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Microfabricated Sensor Arrays for Life Science Applications

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2D Passive Cantilever Array

It has been recently shown that the stiffness of cancer cells affects the way they spread in the body [1]. Equally important is the adhesion forces of those ones to other cells. The measurement of nanomechanical properties of cells as well as cell-cell interactions are therefore of particular interest in cancer research.

Single cell nanomechanical experiments are time consuming, and acquiring reasonable statistics for a single set of parameters is a matter of days, even for experienced researchers. For this method to be more efficient, we suggest a probe array system that allows measuring multiple cells in parallel :

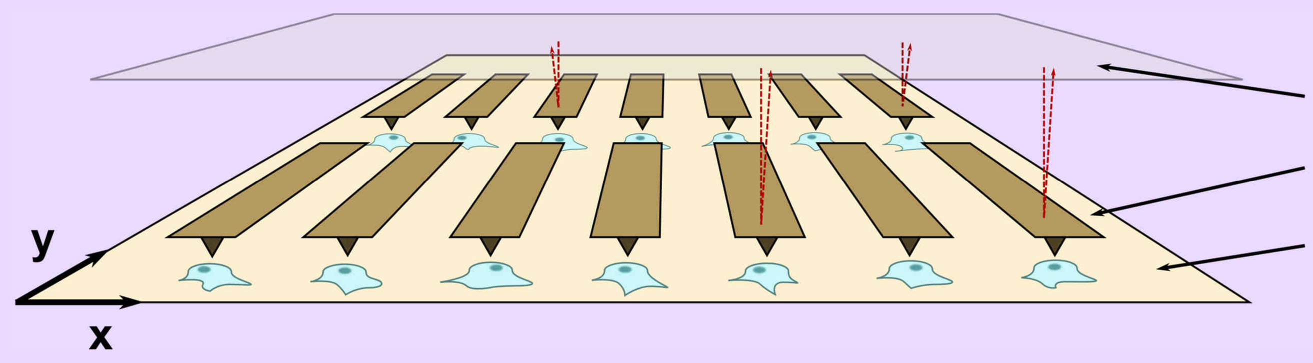

Figure 1: Schematic of the 2D probe array AFM system composed by three distinct platforms, namely the cell grid, the cantilever array and the parallel optical readout.

Theory

In order to perform various experiments, cantilever with different spring constants are required. By changing the area moment of inertia of the cantilever, we are able to modify its stiffness without changing its footprint (Figure 2).

This technique allows us to use cantilever arrays of different stiffnesses without modifying the pitch of either the cell grid or the optical readout.

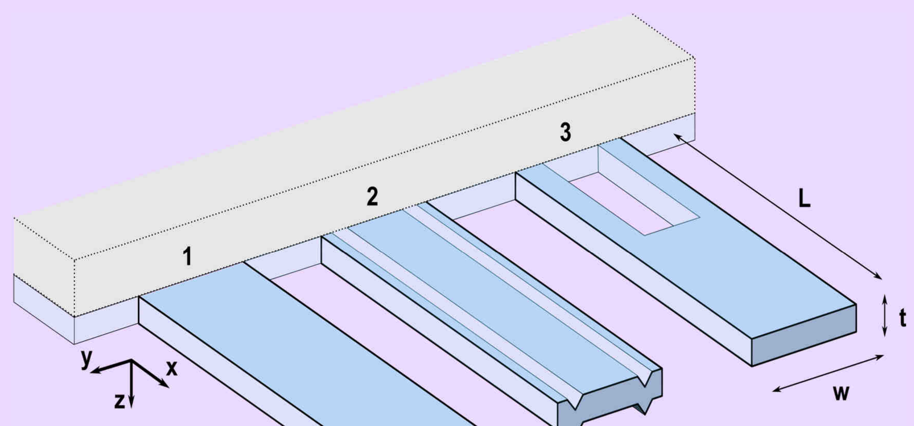

Figure 2: Schematic of three different cantilevers having the same footprint. They have different stiffnesses. Compared to the flat rectangular shape (1), the cantilever with integrated V grooves (2) has a higher spring constant. In contrast, the one with the slit (3) has a lower spring constant.

