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PAPER

# Adsorption induced surface-stress sensing signal originating from both vertical interface effects and intermolecular lateral interactions

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This research investigates the origin of specific molecule-adsorption induced surface-stress for micro/nano-cantilever bio/chemical sensors. Systematic discussion is presented on the contribution from types of molecule interactions to the generated surface-stress sensing signal. With the main arguments verified by our micro-cantilever sensing experiments, the origin of the adsorption induced surface-stress is, for the first time, clearly categorized into interface vertical effects and lateral interactions, which helps to comprehensively understand the surface-stress generation and overall to optimize the sensing performance of micro-cantilever chemo-mechanical sensors. The key findings of this research are that, vertically at the molecule adsorption surface, interfacial energy change and charge redistribution are the main origins of the generated surface-stress. More importantly, intermolecular lateral interactions may make a more significant contribution to the nano-mechanical surface-stress response. Compared with other lateral interactions like van der Waals force and the electrostatic coulombic effect, intermolecular hydrogen-bond intensity and steric factor easily cause much greater disparity in surface-stress.

## 1. Introduction

Used as sensing platforms, micro/nano cantilevers have been increasingly employed as chemical/bio-chemical sensors. Cantilever bio/chemical sensors offer substantial advantages, such as high sensitivity, fast response, low cost and on-chip integration capability. By translating molecular recognition into a micro/nano-mechanical sensing signal, the mechanical bending (deflection) response of a static cantilever or frequency-shift of a resonant cantilever has shown great promise for the highly-sensitive detection of bio-molecules like DNA,<sup>1–3</sup> RNA,<sup>4</sup> protein<sup>5,6</sup> and pesticides,<sup>7</sup> as well as, chemical gases like volatile organic compounds (VOCs),<sup>8,9</sup> explosives,<sup>10</sup> and mercury vapors.<sup>11</sup> Currently, both the static and dynamic sensing modes are used for cantilever sensors. Accordingly, the sensing signal of the static mode is induced by a change in the surface-stress, and the dynamic sensing mode is based on the specific mass loading. Since the mass adsorption induced frequency-shift of the resonant cantilever sensor is well defined, the sensor performance optimization mainly concerns improving the specific adsorption

capability to obtain as large a mass change as possible. For the static cantilever, unfortunately, an overall understanding of the surface-stress generation mechanism still remains obscure so far, due to the fact that the surface-stress generation process involves a complicated molecular mechanism. In addition a quantitative modelling, a quasi-quantitative or even a qualitative explanation to the relationship between the specific molecule reaction at the cantilever surface and the generated surface-stress signal is still difficult to provide clearly. The sensor sensitivity can only be determined by assessing sensing experimental results. In comparison to the established physical micro-cantilever sensors such as the cantilever beam-mass structural accelerometers, the sensitivity (to bio/chemical target molecules) of a static bio/chemical cantilever sensor is hard to determine well at the sensor design stage.

Obviously, in order to increase the surface-stress sensitivity and optimize the design of static cantilever sensors, exploring the origin of surface-stress generation is highly desirable.<sup>12,13</sup> In other words, a comprehensive understanding of the nano-mechanical sensing mechanism is essential for developing high-performance cantilever sensors. To measure the surface-stress induced deflection of a cantilever, only one side of the cantilever is coated with the receptor molecules for specific adsorption. Induced by molecule specific adsorption, the surface-stress is generated probably from quite a few interaction effects, which have been individually proposed as the electrostatic interaction (dipole–dipole interaction),<sup>14</sup> van der Waals (vdW) forces,<sup>15</sup> configuration entropy,<sup>16</sup> changes in the charge distribution of surface atoms<sup>17</sup> and so on. Although preliminary models and simulations

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have been raised sporadically,<sup>15,18,19</sup> the mechanisms proposed lack multi-interaction association and systematic consideration. Compared with individual studies on finding cantilever surface-stress sensing for certain kinds of target molecules, there have been relatively few systematic investigations exploring the origin of surface-stress generation. In our previous experiments, a striking difference was observed in the generated surface-stress when we self-assembled similarly-structured sensing-layers (all with an identical –COOH sensing terminal) on a cantilever surface to detect trinitrotoluene (TNT) vapor. The adsorption of TNT vapor on a sensing SAM (self-assembled monolayer) modified Au surface was reported<sup>10,20</sup> to always produce compressive surface-stress. In contrast, an opposite response indicating tensile surface-stress was experimentally obtained, when we modified the SiO<sub>2</sub> surface of the cantilever still with the –COOH terminated sensing-layer.<sup>21</sup> The contradictory phenomena as well as many other confusing results have not been clearly explained by previous studies. How do those individual interactions affect the final generation of surface-stress, and, what is the main concern for optimizing the surface-stress sensitivity? In order to answer these questions, we carried out this study to explore the origin of the surface-adsorption induced surface-stress.

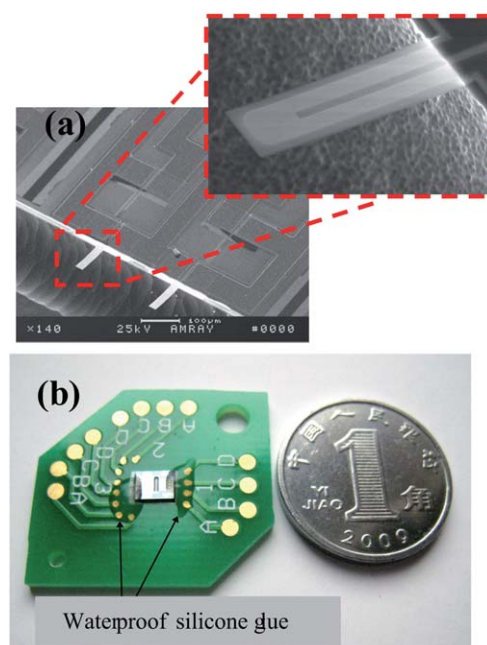
Based on the cantilever-sensing experiments that were specifically designed by us and theoretical analysis, we have tried to model the adsorption-induced surface-stress in a more overall way than that carried out before. In particular, we propose to distinguish the origin of the specific adsorption induced surface-stress by the vertical interface interaction and the lateral inter-molecular interaction on the surface. Of course, there is still a mutual influence between the vertical and the lateral effects, and we have included the mutual influence into our modelling consideration. With the multiple interactions associated, the various roles of concrete interaction factors are given for the design optimization of cantilever sensors.

