A contractility platform for engineered 3D muscle tissues

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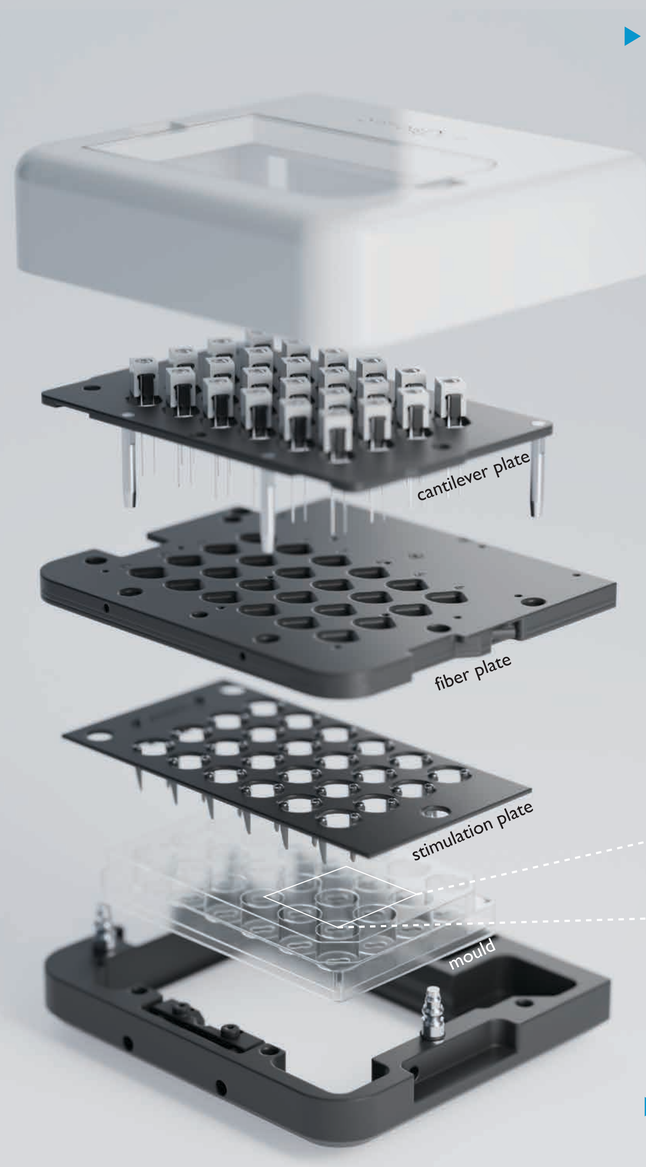
Elizaveta Loseva, Giulia Pilia, Tom Berkers, Svetlana Pasteuning, Massimiliano Berardi

The advancements of muscle biology research, disease modelling, and drug development are hindered by the challenge of generating human-relevant data in scalable and controllable settings. Conventional 2D cell cultures and lab animals are limited in accurately representing human physiology.

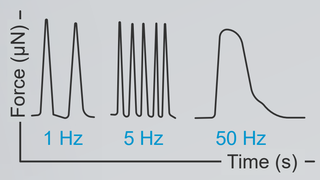
Engineered 3D muscle tissues are emerging as promising models, by enabling functional measurements while maintaining the advantages of in vitro assays. However, their wide adoption is limited by complexity and a lack of standardization in both model manufacturing and assays.

Cuore platform is designed to integrate long-term culturing of 3D engineered muscle tissues with their electrical stimulation and contractility measurement, offering a broad range of assays in fundamental research and preclinical drug development.

Cuore platform

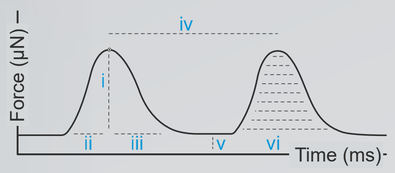


- Autoclavable & reusable
- Absolute force readout with µN and ms precision
- Integrated electrical stimulation



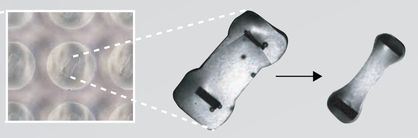
- Twitch
- Tetanus
- Exercise
- Fatigue
- Force-frequency relationship

