Atomic Force Microscopy: a multifunctional tool for imaging of biosystems from single molecules to cells.

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The Atomic Force Microscopy (AFM) provides a multifunctional imaging platform that allows biosystems, ranging from nucleic acids and proteins to cells and tissues, to be visualized, analyzed and manipulated. Since its invention in 1986 [1], many different operating systems have been devised, not only to obtain images, as it was originally conceived.

AFM images are achieved by scanning a probe, mounted to a cantilever spring, over the surface of a sample and by controlling the interaction forces between the probe and the sample surface. A very attracting feature of AFM is the possibility to operate also in liquid environments and at room temperature in which the native state and dynamics of the systems are preserved. Owing to this peculiar feature, AFM moved towards biology since it allows exploring biological structures, at the single molecule level providing three-dimensional views of specimens with nanometric resolution and with minimal sample preparation.

In addition to the traditional optical detection system and liquid cell enabling contact and dynamic mode AFM to operate in aqueous solution, a variety of AFM modes have been developed to characterize biological systems and their components [2], as illustrated in Figure 1. The main AFM-based techniques and their applications will be overviewed. In particular, the force-distance curve-based AFM, which contours the surface of a biological system, the multiparametric AFM, which contours the sample while mapping multiple physical or chemical properties, the molecular recognition, which images and maps specific interactions of biological samples, high-speed AFM, which decreases the acquisition time by a factor of ~10^3, providing access to process dynamics, will be discussed.

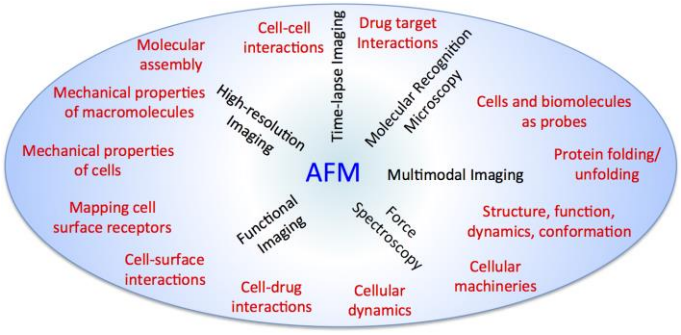

Figure 1. Main AFM techniques used to characterize biosystems ranging from single-molecules to cells.

[1] Binnig, G.; Quate, C. F.; Gerber, C., *Phys. Rev. Lett.* **1986**, 56, 930-933.
[2] Dufrene, Y. F.; Ando, T. et al., *Nature Nanotechnol.* **2017**, 12, 295-307.