High Sensitivity Detection Schemes for Force Microscopy and Biosensing

Hideki KAWAKATSU, Daisuke SAYA, Dai KOBAYASHI and Denis DAMIRON

Abstract

The paper reports on heterodyne laser doppler interferometry and photothermal excitation applied to Atomic Force Microscopy. The combination of the above mentioned interferometry and excitation methods allows the use of small and stiff cantilevers or higher oscillation modes up to the 100MHz regime, as well as the use of multimodal vibrations and amplitude of drive in the 10 pm order. Since excitation acts directly on the oscillator, surrious free excitation is implemented both in liquid, air and vacuum. Phase rotation around modes are clean, allowing multiple modulation schemes such as phase modulation and frequency modulation to be employed.

This paper reports on a new optical system for atomic force microscopy and biosensing utilizing heterodyne laser doppler interferometry and photothermal excitation. The optics was introduced to accommodate small cantilevers with high natural frequency. The merits of using such cantilevers are reduced thermal noise, improvement of scanning speed and reduction of size of biosensing cantilever arrays. Photothermal excitation and magnetic excitation of the cantilever is effective in eliminating surrious noise, especially in liquid. The latter also has the ability to control the DC value of the force.

Although the optical setup is rather cumbersome, it has the merit of improved signal to noise ratio at higher frequencies due to detection of velocity. Up to around 2MHz, decrease in effective displacement detection was confirmed to be as low as a few fm/√Hz.

1. Optics

The optical system is depicted in Figure 1. The laser source used ranged from 0.3 mW to 1mW, depending on the laser mode. For the generation of the carrier frequency, acousto optic modulators (AOM) or the beat frequency of adjacent longitudinal modes were used. For generation of carrier frequency above 1GHz, two AOM were used in cascade, or an AOM was used to add to the intrinsic beat of the HeNe laser. For photothermal excitation, a power modulated laser diode (LD) was used. Excitation and detection was confirmed up to around 160 MHz, which came from the limitation of finding an oscillator with a higher frequency. In principle, with a carrier frequency of 1.1GHz, oscillation up to 200MHz can be measured. Due to the simple measurement scheme, where it suffices to place two optical spots on the oscillator, measurement of such samples as (i) various silicon based oscillators, (ii) graphene sheets, (iii) AFM cantilevers, (iv) tungsten sub oxide whiskers, (v) membranes could be measured. Optical power used for the photothermal excitation was in the order of a few mW or less, and comparable to the power used in most optical lever detection. The wave length used was 405nm and 780 nm. The former showed around three times better excitation efficiency for the same optical

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*IIS, UTokyo
**LIMMS (CNRS/IIS)
***IIS, UTokyo / LIMMS (CNRS/IIS) / C2C JSPS
****LIMMS (CNRS/IIS) / JSPS / C2C JSPS

Figure 1. Heterodyne laser doppler interferometry and photothermal excitation applied to a liquid AFM.
power. This is due to the fact that at 780nm, silicon appears to be semi-transparent. From experience, and as found in literature, intentionally making the cantilever surface black helped improve the excitation efficiency.

2. Excitation of higher modes

Figure 2 shows an example of excitation and detection with the optical scheme introduced\(^7\). For comparison, piezo excitation was carried out to achieve equal level of amplitude of drive. It can be seen that the excitation is clean and free of spurious noise. Phase rotation around each eigen mode was also clean, implying that the method is well suited for phase modulation techniques. Using this detection method, we have confirmed for example, (i) imaging of Si(111) 7x7 surface with an amplitude of drive of 30pm\(^8\) (Figure 3), (ii) imaging of Si(111) 7x7 with the third mode of deflection of a commercial cantilever at 5MHz\(^9\), (iii) atomic resolution imaging with the torsional mode(Figure 4)\(^10-11\), (iv) atomic resolution imaging in liquid with the torsional mode (Figure 5), (v) fast imaging using the amplitude modulation technique in vacuum due to the elevated operating frequency\(^12\).

(vi) manipulation of single atoms at room temperature\(^13\). The result depicted in Figure 4 was obtained by position modulation of the tip apex with an amplitude of drive of about 1 Å while the tip sample distance was regulated by monitoring the tunneling current. Calculation by N. Sasaki showed very good agreement.
with the experimental result, proving that both vertical and lateral force fields could be measured by AFM at the atomic level. Figure 5 shows imaging of structured water molecules on mica. Movement of foggy zones on mica could be seen. The foggy zone itself showed vertical structures with a well defined spacing.

3. Multimode excitation

One merit of photothermal excitation is that simultaneous multimode excitation, including a mixture of deflection and torsion can easily be implemented by choosing the point of excitation on the cantilever and mixing two or more eigen frequencies of the cantilever modes. By changing the power intensity corresponding to each mode, one could sweep the ratio of the multiple modes.

4. Use of multiple modulation frequency for simultaneous detection of force curves

In the case of non-contact AFM, where the cantilever is set to self-oscillate, the oscillation frequency changes under the influence of the potential field between the tip and the sample. The frequency shift to tip sample distance curve, commonly known as the frequency curve (FC) contain information of the potential field in which the cantilever is oscillating. Such was reported at the atomic level in the literature. In the case of our optical setup, due to the ease of modulation and possible operation at elevated frequencies, the scheme is well adapted to extracting information from FC on the fly. We have demonstrated methods to extract parameters defining the potential field as the tip is scanned on the surface. For such detection schemes, various modulation techniques were introduced to scanning probe microscopy. Figure 6 shows detection of FC and its derivative for KBr. Acquisition of the derivative also necessitates position modulation and lock in detection. Acquisition of the derivative with a bandwidth necessary for feedback control of the tip sample distance necessitates choice of higher oscillation frequencies of the cantilever, the use of higher frequency modulation and a fast demodulator.

5. AFM incorporated in other microscopes

As depicted in Figure 1, one need only position the two laser spots on the cantilever to implement an atomic resolution AFM. Combination with other microscopes is relatively simple, such as TEMA FM (Figure 7) and a FIMA FM (Figure 8). The former enabled observation of the AFM tip apex with the sample, and the latter was used to image the AFM tip functionalized with various molecules and then carry out force spectroscopy with the AFM.
6. Application to biosensors

The NOSE project carried out by Ch.Gerber and others is one example of pioneering work in the use of cantilever arrays for biological detection. Figure 9 shows a linear array of cantilevers, called the NanoPiano. Addressing of the cantilevers is accomplished by scanning the detection and excitation laser spots on the NanoPiano and by detecting the shift in frequency of each ‘notes’. An example of the detected frequency peaks is shown in Figure 10. Currently, diagnosis on the condition of the Tau protein is carried out by functionalized cantilevers in a liquid cell. Similar to other cases, no wiring is needed to the microfluidic cells due to the all-optic design. A marked difference was observed between healthy and mutant biomolecules.10

**Conclusion**

The optical scheme introduced here allows large freedom on the AFM head and hybrid systems due to the all-optic configuration. As for the frequency of operation, it is only a matter of choice of the carrier frequency used for the heterodyne detection. In other words, by replacing the AOM, one can aim to obtain best results for the range of frequency in question.

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