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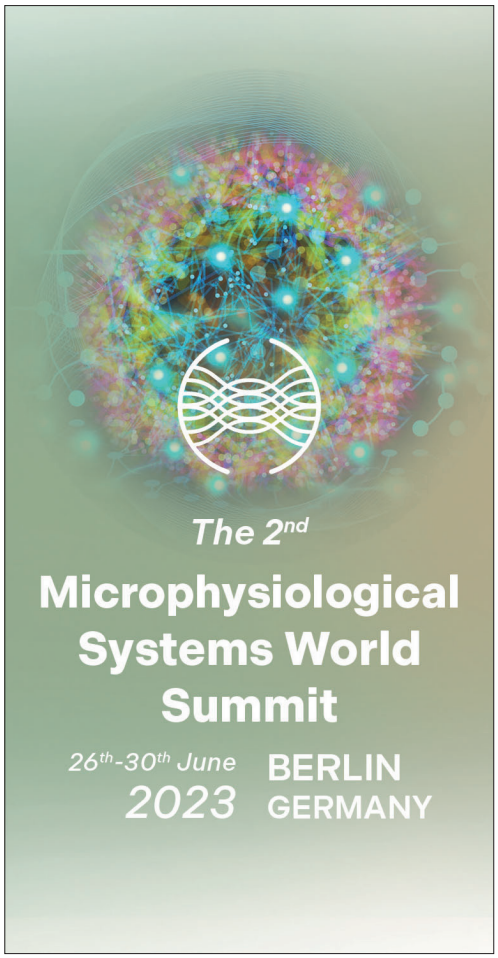
Welcome



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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

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

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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-electrode 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

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

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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