## 2. Experimental

### 2.1 Micro-cantilever sensor

The surface-stress self-sensing microcantilevers used in this study were designed and fabricated in the authors' lab.<sup>9,10</sup> As is illustrated in Fig. 1(a), the cantilever is composed of silicon dioxide, with a thin layer of single-crystalline-silicon piezoresistor embedded near the top side of the cantilever. The bending stress sensitive piezoresistor is encapsulated and insulated by the surrounding silicon dioxide. The dimension of the cantilever is 90 μm in length, 20 μm in broadness and 1 μm in thickness. The cantilever piezoresistive sensitivity to surface-stress is calculated as  $(\Delta R/R)\sigma^{-1} = 8.37 \times 10^{-4} \text{ m/N}$ , where  $\Delta R/R$  is the relative resistance change of the piezoresistor. Therefore, the adsorption induced surface-stress signal can be proportionally characterized and experimentally expressed by the piezoresistive sensor output voltage.

In the sensor, one cantilever serves as the sensing cantilever, with its top surface coated with a gold thin-layer. Without a gold coating, another reference cantilever is used to compensate for the noise from environmental influences such as temperature changes or air/liquid flow. Besides the two piezoresistive cantilevers, two fixed resistors are integrated into the silicon chip



**Fig. 1** (a): SEM image of the piezoresistive cantilever sensor chip, the inset is a close-up view of the sensing cantilever. (b): Digital graph showing the packaged cantilever sensor chip for sensing experiments.

frame. The two piezoresistors embedded in the cantilevers and the two resistors are configured into a Wheatstone bridge for differential voltage output. Fig. 1(b) shows the digital picture of the sensor chip packaged on a printed circuit board for sensing experiments. In our experiments, the Wheatstone bridge was power supplied with a dc of 200 mV. A higher supply voltage was not used to depress the self-heating of the SiO<sub>2</sub> cantilever that causes thermal noise at the output signal.

### 2.2 Cleaning and modification processes to resist against non-specific adsorption

Prior to any further treatment of the cantilever, the Au surface and SiO<sub>2</sub> surface of the cantilevers were carefully cleaned several times with acetone, absolute ethanol, deionized water and Piranha solution (7/3 (vol/vol) of 98% H<sub>2</sub>SO<sub>4</sub> and 30% H<sub>2</sub>O<sub>2</sub>).

When the gold surface of the cantilever is used for sensing, non-specific adsorption of thiols on the SiO<sub>2</sub> surface should be avoided or depressed. The cantilevers were pre-modified with an ultra low surface-energy SAM of heptadecafluorodecyltrimethoxysilane (FAS-17). This pre-modification can change all the hydrophilic SiO<sub>2</sub> surfaces of the two cantilevers to hydrophobic surfaces. The technical details of the pre-modification can be found in our previously published work.<sup>20</sup> In contrast, when the bottom SiO<sub>2</sub> surface of the sensing cantilever is used for specific adsorption, it is not necessary for the clean gold surface to be pre-modified. In this case, the identical surface-stress signals generated on both sides of the reference cantilever will cancel each other out.

### 2.3 TNT detection with different sensing coatings

After the cleaning procedure with Piranha solution, the self-assembly of the sensing monolayer on the gold surface was

implemented by immersing the freshly cleaned cantilevers into a 6 mM solution of 4-mercaptopbenzoic acid (4-MBA) (97%, purchased from Aldrich Chemical) in absolute ethanol for 24 h. After rinsing with absolute ethanol and drying in ambient air, the functionalized cantilever sensor was ready for TNT detection. By exposing the sensor to saturated TNT vapor at 25 °C, a sensing signal for TNT was obtained. For comparing the sensitivity disparity when different sensing layers were used, the same sensor was cleaned and then re-modified with 6 mM solution of 6-mercaptonicotinic acid (6-MNA) (97%, purchased from Acros Chemical) to detect the saturated TNT vapor (at 25 °C) again.

## 2.4 Detection of the generated surface-stress from self-assembling dodecanethiol (DDT; HS-(CH<sub>2</sub>)<sub>11</sub>CH<sub>3</sub>) on gold in various media

Experimentally, after the cleaning and modification procedures for resisting against non-specific adsorption, the cantilever sensor was placed in a closed glass chamber of 50 mL for self-assembly of DDT (purchased from Fluka, with purity > 97%) in the vapor phase. The thiol liquid was injected into the chamber through a port and volatilized into the surrounding air. DDT was adsorbed onto the Au film of the cantilever to form a SAM on gold. In the case of liquid phase self-assembly, the cantilever can be immersed into 20 mL of pure solvent (ethanol, acetonitrile or hexane) to form the initial state. Then 20 µL of thiol liquid is injected into the solvent. All the solvents used in the experiments were of HPLC grade. During the self-assembly process on the Au substrate, the surface-stress change was recorded and read out by the output voltage of the cantilever sensor to reflect the change in surface-stress.

## 2.5 Sensing experiments to detect stereo disparity caused surface-stress

### 2.5.1 TNT sensing experiments for finding stereo effect on direction (or sign) of the generated surface stress.

When the SiO<sub>2</sub> surface of the cantilever was used for specific adsorption (see also the cantilever treatment in subsection 2.2), we used the two reagents *p*-aminobenzoic acid (PABA, purchased from Sigma-Aldrich) and 3-glycidioxypropyltri-methoxysilane (GPTS, purchased from ABCR) as the raw materials for directly constructing the sensing bi-layer on the SiO<sub>2</sub> surface. The sensing bi-layer grafting procedure is as follows. Firstly, 30 mL of GPTS (1 mM solution in anhydrous toluene) was prepared in dry flat-bottomed glassware under N<sub>2</sub> flow. Then, all of the SiO<sub>2</sub> surface of the cantilevers was pre-treated with hot Piranha solution for 3 min. Such a pre-treatment can densify the ≡SiOH groups at the SiO<sub>2</sub> surface. Then, the SiO<sub>2</sub> cantilevers were rinsed with deionized water several times and blow-dried with pure nitrogen gas. The micro-cantilevers with the freshly pre-treated SiO<sub>2</sub> surface were immediately immersed in a GPTS toluene solution to self-assemble the first molecular layer. The self-assembly process was carried out for 12 h at 70 °C under an N<sub>2</sub> atmosphere. Meanwhile, 100 mg mL<sup>-1</sup> aqueous PABA was prepared. The pH value of the PABA solution was adjusted to about 8.0 by adding Na<sub>2</sub>CO<sub>3</sub> powder. Upon completion of the first SAM, the cantilever sensor was removed from the GPTS solution and rinsed several times with toluene and ethanol to remove the

residue. Afterwards, to form the carboxyl-terminated sensing groups on the cantilever surface, the as-modified epoxy-terminated cantilever sensor was immersed, for about 24 h, into the prepared PABA solution to implement the second-layer grafting process. During this process, the epoxy ring was opened and the PABA was grafted on top of the first layer through a linkage between the amino groups and the epoxy groups. After acidification treatment in a pH 4.0–5.0 solution for about 30 min, the sensing terminals were finally grafted on top of the bilayer and the functionalized cantilever sensor was ready for TNT detection. The as-prepared sensor was exposed to saturated TNT vapor at 25 °C.

