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An engineered heart tissue platform with integrated pacing microelectrodes

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1 - Motivation

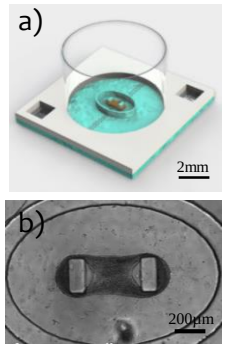

Fig 1. a) 3D model of the EHT platform with integrated electrodes; b) top view of the tissue formed in the EHT platform

Engineered heart tissue (EHT) models demonstrated valuable potential to reproduce the (patho)physiology of human cardiac tissue *in vitro* [1]. Besides the mechanical support, offered by currently used EHT platforms, other biomechanical and electrical stimuli are also significant for recapitulation of human cardiac *in vivo* environment.

This research demonstrates the integration of an electrical pacing system into a miniature EHT platform [2] allowing accurate and precise *in situ* tissue stimulation (Fig 1.).

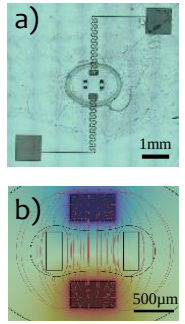

Fig 2. a) Top view of the EHT platform with TiN electrodes; b) FEM simulation of the electric field distribution

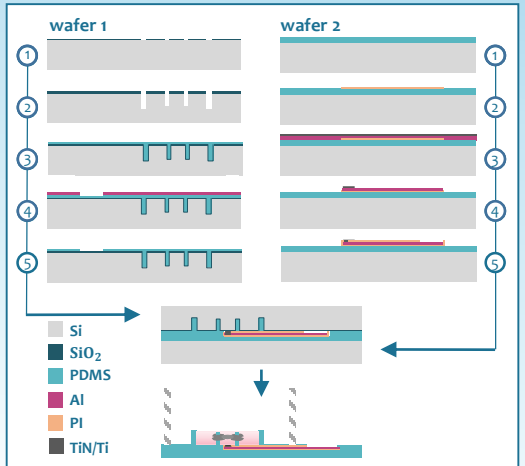

Fig 3. Process flow of the microfabrication

2 - Design and Fabrication

- Wafer-level microfabrication techniques were used to integrate Ti/TiN pacing electrodes into our prior EHT platform [2].
- The electrodes were positioned close to the base of the micropillars (Fig 1a), and designed to create an electric field perpendicular to the direction of tissue formation (Fig 2b).
- Fabrication process included a combination of polymer deposition and molding, metal sputtering, photolithography, dry etching, and wafer bonding (Fig 3).

3 - Electrical stimulation setup

- A portable electronic circuit for electrical stimulation of the tissues has been developed (Fig 4, center)
- The circuit generates rectangular bipolar pulses (0-30V peak-to-peak) and with frequency (0-5Hz) and duty cycle tunable through a user-friendly graphical interface. (Fig 4, right)
- The fabricated chips were fitted into a 96-well plate format (Fig 4, left)

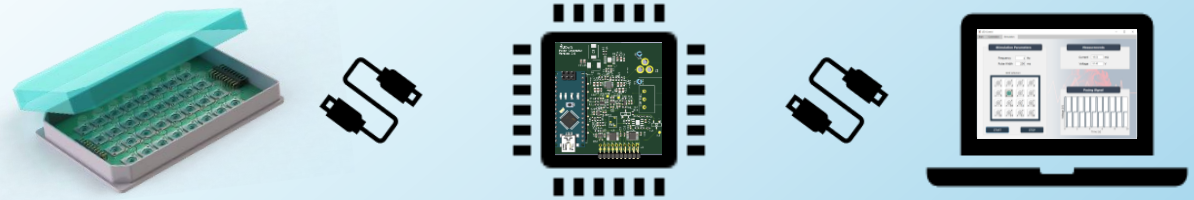

Fig 4. a) 3D model of the array of EHT platforms in the multi-well plate format; b) custom-made bipolar pulse generator; c) user interface of the app for control of the stimulation

4 - Conclusions and Outlook

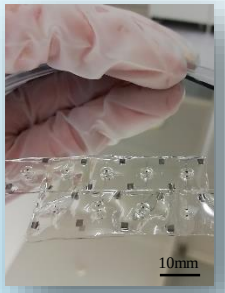

Fig 5. Fabricated EHT platforms with electrodes

- The TiN electrodes were successfully integrated into our EHT platform using silicon-based micromachining and polymer processing (Fig 5).
- The designed electronic circuit board was tested for the required pacing signals
- The whole system was configured into a 96-well plate format for forthcoming high-throughput biological assays.

References

[1] Stein, J. M. *et al.*, *Stem Cell Reports*, **16**, pp. 1-9. (2020)
[2] Dostanić, M. *et al.*, *Journal of Microelectromechanical Systems*, **29** (5), pp. 881–887. (2020)

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