Receptor-free nanomechanical sensors

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ABSTRACT

Nanomechanical response of molecular adsorption has been demonstrated as the basis for a number of extremely sensitive sensors. Molecular adsorption on microcantilevers results in nanomechanical motion due to adsorption-induced surface stress variation. Chemical selectivity in nanomechanical sensors is achieved by immobilizing receptors on the cantilever surface. Although receptor-based detection has high selectivity for biomolecular detection, it fails when applied to small molecule detection. Nanomechanics, however, offer new possibilities for achieving chemical selectivity that do not use any receptors. For example, small thermal mass or high temperature sensitivity of a cantilever beam could be used for detecting molecular adsorption using photothermal effects and physical property variation due to temperature. Here we describe two such techniques for achieving chemical selectivity without using any receptor molecules.

Keywords: Cantilever sensors, sensor arrays, explosive vapor detection, cantilever bending, adsorption-induced stress, photothermal spectroscopy

1. INTRODUCTION

Molecular adsorption on surfaces results in surface stress variation due to adsorption-induced forces. These adsorption-induced stresses can be observed as deflections of a miniature cantilever beam provided the adsorption is confined to a single surface[1-4]. This mechanical effect of molecular adsorption can be the basis for a novel signal transduction method. Nanomechanical signal transduction can be complementary to the other signal transduction processes such as variations in mass, electrical and optical properties caused by molecular interactions. Optimization of nanomechanical signal induced by interaction between analyte molecules and the sensor elements is critical in designing an ideal sensor.

Recently many sensor have been demonstrated where molecular adsorption on a cantilever surfaces results in surface stress variation, which in turn results in nanometer deflection of the cantilever[5-6]. Molecular adsorption reactions on a surface are driven by free energy reduction of the surface, and the free energy per unit area (J/m^2 or N/m) is the surface stress. While molecular adsorption processes produce no observable macroscopic mechanical change on the surface of a bulk solid, the adsorption-induced surface stresses are sufficient to bend a cantilever if two conditions can be satisfied. The first condition is that the adsorption must be confined to one surface of the beam, and the second involves the small force constant of the cantilever. Reduction in free energy due to molecular adsorption on one side of the cantilever results in a differential surface stress. This differential surface stress leads to bending of the cantilever. The adsorption-induced bending of a cantilever is easily observed using a cantilever with a very small spring constant. Adsorption-induced forces, however, should not be confused with bending due to dimensional changes such as the swelling of thicker polymer films on cantilevers.

The microcantilever sensor platform is the simplest micromechanical systems that can be mass-produced using conventional micromachining techniques. Typical dimensions of a cantilever are 100 μm in length, 20 μm in width and 1 μm in thickness. A typical cantilever has a spring constant of 0.1 N/m, and a resonance frequency of 50 kHz in air. Extremely high sensitivity has been demonstrated for detection of chemical vapors using cantilever bending. In addition to bending, molecular adsorption can also be detected using changes in resonance frequency of the cantilever. Depending on the mass and resonance frequency of the cantilever, a mass adsorption sensitivity of picogram to femtogram can be achieved. Using nanocantilevers, a mass sensitivity three orders of magnitude higher has been demonstrated.

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Although molecular adsorption-induced bending and resonance frequency variation can be observed simultaneously, dimensional requirements for these two modes are opposite. Cantilevers with very small spring constant and longer lengths are ideal for observing adsorption-induced cantilever bending, while short cantilevers with very high spring constant are essential in achieving high mass resolution. Cantilevers with dimensions in the mid range can be ideal for simultaneously observing both these modes of operation with reasonable sensitivity.

Another interesting physical property of a cantilever is that it can be made extremely sensitive to temperature by making it bi-material, a property similar to that used in thermostats[1,3]. Cantilevers can be made bi-material applying a metallic coating to one side of the cantilever. Changes in temperature result in unbalanced thermal expansion of the bi-material components, which results in cantilever bending. Thermal sensitivity of sub pico Joule has been demonstrated using bi-material cantilevers. In fact, microcantilever temperature sensors are one of the most sensitive temperature sensors available today.

