Advances with Acoustics

Evolution of Acoustic Dispensing and Next Generation Developments

SLAS Europe Compound Management
March 14, 2017
Corporate History

2000
Labcyte founded

2004
First Echo® Liquid Handler shipments
initial focus on early stage pharmaceutical discovery

2006
Launched Echo® 555 Liquid Handler
targeting high-throughput pharmaceutical discovery

2011
Release of Dynamic Fluid Analysis™
dramatically expanding addressable applications

2013
Launched Echo® 525 Liquid Handler
25 nL drop expands dynamic range

2014
Initiated Echo-MS Project
direct loading of mass spec using acoustic energy

2015
Initiated Acoustic Tube and Instrument program
collaborative with AstraZeneca

Labcyte 1.0
First-Gen technology that enabled delivery of compounds stored in DMSO, for early stage drug discovery

Labcyte 2.0
Introduced Dynamic Fluid Analysis™, which enables self-adjustment to transfer most liquid types and expansion into genomic research, cancer research and molecular diagnostics

Labcyte 3.0
Development of novel systems that will substantially expand the application of acoustic liquid transfer into new markets
Broad Range of Applications

Used in life sciences, research, drug discovery and personalized medicine

<table>
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<tr>
<th>Genomics</th>
<th>Translational</th>
<th>Drug Discovery</th>
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<tr>
<td>Synthetic Biology</td>
<td>Sequencing</td>
<td>Epigenetics</td>
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<td>Increase efficiency and speed while reducing costs</td>
<td>Low cost, highly efficient library preparation</td>
<td>Enabling high-throughput epigenetic screening</td>
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- **Drug Discovery**: Enabling miniaturization with unparalleled throughput and accuracy
  - **Result**: New drugs discovered

- **Genomic Research**: Overcoming traditional barriers by dramatically reducing sample and reagent volume requirements
  - **Result**: Better experimental data at a fraction of the cost

- **Cancer Research**: Helping research programs drive down assay costs while enabling new experimental workflows
  - **Result**: Patient sample targeted therapy

- **Molecular Diagnostics**: Eliminating cross-contamination and other data errors while dramatically reducing running costs
  - **Result**: Lower operational costs (critical with reimbursement pressures)
Acoustic Tubes and Instrumentation
Drivers for Acoustic Tube

▸ **Data quality**
  - Eliminate all tip based liquid handling
  - Sample integrity assurance throughout system

▸ **Flexibility / scalability**
  - Modular and configurable liquid handling instruments
  - Modular tube and plate storage
  - Standardization across sites, research partners, CRO’s

▸ **Reduced running costs**
  - Eliminate tips and DMSO wash
  - Reduce additional plastic-ware
  - Reduce maintenance and intervention intervals

▸ **Footprint reduction**
  - Reduction in total compound volume in storage
  - High density tube and plate storage
Acoustic Tube System

▸ Echo Qualified Acoustic Microtube
  - 96/per rack
  - Screw Cap and 2D Barcode
  - ~70 uL working volume
  - ~15 uL dead volume

▸ Echo System for Tube Transfer
  - Capable of 555 transfer speed
  - Dynamic fluid analysis enables DMSO, and aqueous without calibration
  - Will support transfer from microplates

▸ Access Workstations for Tube Processing
  - Dual Echo, dual robot base system
    • Option to configure as single Echo & robot
  - Advanced integration with LIMS to support order management across multiple workstations
Configurable and expandable

- Up to 2 Echo Liquid Handlers
  - Transfer from tubes or microplates
- Up to 2 plate handling robots
- Capper/decapper units
- Highspeed centrifuges with imbalance management
- Thermal sealers
- Bulk reagent dispensers
- Microplate labeler
- FILO storage up to 770 plates
- Random access storage of 672 tube racks
- Dockable, configurable carts
Flexibility & Expandability
Project Milestones

- **Specifications complete**
  - Tube, Echo, Workcell, Titian integration

- **Beta system running in Sunnyvale, CA**
  - April 2017

- **Validation testing**
  - Lifetime sample integrity (hydration, DMSO evaporation)
  - Tube handling cycle testing (cap/decap, pick/place, Echo dispensing)
  - System testing (Titian/Brooks/Labcyte)

- **Production tubes available**
  - Q4 2017

- **Hardware available**
  - Q2 2018
Acoustic Mass Spectrometry
Echo-MS — Acoustic Mass Spec Interface

Technical Challenge

- Demand for a new approach to mass spectrometry sampling
  - Higher throughput
  - Lower sample requirement

- Can we dramatically reduce assay development time?
  - Kinetic sampling

- Need detection of a wide range of end points
  - Proteins
  - Small molecules
  - Lipids
  - DNA
  - Sugars
Echo-MS — Acoustic Mass Spec Interface

Technology Overview

- Patented Labcyte acoustic technique proven to provide strong signal directly loading a mass spec
  - Novel technique creates a focused mist
  - Dynamic adjustment to handle a wide range of fluids
  - Electrospray methodology for ionization

![Image of acoustic interface with volume and micron measurements]
Echo-MS — Collaborative Development

- **Initial research phase funded by AstraZeneca**
  - Research partnership with Waters

- **Most recent assay results**
  - Sampling rate of 3 samples per second achieved
  - Demonstrated reagent savings of $150,000 in one screen
  - Reduced assay development time from 4 months to 4 days
    - Unique ability to analyze enzyme kinetics, readdressing the same well multiple times
Example materials tested

- **Solvent Systems**
  - Buffers
  - Water/alcohol
  - Cell lysate
  - DMSO/water

- **Small Molecules**
  - Caffeine
  - Verapamil
  - Sulphadimethoxine (SDM)
  - Warfarin

- **Proteins & Peptides**
  - Up to 40 kDa to date

- **Double Strand DNA with/without Intercalating Compound**
Next Steps

- Adding additional early access partners now
- Investigations will expand to include:
  - Multi-component reaction chemistry QC
  - Cell based systems
  - Metabolomics