

Development of a Fully-Integrated ECHO Dosing System for Cell-Based Assays

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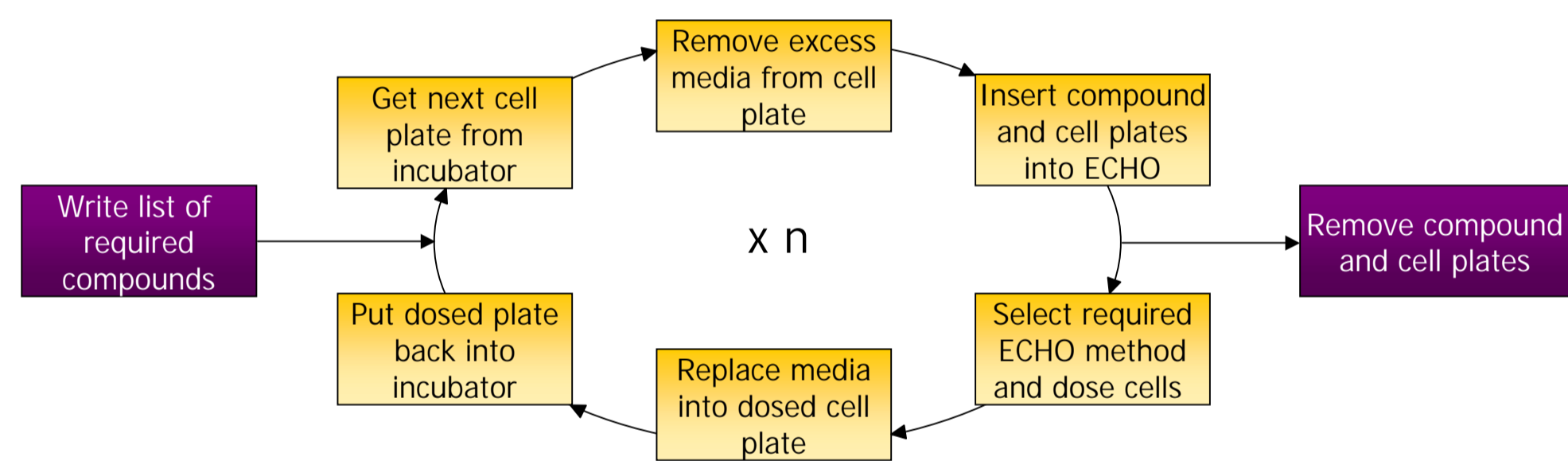
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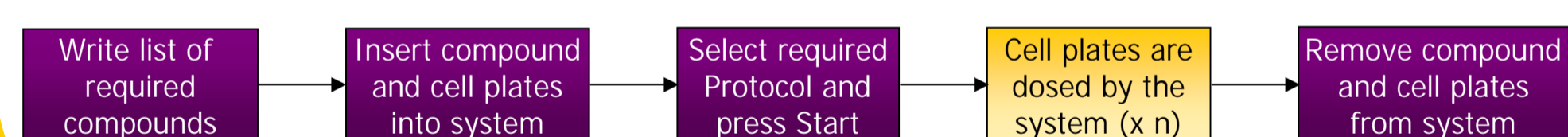
1. The Requirement for an Integrated ECHO System

The Labcyte ECHO acoustic reformatter is routinely used in AstraZeneca Cancer Bioscience in Alderley Park to dose cell-based screening assays, due to its non-contact dispense method, high precision and accuracy and a dispense volume range down to 2.5 nl. Although there have been significant increases in throughput compared to manual dosing, the ECHO dosing step is still time-consuming. In addition, the creation of IC50 dosing platemaps originally required a vast number of worklist files to be manually-generated (often one worklist per cell plate). However, large assay batches (>50 plates) and the requirement for identical treatment of each cell plate make the ECHO dosing process an extremely suitable candidate for automation.