The sensing action of a cantilever is based on monitoring the displacement of a cantilever with sub nanometer resolution. There exist a number of readout techniques that can be used for detecting the displacement of a cantilever beam such as optical beam deflection, variation in capacitance, piezoresistance, and piezoelectricity[7]. Optical beam deflection such as that perfected for atomic force microscopy has excellent sensitivity. This was the most common readout technique for cantilever deflection in the early days of cantilever sensing. Bending of a cantilever is determined by reflecting a focused light beam off of the free end of the cantilever into a position sensitive detector. Interferometry optics has also been adapted to read out cantilever motion, in which the deflection is detected by its relative movement to a reference cantilever or substrate. However, optical beam deflection makes the device bulky and complicated due to optical beam alignment problems. In addition, refractive index effects should be compensated using reference cantilevers to avoid artifacts. The piezoelectric method is more suited for the resonance frequency based detection method than for the mode based on cantilever bending. The capacitive method is not suitable for liquid based applications. Another attractive readout technique is based on piezoresistivity, whereby the bulk electrical resistivity varies with applied stress.

Electrical readout techniques have several advantages over the optical beam deflection method. For example, the optical beam deflection probes the bending of the free end of the cantilever[8-10]. It is assumed that the cantilever bending is uniform along the length of the cantilever. The piezoresistive method, on the hand, measures the integrated bending of the cantilever. Piezoresistive cantilevers can be encapsulated in silicon nitride for operation under solution thus avoiding the longstanding problems associated with optical path lengths and refractive index variation. In addition, because no external optical components are required, the electronic readout is more amiable for miniaturization and ideal for portable devices. Electronic readout is compatible with array arrangements since both cantilevers and readout circuits can be fabricated simultaneously on the same chip. However, currently available piezoresistive cantilever sensors are an order of magnitude less sensitive than those using optical readout techniques. This discrepancy in sensitivity, however, is vanishing fast due to the recent progress in piezoresistive cantilever development.

1.1 Chemical selectivity

As pointed out earlier molecular adsorption results in cantilever bending which can be the basis for a plethora of chemical and biological sensors. Despite its high sensitivity, a cantilever sensor does not have any chemical selectivity. A cantilever sensor is essentially an extremely sensitive displacement sensor. Chemical selectivity, however, can be achieved by using immobilized receptors on the cantilever surface. The receptors adsorb certain analyte molecules with higher affinity than other molecules impinging on the receptor surface. Examples of the receptors include self-assembled monolayers, polymer films, biomolecules, etc. Monoclonal antibodies are extremely selective to their antigens. Biomolecular detection using biomolecules is extremely selective. Biomolecules, such as DNA, RNA and proteins, interact with each other through highly specific reactions which are determined by the structures of the macromolecules and various interaction forces in between. The interaction forces include hydrogen bonding, electrostatic interactions, van der Waals interactions and hydrophobic force. Since all reactions are driven by the reduction of free energy, and because the free energy of biomolecules is related to their mechanical compliance in conjunction with the interaction forces, mechanics of biomolecules can play a critical role in reactions.

Selective detection of small molecules such as vapor phase analytes is a challenge. Unlike biomolecules where a large number of bindings take place between the analyte and the receptor, only a single interaction takes place between receptor and the small molecule analyte. These are generally very weak interactions such as van der Waals, hydrogen bonding, etc. These interactions are weak and therefore very unspecific. Although there exist some receptors that can bind the analytes with strong interactions, they cannot be regenerated at ambient temperature. These receptors, therefore, can be used only as dosimetric sensors. Chemical selectivity based on weak interactions are, therefore, very unselective. An array of sensors where each sensor element is coated with a different weak interacting receptor combined with pattern recognition may be able to bring some selectivity to chemical sensing. However, each selective coating should provide a unique signal for the pattern recognition to work. Simply increasing the size of the array will not increase the selectivity. This is mostly due to the limited number of interactions that can serve as the basis for a given interaction.

It has been demonstrated that small molecules can be detected with high sensitivity and specificity in the absence of other interfering molecules. A pattern recognition algorithm can identify the chemical with certainty. However, the confidence level of the pattern recognition goes down with binary mixtures, and totally fails for mixtures of three or more. This failure is directly related to the weak molecular interaction between the analyte and the receptor.

It is, therefore, doubtful that any sensors based array and pattern recognition will achieve selectivity when relying on simple interactions for speciation of small molecules. It should be stated that there exists a limited number of coatings that are extremely specific. As long as there exists a lack of highly selective coatings that can provide a unique signal in an array format, selectivity will remain a formidable challenge.