Results and Characterization

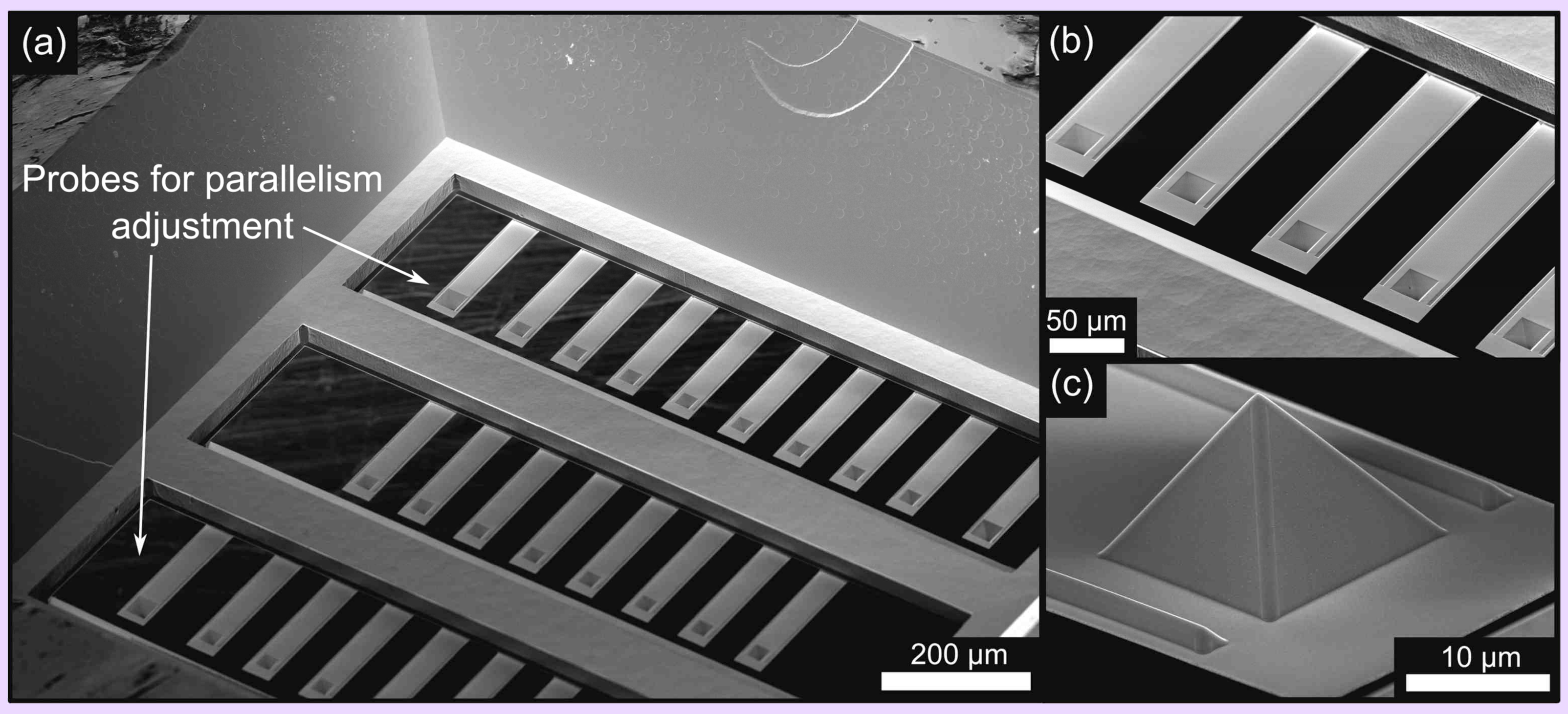

Figure 3: SEM observations: (a) 2D cantilever array, cantilevers (200 µm x 50 µm x 0.45 µm) are placed in a 1 mm2 working area, (b) four typical cantilevers with integrated V-grooves and (c) a close up view of cantilever end with the molded tip and V-grooves.

