Abstract

Traditional sample management and high throughput screening has relied heavily on high density microplates for compound storage and tip-based liquid handling solutions for processing. Drawbacks of these technologies have included increased microplate storage space requirements (empty wells cannot be excluded), sample integrity challenges (accessing sample subsets in a microplate requires thawing the entire plate) and compound loss during transfer (due to adhesion to or contamination from the tip plastic itself). Adaption of individual tubes for storage and acoustic liquid handling technologies for transfer have addressed most but not all these drawbacks. To date, sample tubes have not been compatible with acoustic liquid handling technology – necessitating creation of working microplates using tip-based liquid handling systems. We present an overview and performance details for a new acoustic liquid handling technology and compatible acoustic tubes that offers the full benefit of tube storage and acoustic liquid handling without the historical drawbacks.

We will demonstrate the utility of the technology in maximizing compound storage both in terms of maximizing space and maintaining sample integrity. The combination of acoustic tubes and acoustic liquid handling offers a more efficient, streamlined approach to non-contact acoustic transfer of samples and reagents for sample management and small molecule screening groups.

Advantages of Echo Acoustic Liquid Handling

- Maximize Reagent Savings
- Maximize Time
- Maximize Results

Figure 1. Advantages of Acoustic Liquid Handling. A. A highly precise nanoliter transfer volumes enable assay reactions to be miniaturized. Common genomics workflows have been miniaturized, up to 100-fold B. Due to Echo Liquid Handler any-well to any-well transfer capabilities, time to complete complex workflows can be significantly shortened. An 80% time savings was achieved with a complex pooling and assembly workflow. C. Replacing tips with non-contact dispensing of compounds improves IC50 values. In a study performed by Bristol-Myers Squibb, researchers found ~12% more hits using an Echo Liquid Handler compared to a tip-based system (Spicer T., et al. Pharmacological evaluation of different compound dilution and transfer paradigms on an enzyme assay in low volume 384-well format. Poster – Drug Discovery Technology, August 2005, Boston, MA).

How Does Acoustic Transfer Work?

An acoustic transducer is positioned below a source plate or acoustic tube. Water flowing between the transducer and well bottom couples the transducer to the well of interest enabling sound energy to propagate into the fluid in the well. Acoustic energy focused at the fluid surface by the transducer enables droplets of a predetermined volume (2.5 nL in the case of Echo 650 Series Liquid Handlers) to be ejected. Larger volumes are achieved by serially ejecting droplets. Ejected droplets are collected in an inverted destination plate positioned immediately above the source plate. Droplets can be transferred to either a dry well or a well already containing fluid.

Next-Generation Echo Liquid Handlers

Echo 650 Series Liquid Handlers represent the most flexible line of instruments for low volume acoustic liquid handling. The Echo 65ST and 650T Liquid Handlers offer the ability to transfer from acoustic sample tubes and Echo Qualified Microplates. Echo 65ST and 650T Liquid Handlers natively transfer from Echo Qualified Microplates and can be upgraded to transfer from acoustic sample tubes in the future. The benefits of this new instrument include:

- Improved fluidics handling for simpler maintenance and quieter operation
- Simplified architecture to improve robotic integration
- Seamless upgrade path to enable transfer from acoustic tubes
- High speed transfer with Echo 65ST and 650T Liquid Handler models

Echo 650 Series Performance

Equivalent high performance was demonstrated for Echo 65ST and 555 Liquid Handlers for transfers from 1536LDV, 384LDV, 384PP and 96TR source plate types filled with DMSO and aqueous fluids to 384-well destination plates (DMSO-only data is presented since aqueous results were highly similar). Testing was performed independently on four Echo 65ST and four Echo 555 Liquid Handlers. Transferred volumes were determined using a fluorescence assay. For each fluid, average volume and CV for all 384 well transfers was calculated. Data was plotted with x-axis “jitter” to artificially offset data points for better visualization.

Conclusions

Unlike tip-based liquid handlers that can result in compound loss, carry-over, cross contamination, or introduction of harmful plastic leachates, the Echo 650 Series of Liquid Handlers transfer without any contact being made with the sample. Non-contact transfer also reduces volumes and reagent costs while improving accuracy and precision. Echo Systems support microplate set-up from Echo Qualified Liquid Handler models to many destination wells, a series of 14 consecutive 5 µL transfers was tested for both DMSO (Dimethyl sulfoxide) and aqueous fluids (DMSO-only data is presented since aqueous results were highly similar).