1.2 Receptor-free chemical sensing

The selectivity issue can, however, be addressed using non receptor-based approaches that utilize nanomechanics. As pointed out earlier a bimaterial cantilever is extremely sensitive to temperature variation. The mass of a cantilever is a few nanograms and, therefore, has a very low thermal mass. Since the thermal mass of the cantilever is extremely small, they can be heated to a high temperature in a few milliseconds. Heating of the cantilever can be accomplished by passing the current through electrical channels in the cantilever. As soon as the power is switched off the cantilever cools to the ambient temperature in milliseconds.

Here we will discuss two techniques by which chemical specificity can be achieved without using any receptors. The first method is based on calorimetry where the adsorbate-covered cantilever is heated in milliseconds to initiate a response that is very specific to the adsorbate[11]. The second method is a variation of photothermal calorimetry where an adsorbate covered bimaterial cantilever is exposed to specific infrared waves to initiate thermal response due to the absorption of specific IR waves by the adsorbate[12]. The cantilever bending response as a function of the exposing IR wavelengths resembles IR absorption spectra.

2. EXPERIMENTAL

2.1 Response of a heated cantilever

Thermal response experiments were carried out using custom designed and manufactured piezoresistive microcantilevers. Each cantilever has two doped poly-silicon piezoresistive tracks which change resistance in response to temperature. One track was used to heat the cantilever during the experiments, while the second track was used in a Wheatstone bridge circuit to monitor changes in the device resistance. The voltage for the heating track was supplied by a function generator in the form of a single 10 millisecond square wave pulse. A computer program written in LabVIEW was used to trigger the heating pulse and to measure and record the voltage across the Wheatstone bridge. Device exposure to TNT vapor was provided by an explosive vapor generated developed at Idaho National Laboratory.

2.2 Photothermal response

Photothermal experiments were carried out using commercially available silicon nitride AFM (atomic force microscope) cantilevers. Optical beam deflection was used to detect the cantilever motion. The silicon nitride cantilevers were deposited with a 30 nm gold layer in a vacuum evaporator. A 5 nm thick layer of Cr served as an adhesion layer. IR illumination of the cantilever was provided by a custom built filter wheel based monochromator. IR radiation from a glow bar was focused by a spherical mirror through a filter wheel and beam chopper onto the cantilever surface. The filter wheel had three filter segments which allow wavelength scans from 2.5 to 14.5 μm. Bending of the microcantilever was measured by reflecting a visible laser beam off the cantilever surface and into a position sensitive detector (PSD). The signal from the PSD was monitored using a lock-in amplifier utilizing the IR beam chopper as the reference.

3. RESULTS AND DISCUSSION

3.1 Response of a heated cantilever as a sensor signal

Adsorbates on a cantilever undergo phase transitions when the cantilever is heated, and these phase transitions result in variations in the cantilever heating rate as compared to the heating rate of a cantilever with no adsorbate. Since the mass of a cantilever is very small, small variations in heat energy can be easily detected with a cantilever. When a voltage pulse is sent through the heating track of the cantilever, the temperature of the cantilever increases as a function of time, constrained by the geometric and thermal properties of the cantilever. If an adsorbate is added to the cantilever surface, the added mass and thermal properties of the adsorbed material will cause a change in the rate at which the temperature increases. The added mass of the adsorbate adds to the overall thermal mass which in turn retards the rate of temperature increase.

Species specific adsorbate thermal properties of interest include: specific heat capacity, melting point, boiling point, heat of fusion, and heat of vaporization. For a given fixed rate of heat input into the adsorbate, the thermal properties of the adsorbate determine the shape of the temperature response curve. The specific heat capacity determines the slope of the response as the temperature increases. The phase changes occur at characteristic temperature points given by the melting point and boiling point and appear as changes in slope in the temperature curve. At the phase change points, the slope of the temperature curve reduces sharply due to the fact that the temperature of the adsorbate remains at the phase change temperature while the heat required to make the phase change is being absorbed. The time required for the heat absorption is given by the heat of fusion and heat of vaporization, and leads to plateaus in the temperature curve.

For the piezoresistive cantilever, temperature changes cause electrical resistance changes in the cantilever measurement track which are then measured in a Wheatstone bridge circuit. The temperature response of the cantilever is therefore directly related to the resistance curve. By subtracting the temperature response curve of the unloaded (no adsorbate) cantilever from the response curve of the same cantilever with adsorbate on its surface, a response signature which is characteristic of the adsorbate can be produced.