Figure 3 shows a backside SEM observation of the fabricated cantilever array. The array has 1 mm x 1 mm working area and the cantilevers are supported by the silicon frame.

An analytical model and experimental results confirmed that the spring constant of the cantilever (200 µm x 50 µm x 0.45 µm) could be increased up to two decades (0.03 N/m – 5 N/m) by changing the depth of the V-grooves (Figure 4).

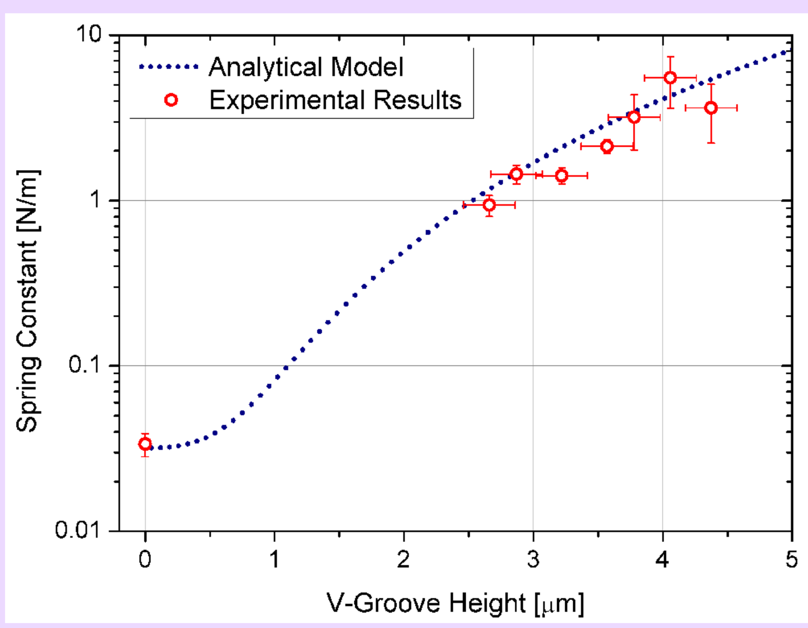

Figure 4: Variation of cantilever spring constant as a function of V-groove heights.

Piezoresistive Membrane-Type Sensor

While cancer is still one of the most lethal diseases in the world, it is mostly highly curable if detected early. Cancer diagnosis is usually performed by endoscopy and taking a biopsy of suspect lesions. In order to reduce the complexity and the risks of such operations, non-invasive diagnosis tools can be developed with the use of biosensors or artificial noses [2].

Theory

We developed a membrane-type surface stress sensor (MSS) with a sensitivity increased by a factor of 20 compared to a piezoresistive cantilever-type sensor [3].

Made out of an SOI substrate, the membrane is coated with a polymer that reacts with volatile molecules and produces its deflection. The latter is detected by four piezoresistors integrated on suspended beams (Figure 5).

The membrane has a thickness of 2.5 µm and a diameter of 500 µm.

