

High-definition microelectrode arrays with scalable, integrated microfluidics in multi-well format for drug screening in a heart-on-a-chip application

Cóndor, Mar ; Braeken, Dries; Rushdy Ahmed, Alaa; Labie, Riet ; Abeille, Fabien ; Meucci, Sandro ; Brandstätter, Birgit ; de Moura, Thiago ; Mastrangeli, Massimo; Stakenborg, Tim

Publication date

2023

Document Version

Final published version

Citation (APA)

Cóndor, M., Braeken, D., Rushdy Ahmed, A., Labie, R., Abeille, F., Meucci, S., Brandstätter, B., de Moura, T., Mastrangeli, M., & Stakenborg, T. (2023). *High-definition microelectrode arrays with scalable, integrated microfluidics in multi-well format for drug screening in a heart-on-a-chip application*. 263-263. Abstract from 2nd Microphysiological Systems World Summit 2023, Berlin, Germany.

Important note

To cite this publication, please use the final published version (if applicable).
Please check the document version above.

Copyright

Other than for strictly personal use, it is not permitted to download, forward or distribute the text or part of it, without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license such as Creative Commons.

Takedown policy

Please contact us and provide details if you believe this document breaches copyrights.
We will remove access to the work immediately and investigate your claim.

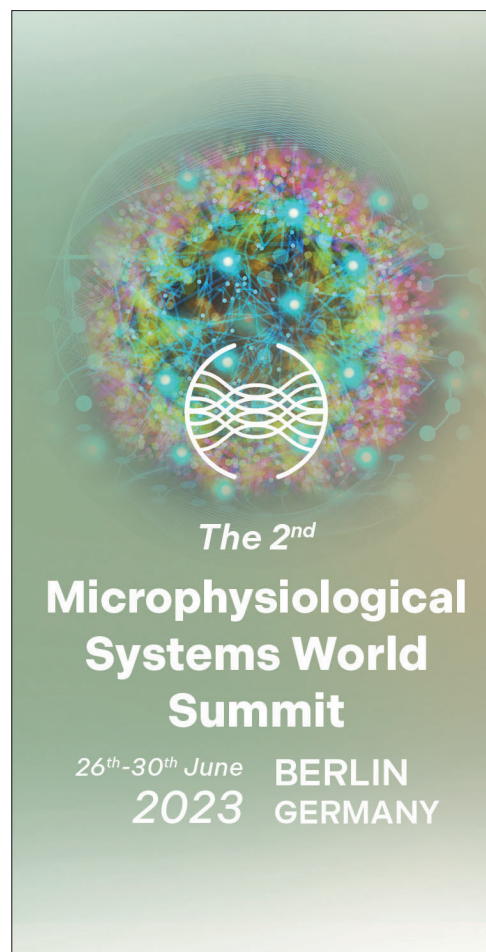


Abstracts of the 2nd Microphysiological Systems World Summit, Berlin, 2023

Volume 11, No. 1
ISSN 2194-0479
doi:10.58847/ap.2301 (2023)

ALTEX Proceedings

Marcel Leist, Uwe Marx
and Peter Loskill
Welcome



Track 1:
**MPS Development:
Bioengineering Models
and Readouts**

Track 2:
**MPS for Industrial and
Regulatory Application:
Standardization,
QA, Parallelisation and
Automation**

Track 3:
**MPS for Disease
Modelling, Safety Testing
and Basic Research**

Track 4:
**MPS Highlights Across
Disciplines**



496

High-definition microelectrode arrays with scalable, integrated microfluidics in multi-well format for drug screening in a heart-on-a-chip application

Mar C ndor¹, Dries Braeken¹, Alaa Rushdy Ahmed¹, Riet Labie¹, Fabien Abeille², Thiago Moura³, Birgit Brandst tter³, Massimo Mastrangeli⁴, Sandro Meucci⁵ and Tim Stakenborg¹

¹imec, Leuven, Belgium; ²micronit BV, Enschede, The Netherlands;

³Besi Austria GmbH, Radfeld, Austria; ⁴TU Delft, Delft, The Netherlands;

⁵Micronit BV, Enschede, The Netherlands

lei.zhang@imec.be

Towards increased throughput and automated workflows for organs-on-a-chip, a novel high-definition electrophysiology multi-well plate is developed in the Moore4Medical project [1]. It consists of an advanced CMOS microelectrode array (MEA) chip with 16 sampling areas, each featuring 1024 electrodes [2], and of a polymeric fluidic cartridge with 16 corresponding microchambers, each connected to an integrated pneumatic peristaltic pump [3]. It can perform 16-well assays with single-cell-resolution electrical recording and integrated microfluidics. Building on an earlier prototype, we present recent developments showing a scalable integration route and excellent fluidic and electrical functionalities of the plate in an easy-to-use system.