We have demonstrated changes in a cantilever heating response due to melting and vaporization of adsorbed species. Energetic materials such as TNT undergo deflagration when heated rapidly using a cantilever. Since the amount of material adsorbed on the surface is very small, the deflagration should be considered as a fast evaporation rather than an exothermic process. Evaporation occurs at a definite temperature and can be used for speciation.

When a cantilever with adsorbed TNT is heated rapidly with a very high temporal gradient of 10^6 degree/s or higher, the adsorbed TNT undergoes deflagration. The cantilevers were first deposited with controlled amounts of TNT vapor from the vapor generator. The mass of adsorbed TNT on the cantilever was calculated from the resonance frequency variation by measuring the resonance frequencies before and after TNT adsorption. The cantilever was then heated by applying a 10 millisecond voltage pulse of 10V (current of ≈ 5 mA). The estimated temperature of the cantilever due to pulse heating was around ≈ 700^0C. This rapid heating makes the resistance of the piezoresistive cantilever increase to a maximum in a time of about 2 milliseconds.

The dashed curve in Fig. 1 represents the cantilever response to the heating pulse in the absence of TNT. The amplitude of the response is displayed as the voltage across the Wheatstone bridge and therefore corresponds to the temperature induced resistance change of the cantilever. The solid curve represents the cantilever response to the heating pulse when TNT is present on the cantilever surface. Since the gradient of the response curve is lower when adsorbed TNT is present, the response should be characterized as fast evaporation. No exothermic process was observed during these experiments. From Fig. 1 it is clear that the cantilever comes to thermal equilibrium during heating within a few milliseconds, and the temperature/resistance reaches an equilibrium value. When the voltage pulse is turned off, the cantilever comes back to ambient temperature within about a millisecond and the resistance returns to its original value. Since the resonance frequency of the cantilever returns to its original value after rapid heating it can be assumed that all the adsorbed TNT desorbed from the surface. The sensitivity of detection is estimated to be around 50 pg.

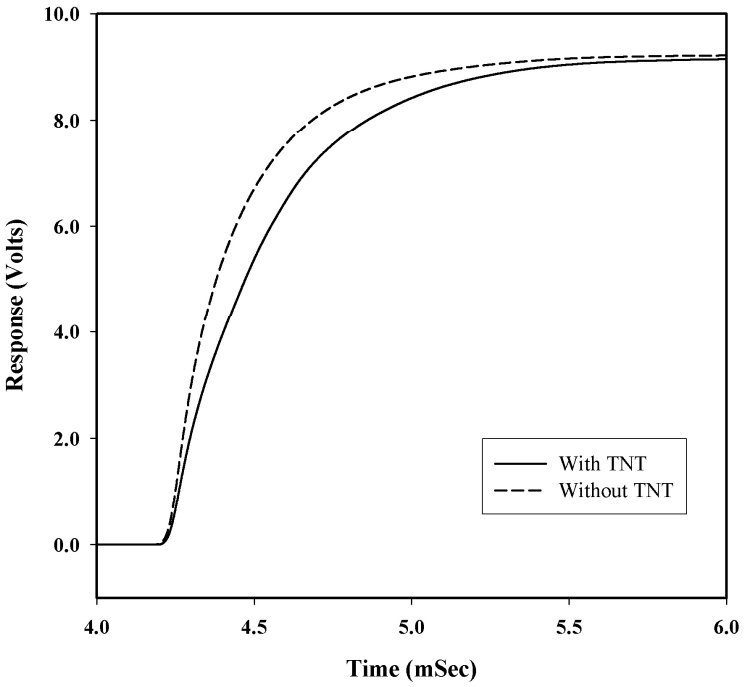

Fig. 1. Heated cantilever response. The signal amplitude is the output voltage across the Wheatstone bridge used to monitor changes in resistance of the piezoresistive cantilever as its temperature changes. The cantilever heating pulse turns on at the 4.2 mSec point in the plot, and the temperature of the cantilever reaches the maximum value of about 700 degrees C in less than 2 mSec. The response curve for the cantilever with adsorbed TNT lags behind the response for the unloaded cantilever indicating that the TNT desorption is an endothermic process.

