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Breathe NTF

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Transparent elastomeric sensors for the interrogation of smooth muscle cells

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The project Breathe aims to develop a highly parallel in-vitro platform for direct measurement of the force applied by smooth muscle cells. This requires, first, the growth of smooth muscle cells into a functional muscle tissue with interconnected cells and, second, measurement of the contractile force of the model. Cells will be cultured on a thin, ultrasoft elastomer membrane with printed strain transducers whose stiffness is only one order of magnitude larger than the cells. Drug screening applications are envisioned.

Smooth muscle cells

Smooth muscle disorders are an integral part of diseases such as asthma, chronic obstructive pulmonary disease and emphysema as well as atherosclerosis and inflammatory bowel disease. For example, asthma is characterized by contraction of the bronchial smooth muscle, causing difficulties in breathing.

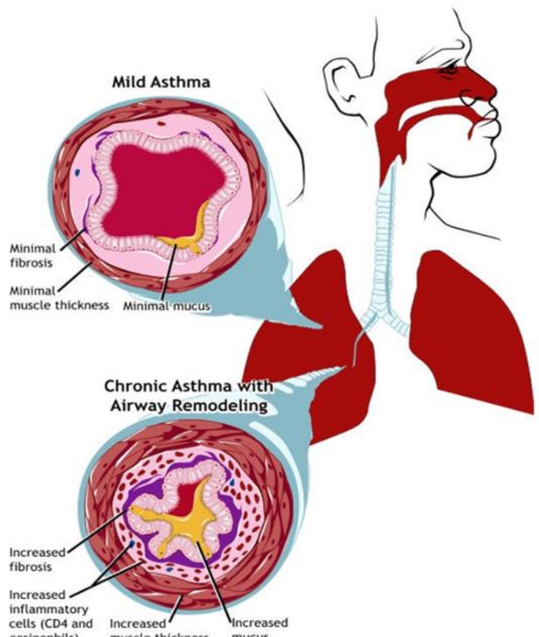


Image from the US National Institute of Allergy and Infectious Diseases (NIAID)

Needs in toxicology and pharmacology:

- *in vitro* models of smooth muscle (healthy and diseased)
- tests of function: contraction forces, displacement
- high throughput: numerous tests in parallel
- compatible with existing lab equipment
- easy to make and use

State of the art

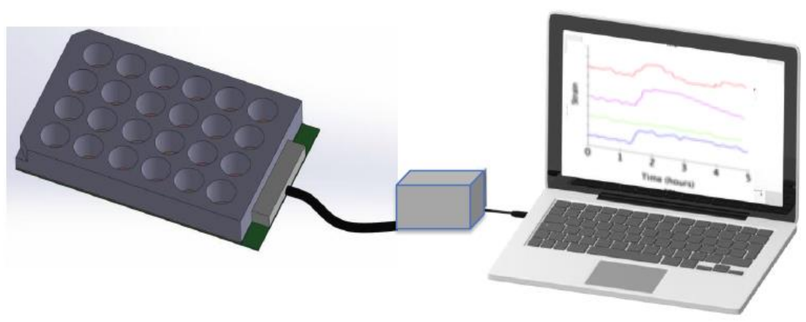
Analysis of Muscle Contraction

Method	Problems
Use of a muscle portion excised from an animal and attached to a force transducer [1]	• Ethical issues • Low throughput • Limits due to differences between animal and human physiology
Use of single muscle cells whose contraction is characterized by their deformation of a soft material on which they are cultured [2]	• Lack of aligned and interconnected cells with synchronized contractions • Limited physiological relevance
Muscle cells cultured on layers of soft polymers that can be bent by the muscle cells allowing quantification of the forces exerted [3,4]	• Soft polymer support fabrication is complex and expensive. • Optical readout of cell contraction : hard to parallelize

Device

We will develop an array of low-cost cell culture supports, each with an electrical strain readout (based on soft and transparent nanocomposite piezoresistors) allowing:

- Parallel operation
- Continuous measurements
- Use in an incubator
- Scaling to a large number of wells.