Direct bonding of the MEA chip and the cartridge was achieved using accurate glue deposition and a high-precision pick-&-place procedure, resulting in 16 well-aligned, sealed microchambers on top of the MEA. This method is developed for high-volume production. To run the plate, a user-friendly toolbox, which can be placed inside an incubator, is made together with a data acquisition unit, a pneumatic control unit, and custom software. The plate can be clamped directly inside the toolbox, ensuring communication of the MEA with the data acquisition unit by a pogo-pin connection. The pneumatic control unit actuates the 16 integrated pumps simultaneously via three pressure lines. Hence, 16 assays can run in parallel, with simple pipetting steps for cell seeding and media perfusion.

To demonstrate the plate's functions, all the 16 microchambers were primed and filled with water and 1% PBS buffer sequentially. No liquid leakage or bubble entrapment was observed. The voltage scan of the 16 MEA areas showed uniform signals and a clear difference between the two liquids (0.08 mVrms for water; 0.02 mVrms for PBS). Plate biological-validation is currently on-going to study the effect of drugs on electrical and contractile properties of human stem-cell derived cardiomyocytes and to demonstrate the plate potential for OoC standardization and workflow streamlining.

References

[1] https://moore4medical.eu/organ_on_chip

[2] Miccoli, B. et al. (2019). High-density electrical recording and impedance imaging with a multi-modal CMOS multi-elec-

trode array chip. *Front Neurosci* 13, 641.

[3] Aksoy, B. et al. (2019). Latchable microfluidic valve arrays based on shape memory polymer actuators. *Lab Chip* 19, 608-617.

Presentation: Poster

497

Complementing MPS with mechanistic computer models helps overcome limitations: Translating the drug exenatide from MPS to humans

Oscar Arrestam^{1,2}, Sophie Rigal³, Katharina Schimek³, Christian Simonsson¹, Tilda Herrg rdh¹, Belen Casas Garcia¹, Kajsa Kanebratt⁴, Uwe Marx³, Liisa Vil n^{4,5}, Peter Gennemark^{1,4} and Gunnar Cedersund^{1,2}

¹Department of Biomedical Engineering, Link ping University, Link ping, Sweden; ²SUND sound medical decisions, Link ping, Sweden; ³TissUse GmbH, Berlin, Germany; ⁴Drug Metabolism and Pharmacokinetics, Research and Early Development, Cardiovascular, Renal and Metabolism (CVRM), BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden; ⁵Division of Pharmaceutical Biosciences, Drug Research Program, Faculty of Pharmacy, University of Helsinki, Helsinki, Finland

gunnar.cedersund@gmail.com

Today, realistic organoids can be combined into microphysiological systems (MPS), which are useful for a growing list of applications. Because of this combination, one can study dynamic cross-talk between organs, otherwise only observable in animals. This improved realism creates the potential to replace animal experiments, improve drug development, etc. However, using a purely experimental approach, there are certain limitations that are hard to overcome: the dynamic cross-talk makes data interpretation difficult, and today's MPS still display critical differences to humans, in terms of functionality, volume differences, and missing organs. We therefore propose to combine MPS with mechanistic computer models, which can help overcome these short-comings.

In this presentation, we demonstrate this potential for our two-organ MPS, with liver spheroids and pancreas organ model. Using this MPS, we can study central metabolism, in both healthy conditions and disease states, such as type 2 diabetes and liver steatosis. We develop the computer model by mechanistic hypothesis testing and validate the model by comparing experiments first done in the computer with subsequent MPS results. Using the validated computer model, we can also create more human-like versions of the MPS system. We can, for instance, scale the volumes of the organoids and the circulating media to the human proportions; this makes the consumption of a glucose tolerance test go from the unrealistic 48 h to the typical human timescale of 2-4 h. We can also add already developed computer models for the missing organs – muscle, fat, brain, etc. We demonstrate how this assembling into a