Imaging of Molecules by Dynamic Force Microscopy in Liquid

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Dynamic force microscopy (DFM) using frequency modulation (FM) detection has been widely used for the atomic scale investigations of various materials. In FM detection tip-sample short-range interaction forces are sensitively detected by the frequency shift of a sharp cantilever resonance. In fact most of the high-resolution observations were performed in UHV condition because of the high quality (Q-) factor of the cantilever resonance in vacuum, which usually exceeds 10,000. Imaging in liquid, however, is indispensable for the applications to nanobiology where visualization of individual biomolecules such as proteins and DNAs is essentially important. A major difficulty in DFM working in liquid comes from the fact that the Q-factor is extremely reduced due to the hydrodynamic interaction between the cantilever and the liquid. This reduction of the Q-factor directly connects to the decrease in the force sensitivity and consequently in the spatial resolution. In addition, the stable cantilever oscillation in FM detection is often heavily perturbed.
The difficulty was overcome mainly by the use of the small amplitude mode ($A < 1$ nm) and the noise reduction (17 fm/$\sqrt{\text{Hz}}$) in the cantilever deflection sensor, leading the success in high-resolution DFM imaging in the low Q-factor environment. In this paper we describe subnanometer-resolution imaging of organic molecules in liquid. Figure 1(a) is an FM-DFM image of a cleaved surface (bc-plane) of a polydiacetylene single crystal (poly-PTS) taken in pure water. A herring bone structure of the side groups (*p*-toluene sulfonate) is clearly seen. Furthermore, purple membrane consisting of hexagonally packed bR (*bacteriorhodopsin*) protein trimers was imaged in buffer solution as shown in figure 1(b). The success in high-resolution FM-DFM imaging in liquid has opened the new way to direct visualization of *in vivo* molecular-scale biological process.

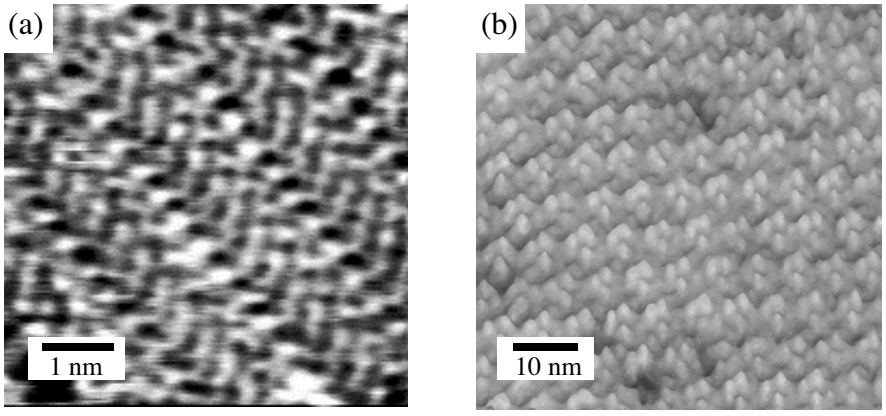

Figure 1 FM-DFM images of polydiacetylene single crystal surface taken in pure water (a) and of purple membrane obtained in phosphate buffer solution (b).

[1] T. Fukuma, K. Kobayashi, K. Matsushige and H. Yamada, *Appl. Phys. Lett.*, **86** (2005) *in press*.
[2] T. Fukuma, M. Kimura, K. Kobayashi, K. Matsushige and H. Yamada, *Rev. Sci. Instrum.* **76**, 053704 (2005).