#64 -AUTOMATED ORGANS-ON-CHIP PLATFORM TO REDUCE INTRA-LABORATORY CELL CULTURE VARIABILITY

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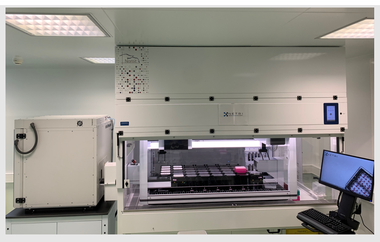
BACKGROUND

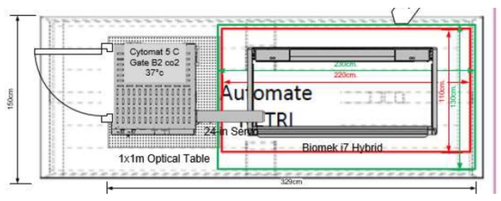


Pushed by the necessity to boost drug development by giving access to relevant models, legislative bodies are expanding the usage of Organs-on-Chips (OoCs) submissions. There are still some significant challenges that need to be overcome to fully enable this transition. The lack of trained technicians in microfluidic operations, the high exigence of the industry (high throughput screening and high reproducibility), and the integration with their current technologies and readouts constitute some of these roadblocks. Here we present the development of our automated cell culture platform, a technological response to these issues.

MATERIAL

AUTOMATED CELL CULTURE-PLATFORM.

To address this challenge, we present an automated cell culture-on-chip platform (Biomek 7, Beckman Coulter), and illustrate its impact on neuronal cells.



NETRI's microfluidic technology is compatible with automated cell culture.

NETRI's microfluidic devices

- NeuroFluidics line
- In **96-well SBS format**, NeoBento™

Cells

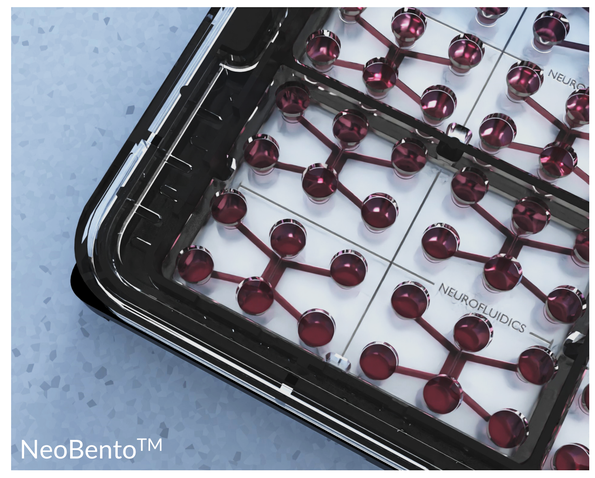
- **Rat Primary Hippocampal neurons**

Methods

- Cells were maintained in culture for more than three weeks
- Obtained **manually versus using automated cell culture-platform**

Competitor

- **Human laboratory technician** (Manual)



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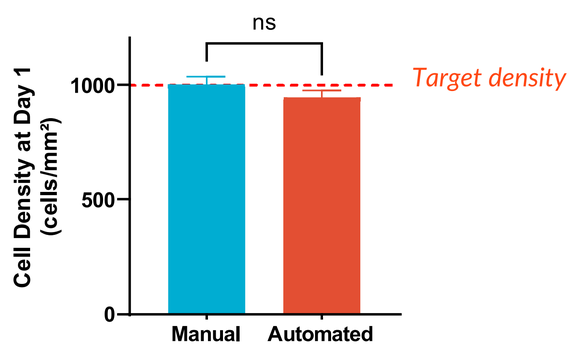
RESULTS

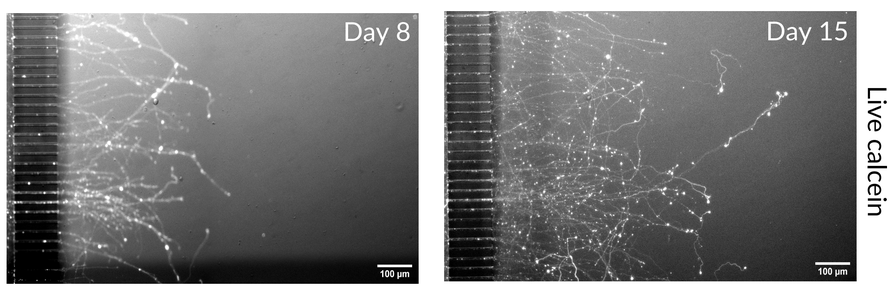
COMPARABLE DATA BETWEEN MANUAL AND AUTOMATIC CULTURE

Biological relevance with automated cell culture-on-chip platform.