In another case when the gold surface of the cantilever was used for sensing, hydrophobic heptadecafluorodecyltrimethoxysilane (FAS-17, 99%, purchased from Fluoro Chem) was firstly immobilized on all the SiO<sub>2</sub> surfaces to resist against non-specific adsorption of humidity, by immersing the pre-cleaned cantilever in 0.2 mM FAS17/ethanol solution (with 1% water added). Upon removal from the FAS-17 solution, the cantilever was rinsed several times with absolute ethanol, and then activated at 120 °C for 1 h. The SAM of FAS-17 was selectively modified on the SiO<sub>2</sub> surface, and did not contaminate the Au substrate at the top surface of the sensing cantilever. The Au surface was further functionalized with a specific sensing SAM for TNT sensing. The thiol-based sensing layer was formed by self-assembly of 4-mercaptopbenzoic acid (4-MBA, 97%, purchased from Aldrich). After the cleaning procedure with Piranha solution, self-assembly of the sensing monolayer on the gold surface was implemented by immersing the cantilever sensors into absolute ethanol solutions of 2 mM 4-MBA. The self-assembly process normally takes 24 h. After rinsing with absolute ethanol and drying in ambient air, the cantilever sensors are ready for detection of the vapor. In the TNT detecting experiment, the 4-MBA coated sensor was exposed to saturated TNT vapor concentration at 25 °C.

### 2.5.2 Stereo disparity experiments with 3-MPA (mercapto-propionic acid) coating to detect molecules with big steric disparity.

The experimental procedure used was similar to that described before. After a similar pre-treatment procedure, self-assembly of the sensing monolayer on the gold surface was implemented by immersing the cantilever sensors into absolute ethanol solutions of 6 mM 3-MPA (99%, from Aldrich). The self-assembly process lasts for about 24 h. After rinsing with absolute ethanol and drying in ambient air, the cantilever sensors were ready for detection of the vapor. The sensitive response to 2,4-dinitrotoluene (DNT) and tetramethylammonium hydroxide (TMAH) was examined by exposing the 3-MPA coated sensor to the saturated DNT and TMAH vapor at 25 °C, respectively.

## 2.6 Sensing experiments to detect electrostatic attraction effect

Firstly, all the SiO<sub>2</sub> surface of the cantilevers was functionalized with CES as described before (see subsection 2.5.1). Then the cantilever sensor modified with the siloxane-based sensing layer was immersed into 9 mL of deionised water for signal baseline recording. 1 mL of 25% aqueous TMAH was injected into the solution for detection of the specific adsorption.



## 2.7 Sensing experiments to obtain surface-stress disparity induced by hydrogen-bond capability between adjacent molecules

For detection of amine homologues, the cantilever sensor coated with 3-MPA (see subsection 2.5.2) was sequentially exposed to 500 ppm each of our lab-made trimethylamine (TMA) vapor, dimethylamine (DMA) and monomethylamine (MMA).

## 3. Results and discussion

### 3.1 Overview of the surface-stress and the self-sensing cantilever sensor

It has been widely accepted that micro-cantilever bending is associated with the surface-stress disparity between its double sides and can be expressed by the Stoney equation.<sup>22</sup> The cantilever bending (characterized by the curvature radius  $r$ ) can be subsequently converted into the difference in surface-stress between the top and the bottom surfaces of the cantilever,  $\sigma_s$ , as

$$\frac{1}{r} = \frac{6(1-\nu)}{Et^2} \sigma_s \quad (1)$$

where  $t$  is the cantilever thickness,  $E$  is Young's modulus and  $\nu$  is the Poisson ratio of the cantilever material. Therefore the micro-cantilever is a good tool for experimentally testing surface-stress. Conversely, appropriately designed specific surface adsorption can generate an optimized surface-stress signal for a highly-sensitive cantilever sensor. A self-sensing cantilever sensor was used in our experiments, where the embedded piezoresistor can translate the surface-stress induced bending signal into output voltage.

From the view of chemistry, surface-stress is the reversible work per unit area required to elastically strain a surface and to increase the surface area. The surface-stress can be expressed by the Shuttleworth equation as

$$\sigma_s = G + dG/d\varepsilon \quad (2)$$

where  $G$  and  $\varepsilon$  are surface free energy and surface-strain, respectively. For typical micro-cantilever structures, the contribution from the surface-strain can be neglected and the surface-energy change directly equates to the variation in surface-stress.<sup>23,24</sup> Thus, eqn(1) can be approximately but simply expressed as

$$\Delta\sigma_s = \Delta G \quad (3)$$

Hence, the generated surface-stress can be considered to be a measure or expression of the variation in surface energy. When the topside of the cantilever is used for adsorption and sensing, upward or downward bending of the cantilever is normally considered to be due to the generation of tensile stress or compressive stress, which reflects an increase or decrease in the surface energy.

For simplicity, we assume that the sensing surface of the cantilever is chemically homogeneous, thus the adsorbates are distributed statistically uniformly on the sensing surface that can be expressed with the mean interspacing distance between two adjacent adsorbates along the direction of the length. Herein we also assume that the first layer of the adsorbates on the cantilever

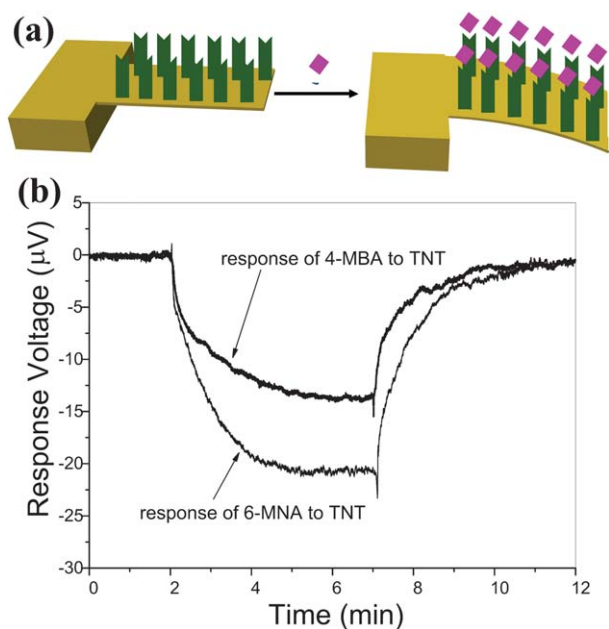
surface plays a dominant role, with the influence from the second and upper layers of the adsorbates ignored.<sup>12,17</sup> From an atomistic point of view, the surface-stress generated by the adsorption of target molecules can be understood in the following way: the surface layer of the substrate (*e.g.* the original molecular layer or the modified surface) is in an equilibrium state with its initial surface-stress,  $\sigma_{s0}$ , determined by the initial state of the substrate surface and the adsorbed environmental molecules (*e.g.* air molecules for gas/solid interface or solvent molecules for liquid/solid interface). The adsorbate molecules replace the former non-specifically adsorbed molecules and, therefore, change the substrate surface. Accordingly, the surface-stress changes at the newly formed interface to achieve a new equilibrium. The change in the surface-stress originates from both the interfacial interaction (herein named as vertical effects) and the adjacent-molecule interactions on the surface (herein named as lateral interactions). Accordingly, we distinguish the surface-stress origin into two parts, *i.e.* the origin from the specific binding between the adsorbate and the coating molecules at the interface, as well as, the origin from the surface molecular re-ordering caused by lateral intermolecular interaction.

