

C4: Frictional and adhesive properties of polymer surfaces

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Presentations

- 3 oral IRTG
- 5 posters IRTG
- 2 oral other
- 3 posters other

Publications

- [1] Grespan E., Martewicz S., Le Houerou V., Elvassore N. and R  he J. (in preparation)
- [2] Grespan E., Giobbe G., Badique F., Anselme K., R  he J. and Elvassore N. (in preparation)

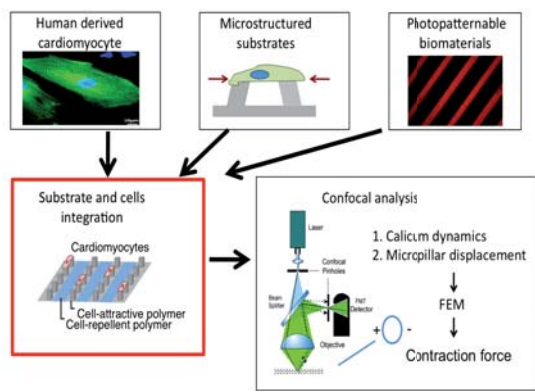
Motivation

Contraction of heart muscle cells (cardiomyocytes (CMs)) is a key parameter which determines the beating of the heart and the flow of blood. Isolated cardiac cells can be used to study fundamental myocardial biology as well as physiological and patho-physiological responses. Information on the forces in the contraction process combined with analysis of calcium dynamics are important for understanding molecular alteration in diseased heart cells [1,2].

Aim

The aim of this work is to realize an *in-vitro* set up which allows to **simultaneously** detect and analyze the calcium dynamics and the contraction force, in **human CMs** derived from pluripotent stem cells. Key to the study is to study cells with a **highly oriented structure** induced by a substrate with a precisely tailored surface topography and substrate chemistry.

Strategy



Experimental

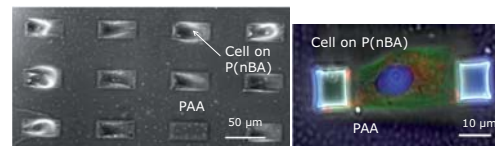
Cell source

Human cardiomyocytes were obtained from human pluripotent stem cells adapting the protocol of Lian et al. [3].

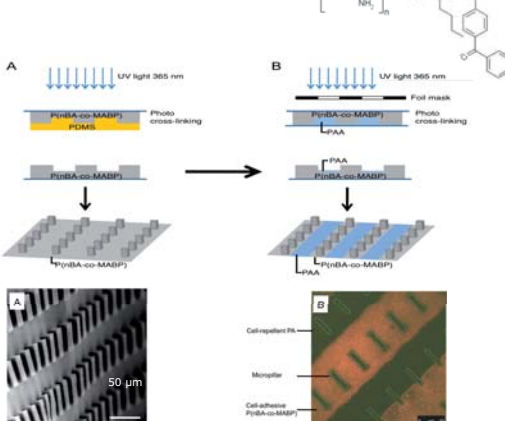


Substrate fabrication

Cells on micropatterned substrates (left) and cells on micropatterned and micropillared substrates (right).



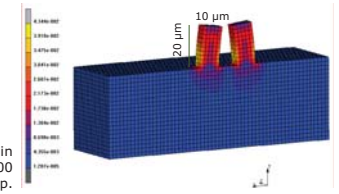
- 1) Generation of a substrate covered with elastomeric µ-pillars (e.g. 10 µm width, 20 µm height, 20 µm interaxial distance) from P(nBA)
 - 2) Generation of a chemical pattern to realize cell adhesive and cell-repellent areas that induce a physiological shape and growth of the cells through photochemical attachment
- Cell-adhesive polymer:** P(nBA-co-MABP)
Cell-repellent material: P(AA).



Finite Element Model

A Hookean constitutive model can be adopted to model the material and a quantitative estimation of the global force of contraction exerted by a single cell can be assessed.

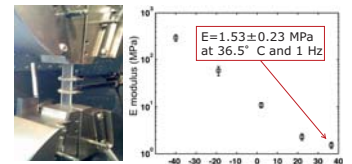
Equivalent of elastic strain at an applied force of 600 nN on each pillar top.



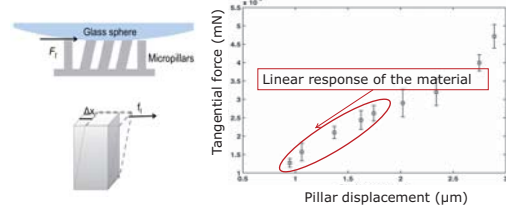
Results

Mechanical characterization

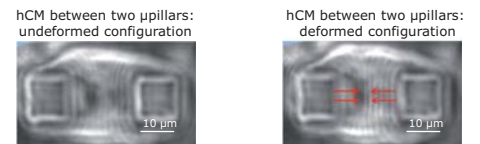
Young's modulus of P(nBA-co-4%MABP) networks is evaluated through DMTA analysis.



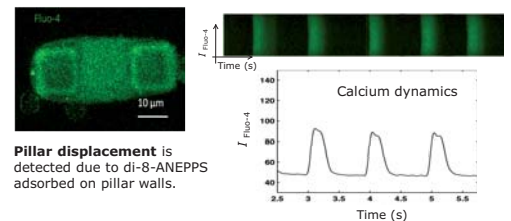
Micropillar response to tangential force is recorded through nanoindentation tests.



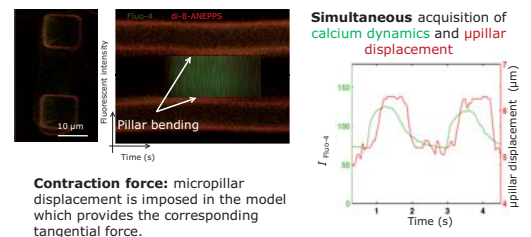
Calcium dynamics and contraction force in human derived CMs



Calcium dynamics: confocal microscopy /w calcium dye Fluo-4.



Pillar displacement is detected due to di-8-ANEPPS adsorbed on pillar walls.



Contraction force: micropillar displacement is imposed in the model which provides the corresponding tangential force.

Conclusions

A system which allows high-throughput simultaneous *in-vitro* analysis of calcium dynamics and contraction force of human pluripotent stem cells derived cardiomyocytes has been developed. Through appropriate design of the surface topography and chemistry the cells are guided into a physiological shape. The described method can be used to evaluate cell performance of CMs differentiated from pluripotent stem cells and can provide quantitative information on cells affected by specific pathologies.

- References:
1. Kim K. et al., *Micro-Nano Letters*, 2001
2. Rodriguez A.G. et al., *Biophysical Journal*, 2011
3. Lian X. et al., *Nature Protocols*, 2013