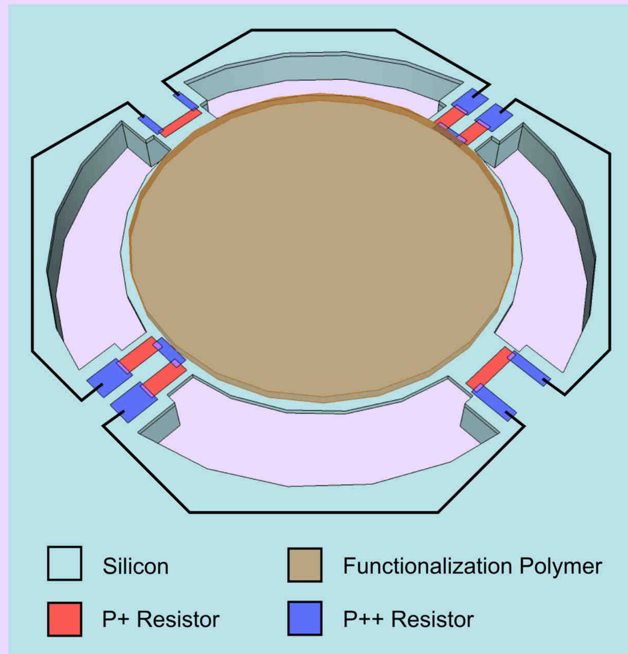

Figure 5: Graphical representation of a membrane suspended by four constricted beams with integrated piezoresistors connected in a Wheatstone bridge. The membrane is coated with a polymer that reacts to surrounding molecules.

