Nanomechanical sub-surface mapping of living biological cells by force microscopy

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Mapping force versus distance curves with an atomic force microscope and the local evaluation of soft samples allows the operator to “see” beneath the sample surface and to capture the local mechanical properties [1]. In this work, we combine atomic force microscopy with fluorescence microscopy to investigate cancerous epithelial breast cells in culture medium. With unprecedented spatial resolution, we provide tomographic images for the local elasticity of confluent layers of cells. For these particular samples, a layer of higher elastic modulus located directly beneath the cell membrane in comparison with the average elastic properties was observed. Strikingly, this layer appears to be perforated at unique locations of the sample surface of weakest mechanical properties where distinct features were visible permitting the tip to indent farthest into the cell’s volume. We interpret this layer as cell membrane mechanically supported by the components of the cytoskeleton that is populated with sites of integral membrane proteins. These proteins act as breaking points for the indenter and thus explaining the mechanical weakness at these locations. Contrarily, the highest mechanical strength of the cell was found at locations of the cell cores as cross-checked by fluorescence microscopy images of staining experiments, in particular at nucleoli sites as the cumulative elastic modulus of the cell membrane comprising cytoskeletal features and the tight packing ribosomal DNA of the cell [2].

[1] C. Dietz, Sensing in-plane nanomechanical surface and sub-surface properties of polymers: local shear stress as function of the indentation depth, Nanoscale 10, 460 (2018).

[2] L. Stühn, A. Fritschen, J. Choy, M. Dehnert, and C. Dietz, Nanomechanical sub-surface mapping of living biological cells by force microscopy, Nanoscale 11, 13089 (2019).