Fabricating ultrasoft elastomeric electrodes

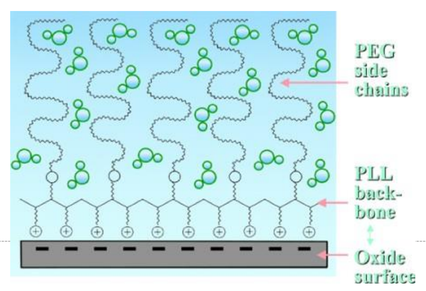
Electrodes are fabricated on thin elastomeric membranes using pad printing. Different printing processes are under test to avoid damaging the ultrasoft membrane.

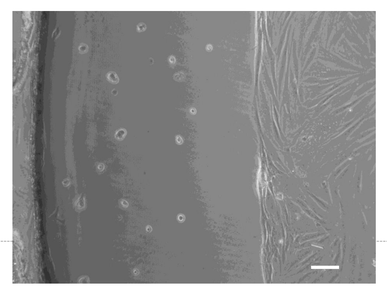
Example of a pad printing process

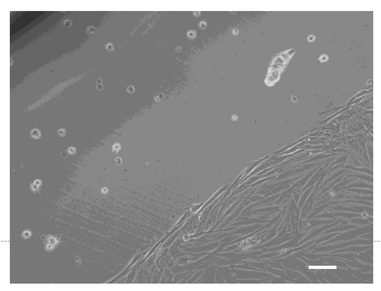
1. Place membrane in contact with PET (electrostatic adhesion)	
2. Pad print	
3. Remove PET support by dissolving sacrificial layer	

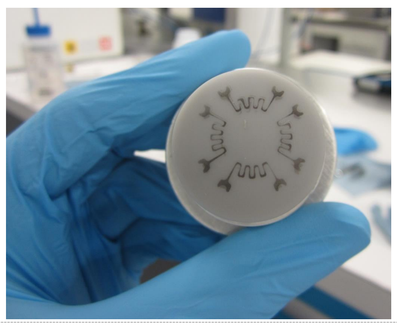
Patterning muscle cells on the sensors

The muscle cells are cultured on specific areas of the elastomer membranes. The cells must also be aligned relative to the electrodes. Cell patterning will be based on PLL-PEG non-adhesive areas, and fibronectin cell-adhesive areas. Photolithography will be used to pattern the surface chemistry of the elastomer.

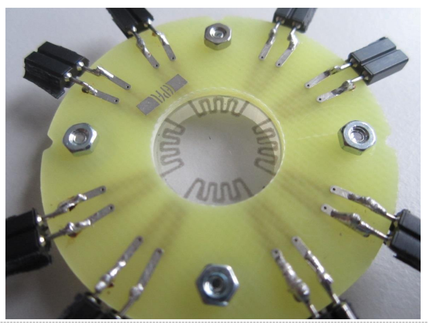








Patterned ink on a printing pad



First test electrode structure

References

1. "Calcium sensitization of smooth muscle mediated by a Rho-associated protein kinase in hypertension." Uehata et al., Nature, 389, 990–993 (1997)
2. "Substrate stiffness affects the functional maturation of neonatal rat ventricular myocytes". Jacot, J. G., McCulloch, A. D.,Omens, J. H. Biophysical Journal, 95, 3479–3487. (2008).
3. "Muscle on a chip: In vitro contractility assays for smooth and striated muscle." Grosberg et al, Journal of Pharmacological and Toxicological Methods, Volume 65, Issue 3, (2012), Pages 126–135
4. "Ensembles of engineered cardiac tissues for physiological and pharmacological study: Heart on a chip." Grosberg et al., Lab on a Chip, 11, 4165–4173. (2011).

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