

Optimizing Assay Plate Preparation Automation Using a Flexible High-Throughput Application Architecture

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Abstract

Creating assay plates in a typical high-throughput research laboratory requires the coordination of several instruments and robotics. Protocol creation processes can be wearisome if the chosen software tool lacks application focus and is simply a hardware "driver". New assay-plate driver software coupled with a revolutionary scheduler dramatically improves workflow and throughput while eliminating the need for trained software experts.

We have designed three software applications specifically to allow end-users to take full advantage of the Labcyte® Echo® liquid handlers and the unique capabilities of acoustic droplet ejection technology. *Echo Cherry Pick* enables accurate "touchless" low-volume sample transfer from any source well to any assay well. *Echo Plate Reformat* provides plate replication, reformatting, and region-based mapping tools that facilitate sample pooling into assay plates. *Echo Dose-Response* automates the "direct" sample dilution process for dose-titration studies. In each of these applications, the user employs an assay plate designer to specify the layout of the assay plates. The software automatically creates the protocol necessary to achieve the desired layout, manages the plates and their contents from protocol start to finish, and generates user-customizable reports in XML or CSV formats for easy import into LIMS systems.

We present case studies utilizing these software applications and explain how the revolutionary *Intellectual Scheduler*, a priority-based dynamic scheduler used in the POD™ 810 plate assembler, coordinates the activities of these software tools to fully optimize assay plate preparation without sacrificing flexibility in assay design or application process mapping.

Replicating, Pooling, Reformatting

The Echo Plate Reformat software simplifies a wide variety of plate transfer functions – plate replication, up-stack/down-stack plate reformatting, and custom regional mapping. This Echo application software offers great flexibility in specifying the number of source plates, transfer regions and transfer volumes. The drag-and-drop interface combined with color-coded plate preview simplifies the setup process for even the most complex cross-pooling protocols.

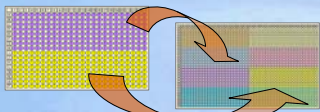


Figure 1: One example of regional 384→1536 sample pooling



Echo® Liquid Handler

- Utilizes acoustic droplet ejection technology
- 2.5 nL and up with high accuracy and precision
- No tips, no washing, no waste



Echo Plate Reformat

- Regional-based transfers for sample distribution, pooling or simple replication or reformatting
- Optional reference addition eliminates the need to run multiple protocols
- Perfect for screening libraries



Echo Cherry Pick

- 1→N, N→1, M→N wells or plates transfers
- User provides CSV-file pick lists in implicit or explicit format.
- Perfect for picking samples from a large pool or creating complex transfer patterns



Echo Dose-Response

- 1→N transfers to build sample dose titration curves: up to 24 points for 384-well format and 48 points for 1536-well format
- Optional DMSO back-filling, reference addition, replications
- Supports pick lists for transferring directly from original library plates, and eliminates separate pooling steps

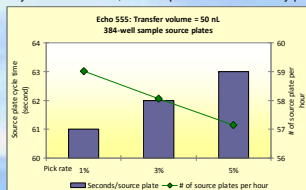


Figure 2: Dependence of source plate cycle time on pick rate in Echo Cherry Pick software.

Making Dose-Response Curves

The Echo Dose-Response software enables you to prepare IC₅₀, EC₅₀ or any type of dose-response curves using the unique capabilities of the Echo liquid handler. This software simplifies the creation of assay-ready plates for dose-response studies by consolidating compound distribution, DMSO back-fill and control compound transfer in a single, easy-to-use graphical interface.

Source Concentration	Transfer Volume (µL)	Backfill Volume (µL)	Assay Volume (µL)	Final Concentration
1.000E-02	200.0	0	20	1.270E-04
1.000E-02	75.0	175	20	3.760E-05
1.000E-02	25.0	225	20	1.270E-05
1.000E-02	7.5	242.5	20	3.760E-06
1.000E-02	2.5	247.5	20	1.270E-06
1.270E-04	200.0	0	20	1.620E-04
1.270E-04	75.0	175	20	4.974E-05
1.270E-04	25.0	225	20	1.620E-05
1.270E-04	7.5	242.5	20	4.974E-06
1.270E-04	2.5	247.5	20	1.620E-06
1.270E-06	75.0	175	20	4.030E-08

Figure 3: Sample 11-point curve covering over 5 logs of dose titration range



Intellectual Scheduler

Maximizes Productivity
High-Throughput Automation
With Intellectual Scheduler

- Task scheduling to effectively utilize idle devices
- Devices are reserved for tasks and unreserved when a task is completed
- Non-sequential execution of tasks – Dynamic reordering of tasks based on priority and device availability
- Plate lidding and delidding task is automated

The Power of the Intellectual Scheduler

The Intellectual Scheduler is an event-based scheduler with built-in intelligence for maximum throughput based on device availability and task priority. Developed by Labcyte, it is the core of the POD™ 810 plate assembler that ties together multiple assay plate preparation devices for cohesive operation.

Users can configure devices, create protocols, schedule runs and monitor run progress with the intuitive graphical user interface. No software programming or lengthy scripting is required when changing research methods. The Intellectual Scheduler is the key to increasing productivity and faster return on investment. Runs can be started right away or scheduled for a later time, and multiple runs can be queued in the scheduler for sequential execution. The flexible run scheduling feature of the Intellectual Scheduler enhances device efficiency and maximizes productivity.

Summary

While the various software applications enable the Echo system to perform complex liquid handling tasks, the POD 810 plate assembler together with the Intellectual Scheduler maximize the utilization of the Echo system. The core protocol execution engine of the Intellectual Scheduler is identical to all Echo applications software and provides forward compatibility with future applications for the Echo instruments. It not only automates plate replication and cherry picking, but also enables high-throughput dose-response curve generation for assay-ready plates.

In summary, the combined application architecture of the Echo system and the POD 810 plate assembler optimizes assay plate preparation automation in the following ways:

Event-based integration with Echo applications

- Intellectual Scheduler receives events (requests) from the Echo applications
- Schedules requests in processing queues for each device
- Plate-specific tasks are maintained and tracked to completion

Priority-based dynamic scheduling

- Resource reservation.
- Avoids deadlocks through unique system design.

Optimization of resources

- Priority given to the Echo system to keep the Echo system fully utilized.
- Devices request work and notify scheduler when the previous task is completed.