- Automated analysis of contractility parameters



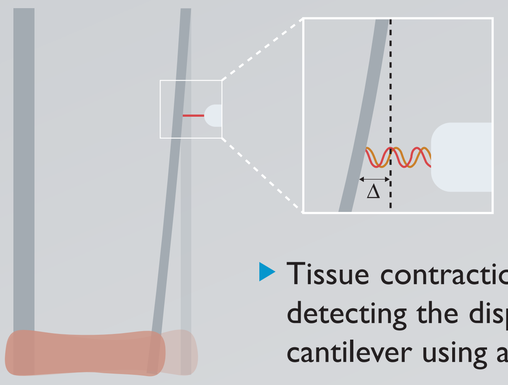
i. Maximum force
ii. Contraction time
iii. Relaxation time
iv. Frequency
v. Tension build up
vi. Peak widths

- 24-well casting mould facilitates tissue formation



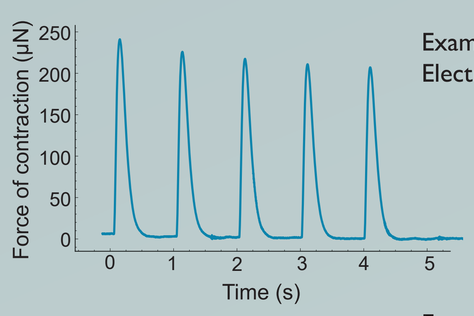
After compaction around the cantilevers, tissues are transferred to a regular 24-well plate

- Transparent bottom allows combining contractility measurements with imaging
- Tissues can be harvesetd for downstream biochemical analysis

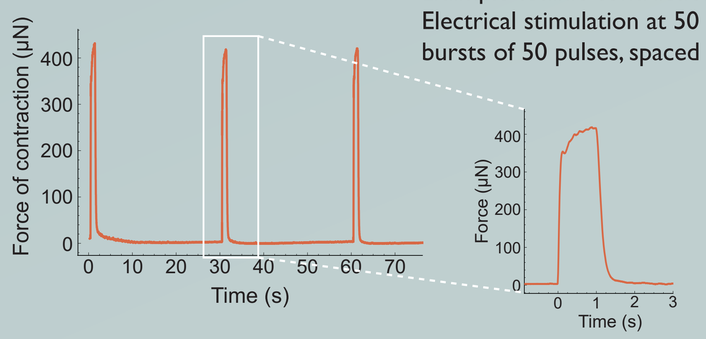


- Tissue contractions are measured by detecting the displacement of a flexible cantilever using an optical fiber sensor.

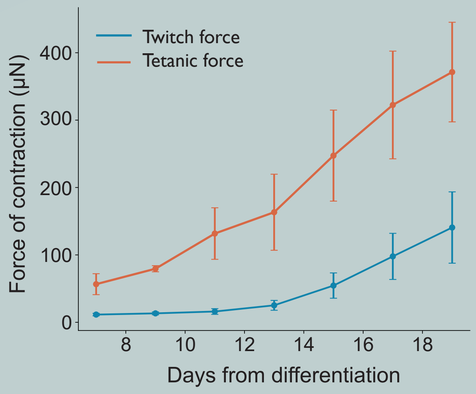
Skeletal muscle



Example twitch contractions
Electrical stimulation at 1 Hz, 5 V



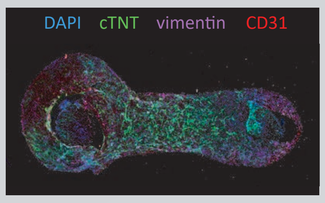
Example tetanic contractions
Electrical stimulation at 50 Hz, 5 V, bursts of 50 pulses, spaced 30 s apart



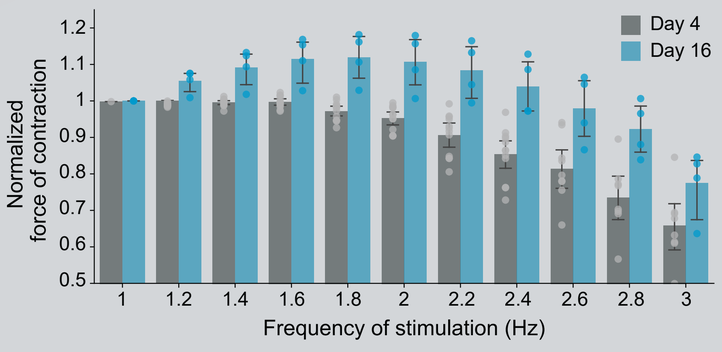
Evolution of twitch and tetanic force of contraction over time in tissues produced from hiPSC-derived myogenic progenitors (n=7 tissues).