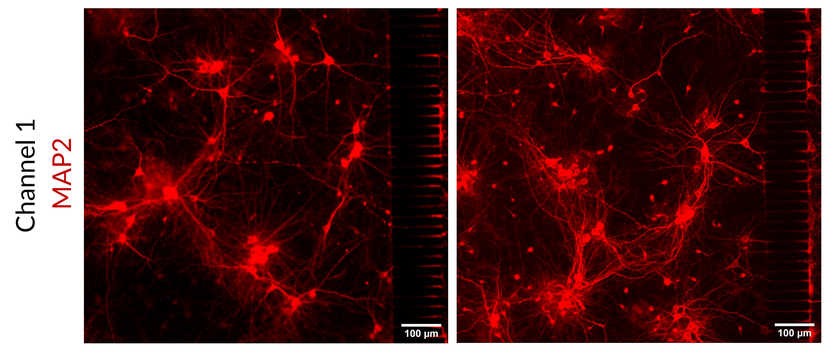
- **Standard Operating Protocol** enabling consistent cell seeding density
- **Cell viability** up to day 23
- Following **axonal growth** during culture
- **Neuronal phenotypic expression** of: vGlut1, MAP2, βIII-Tubulin,



Quantification of cell density using automatic proprietary software (n=16, N=4 runs).



Dynamic neurite outgrowth of rat primary hippocampal neurons with Calcein live staining (0.1 µg/mL)

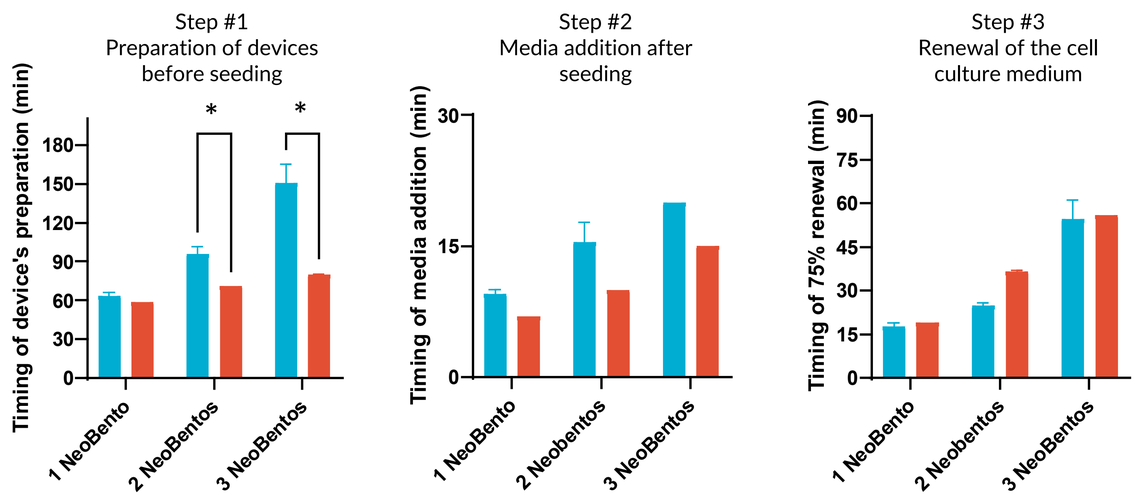


Immunofluorescence pictures of primary hippocampal neurons cultured in microfluidic devices at Day 23 (n=3, N=4 runs).

HIGH THROUGHPUT STANDARDIZED NEURO-ORGAN-ON-CHIP.

Processing time and high throughput capacity thanks to automated cell culture platform:

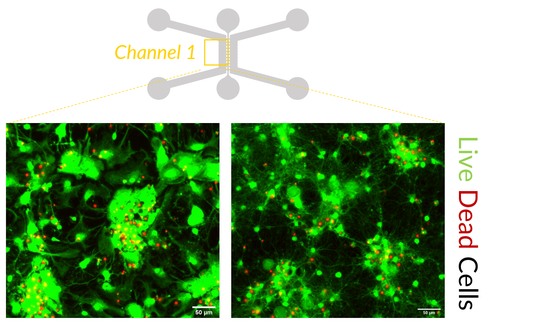
- **Time-saving** at various stages
- **Reproducible time** at each stage of the cell culture protocol
- Improved **reproducibility**



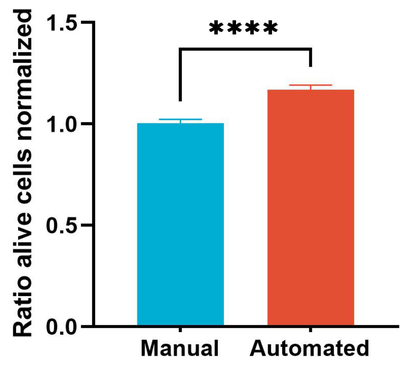
Timing of the experiment for three stages of the cell culture protocol (unpaired t-test, *p-value <0.05).

Automated cell culture improves the viability of neuronal cells.

- Death/live **quantification method**
- Platform compatible with **non-invasive analysis in the supernatant**



Illustrative pictures of primary hippocampal neurons in channel 1 at day 23.



Quantification of alive cells at Day 23 using automatic proprietary software (n=7, N=4 runs, unpaired t-test, ****p-value <0.0001).

CONCLUSION & PERSPECTIVES

Approval of our tool and automated cell culture method

- Biological relevance, repeatability, reproducibility of models, and user experience efficiency
- Quality control to ensure model conformity
- High throughput capacity

A production line for tomorrow's products to

- Access to pre-seeded human organs-on-Chip
- Increase the number of readouts (particularly for real-time monitoring)
- Use human cells derived from iPSCs

Continuous improvement

- Optimization of automated protocols to move away from humans (i.e., for cell culture medium renewal step #3)
- Development of online quality control

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