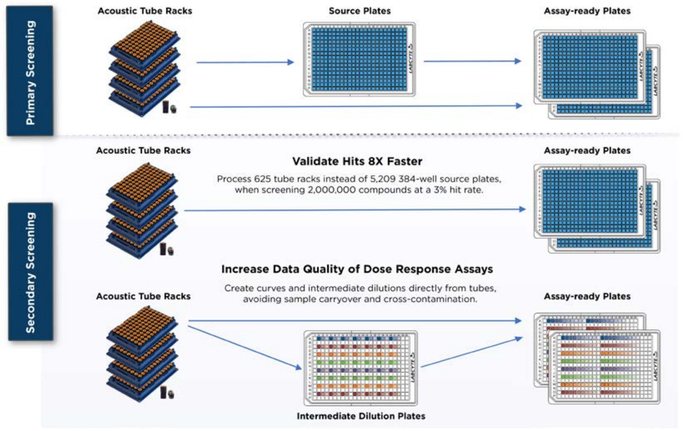


FIGURE 2: Example of the advantages to moving towards an acoustic tube centric assay-ready plate workflow in comparison to a traditional, large volume tube process that involves tip based liquid handler steps to prepare Echo qualified source plates.

Workflow Steps:

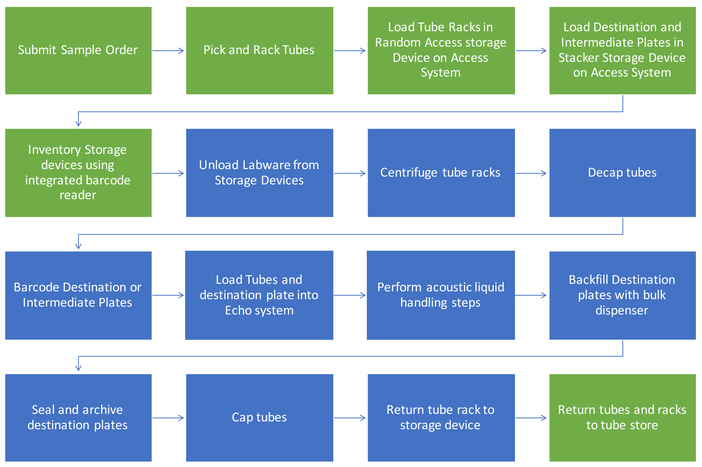
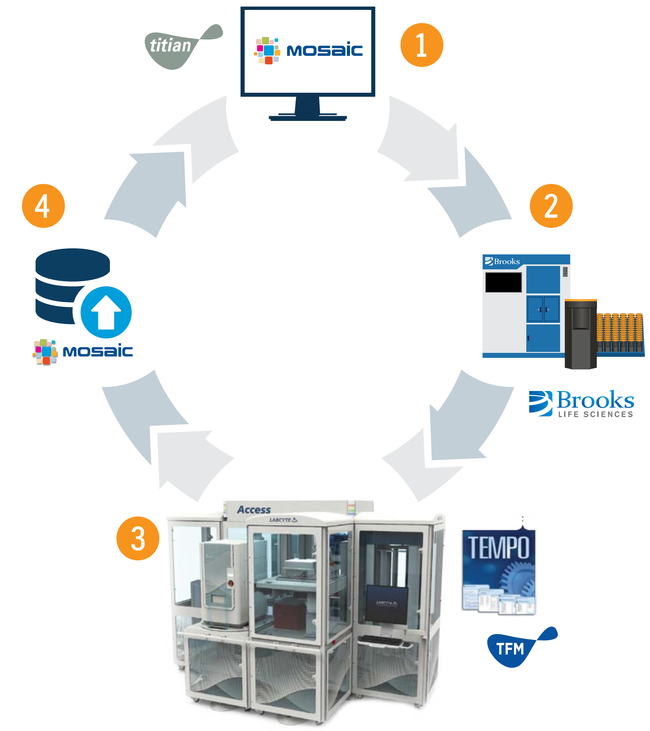


FIGURE 3: Overview of a typical process workflow for creating assay-ready plates using the Access Dual Robot System. Items in green are offline, while items in blue are in performed by the system. Tempo™ Automation software manages and controls each step for an optimized throughput with a main focus around the Echo. In additional Tempo records, in detail, all actions for each plate in order to provide a complete audit trail for a given run.