User Workflow for Manual ECHO Dosing



User Workflow for Integrated ECHO System Dosing



2. Hardware in the Integrated ECHO System

- Labcyte ECHO 555 acoustic reformatter for dosing down to 2.5 nl from 384-well compound plates
- Velocity 11 VPrep® pipetting station for media handling in 96-well plates
- Peak KiNEDx robotic arm for plate movement and lid handling
- LiCONiC StoreX 220 incubator with rotating plate transfer station and internal barcode reader
- Custom-built storage hotel for 12 compound plates, incorporating a delidding/ relidding station and mobile barcode scanner

Introduction

The Section for Cell Assays in AZ Cancer Bioscience has proven that the Labcyte ECHO acoustic reformatter is a reliable and accurate platform for the dosing of test compounds in cell-based screening. As the compound dosing step can be time-consuming, and it is important to minimise the duration that cell plates are outside the incubator environment, we have developed a fully automated system which can process up to 200 cell plates in a single screening batch. Here we describe the design and development of this integrated system, as well as its benefits when used for routine cell-based assays.



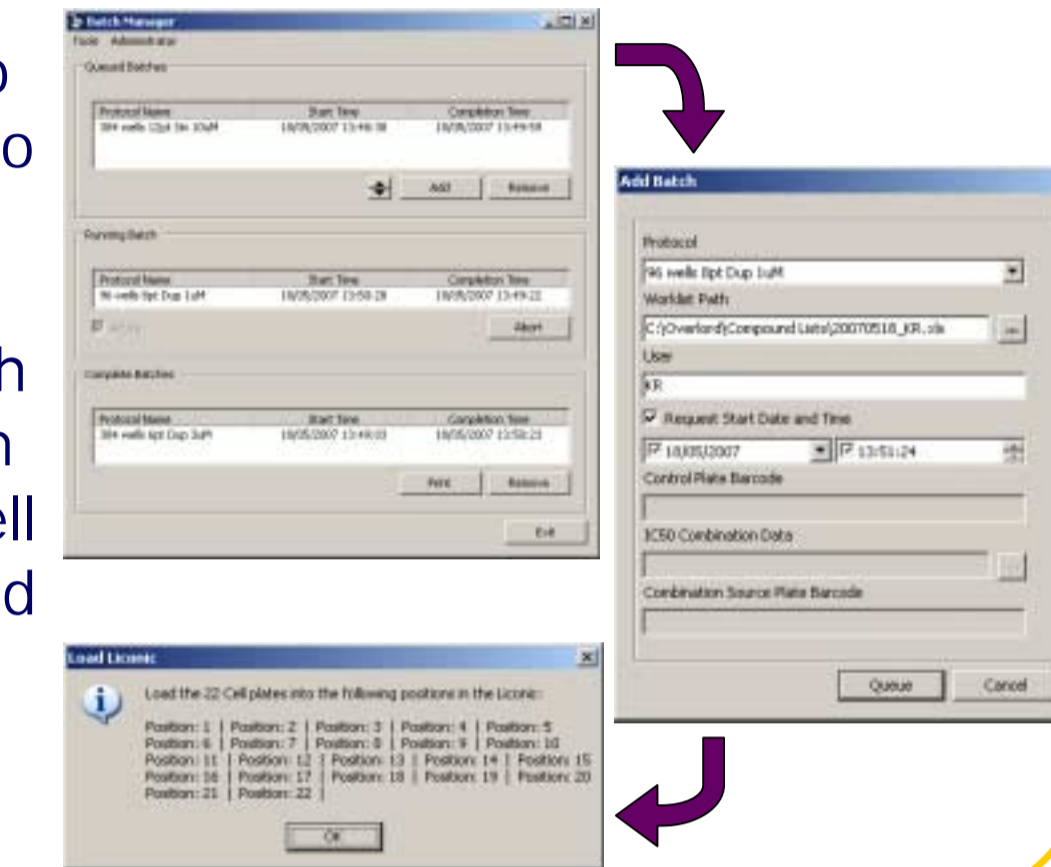
3. OVERLORD Software

A specific application module was developed by PAA to run the integrated ECHO system, operating under the OVERLORD automation control software. The main functional highlights of this system are:

- Compatible with 96- and 384-well lidded plate formats, with an extra media handling step included for 96-well plates
- User-defined protocols allow any combination of dose range, DMSO backfill, control compound concentration and platemap
- Automatically generates IC50 method files for the ECHO dosing step, based on the selected protocol and a list of required compounds
- Full compound cherry-picking capability - a single cell plate can be dosed from multiple compound source plates
- Multiple assay batches can be queued, each with a different protocol and compound list, and each batch can be given a scheduled start date and time
- A detailed report generated at the end of each batch includes ECHO survey and dispense results for each compound and cell plate barcode