This method has high selectivity for very sticky molecules such as TNT. Experiments conducted by exposing the cantilever to common interferents such as vapors of water, gasoline, acetone, and alcohols show no thermal response. This is mostly due to the fact that these molecules do not stick to the surface because of their high vapor pressures. TNT molecules, on the other hand, have very low vapor pressure at ambient conditions and condense on surfaces.

The details of the response variations are more easily seen if the null response (the response with no adsorbate present) is subtracted to create a differential response. In Fig. 2 is shown the differential responses for exposure to TNT and to NH_4Cl. The solid lines show the responses to three separate TNT exposures, while the three dashed lines show the responses to three separate exposures to NH_4Cl. Phase shifts are clearly visible in the NH_4Cl responses. The response signatures are repeatable and differentiable.

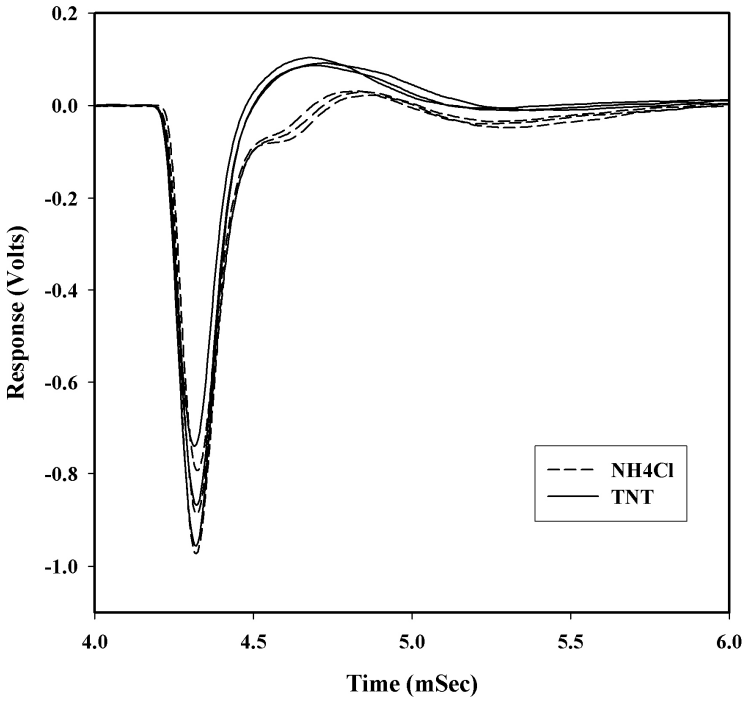

Fig. 2. Heated cantilever differential response for two adsorbates. The differential response is created by subtracting the heating response of the unloaded cantilever from the heating response of the adsorbate loaded cantilever. The melting point of NH_4Cl is about 340 degrees C. This temperature is reached at approximately the 4.5 mSec point where the response for NH_4Cl shows the short plateau region we would expect due to the absorption of the heat of fusion energy at the phase change. The response of the TNT is easily differentiable from the NH_4Cl response.

3.2 Photothermal response

Adsorbates on a cantilever surface absorb IR radiation at specific wavelengths which are characteristic of the vibrational modes of the molecules. As the adsorbate covered bi-material cantilever is illuminated with IR radiation, the absorbed wavelengths heat the cantilever and cause the cantilever to bend due to the bi-material effect. The nanomechanical motion of the cantilever as a function of illuminating wavelengths resembles IR absorption spectra of the adsorbed molecules.

We have demonstrated photothermal deflection of a bi-material cantilever due to absorption of IR radiation. Further, we have used the technique to acquire photothermal signature spectra of the explosive TNT, the biological spores of the bacterium *Bacillus cereus anthracis* (BA) more commonly known as "Anthrax", and *Bacillus cereus* (BC), a species commonly used as a simulant for BA. BC shares many similar chemical and physical properties with BA without the devastating health effects.

The TNT vapor was applied to the cantilever as described above, and the IR monochromator source was scanned from 2.5 μm to 14.5 μm wavelength. The cantilever response is shown in Fig. 3. The major peaks correspond well with traditional absorption spectra taken with a high resolution IR spectrometer[13].