Integrated Solution Workflow

1. **Create Order:**
   - Using Titian's Mosaic Software, a remote user requests an order by selecting from a set of templates and inputting parameters that include samples required and their respective concentrations needed, bulk dispenser reagent types, plate layouts, number of copies, destination labware types, device parameters, batch size etc..
2. **Retrieve Samples:**
   - Mosaic sample management software provides a worklist for the tube store to retrieve the necessary samples. The tube store will pick tubes, place them in SBS 96w tube racks, scan tube and rack barcodes to validate and update sample locations/inventory.
3. **Process Order on Access:**
   - At the Access DRS, a user opens Titian's Tempo Fulfillment Module (TFM), selects an order to process, and is then guided to load tube racks, destination, source, or control plates into storage devices that are integrated on the system. Once loaded, Tempo inventories these storage devices using their integrated barcode readers and updates the system inventory in real time. When ready to run, TFM schedules and initiates Tempo to start processing. During order processing, detailed run reports are generated by Tempo to provide TFM the necessary information to maintain a complete audit trail for a given order.
4. **Upload Order Data:**
   - At run time, Tempo run reports are automatically parsed by TFM and plate layouts, sample inventory and workflow history and uploaded to Mosaic. After run completion, the user unloads labware and sends back to tube store to be placed back into inventory.



Tempo Fulfillment Module (TFM) and Mosaic Integration Key Benefits:

- Only module that integrates directly with ECP, EDR, ECS and EPA Echo® software applications on an automated system
- User friendly interface to guide the fulfilment from sample requests to automated protocol creation
- Leverages 2D tube barcodes and 1D tube rack or plate barcodes for fully automated result processing and sample tracking
- Complete Source, Intermediate and Destination plate sample transfer report, including controls and standards
- Captures exact volume and concentrations transferred by the Echo
- Survey volumes and DMSO% of source wells are used to update the Mosaic inventory.
- Tracks sample integrity information such as number of times used, freeze thaw and cap + decap cycles
- Generates email reports that highlight and provide visible plate map indications for any processing errors.

Overview of System Devices:

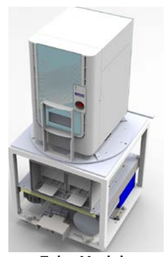
Device		Device Type	#	Description
Labcyte Echo 655T	A	Acoustic Liquid Handler	2	• New Acoustic Tube Compatible Echo • Can also process Echo Qualified plates • DMSO and aqueous capability
Precise Flex PF400	B	Microplate Handling Robot	2	• 4 axis robot with servo gripper
Brooks Life Sciences IntelliXCap	C	Capper / De-Capper	4	• Capper and Decapper for acoustic tubes
F&G Certus Flex	D	Bulk Dispenser	1	• Nanofilter bulk dispenser that supports up to 8 different reagents an a wide range of fluid types
Brook Life Sciences XPeel	E	Microplate Seal Remover	1	• Seal remover • Uses adhesive tape roll to remove seal • Compatible with heat and adhesive seals • ~400 plates per roll
BioNex HiG3	F	Centrifuge	2	• Centrifuge device capable of up to 5000 rpm speed • Very high imbalance tolerance (100g) • Capable of spinning partial and full tube racks
Agilent Microplate Labeler	G	Microplate Labeler	1	• Microplate barcode labeler, • CAB printer
Agilent PlateLoc	H	Microplate Sealer	2	• Heat Sealer • Compatible with broad range of ANSI/SLAS format plates
HighRes Biosolutions Ambistore	I	Storage Device	1	• High capacity ambient storage • Storage of up to 672 acoustic tube racks or microplate
HighRes Biosolutions MicroServe	J	Storage Device	1	• High Capacity FILO storage of 770, 384/96-well micro-plates and tube racks or 1120 384/1536-well LDV plates

Overview of System Devices

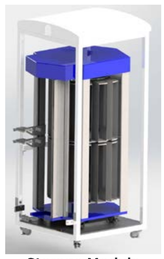
The Access Dual Robot System is a modular system that allows for flexibility and scalability. Below is an overview of the different module types and their features.

