High-resolution AFM of membrane proteins in native membranes

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The atomic force microscope (AFM) has become a powerful tool in structural biology allowing the investigation of biological samples under native-like conditions: experiments are performed in physiological buffer at room temperature and under normal pressure. Topographies of membrane proteins can be acquired at a lateral resolution of ~10Å and a vertical resolution of ~1Å. Importantly, the AFM features an extraordinary signal-to-noise ratio allowing imaging of individual membrane proteins in prokaryotic (1) and eukaryotic (2) native membranes that participate in supramolecular assemblies.

Imaging techniques in medicine are important for our understanding of pathologies and potential development of cure approaches. It is now clear that many pathologies are based on molecular disorders – therefore techniques capable to image at a resolution sufficient to observe single molecules and better must be developed and adapted for medical issues. Membrane proteins are involved in many vital processes and their malfunctions often have a serious impact on an organism's state. Nowadays, AFM is a recognized technique able to reveal the structure of supramolecular assemblies of membrane proteins (1). Using AFM as a medical nano-imaging tool, we imaged healthy (2) and cataract affected (3) eye lens membranes at unprecedented resolution. Crucial differences in organization of the two membrane proteins, aquaporin-0 and connexin, are distinguished between healthy and pathological cases.

Most recently, the power of high-speed atomic force microscopy (HS-AFM, (4)) was used to investigate dynamic membrane processes (5). The perspectives of this novel technology will be discussed.

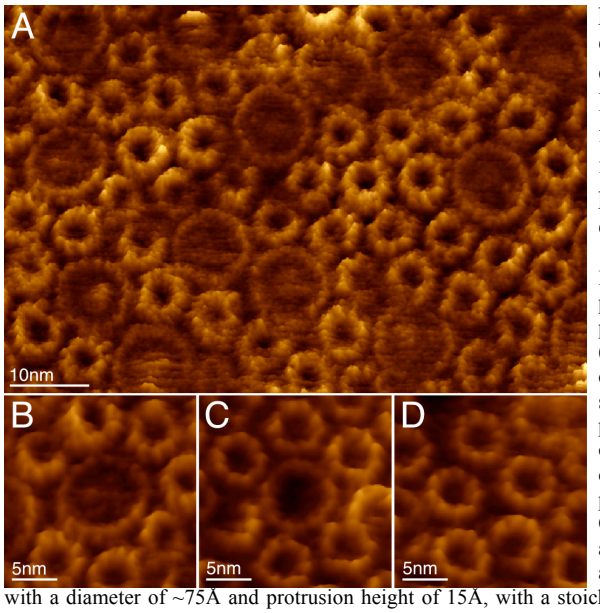

Figure Caption. Structure and supramolecular assembly of photosynthetic complexes in chromatophores of Rsp. photometricum. Containing light-harvesting complexes 2 (LH2), light-harvesting complexes 1 (LH1) and reaction centers (RC). A) High-resolution AFM topograph of the supramolecular assembly of a high-light adapted photosynthetic membrane. The ratio of LH2 rings / core-complex is ~3.5. The core-complexes are homogeneously distributed within the membrane, the most favorable assembly pattern is LH2-LH1-RC-LH1-LH2-LH1-RC- and so on. B) Core-complex imaged at high-resolution. The LH1 assembly around the RC forms a closed ellipse (long axis 99Å; short axis 83Å protruding 15Å with 16 subunits. C) LH complex with a diameter of ~75Å and protrusion height of 15Å, with a stoichiometry between 12 and 14 LH subunits. D) High-resolution topograph of nonameric LH2 complexes. LH2 have a top ring diameter of 50Å and protrude 16Å. Bottom: 'moon-shaped' molecule formed by 6 subunits.

References

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