Integration of Optical Tweezers with Atomic Force Microscopy – The Ultimate Nano-Force Toolbox

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In recent years, optical tweezers (OT) have generated remarkable interest in research areas other than fundamental physics, including biochemistry, biology, and medicine. The ability to gain insight into the mechanical processes and miniscule forces underlying protein folding, DNA-ligand interactions, cell adhesion, and cell mechanics opens a broad range of new applications. Atomic force microscopy (AFM) currently offers premium spatial resolution of the analysed samples while simultaneously being able to correlate topography and mechanics at near native/physiological imaging conditions.

A range of biological and biophysical experiments benefit from a significant increase in spatial and temporal control over sample dynamics. Optical traps can be used to manipulate or hold sample components with the ability of precise force application. By further utilizing motorized stages, three axis piezo-driven sample scanners and multiple traps, up to 14 degrees of freedom for positioning, force application and measurement are available. The combination with AFM allows force measurements over four orders of magnitudes (femtonewtons – nanonewtons) in the same sample.

We will demonstrate the application of the first commercially available OT-AFM Combi-System pairing the exceptional surface force measurement and imaging capabilities of AFM with the ability of OT to apply the smallest forces and to do precise micromanipulations in 3D. The combined setup fulfills the highest demands on mechanical stability, flexibility, and modularity. A specially designed OT-AFM ConnectorStage™ is the key to combining any AFM of the NanoWizard® or CellHesion® family with the latest NanoTracker™ 2 optical tweezers on a research-grade inverted optical microscope.

The unique combination of 3D positioning, detection, and manipulation provided by OT and the high-resolution imaging and surface property characterization of AFM opens up a whole new spectrum of applications, such as cellular response, cell-cell or cell matrix interactions, immune response, infection or bacterial/virus/nanoparticle uptake processes, and more.

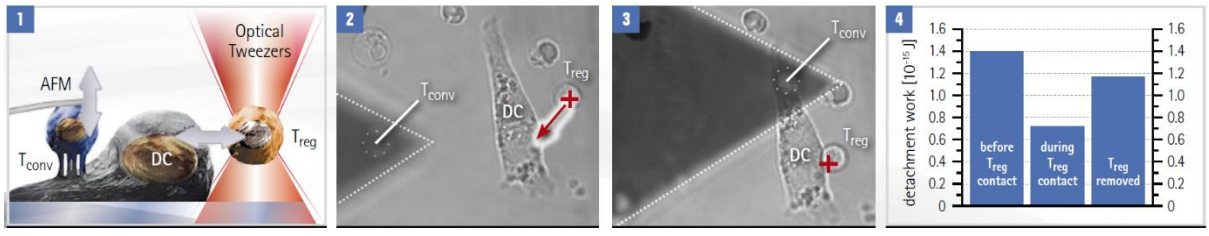

Figure 1. (1) Adhesion experiment with dendritic cells (DC) and conventional T-cells (T_{conv}). The T_{conv} is attached to a tipless cantilever, then approached to the surface-bound DC. The cantilever is pulled up and the adhesion forces are measured. A regulatory T-cell (T_{reg}) is attached to and removed from the DC with optical tweezers to test its influence on the binding strength.
(2) and (3) Measurement setup. The optical trap (red cross) moves the T_{reg} while adhesion measurements are performed with a cantilever-attached T_{conv}.
(4) Detachment work measured for the three situations. Treg attachment reduces DC-T_{conv} interactions. After the T_{reg} is removed, the adhesion level is almost restored. Sample courtesy of Yan Shi, University of Calgary / Tsinghua University, Beijing. The results of the original experiment designed by Yan Shi et al. (publication in print).