Robot Module

Device Module



Echo Module



Storage Module

1. **Robot Module:**
   - Core for electronice, power, and utilities
   - Equipped with environmental features
   - Docking features
   - Different deck heights to accomodate different robot models
   - Random Access Temporary Hotels
   - De-lid station, Regrip and Barcode reader
2. **Device Module:**
   - Configurable shelfs
   - 1-4+ depending on device types
   - Retractable or fixed
   - Docking features
   - Equipped with environment features
   - Safety door sensors
   - Doors on 2 sides
3. **Echo Module:**
   - Turntable
   - 2X Capper/Decappers on shelf (retractable) underneath in environment box
   - Echo accessories on the bottom shelf
   - Docking features
   - Monitor mount option
4. **Storage Module:**
   - Holds large storage devices
   - Fans to vacate heat
   - Safety interlocks
   - Main PC/Monitor mount

Docking Features and Benefits:

The Access Dual Robot System is a compact design, but with a docking option users are able to access the inside of the robot modules for teaching, recovering, and maintenance. Features and benefits of the docking option are listed below.

Floor plate for alignment and hold weight of cart
- Repeatability of +/-100u, (x/y) +/-200um (z)
- No re-teaching necessary

Screw + Motor Assembly:
- Push-button automated dock and undock

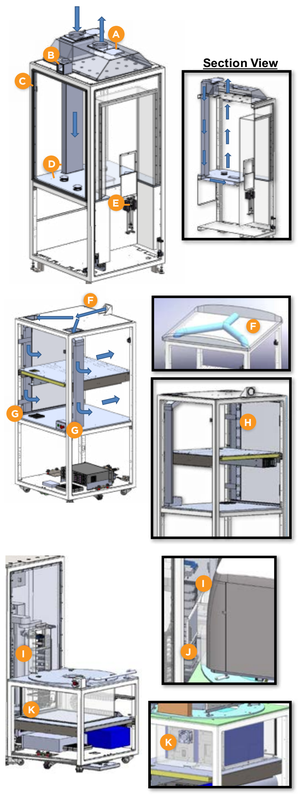
Spring loaded casters:
- Cart requires less force to move

Guides on cart to facilitate alignment:
- Easier to locate cart for docking

Retractable umbilicus containing all cart utilities:
- Single bundle of cables to disconnect to remove cart
- 1 Meter umbilicus length.
- Users can recover from errors easier.
- Can undock a cart and access the inside of the robot cell without cutting power to devices.
- System pauses when undock is initiated. Once reconnected, system can resume run in progress.

Integrated Environment Features:

Hydration of samples in DMSO can lead to assay quality issues due to changes in sample concentrations. To prevent hydration, Labcyte has designed and integrated a series of unique environment features that allows house HVAC systems to connect to the system to maintain an ambient (19 – 26°C) and low %RH (10 – 30%) environment. Each system module has its own features and when integrated together deliver a complete solution.



Robot Module HVAC Connections	A	• 1 Input and 1 Output per Robot Mofule (2 robot module total) • Air distributed to robot cell and device module • Air returned and recirculated
Device Module Duct	B	• Duct that directs air to device cart • Hinged to provide ability to close duct when device module is not present allowing the system to operate without compromising environment when a mofule is removed
Gasket Seals	C	• Prevent environment leaks when mated to module or blanking panel
Robot Deck Ducting	D	• Directs air through a duct located behind robot (see section view), distributes the air from base of robot deck and returns air to HVAC via plenum above
Inlet Panels and Actuating Door	E	• Located in front of storage device modules • Open only when robot needs to access storage device • Allows user interaction with storage cart during operation • Prevent external environment intrusion
Device Module Top Ducting	F	• Ducting that directs robot cell input air to the device cart • Hidden by device top cart
Device Module Rear Duct	G	• 2X Ducts located at the rear of the device cart • Airflow is directed from back of devices towards the robot cell
Duct Tuning Features	H	• Adjustable to optimize the rate of airflow
Echo Tunnel	I	• Facilitated diffusion of internal environment to echo • Safety shield • Echo has own internal dedicated CDA source to saturate the inside of the Echo with a low RH, ambient environment
Sliding Door	J	• Close door when Echo is rotated or in service to close opening, maintain environment and operate system • Integrated safety sensors to check door state or prompt users
IntelliXCap Enviroment Enclosure	K	• Gasketed interface and boarder to seal IntelliXCap to prevent external environment intrusion • Rear fan to draw robot cell environment to IntelliXCap enclosure

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