Data generated by A. Iuliano and P. Pijnappel at Eramus MC, Rotterdam, The Netherlands, as part of NXTGEN consortium

Cardiac muscle

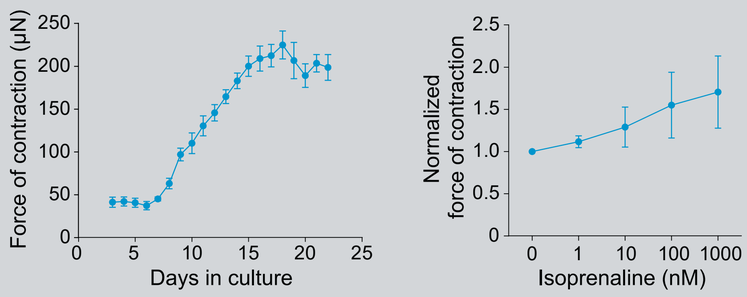


Immunostaining demostrates homogeneous distribution of cell types in tissues composed of 70% hiPSC-cardiomyocytes, 15% hiPSC-endothelial cells and 15% hiPSC-cardiac fibroblasts.



Improved FFR over time indicates cardiac tissue maturation.

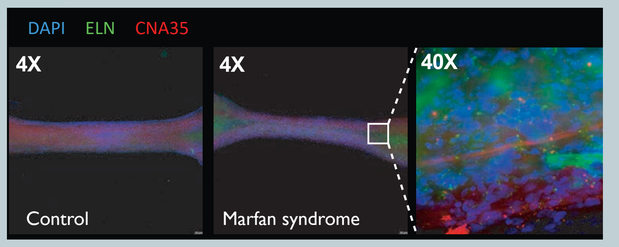
Data generated by M. Dostanic, V. Orlova and C.L. Mummery at Anatomy & Embryology, LUMC, Leiden, The Netherlands.



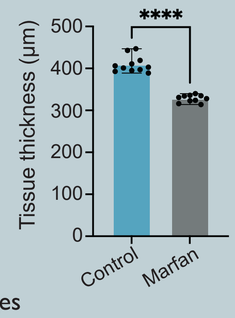
Spontaneuos contractions (left) and chemical challenging (right) of 3D tissues composed of 70% axoCells™ ventricular cardiomyocytes and 30% Innoprot human cardiac fibroblasts.

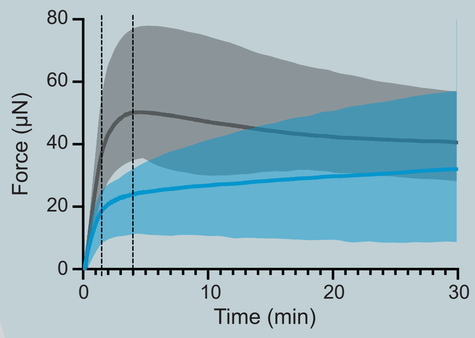
Data generated by E. dos Santos, K. Kmiotek-Caller, R.A. Kumar and A. Zoccarato at the School of Cardiovascular & Metabolic Medicine and Sciences, King's College, London, United Kingdom. The cells were kindly provided by Axol Bioscience.

Smooth muscle

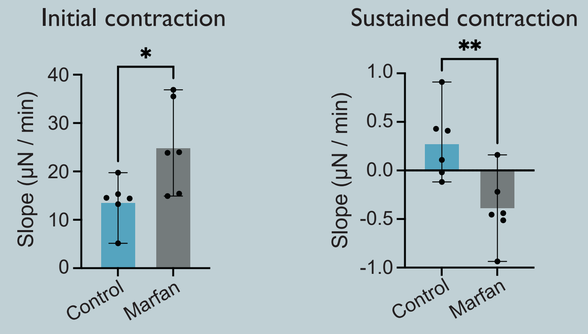


Tissues generated from Marfan syndrome (MFS) patient-derived cells demonstrate structural ECM changes





Smooth muscle contractions induced by thromboxane agonist, using a custom-made drug pump, in control and MFS tissues.



MFS tissues show higher initial contraction (left), but cannot sustain it over a 30-minute period (right).

Data generated by P. Saraber, K. Reesink, L. Schurgers at Maastricht University, Maastricht, The Netherlands.

We thank our partners for kindly providing the data presented in this poster

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