

Single Molecule Experiments by Evanescent Wave Scattering.

We have developed a new single-molecule method which is a kind of cantilever-less AFM. The method is based on tracking the motion of a micron-size bead attached to a solid surface through a single molecular contact. The bead's motion is monitored with sub-nm resolution by evanescent wave microscopy, while a force is exerted through a flow. The method allows to exert a non-destructive force on a single molecule while simultaneously monitoring nm scale conformational motion of the molecule.

We have demonstrated the method by measuring the entropic elasticity of a long polymer chain [1], by reproducing previously known biotin-avidin bond rupture forces [2], and by detecting nm scale conformational changes of proteins and DNA [3, 4].

[1] H. Jensenius and G. Zocchi, "Measuring the spring constant of a single polymer chain", *Phys. Rev. Lett.* **79**, 5030 (1997).

[2] G. Zocchi, "Force measurements on single molecular contacts through evanescent wave microscopy". *Biophys. J.* **81**, 2946-53 (2001).

[3] G. Zocchi, "Proteins unfold in steps", *Proc. Natl. Acad. Sci. USA* **94**, 10647 (1997).

[4] M. Singh-Zocchi, S. Dixit, V. Ivanov, and G. Zocchi, "Single molecule detection of DNA hybridization", *Proc. Natl. Acad. Sci. USA* **100**, 7605-10 (2003).