A highly-sensitive integrated capacitive sensor for contractile force measurement in an engineered heart tissue platform

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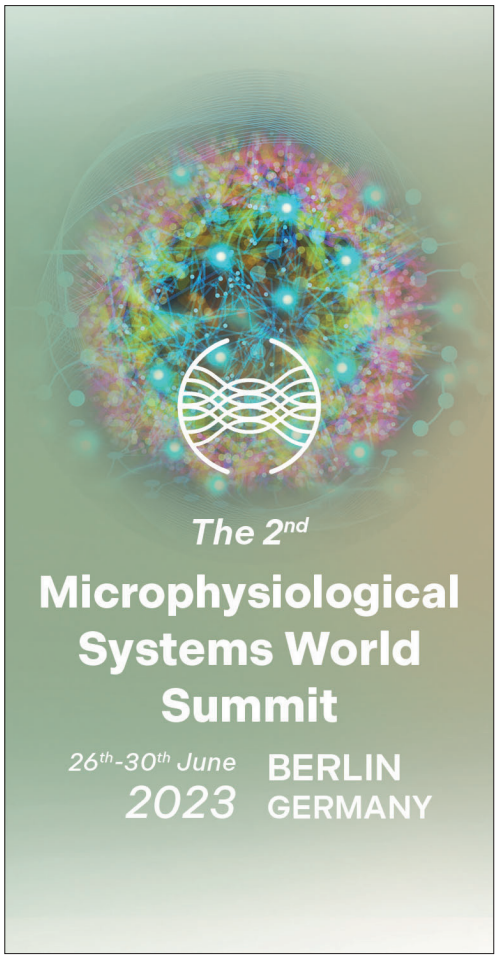

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A highly-sensitive integrated capacitive sensor for contractile force measurement in an engineered heart tissue platform

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Engineered heart tissues (EHTs) showed great potential in recapitulating tissue organization and function of the human heart *in vitro* [1]. Contractile kinetics is one key hallmark of cardiac tissue function and maturation level of cardiomyocytes, and a critical readout from EHT platforms. Typically-used optical methods to track elastic micropillar displacement upon tissue contraction are laborious and in most cases not conducted in real-time. This hampers automation and precise control of the EHT microenvironment. We address these unmet needs by developing a co-planar capacitive displacement sensor for tissue contraction force measurement integrated within an EHT platform.

The working principle of the displacement sensor relies on the deformation of the substrate wherein the sensors are integrated. Bending of each micropillar, caused by tissue contraction, results in local anti-symmetric out-of-plane deformation of the substrate. Two spiral capacitors are integrated below each micropillar of a previously developed EHT platform [2] to exploit the maximum substrate deformation.

The capacitive sensors were fabricated using a combination of wafer-level micromachining and polymer processing. The mould for the micropillars and elliptic well was fabricated by deep reactive ion etching of a Si wafer. Another Si wafer was covered with an 80 µm-thick polydimethylsiloxane (PDMS) layer, whereupon sputtered Al was photolithographically patterned into sensor designs. De-moulded micropillars and wells were aligned and bonded to the wafer with sensors. Single 10 x 10 mm^2 PDMS chips with integrated sensors were wire-bonded to custom-designed printed circuit boards. Analog Device AD7746 was selected to readout the expected aF-range change in base capacitance.

Static characterization of the sensors showed good agreement between measured and FEM-simulated values of base capacitance. The dynamic behavior was tested using a nanoindentation setup by applying specific force at different positions along the micropillars length while measuring the electrical response. Responsivity of 0.35 ± 0.07 fF/µN was measured. Preliminary experiments with EHTs proved the biocompatibility of the new platform with integrated sensors, as tissues were functional and in culture for at least 14 days.

References

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[2] Dostanić, M. et al. (2020). *Journal of MEMS 29*, 881-887.

Presentation: Poster

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Human-based placenta-embryo chip for developmental toxicity assessment of nanoparticles

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Nanoparticles (NPs) are emerging materials enabling a wealth of novel applications, but little is known about their effects during pregnancy. Understanding developmental toxicity of NPs is indispensable to protect pregnant women and the developing fetus as well as to support the study of novel safe nanomedicines. However, there is a lack of physiologically relevant human *in vitro* models to study NP transfer and effects along the maternal-embryonic axis.

The aim of our project is to develop a fully human-based microphysiological platform, which recapitulates systemic effects of the maternal-fetal interface by realizing a placental barrier model in close vicinity to an embryonic model. Such a dynamic co-culture configuration is a prerequisite to capture not only direct embryotoxic effects from translocated NPs but also indirect effects from NP interference with placental functions and signaling factors that are essential to embryo-fetal development.

We have previously established a user-friendly microphysiological system that combines a placental barrier (BeWo trophoblast cell line) on a microporous membrane with murine embryoid bodies cultivated in a subjacent hanging drop [1]. To achieve a more predictive placental model, we replaced the BeWo cell line with a co-culture of primary cytotrophoblasts (CTBs) isolated from human term placenta and human placental vascular endothelial cells (HPVEC). We established a confluent co-culture barrier and verified spontaneous syncytialization of the CTBs. To verify the predictive value of the model for NP transport studies, we are studying size-dependent translocation of differently sized polystyrene NPs under static versus dynamic conditions and comparing the results to those obtained with a human *ex vivo* placenta perfusion model. As next steps, we will integrate a 3D embryoid body, derived from human induced pluripotent stem cells (iPSCs), in our microfluidic platform and verify developmental toxicity of selected NPs previously shown to be associated with adverse pregnancy outcomes.

The microphysiological placenta-embryo model will enable to gain novel mechanistic insights important to design safer NPs, to