Monitoring Cell Traction

F. Sorba, M. Giazzon, R. Ischer, M. Liley, C. Martin-Olmos

CSEM is developing hybrid stiffness microelectromechanical systems (MEMS), which combine materials with elastic moduli that differ by several orders of magnitude. The goal is to develop a very sensitive mechanical device that is able to both detect and apply extremely small forces on large numbers of living biological cells in parallel.

Europe needs to respond to the growing challenge of chronic diseases: cancer, diabetes, chronic respiratory and cardiovascular diseases, all affecting the aging quality of the population and increasing health care costs. In order to address this challenge, not only are more effective therapeutic agents necessary, but also better tools for early diagnoses.

Mechanobiology is potentially a powerful approach to the recognition of early stages of many chronic diseases. Numerous mechanoreceptors, such as extra cellular matrix molecules, transmembrane proteins, cytoskeleton, exist in the cells and tissues of our body, and many diverse diseases are associated with changes in their mechanical properties. These mechanical properties open a new perspective on disease development, and thus, new possibilities for early diagnosis.

However, in order to advance significantly in this field, a measurement device is needed [1] that is capable of:

- Real-time measurements
- Parallel operation
- Incubator compatibility

Our goal in this project is to develop high throughput and easy to use measurement platforms for the mechanobiology of single cells (Figure 1). In contrast to existing, mostly optical, methods, we intend to determine the cell's mechanical properties electrically. An electrical approach allows parallel measurements and easy computerized data acquisition.

Figure 1: A platform tool that can be plugged into a PC for operation, data acquisition and analysis is highly preferred by the end users for its simplicity.

The first challenge is to detect the traction forces exerted by living cells on their culture support. Single cells exert very small forces (in the range of 1-40 nN [2]). A measurement device will require materials with alike Young's Moduli and structures with extremely low spring constants to produce measurable deformations with such small forces. For this reason, softMEMS devices using very low Young's Modulus polymers are good candidates for the measurement platform.

A first series of softMEMS devices was fabricated using SU-8 as a structural material (Figure 2). SU-8 is biocompatible, stable in an aqueous environment, and chemically inert. These properties, together with its mechanical properties (4 GPa), make it an ideal candidate for this application.

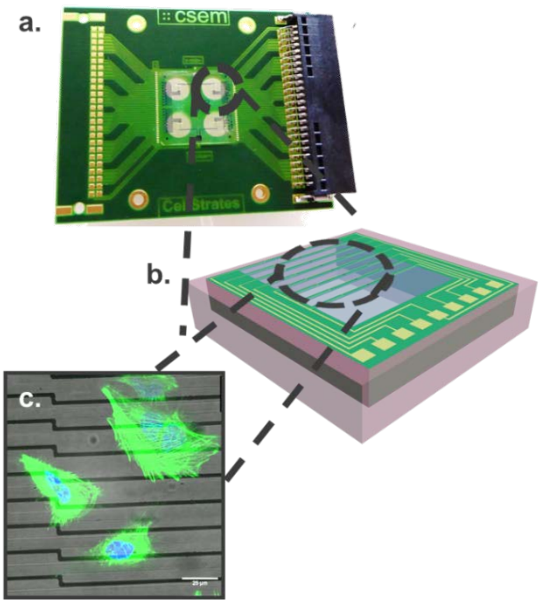

Figure 2: A softMEMS device for measurement of cell mechanical properties. a) A disposable PCB serves as mechanical support for the soft biocompatible chip and provides electrical connection for data acquisition; b) Schematic drawing of the hybrid polymer chip; c) Fluorescence image of osteoblast cells successfully attached to the flexible beams in the sensing areas of the chip.

The current softMEMS device uses gold wires as gauges embedded in self-standing SU-8 beams for detection of cell traction forces. Changes in the resistance of the wires occur when the beams are deformed.

Currently, the development of highly sensitive and multiplexable circuitry is in progress, together with the design of a method to calibrate the platform. A robust setup, like the one CSEM is envisioning with this project, has great potential to be used by a large variety of laboratories and clinics; and it will have a large impact on both the knowledge of fundamental processes of single cells and the early detection of diseases.

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[1] J. Guck, E. R. Chilvers, Science Translational Medicine 5, 212 (2013)

[2] O. du Roure, *et al*., PNAS 102, 7 (2005)