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Development and applications of atomic force microscopy combined with optical tweezers (AFM/OT)

F Pierini, P Nakielski, S Pawłowska, I Piechocka, K Zembrzycki and T A Kowalewski

Institute of Fundamental Technological Research, Polish Academy of Sciences, ul. Pawinskiego 5B, Warsaw, Poland

Atomic force microscopy (AFM) is an evolution of scanning tunnelling microscopy that immediately gained popularity thanks to its ability to analyse nanomaterials. Initially, AFM was developed for nanomaterials imaging purposes, however the development of new features made it the most commonly used tool for studying the biophysical properties of biological samples. On the other hand, atomic force microscopy has limited use for examining sub-piconewton forces. Few techniques have been developed to measure forces below the AFM limit of detection. Among them, optical tweezers (OT) stand out for their high resolution, flexibility, and because they make it possible to accurately manipulate biological samples and carry out biophysics experiments without side effects thanks to their non-invasive properties.
The combination of AFM with other techniques in the last decades has significantly extended its capability. The improvement of the AFM force resolution by developing a hybrid double probe instrument based on the combination of AFM and OT has great potential in cell or molecular biology. [1]
We outline principles of atomic force microscopy combined with optical tweezers (AFM/OT) developed by our team underlying the techniques applied during the design, building and instrument use stages. We describe the experimental procedure for calibration of the system and we prove the achievement of a higher resolution (force: 10 fN – spatial: 0.1 nm – temporal: 10 ns) than the stand alone AFM.
We show the use of the hybrid equipment in a number of different biophysics experiments performed employing both AFM and OT probes. The presented studies include the demonstration of simultaneous high-precision nanomanipulation and imaging, the evaluation of single biomolecule mechanical properties and the single cell membrane activation and probing. Finally, we show the further potential applications of our AFM/OT.

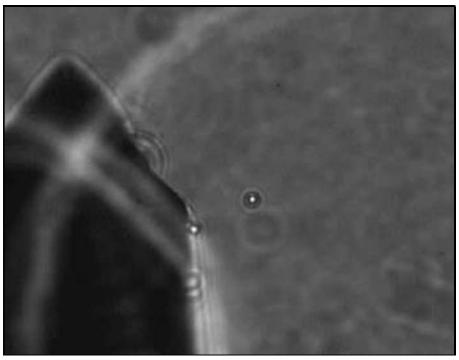

Figure. Stretching of a single DNA molecule by AFM/OT

References:
[1] F. Pierini, et al. Meas. Sci. Technol. 27 (2016) 025904.