4. System User Interface

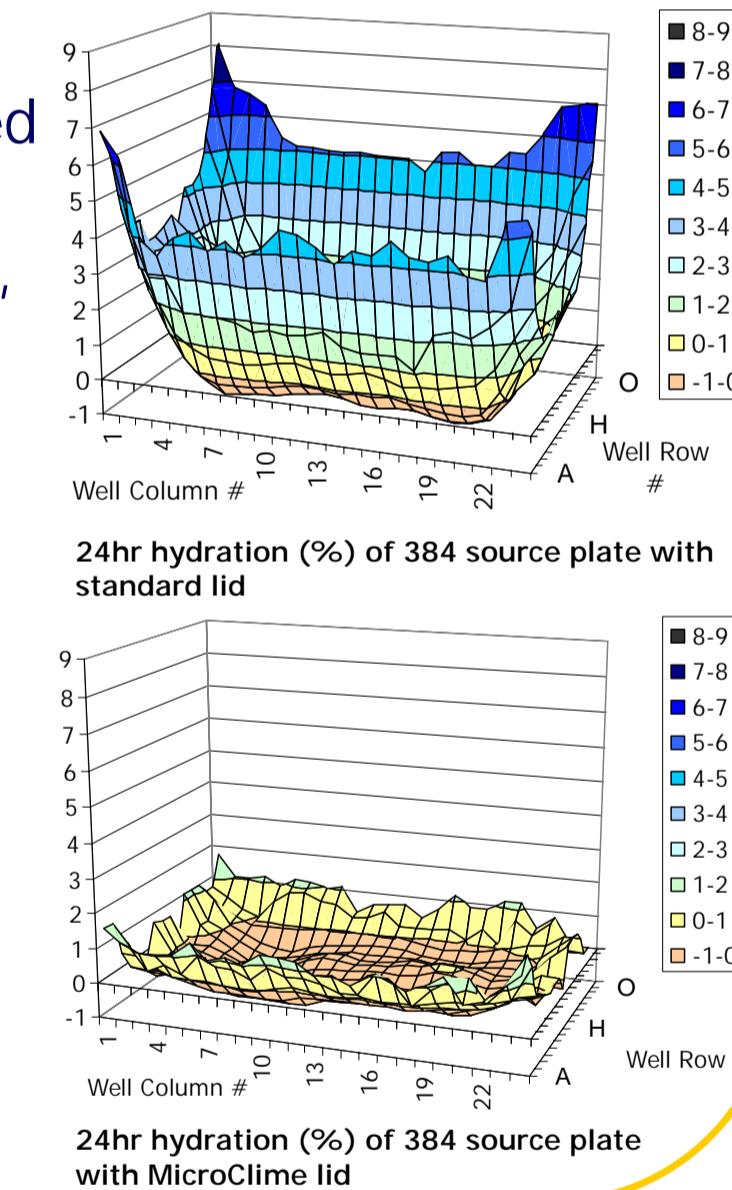
Users of the system are asked to choose an appropriate protocol to run, and then load a simple MS Excel file that lists the plate barcode and well location of each required compound. The system then calculates the number of cell plates needed to fulfil this list and instructs the user to load the system with the necessary cell and compound plates.



5. Labcyte® Microclimate™ Lids for Compound Plates

Long or scheduled dosing runs mean that compound plates remain inside the integrated system for extended periods. DMSO rapidly hydrates under normal laboratory conditions, and increased hydration in edge wells leads to variations in compound concentration across a plate.

We compared DMSO hydration across compound plates between standard microplate lids and Labcyte's MicroClimate™ Environmental lids. MicroClimate™ lids were injected with DMSO to form a vapour barrier over the wells, significantly reducing DMSO hydration and edge effects over 24hrs.



6. Benefits to Cell-Based Assays

- The Integrated ECHO System allows greater flexibility in dosing cell assays due to full cherry-picking capability for compounds
- Time scheduling allows dosing to occur 24 hours a day, 7 days a week
- Automation guarantees that each cell plate is treated identically and incubated for the same amount of time