

An engineered heart tissue platform with integrated pacing microelectrodes

Dostanic, M.; Windt, L.M.; Stein, J.M.; van Meer, B.J.; Diakou, A.; Mummery, C.L.; Sarro, P.M.; Mastrangeli, M.

Publication date

2021

Document Version

Final published version

Citation (APA)

Dostanic, M., Windt, L. M., Stein, J. M., van Meer, B. J., Diakou, A., Mummery, C. L., Sarro, P. M., & Mastrangeli, M. (2021). *An engineered heart tissue platform with integrated pacing microelectrodes*. Poster session presented at European Organ-on-Chip Society Conference 2021.

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.

M. Dostanić^{1,*}, L. M. Windt², J. M. Stein², B. J. van Meer^{2,3}, A. Diakou¹, C. L. Mummery^{2,4}, P. M. Sarro¹, M. Mastrangeli¹

¹ Microelectronics, TU Delft, Delft, The Netherlands. ² Anatomy and Embryology, LUMC, Leiden, The Netherlands. ³ Organ-on-Chip Center Twente, MESA+, University of Twente, Enschede, The Netherlands. ⁴ Applied Stem Cell Technology, University of Twente, Enschede, The Netherlands.

1 - Motivation

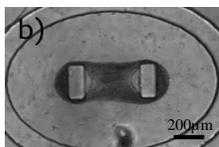
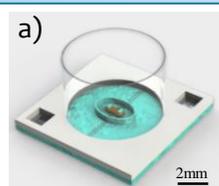


Fig 1. a) 3D model of the EHT platform with integrated electrodes; b) top view of the tissue formed in the EHT platform

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).

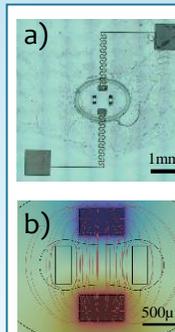
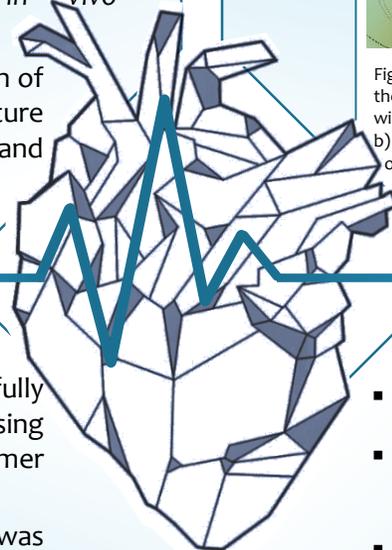


Fig 2. a) Top view of the EHT platform with TiN electrodes; b) FEM simulation of the electric field distribution

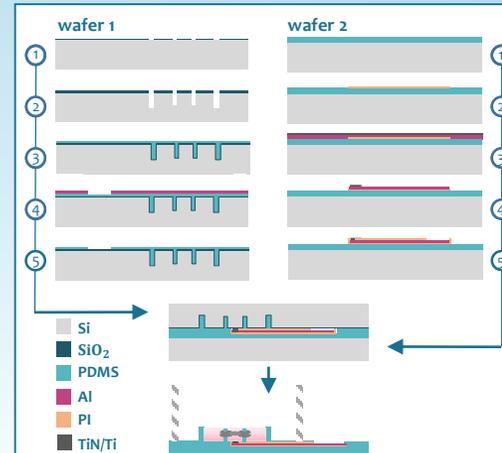


Fig 3. Process flow of the microfabrication

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).

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)

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)

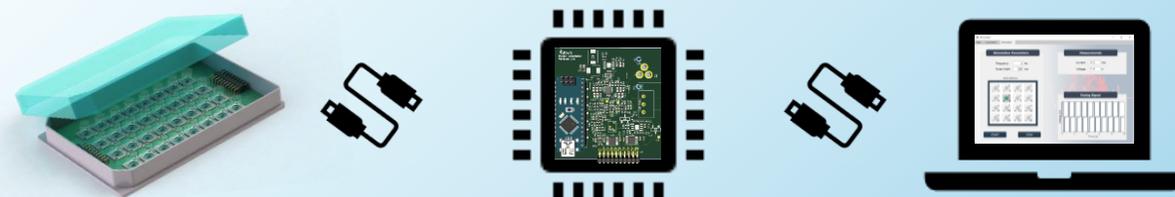


Fig 4. a) 3D model of the array of EHT platforms in the multi-well plate format; b) custom-made bipolar pulse generator; c) user interface of the app for control of the stimulation