From Molecules to Cells: Sensing the Nanomechanical Way

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INTRODUCTION: Micromechanical cantilevers are tiny mechanical sensors which bend in response to expansion and contraction reactions on their surface. Such bending responses have been observed upon molecular interactions of various ligands with cantilever immobilized receptor molecules such as ssDNA, antibodies, enzymes and also with synthetic receptor molecules[1]. Here we will present examples for this application of cantilever sensors as biosensors and the recent use as a research tool for surface sciences and cell biomechanics.

METHODS: Nanomechanical silicon cantilever sensors with typical dimensions of 500 x 100 x 1 µm, which allow the detection of forces as small as 0.01 mN/m, have been applied for the experiments. Following gold-coating of the top side of the cantilevers molecules can be immobilized selectively on either the top or the bottom side by thiol or silane chemistry. Subsequently cantilever sensors are transferred to the Cantisens Research detecting system (Concentris GmbH, Switzerland) and surface stress induced changes in cantilever bending are monitored via the beam deflection principle (*Fig. 1*).

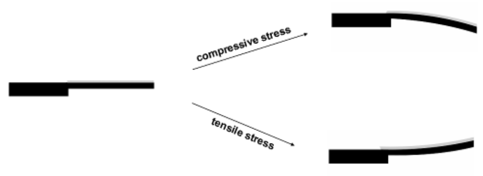

Fig. 1: Cross section view of the cantilever sensor based surface stress sensing principle.

RESULTS: As an example for the use of cantilevers as biosensors data will be presented for the label free real time detection of DNA using this measurement principle.
Another application of cantilever sensors is the monitoring of layer formation processes such as protein immobilization on a sensor surface or the build-up of multilayered structures (polyelectrolyte multilayers, layer-by-layer, LBL) which can be followed in real time and whose internal stresses can be determined[2]. We will present data on the kinetics of multilayer formation as well as the influence of polyelectrolyte concentrations on the internal stress of such multilayer surface coatings (*Fig. 2*).

Fig. 2: Surface stress in LBL coatings.

Recently we have gone one step further in size scale and have applied cantilever sensors for the quantification of forces exerted by whole cells growing on hard surfaces like medical implants or standard tissue culture dishes. To this aim cells are plated on cantilever sensors, are allowed to adhere and develop contractile cell forces which bend the cantilever. Subsequently the cells are enzymatically released and the concomitant relaxation of the support is recorded (*Fig. 3*). Multiplexing this measurement principle will allow in the future the biomechanical characterization of cells growing on surfaces with different molecular and topographical characteristics thus having practical implications for medical implant design.

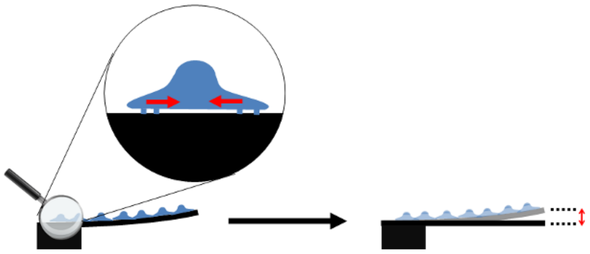

Fig. 3: Principle of a cantilever sensor based cell force quantification assay.

DISCUSSION & CONCLUSIONS: Sensors based on nanomechanical cantilevers have matured over the years and are now used for a wide range of applications. Their unique mechanical sensing principle makes them a useful tool not only for bio- and chemical sensing but also in the areas of surface sciences and complex cell biological studies.

REFERENCES: [1] Vashist, *Journal of Nanotechn. Online* (2007), [2] Koeser *et al.*, *J. Nanoscience and Nanotechnology* **10 (4)**, 2578-82 (2010).

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