

## High-speed AFM and Video Shooting of Dynamic Biomolecular Processes

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Dynamic processes of single biomolecules have been studied mainly by fluorescence microscopy. Because of the insufficient spatial resolution in optical microscopy, dynamic biomolecular processes have been indirectly examined through dynamic behavior of fluorescent spots emitted from fluorophores attached to biomolecules. The atomic force microscope (AFM) has sufficient spatial resolution for directly observing unstained protein and DNA molecules in liquids. Unfortunately, the imaging rate of conventional AFMs is much lower than that of optical microscopy, and hence, they can capture only stationary images. We need a microscope that has both high-spatial and high-temporal resolutions. To materialize such a microscope, we have been developing a high-speed AFM by optimizing various devices for high-speed scanning [1, 2, 3]. The current high-speed AFM can capture an image at 30-60 ms/frame for a scan range of ~250 nm, with 100 scan lines. Importantly, the tip-sample interaction force is reduced greatly without sacrificing the imaging rate, so that delicate interactions between biological macromolecules are not disturbed significantly. Several dynamic biomolecular processes have been successfully captured on video, some of which have revealed the functional mechanisms of proteins [3, 4]. Visualization of this sort is absolutely impossible to perform with other techniques. In this talk, I review various techniques involved in the instrumentation, application to biological studies, current capabilities and limitations, and future prospects.

[1] T. Ando, N. Kodera, E. Takai, D. Maruyama, K. Saito, A. Toda, "A high-speed Atomic force microscope for studying biological macromolecules," *Proc. Natl. Acad. Sci. USA* **98**, 12468–12472 (2001).

[2] N. Kodera, H. Yamashita, T. Ando, "Active Damping of the Scanner for High-speed Atomic Force Microscopy," *Rev. Sci. Instrum.* **76**, 053708 (5pp) (2005).

[3] T. Ando, T. Uchihashi, N. Kodera, A. Miyagi, R. Nakakita, H. Yamashita, M. Sakashita, "High-speed Atomic Force Microscopy for Studying the Dynamic Behavior of Protein Molecules at Work," *Jpn. J. Appl. Phys.* **45B**, 1897–1903 (2006).

[4] T. Ando, T. Uchihashi, N. Kodera, D. Yamamoto, A. Miyagi, M. Taniguchi, H. Yamashita, "Invited Review: High-speed AFM and nano-visualization of biomolecular processes," *Pflügers Arch – Eur. J. Physiol.* (in press).