### 3.2 Vertical interface effects on surface-stress

The vertical interfacial interaction involves the direct bio/chemical reaction that captures the adsorbate molecules. This has been considered to be an important aspect for surface-stress generation. Improving this specific-reaction intensity has also been considered to be the main optimizing strategy for cantilever sensors.

When the the specific binding between the adsorbate and the coating molecules occurs vertically at the interface, the target molecules are specifically adsorbed at the original surface with a surface coverage  $\theta$ , which is determined by the specific binding intensity. In the case of  $\theta < 0.2$ , a linear dependence of the surface-stress on surface coverage has been frequently reported.<sup>25–27</sup> In the low coverage cases, compressive surface-stress scaling linearly with the coverage was observed for the adsorption of sulfur on Ni(100) and carbon on Ni(111).<sup>28,29</sup> Thus, in trace-lever molecule detection where the generated surface-stress is highly dependent on  $\theta$ , increasing the specific binding intensity is indeed an effective way to enhance the sensitivity of the cantilever sensors, especially when  $\theta$  is so small that the inter-molecular interactions can be neglected. Our previous studies on the detection of trace TNT and dimethyl-methylphosphonate (DMMP) determined the relationship between the surface-stress signal and vapor concentration, which was found to fit the Langmuir adsorption isotherm model well.<sup>9,20</sup>

To investigate the effects of specificity to generated surface-stress at low surface coverage, we used two different sensing SAMs to detect the same kind of trace-concentration molecules. Fig. 2 schematically shows the specific adsorption induced cantilever downward bending in (a) and the sensor responded surface-stress signals to TNT vapor in (b). The same cantilever sensor sequentially modified with different SAMs of 4-MBA and 6-MNA were used to sequentially detect the same concentration of TNT. In our experiments, the two sensing SAMs captured TNT molecules both by hydrogen-bond interaction between  $-\text{NO}_2$  group and  $-\text{COOH}$  group. Since the surface  $\text{p}K_a$  values for



**Fig. 2** (a): Schematic showing the surface adsorption induced cantilever bending. (b): Different surface-stress (or surface-energy change) signals are generated by using the different sensing layers of 4-MBA and 6-MNA to detect saturated TNT vapor at 25 °C.

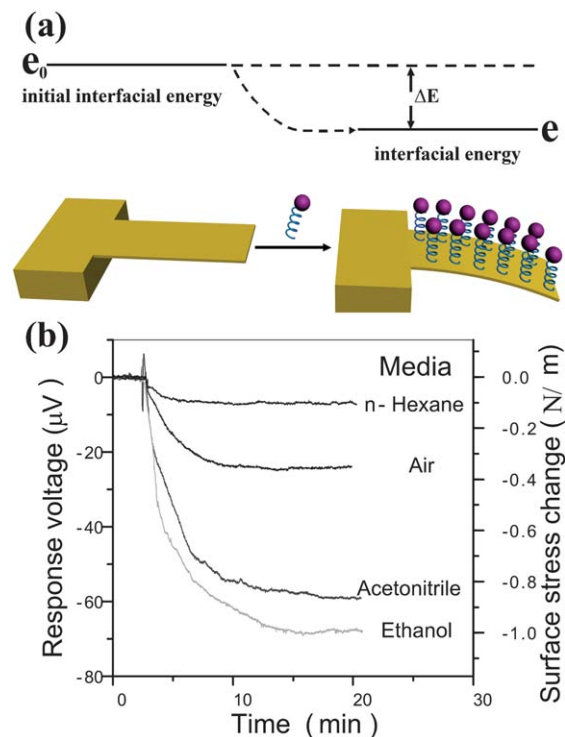
the SMAs of 6-MNA and 4-MBA were experimentally measured as 5.5 and 5.9, respectively,<sup>30,31</sup> the specificity to TNT of 6-MNA is obviously higher than that of 4-MBA, and the cantilever sensor modified with 6-MNA has a stronger capability to capture TNT molecules than that modified with 4-MBA. According to the experimental results, about a 30% increase in surface-stress sensing signal was obtained when the modified SAM of 4-MBA was replaced by 6-MNA which possesses a higher specificity for TNT adsorption. The specific binding intensity not only decides the surface adsorption coverage, but also has an influence on the molecule adsorption speed. It can be observed from the results of Fig. 2(b) that, besides the obtained increase in the finally saturated surface-stress amplitude, the 6-MNA coated cantilever sensor, which has a higher specificity with TNT compared to the 4-MBA coated case, features a higher adsorption rate (especially at the early stage).

Although the specific binding intensity determines the surface coverage  $\theta$  of the adsorbate and influences the adsorption speed, there is no direct relationship with the final amplitude of the generated surface-stress signal, especially for the situation of high surface coverage. Our experimentally obtained opposite-signed surface-stress (generated by the same adsorbed molecules on similarly-structured SAMs) indicates that, despite the influence on surface coverage of  $\theta$ , the adsorbing specificity is not the dominant factor for the amplitude of the generated surface-stress signal. By using a series of homologues, which feature an increasing order of adsorbing specificity onto the same substrate coating, our cantilever sensing experiment verified that instead of showing an increasing order in the generated surface-stress, the response signals showed a reverse order (*i.e.* decreasing order of surface-stress amplitude). The technical details are given in the following section. Under such situations, the vertical molecular interaction specificity (*i.e.* the sensing selectivity) does not

directly dominate the induced surface-stress signal (*i.e.* the sensitivity).