Results and Characterization

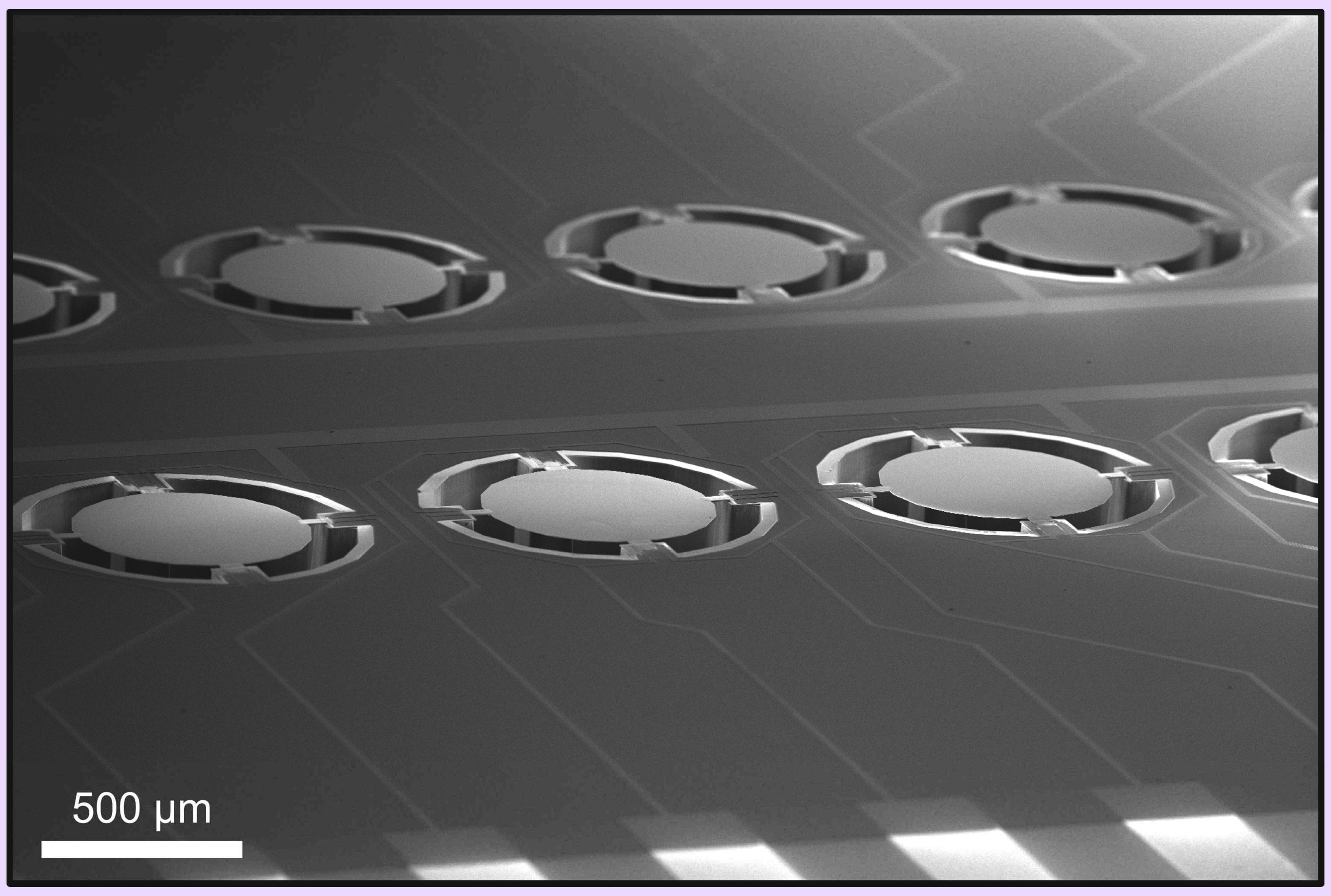

Figure 6: SEM observation of a silicon chip containing two arrays of membrane-type sensors. The membranes are 2.5 µm thick and have a diameter of 500 µm.

Figure 6 shows an SEM observation of the fabricated membrane-type sensor array.

Two membranes within an array were functionalized by inkjet spotting with Cellulose Acetate Butyrate (CAB) diluted in Hexyl Acetate. The membranes were tested as humidity sensors since polymers react strongly with water molecules. Figure 7 shows their dynamic response to four relative humidity pulses of 62% with an amplification gain of 500.

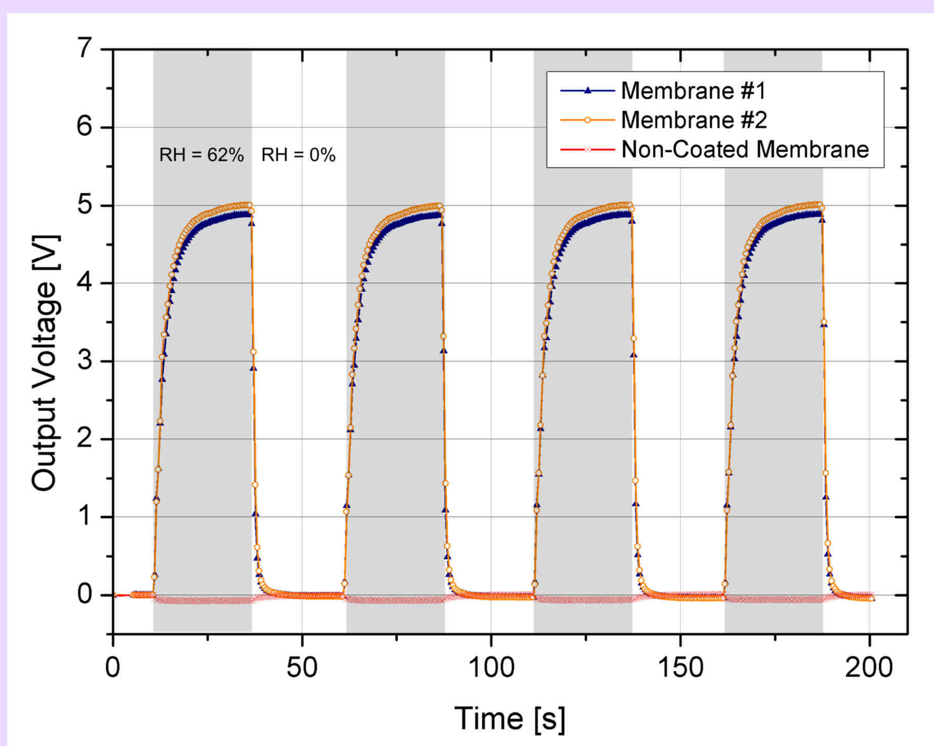

Figure 7: Dynamic response of three membranes to four humidity pulses of 62%. One of the membranes was used as a reference without the functionalization of the CAB polymer. The others showed a response time of 6.1 s. The gain of the amplification stage is 500.

References

[1] S. E. Cross et al., Nanomechanical analysis of cells from cancer patients, *Nature Nanotechnology* **2**,780-3 (2007)
[2] M. Baller et al., A cantilever array-based artificial nose, *Ultramicroscopy* **82**, 9 (2000)
[3] G. Yoshikawa et al., Nanomechanical membrane-type surface stress sensor, *Nano Letters* **11**, 1044-8 (2011)

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