# QUANTITATIVE CHARACTERIZATION OF BIOMATERIALS AND THEIR INTERACTION WITH LIVING CELLS BY AFM

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## Introduction

Topography, roughness and mechanical properties of biomaterials are crucial parameters influencing cell adhesion/motility, morphology and mechanics as well as the development of stem/progenitor cells [1,2,3,4]. Atomic force microscopy (AFM) is a powerful tool not only to study the morphology in terms of high resolution imaging and roughness measurements, but also to map mechanical and adhesive properties. Combining these remarkable abilities with advanced optical microscopy allows for extensive characterization of biomaterials.

## Methods

AFM is based on a flexible cantilever stylus that is scanned over the sample. The probe-sample interaction induced deflection of the cantilever is finally converted into sample topography and interaction force. The sensitivity of the detection system and the accuracy of piezo actuators with capacitive sensors allow for resolving structures of less than 1 nm and forces on the pN scale. Different imaging modes can resolve structures of biomaterials in physiological conditions without the Abbe diffraction limit. In force spectroscopy mode, interaction forces between the (modified) cantilever and any substrate can be investigated. Using Single Cell Force Spectroscopy (SCFS), cell-substrate or cell-cell interactions can be measured down to single protein unbinding (fig. 1). The cantilever can also serve as nano-indentation tool to analyse mechanical properties like the Young's modulus of biomaterials or cells.

## Results

Using AFM imaging, the nanostructure of biomaterials like aligned collagen matrices have been resolved as well as cell alignment on such structures [4,5]. SCFS quantified the adhesion force and the contribution of different components, e.g. from the extra cellular matrix of living cells to implant materials as from cochlear implants [6]. Force-indentation measurements on cells using colloidal probes showed a significant effect of micro-patterned substrates on cellular elasticity [2].

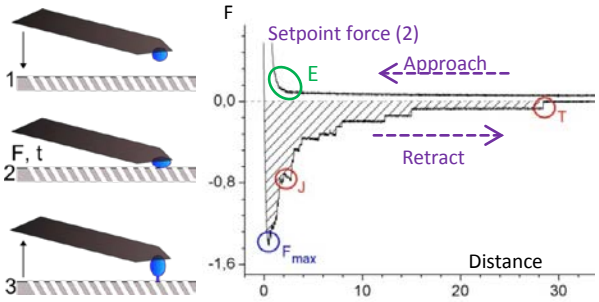


*Fig. 1: Sketch of a SCFS experiment. The probe cell is approached to (1) and pressed against the substrate (2) with a defined Setpoint force (F) for a defined time (t). When the cell is separated from the sample (3) interactions like maximum adhesion force ($F_{max}$) and single unbinding events (force jumps (J) and those that are preceded by membrane tethers (T)) are visible in the force distance curve. The contact part of the Approach curve allows for applying elasticity models (E).*

## Discussion & Conclusions

AFM is a multipurpose technology which is much more than simple imaging. Interaction forces from single molecule unbinding to cell adhesion and analysis of surface and mechanical properties of biomaterials and cells make AFM to a key technology in biomaterial research. Nano-mechanical analysis of cells increasingly gains in importance in different fields in cell biology like cancer research [7] and developmental biology [8]. We present a strategy to comprehensively characterize biomaterials as well as their interaction with cells and influence on cell behavior.

## References

[1]Elter et al., Eur Biophys J 2011:40(3): 317-327. [2]McPhee et al., Med Biol Comput 2010:48(10):1043-53. [3]Engler et al., Cell 2006:126(4):677-689. [4]Kirmse et al., J Cell Sci 20100:124(11):1857-66. [5]Cisneros et al., Small 2007:3(6):956-63. [6]Aliuos et al., Biomed Tech 2010:55:66-68. [7]Cross et al., Nat Nanotech 2007:2(12):780-783. [8]Krieg et al. Nat Cell Biol 2008:10(4):429-36.