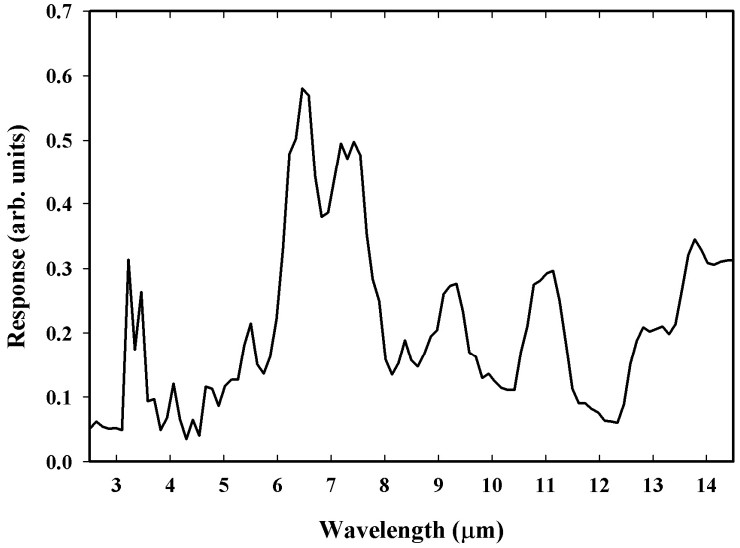

Fig. 3. Photothermal response for TNT. The TNT coated bi-material cantilever bends in response to the heat absorbed by the TNT as the wavelength of the illuminating IR source is scanned over the mid-IR range. This range corresponds to the molecular vibration region of most molecules and is therefore very useful for molecular identification.

The BA and BC coatings were produced by physically dipping the cantilevers into a liquid suspension consisting of water and spores[14]. As the water evaporates a thin layer of spores is left behind on the cantilever surface. The photothermal responses for BA and BC are plotted in Fig. 4. The photothermal measurements were made by scanning the IR monochromator through the three filter regions individually. This produced the small gaps in the data at 4.4 and 8.0 μm visible in Fig. 4.

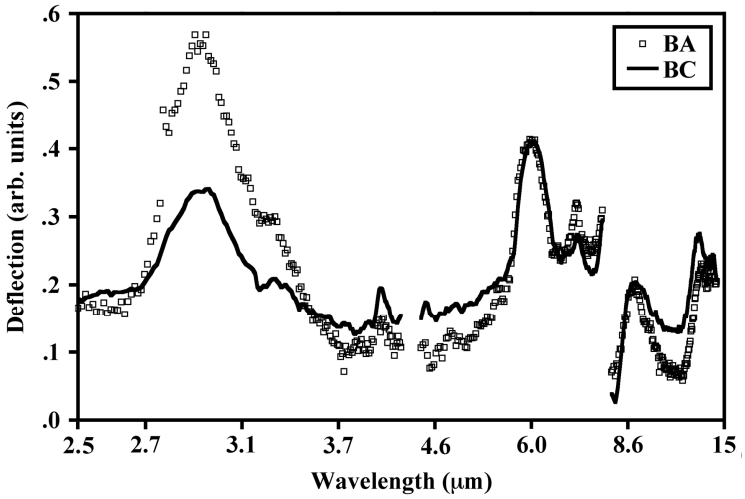

Fig. 4. Photothermal response for *Bacillus cereus anthracis* (BA) and *Bacillus cereus* (BC). The shapes of the two plots are very similar as we might expect since BA and BC share similar chemical and physical properties which are a reflection of the bond energy characteristics of the molecules. We can however see some differences with the amplitudes of the peaks near 3 μm and the inverted amplitudes near 4.6 μm.

4. CONCLUSIONS

Small molecule detection using nanomechanical response of receptor coated cantilevers does not have selectivity since receptors are designed with weak analyte-receptor interaction energy. The method does not show high selectivity even with array arrangements and pattern recognition techniques. Nanomechanical sensors, however, have physical properties that can be exploited for achieving chemical selectivity without using any molecular receptors. The extremely small thermal mass of the microcantilevers allows chemical speciation by measuring physical property variation of adsorbed species when the cantilever is heated rapidly. We also demonstrated chemical selectivity using photothermal effects that exploit extremely high temperature sensitivity of the cantilever when adsorbed molecules absorb infrared radiation. Nanomechanical motion of the cantilever as a function of illuminating wavelengths resembles IR absorption spectra of the adsorbed molecules. These two techniques offer chemical speciation without using any receptors.

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