BraMosA: Our New Smartcel-2 boosting Serial Dilution Preparation

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Introduction

Enhancing throughput while reducing footprint is a recurring requirement in sample management. With the new Smartcel-2 from Flexible Lab Solutions, we have significantly boosted our capability to prepare assay-ready plates in a serial dilution format.

This double-deck automation system features a Bravo from Agilent for high-volume serial dilution plate preparation and a mosquito LV from SPT Labtech for nanoliter dispensing steps. Several peripheral devices, including a peeler, sealer, centrifuge, and plate storage, enable the automation cell to operate around the clock.

Customized User Interface

The scheduler software Director provided by FUJIFILM Wako Chemicals is managing the automation, a customized User interface allows us to:

- Choose between 3 processes: serialise and replicate, serialise only, replicate only
- Upload replication file from Titian Mosaic which secures barcodes, volumes, number of copies
- Select serialisation protocol for the Bravo
- Select suitable tip box layout (only appropriate layouts for selected protocol will be offered)
- Select the use of control plate (Barcode of control plate=Request ID)
- Start several jobs in queue, allow priority jobs to jump the queue and set up delays
- Process multiple orders in parallel with a smart management system
- Monitor and operate remotely with a Camera system in the cell

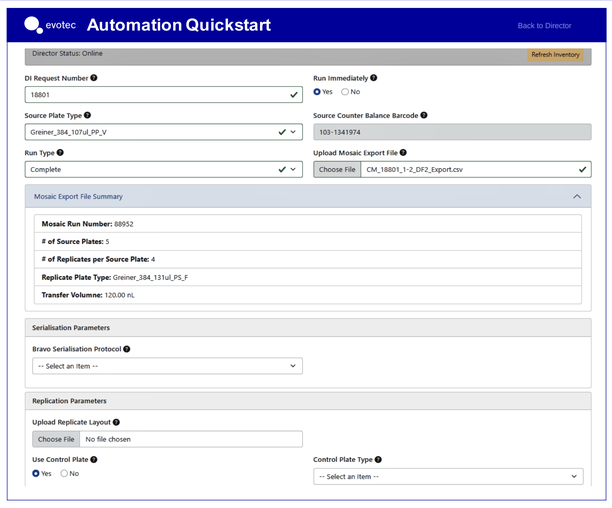


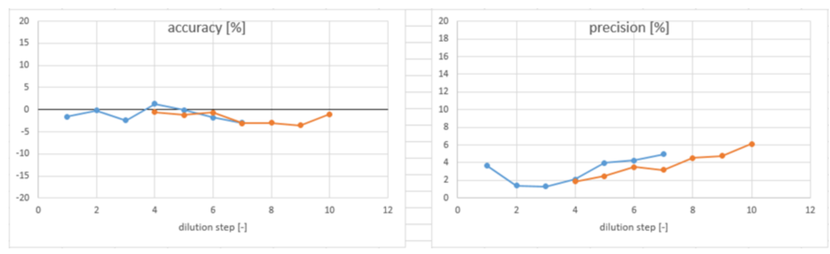
Plate Journey

Mosquito LV Maintenance

The mosquito is mounted onto a dynamic integration stage to enable moving partially out of the cell environment to give better access for Spool changes, maintenance and qualification procedure.

Bravo: Serial Dilution high volume (µl)

- Standard formats available: 4 dilution factors: 1,65 - 2 - 3 - 4 and a restricted number of layouts.
- DMSO reservoirs located on the deck provide a solvent protection from ambient atmosphere with lids fitting to the tip layout.
- Each protocol is carefully set up, including optimal transfer speed, mixing steps, heights and if needed volume corrections.
- The most challenging protocol will be checked monthly to ensure the quality of the process. All protocols are verified yearly.



Quality control with Fluorescence: serial dilution 10pt, Dilution Factor 3, 10µl end volume

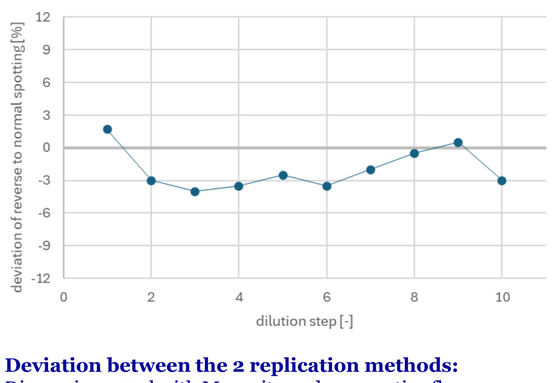
Tip Box Handling

- The Bravo is preparing tip boxes with the different standard layouts that we are offering.
- The tip boxes are barcoded according to their respective layouts and will be offered for selection to the operator during the job creation
- Bulk processing of orders with different layouts.
- The software triggers the change of the Tip Box after a determined number of cycles (customizable)

Mosquito LV: Nanolitre Replication and « Reverse spotting »

For serial dilution format, beside the "regular" replication in nanoliters with the mosquito LV, we introduced an alternative process of "reverse spotting". The dispensing will be done from lowest to highest concentration without tip change
for the same compound. An intensive qualification process showed insignificant differences whether or not tips were changed.

Reverse spotting leads to both speed up the procedure by 40% per plate and minimise material consumption up to 80% per plate.



Deviation between the 2 replication methods:
Dispensing 100nl with Mosquito and consecutive fluorescence measurement

Test of a tool compound in assay:

- Assay system
  - Human microglia Cells in 384 well
  - Antibody based HTRF-assay

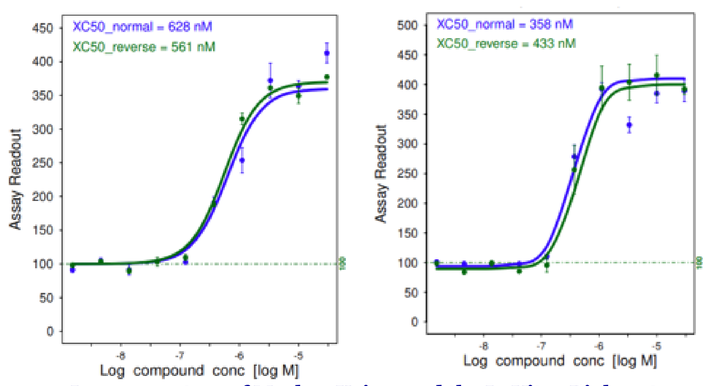


Image courtesy of Markus Keiser and the In Vitro Biology team

Lower Deck

The lower deck holds space for 120 destination plates for maximizing run time up to 24 hours. Racks feature a special positioning system for comfortable manual handling. The process labware is located in the lower deck together with the Mosquito tip waste bin and an auto fill wash fluid reservoir for the dilution process

Conclusion

- To conclude, we would like to highlight that it took less than a year from the design of this automation, tailored to our business process, to the delivery of the Smartcel-2 in our lab that performs exactly as expected. The automation can produce up to 42 "serial dilution" plates in various standard formats, as well as more than 200 replicates in nanoliter volumes (reverse spotting mode) in 24h. Compared to the traditional process, we have increased our throughput by 43% and reduces our resources by 37%. The system includes several control steps to prevent operator errors and enhance our "right the first time" rate. Our next steps will be to integrate this cell into our LIMS system, Mosaic.
- We would like to extend our gratitude to David Reed and Ian Meads from Flexible Lab Solutions for their excellent support during this project, and to Mark Eutizi for developing the awesome UI for Evotec. Finally, we are grateful to the REACT-EU program and the city of Hamburg for their financial support.