We also investigated the effect of adsorption environment on the generated surface-stress by monitoring the self-assembly process of DDT on gold in various media. Fig. 3(a) schematically shows a typical cantilever downward bending induced by thiol self-assembly on gold and the simultaneously accompanying surface-energy decrease during the spontaneous process. Most commonly, the self-assembly generated surface-stress is observed as a compressive one, *i.e.* the surface-stress is negative. For spontaneous self-assembly or surface adsorption, the process should tend to decrease the surface free energy leading to a decrease in the existing surface tension. It is worth pointing out that the spontaneous surface process does not generate compressive surface-stress, but reduces the original surface tension. When the process is on the top surface of the cantilever, the existing surface tension is released, making the cantilever bend downwards. Such a tension release can be equivalently viewed as generation of compressive surface-stress.

Fig. 3(b) shows that the change in surface-stress varies when the media for thiol self-assembly on gold are sequentially ethanol, acetonitrile, air and hexane. The sensor yields a negative voltage when the DDT is injected into every medium, which indicates a downward cantilever bending due to the generated compressive surface-stress on the gold-coated top surface. Nevertheless, quite unequal surface-stress values are measured in different media. The generated surface-stress in air is lower than that in ethanol and in acetonitrile but larger than that in hexane. This phenomenon implies that the self-assembly induced



**Fig. 3** (a): Schematics showing the interfacial energy change induced cantilever bending. (b): Sensing experiment obtained surface-stress (or surface-energy change) generated by sequential self-assembling DDT on gold, in various media of ethanol, acetonitrile, air and hexane.

surface-stress in a polar solvent is much larger than that in a non-polar solvent. This can be mainly attributed to the different initial surface-energy of Au surface in different media. The thiol SAM with identical molecular construction may have undergone largely different surface-stress variations if it was ever self-assembled in different media due to different interfacial energy changes. Moreover, the self-assembly process is usually the first step for specific adsorption of the second layer of target molecules. The successively adsorbed molecule layer would cause a further decrease in interface energy. To increase the interfacial energy at the SAM/media interface is a possible way to enhance the generated surface-stress amplitude of cantilever sensors.

Besides the above discussed factors, at the interface, the charge redistribution is believed to play an important role in the generation of surface-stress.<sup>25,26,32</sup> Godin *et al.* used the charge redistribution to explain the independent surface-stress response of the molecular chain-length of self-assembled thiols on gold.<sup>17</sup> In addition to the molecule adsorption modifying the surface's local free energy, redistribution of the electronic structure of the substrate surface-atoms will change the surface-stress.

No matter whether reversible binding (*e.g.* hydrogen binding) or irreversible binding (*e.g.* covalent binding) had occurred, the specific binding at the interface includes electron transfer. The electron transfer causes charge distribution at the substrate and to vertical dipoles. Such a process also has an effect on the surface coverage of the newly formed surface and, then leads to the generation of lateral interactions between adjacent adsorbed molecules. In general, among the vertical interaction factors, surface energy variation is believed to be the main effect to influence the generated surface-stress. In contrast, the surface binding specificity itself has little direct effect on the value of the generated surface-stress. Alternatively, the specificity influences the adsorption rate and surface coverage, which indirectly influence the lateral intermolecule effects of the adsorbing interface that will be addressed in following section.

### 3.3 Lateral interactions contributing to surface-stress

It is not hard to understand that, after the target molecules adsorbed onto the surface, different kinds of interactions between adjacent molecules begin to influence intermolecular equilibrium distance. Having been previously proposed as Lennard-Jones potential to describe van der Waals force and Pauli exclusion, electrostatic force, conformational entropy, lateral intermolecular interactions can be accepted as the mechanism for surface-stress change. Our experiments have confirmed that lateral interaction often contributes no less to the surface-stress than the above discussed interfacial vertical interactions. Sometimes, the strong lateral intermolecular interactions can cause orders of magnitude higher surface-stress or even generate oppositely signed surface-stress.

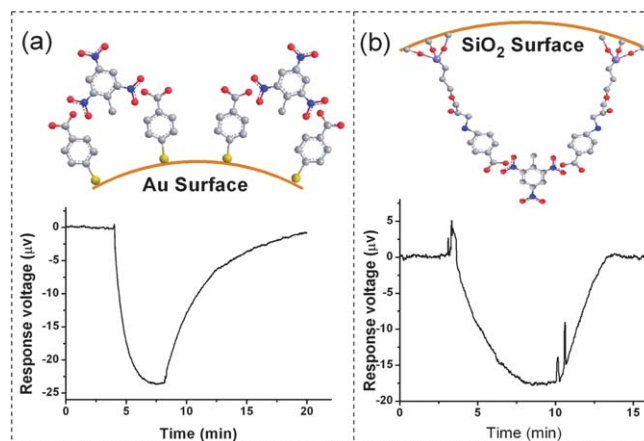
**3.3.1 Stereo effects.** Stereo effects have been found to significantly affect the generated surface-stress. Ss-DNA (single-stranded DNA) hybridization induced configurational entropy change was reported to be capable of controlling the direction of cantilever bending (*i.e.* compressive or tensile surface-stress generation).<sup>16</sup> Besides the DNA macromolecules, we have

experimentally obtained opposite-signed surface-stress signals, by adsorbing TNT molecules on similar-structured sensing layers.

The sensing layers used are thiol-SAM of 4-MBA on Au surface and –COOH terminated bi-layer grafted on SiO<sub>2</sub> surface, respectively. The measured opposite-signed surface-stress sensing responses to identical concentration TNT (saturated vapor at 25 °C) are shown in Fig. 4(a) and (b), respectively. Although the two cantilevers in the two sensing experiments both bend downwards, the adsorbing Au surface is on the top side of the sensing cantilever but the SiO<sub>2</sub> sensing surface of another cantilever sensor is at the backside. Thus, the surface-stress signals in the two experiments should be of opposite signs to each other.

Thiols are believed to form a well-ordered high-coverage monolayer on Au (111) lattice, with the balanced space between two adjacent thiols as 4.97 Å.<sup>33</sup> For the functionalized SiO<sub>2</sub> sensing surface, however, the distance between the two nearest self-assembled –COOH groups will be much sparser and larger than the size of a TNT molecule.<sup>21</sup> The first reason is the sparse –OH groups originally on the SiO<sub>2</sub> surface for siloxane self-assembly. The second reason lies in the condensation reaction between adjacent silanol groups that causes even sparser silanol-group distance for the sensing bi-layer grafting.<sup>21</sup> During the adsorption of TNT molecules, the two –NO<sub>2</sub> groups in the same TNT molecule can be captured respectively by two adjacent –COOH terminals. The calculated distance between the two oxygen atoms, which respectively belong to the two adjacent –NO<sub>2</sub> groups, is about 5.2 Å. Hence, the relatively smaller distance between the two –COOH terminals on the Au surface tends to cause repulsive interaction. In contrast, the relatively larger distance between the two –COOH terminals on the SiO<sub>2</sub> surface easily induce attractive interaction. Thus, either compressive or tensile surface-stress can be generated due to different steric factors.

Opposite-signed surface-stress can also be generated when different-sized molecules are adsorbed on the same SAM sensing



**Fig. 4** Tested cantilever sensor responses and schematic models demonstrating opposite surface-stress signals. (a): Compressive surface-stress signals generated by adsorption of TNT molecules on thiol-on-Au modified cantilever. (b): Tensile surface-stress signal generated from lateral interaction, by adsorption of TNT molecules on siloxane-on-SiO<sub>2</sub> modified cantilever.



layer premodified on gold. We used a 3-mercaptopropionic acid (3-MPA) pre-modified cantilever to detect two kinds of molecules which possess great stereo disparity with each other. The sensing results are shown in Fig. 5. The balanced space of Au(111) modified thiol-SAM is 4.97 Å, while the maximum length of the detected molecules of TMAH and DNT is approximately 4.22 Å and 7.04 Å, respectively. In detection of the relatively smaller TMAH molecules, tensile-stress is achieved. In contrast, since the 4.97 Å interval is not enough to accommodate the big-sized DNT molecules, a repulsive force is generated between adjacent molecules, resulting in a compressive surface-stress.

It is worth pointing out that the stereo effect is closely associated with the density of the active sites and surface coverage  $\theta$  of the bottom sensing layer. As the target molecules are adsorbed onto the sensing layer, the final distance  $r$  between the two adjacent adsorbed molecules (*i.e.* the molecules of newly formed surface) is strongly influenced by the geometric layout and the surface coverage  $\theta$  of the bottom acceptor layer.

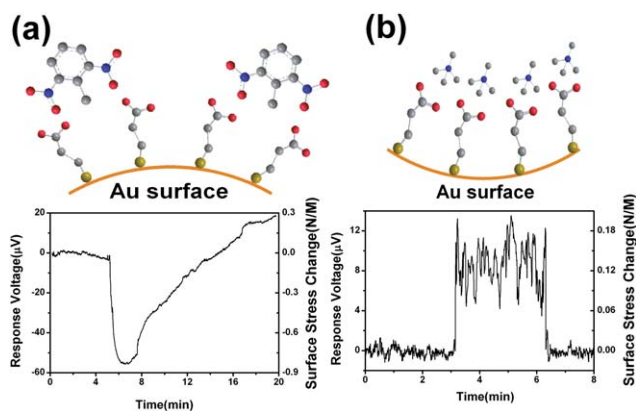
**3.3.2 Van der Waals interaction.** Van der Waals force of attraction has been proposed and discussed in details as a mechanism for adsorption induced surface bending.<sup>15</sup> In our previous self-assembly experiment of DDT and HDT, a small difference in surface-stress amplitude was found. The sensing signal for HDT self-assembly is a bit larger than that for DDT, which could be attributed to Van der Waals force between the adjacent molecule chains. If the self-assembly process of alkyl chains is taken for consideration, van der Waals interaction between the alkyl chains could result in tilt of the self-assembled chains,<sup>17</sup> thereby, constructing an ordered structure of the newly formed surface. Compared with other influences, van der Waals interaction does not directly determine the surface-stress, as it is a short-term weak interaction effect between molecules.

**3.3.3 Electrostatic interaction.** Electrostatic interaction between the adsorbed molecules has been proposed as a possible source of the observed surface-stress, where there are existing charges or charge transfers in the considered system. In many cases, dipolar interaction is considered the dominant factor of

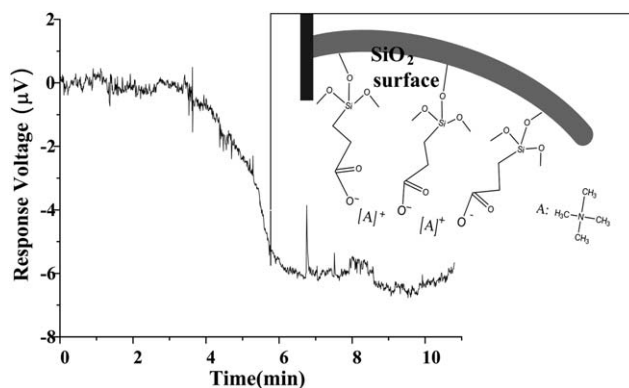
electrostatic interaction. Obviously the dipole-to-dipole lateral interaction between adjacent molecules should generate repulsive force and compressive surface-stress. Such electrostatic repulsion between neighboring ionized carboxylate groups to generate compressive surface-stress was observed by Sushko *et al.*<sup>12</sup> However, in the anionic/cationic case, another kind of electrostatic attractive interaction is also important that generates tensile surface-stress.<sup>34</sup>

To compare the dipolar interaction with the cations-to-anions interaction in terms of the effect on surface-stress generation, we used a cantilever sensor to detect 2.5% aqueous TMAH. The top surface of the sensing cantilever was coated with Au and the bottom SiO<sub>2</sub> surface was modified with a siloxane-based SAM for specific binding. With the results shown in Fig. 6, the sensor yields a large tensile surface-stress signal, where downward bending of the sensing cantilever has occurred. In aqueous solution, the pre-modified carboxyl group (–COOH) dissociates to –COO<sup>1–</sup> and the TMAH molecule dissociates to [N(CH<sub>3</sub>)<sub>4</sub>]<sup>1+</sup>. Therefore, besides the repulsive dipolar interaction between adjacent adsorbate molecules, electrostatic attractive interactions among the cations at the adsorbate and the anions at the double-sided receptors occur. As is schematically modelled in the inset of Fig. 6, the finally observed tensile surface-stress indicates that when strong cation-anion interaction exists, the dipolar electronic interaction can be considered to be a much weaker effect on surface-stress generation.

**3.3.4 Hydrogen-bonding interaction.** In sensing experiments, one sometimes uses identical coating to detect one kind, or a series of similar molecules (*e.g.* homologues), and expect to obtain similar surface-stress signals, as the specificity of the homologues is similar. However, our recent experimental results exceed expectations. In the experiment, we used the same cantilever sensor which was modified with the same –COOH terminated 3-MPA SAM on gold to sequentially detect a series of homologous amines of TMA, DMA, and MMA. According to the theory of gas-phase basicity, their gas-phase basicities are in the order of MeNH<sub>2</sub> < Me<sub>2</sub>NH < Me<sub>3</sub>N which is attributed to an electron-releasing “inductive effect”<sup>35,36</sup> and is illustrated in the top part of Fig. 7. Therefore, the order of the specificity to the –COOH terminated modification should still be MeNH<sub>2</sub> < Me<sub>2</sub>NH < Me<sub>3</sub>N. However, our cantilever sensing experiment



**Fig. 5** Tested sensor responses and schematics models showing opposite surface-stress signals. (a): Compressive surface-stress signals generated by adsorption of DNT molecules on Au. (b): Tensile surface-stress from lateral interaction, by adsorbing TMAH vapor molecules on Au.



**Fig. 6** Sensor response to (CH<sub>3</sub>)<sub>4</sub>N<sup>+</sup> in 2.5% aqueous TMAH, resulting in a compressive surface-stress signal.

results in not only an opposite order of the generated surface-stress but also a huge disparity among the three surface-stress signal amplitudes, *i.e.*,  $\text{MeNH}_2 \gg \text{Me}_2\text{NH} \gg \text{Me}_3\text{N}$ . The signal sequence and the big disparity in the surface-stress can be observed in Fig. 7(a)–(c). If only with the vertical interfacial effects considered that are mainly determined by adsorption specificity, the experimentally observed results cannot be explained.

Although the amine homologues possess many similar properties, among them there are great differences in hydrogen-bond interactive capability. The opposite sequence in the generated surface-stress and the more than one order of magnitude disparity in the signal amplitude can be attributed to the largely different hydrogen bond capability. DMA differs from TMA by the replacement of one methyl group by a hydrogen atom, thereby, resulting in an increase in the carried charge on the nitrogen atom. The appearance of the active hydrogen results in the formation of a hydrogen-bond. In MMA, two methyl groups are replaced by two active hydrogen atoms, which can increase the carried charge on the nitrogen atom. With the increased enhancement of the charge carried on the nitrogen atom, the hydrogen-bond intensity becomes even stronger. With the formation of the inter-molecular hydrogen-bond, the lateral interaction between adjacent molecules becomes dominant by hydrogen-bonding, thereby, inducing a significant signal enhancement by about one order of magnitude. In the case of surface-adsorbed MMA molecules, even more intensive hydrogen bonding occurs leading to a further increase in surface-stress by several times.

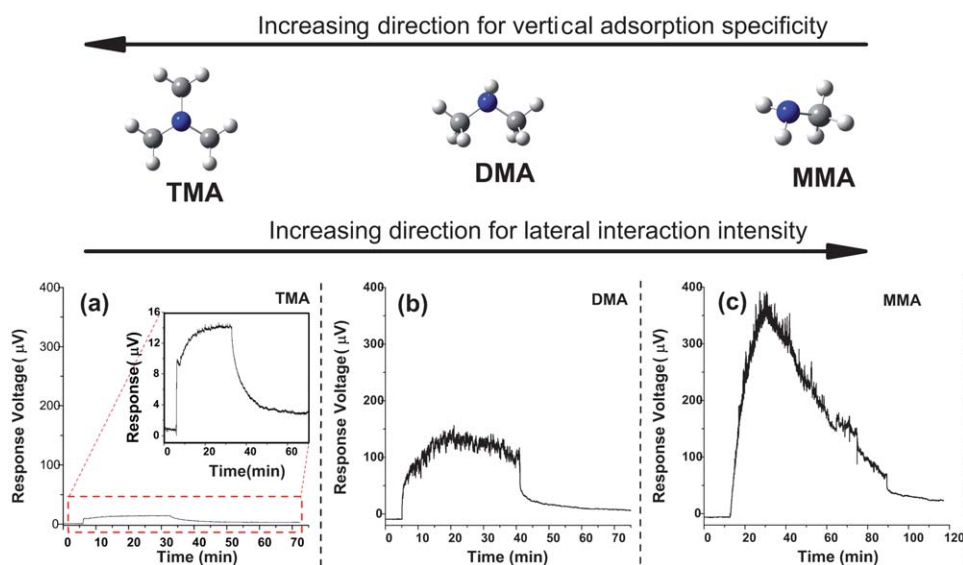
It is well recognized that there are numerous chemical/bio-chemical processes where hydrogen-bonding plays important roles. As a secondary bond with its ordinary bonding energy less than  $42 \text{ kJ mol}^{-1}$ , the hydrogen bond is much stronger than the intermolecular interaction driven by van der Waals force. Vertically at the specific sensing surface, there have been various applications using hydrogen-bond-based sensing coatings (*e.g.* the above-mentioned specific adsorption of amines on 3-MPA

modified surface). However, the hydrogen-bond-based inter-molecular lateral effect on surface-stress has seldom been utilized so far. Compared with the above-described experimental results in Fig. 2, where the very different adsorption specificity at the adsorbate-to-receptor vertical interface [sensing TNT with 4-MBA ( $\text{p}K_a = 5.9$ ) or 6-MNA ( $\text{p}K_a = 5.5$ )] merely causes a 30% difference in surface-stress signal, the huge disparity in surface-stress induced by the lateral intermolecular hydrogen-bonding effect shows more promising prospects in high-sensitivity sensing applications.

## 4. Conclusions

Various interactions can drive molecular adsorption onto surfaces, which results in measurable surface-stress to serve as micro/nano mechanical sensing signals. In most surface-stress induced cantilever-bending sensing applications, interaction specificity between the adsorbate and the surface, which involves the direct binding process, determines the adsorbing speed and the surface coverage of the adsorbate. However, the specificity has no directly absolute relationship with the generated surface-stress amplitude. Vertical to the surface, the adsorption-induced interfacial energy change and charge redistribution can be considered as important but indirect origins of the generated surface-stress value.

On the other hand, lateral intermolecule effects can make significant contributions to the overall mechanical response. In most sensing cases, surface-stress generated from the van der Waals attraction force and coulombic interactions between adjacent adsorbed molecules is relatively small. However, big stereo difference and hydrogen bond intensity can cause great disparity in generated surface-stress. With the size of the adsorbed molecule compared with the balanced space of the receptor molecules at the pre-modified substrate, different disparities in steric factors can even cause oppositely signed surface-stresses. For molecules with a similar stereo-factor, hydrogen-bond



**Fig. 7** Contradictory orders of responses. (a), (b), (c) responses of resonant cantilever sensor to TMA, DMA and MMA, respectively. (d), (e), (f) Responses of surface-stress induced cantilever sensors to TMA, DMA and MMA, respectively.



intensity will dominate the inter-molecular lateral interaction. In the case of amine homologues as absorbates, we have experimentally demonstrated that the hydrogen-bond based lateral effect makes a very significant contribution to the generated surface-stress during specific adsorption.

Current cantilever-based sensing applications can significantly gain in performance by taking these findings into account. Besides improving sensitivity by using optimized coatings to increase the surface adsorbing coverage, more attention should be paid to the following aspects: 1, optimizing the sensing architecture so that the molecular adsorption inherently modifies the charge density; 2, optimizing the sensing coatings so that the interfacial energy changes significantly when the adsorption happens; 3, considering the stereo difference between the balanced space of the sensing coating and the size of the adsorbate and; 4, employing strong intermolecular lateral interactions like the above-described hydrogen-bond-based lateral effect to gain huge disparities in generated surface-stress signals. In general, overall consideration of the various effects on surface-stress signals is helpful for cantilever sensing design optimization and high-performance bio/chemo-mechanical detection.

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## Notes and references

- J. Fritz, M. K. Baller, H. P. Lang, H. Rothuizen, P. Vettiger, E. Meyer, H. J. Guntherodt, C. Gerber and J. K. Gimzewski, *Science*, 2000, **288**, 316–318.
- M. Arroyo-Hernandez, J. Tamayo and J. L. Costa-Kramer, *Langmuir*, 2009, **25**, 10633–10638.
- R. Marie, H. Jensenius, J. Thaysen, C. B. Christensen and A. Boisen, *Ultramicroscopy*, 2002, **91**, 29–36.
- G. H. Wu, R. H. Datar, K. M. Hansen, T. Thundat, R. J. Cote and A. Majumdar, *Nat. Biotechnol.*, 2001, **19**, 856–860.
- W. G. Shekhawat, S.-H. Tark and V. P. Dravid, *Science*, 2006, **311**, 1592–1595.
- J. Zhang, H. P. Lang, F. Huber, A. Bietsch, W. Grange, U. Certa, R. McKendry, H. J. Guntherodt, M. Hegner and C. Gerber, *Nat. Nanotechnol.*, 2006, **1**, 214–220.
- M. Alvarez, A. Calle, J. Tamayo, L. M. Lechuga, A. Abad and A. Montoya, *Biosens. Bioelectron.*, 2003, **18**, 649–653.
- C. Hagleitner, A. Hierlemann, D. Lange, A. Kummer, N. Kerness, O. Brand and H. S. Baltes, *Nature*, 2001, **414**, 293–296.
- G. M. Zuo, X. X. Li, P. Li, T. T. Yang, Y. L. Wang, Z. X. Cheng and S. L. Feng, *Anal. Chim. Acta*, 2006, **580**, 123–127; P. Li and X. X. Li, *J. Micromech. Microeng.*, 2006, **16**, 2539–2546.
- P. Li, X. X. Li, G. M. Zuo, J. Liu, Y. L. Wang, M. Liu and D. Jin, *Appl. Phys. Lett.*, 2006, **89**, 074104.
- B. Rogers, L. Manning, M. Jones, T. Sulchek, K. Murray, B. Beneschott, J. D. Adams, Z. Hu, T. Thundat, H. Cavazos and S. C. Minne, *Rev. Sci. Instrum.*, 2003, **74**, 4899–4901.
- M. L. Sushko, J. H. Harding, A. L. Shluger, R. A. McKendry and M. Watari, *Adv. Mater.*, 2008, **20**, 3848–3853.
- H. F. Ji and B. D. Armon, *Anal. Chem.*, 2010, **82**, 1634–1642.
- Rudiger Berger, Emmanuel Delamarche, Hans Peter Lang, Christoph Gerber, James K. Gimzewski, Ernst Meyer and H.-J. Guntherodt, *Science*, 1997, **276**, 2021–2024.
- D. W. Dareing and T. Thundat, *J. Appl. Phys.*, 2005, **97**, 043526.
- G. H. Wu, H. F. Ji, K. Hansen, T. Thundat, R. Datar, R. Cote, M. F. Hagan, A. K. Chakraborty and A. Majumdar, *Proc. Natl. Acad. Sci. U. S. A.*, 2001, **98**, 1560–1564.
- M. Godin, V. Tabard-Cossa, Y. Miyahara, T. Monga, P. J. Williams, L. Y. Beaulieu, R. B. Lennox and P. Grutter, *Nanotechnology*, 2010, **21**, 075501–075508.
- B. Bar On and E. Altus, *Probabilistic Engineering Mechanics*, 2010, **25**, 228–234.
- X. Yi and H. L. Duan, *J. Mech. Phys. Solids*, 2009, **57**, 1254–1266.
- G. M. Zuo, X. X. Li, Z. X. Zhang, T. T. Yang, Y. L. Wang, Z. X. Cheng and S. L. Feng, *Nanotechnology*, 2007, **18**, 255501–255508.
- Y. Chen, P. C. Xu and X. X. Li, *Nanotechnology*, 2010, **21**, 265501.
- G. G. Stoney, *Proc. R. Soc. London, Ser. A*, 1909, **82**, 172–175.
- H. J. Butt, *J. Colloid Interface Sci.*, 1996, **180**, 251–260.
- R. Shuttleworth, *Proc. Phys. Soc., London, Sect. A*, 1950, **63**, 444–457.
- H. Ibach, *Surf. Sci. Rep.*, 1997, **29**, 195–263.
- W. Haiss, *Rep. Prog. Phys.*, 2001, **64**, 591–648.
- H. Ibach, *J. Vac. Sci. Technol., A*, 1994, **12**, 2240–2243.
- D. Sander, U. Linke and H. Ibach, *Surf. Sci.*, 1992, **272**, 318–325.
- A. Grossmann, W. Erley and H. Ibach, *Surf. Sci.*, 1994, **313**, 209–214.
- C. R. Raj and S. J. Behera, *J. Electroanal. Chem.*, 2005, **581**, 61–62.
- Y. Ji, Q. Zhou, X. W. Li, Y. G. Zhou, Y. Zhuang and J. W. Zheng, *Chin. J. Anal. Chem.*, 2004, **32**, 1050–2.
- F. Amiot, F. Kanoufi, F. Hild and J. P. Roger, *Sens. Actuators, A*, 2009, **152**, 88–95.
- J. C. Love, L. A. Estroff, J. K. Kriebel, R. G. Nuzzo and G. M. Whitesides, *Chem. Rev.*, 2005, **105**, 1103–1169.
- M. Watari, J. W. Ndieyira and R. A. McKendry, *Langmuir*, 2010, **26**, 4623–4626.
- D. H. Aue, H. M. Webb and M. T. Bowers, *J. Am. Chem. Soc.*, 1976, **98**, 311–317.
- G. Bouchoux, *Mass Spectrom. Rev.*, 2007, **26**, 775–835.