

# Nanomechanical Assay to Investigate the Selectivity of Binding Interactions between Volatile Benzene Derivatives

Digvijay Raorane,<sup>†,‡</sup> Si-Hyung “Shawn” Lim,<sup>†,§</sup> and Arun Majumdar<sup>\*,‡,||</sup>

*Department of Mechanical Engineering, University of California, Berkeley, Berkeley, California 94704, School of Mechanical and Automotive Engineering, Kookmin University, Seoul, Korea, and Materials Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720*

*Received March 21, 2008; Revised Manuscript Received May 30, 2008*

## ABSTRACT

Understanding the interactions between aromatic gas molecules and various simple aromatic receptor molecules is important in developing selective receptors for volatile organic compounds (VOCs). Here, five benzene thiols with different functional end groups were used to investigate the weak binding of aromatic vapors such as dinitrotoluene (DNT) and toluene. A multiplexed microcantilever array in conjunction with a very low concentration vapor generation system was developed to study multiple receptor–target interactions simultaneously. Differential nanomechanical responses of such devices provided insight into the influence of various chemical and structural features of such molecules.

**1. Introduction.** Gas detection has been used in a variety of applications such as the detection of pesticides,<sup>1</sup> harmful industrial gases, or environmental pollutants,<sup>2,3</sup> explosives,<sup>4</sup> and so forth. There are various types of gas sensors that exploit either a physical or chemical property of a given gas for detection, such as binding-induced changes in (a) electrical conductance in carbon nanotubes,<sup>5</sup> (b) fluorescence in conjugated polymers,<sup>6</sup> (c) current–voltage ( $I$ – $V$ ) or capacitance–voltage ( $C$ – $V$ ) behavior of Schottky diodes and transistors,<sup>7,8</sup> (d) mechanical resonance in surface acoustic wave (SAW) devices,<sup>9</sup> (e) enthalpy measured by thermoelectric calorimeters,<sup>10</sup> and so forth. However, many of these sensors have limited selectivity because of the lack of target-specific receptors.<sup>11</sup> Increase in selectivity is the key to distinguish target gas molecules in the presence of a background of other similar molecules.<sup>12–15</sup> The origins of selectivity lie in multivalency in binding between the given gas molecule and its receptor because multivalency leads to a higher free-energy change than single-valency ones when individual bonds have similar enthalpic contributions. Apart from selectivity, reversibility is also an important aspect for multiple uses of gas sensors. If an interaction of gas with the receptor/sensor is irreversible, as in case of the formation of a strong chemical bond, then it could lead to sensor poisoning or one-time use.<sup>17</sup> In that respect, an ideal receptor

is that which utilizes multiple weak binding interactions with a target to create large contrasts in reaction free energies or dissociation constants. The genesis of multiple weak binding interactions depends on the chemistry and structure of both the receptor and the target molecule. The structural and chemical complexity of macromolecules such as nucleic acids and proteins allows the creation of highly specific receptors. But for simple volatile organic compounds (VOCs), receptor discovery has remained highly challenging and largely unexplored.<sup>18</sup> The goal of this paper is to study weak interactions between aromatic compounds with various functional moieties in order to provide insight into the origins of multivalency in simple volatile benzene derivatives.

Although selectivity is certainly important in chemical analysis, it must be accompanied by high sensitivity as well: it is the combination of sensitivity and selectivity that leads to the desired receiver operating characteristic (ROC) curves of any sensor system. Although many sensors are available, as indicated earlier, recent studies have shown that microcantilevers that rely on surface stress change due to the interaction between target gas molecules and the receptor molecules are very sensitive indeed.<sup>19</sup> Borrowed from the atomic force microscope (AFM), the optical readout can measure cantilever deflections of  $\sim 1$  nm. We have developed a multiplexed microcantilever chemical sensing platform, which consists of two-dimensional cantilever sensor arrays, a very low concentration target vapor generation system, an optical setup consisting of laser and CCD, and so forth.<sup>20</sup> It allows us to immobilize microcantilevers with different

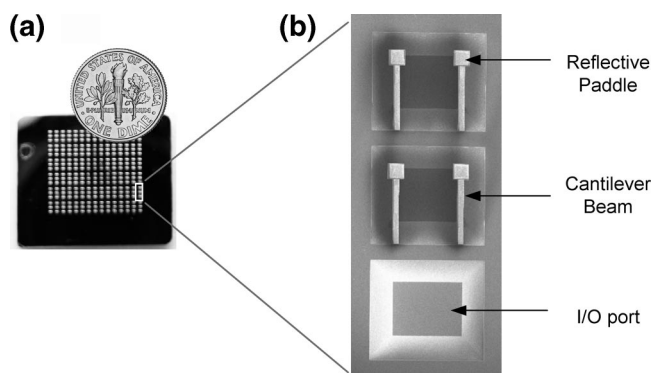
\* Corresponding author. E-mail: majumdar@me.berkeley.edu.

<sup>†</sup> These authors contributed equally to this paper.

<sup>‡</sup> University of California, Berkeley.

<sup>§</sup> Kookmin University.

<sup>||</sup> Lawrence Berkeley National Laboratory.

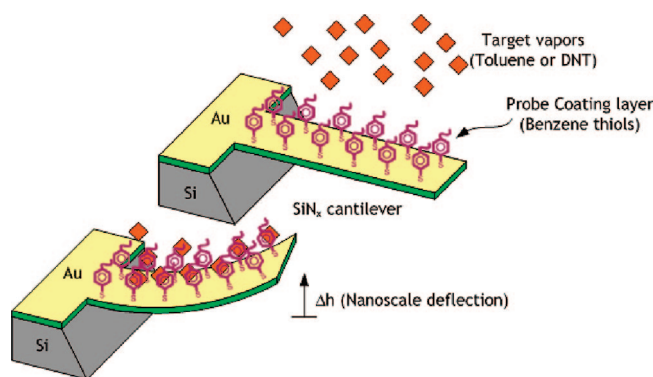


**Figure 1.** (a) Cantilever array chip containing a 2D array cantilevers in reaction wells (b) SEM picture of a single microcantilever well. Each cantilever is 200  $\mu\text{m}$  long, 40  $\mu\text{m}$  wide, and 0.5  $\mu\text{m}$  thick in size.

receptors and study their interactions with a given target vapor simultaneously.

Recently, microcantilevers have been used to detect various gases,<sup>4,10,11,21</sup> although explosives such as trinitrotoluene (TNT) has received much attention.<sup>6</sup> Previous attempts have used mercaptobenzoic acid as the receptor for TNT.<sup>24</sup> However, it is not clear if it is the most selective candidate. Also, it is also not apparent if hydrogen bonding or electrostatic interactions between nitroaromatic compounds and the  $-\text{COOH}$  group is dominant, and whether that provides the optimal response. Because of the very low vapor pressure at the room temperature, TNT is present at very low concentrations (5 parts per billion- ppb) in gaseous form and is, therefore, a difficult target to detect. However, gaseous dinitrotoluene (DNT), which is a decomposition product of TNT, is present at relatively higher concentrations (100 ppb)<sup>22</sup> due to higher vapor pressure. Hence, DNT is often used as a surrogate for TNT. To understand the role of nitrogroups, we have studied the interactions of two aromatic gases (DNT and toluene) with five types of benzene thiols with different end groups. The target gases and receptors are so chosen to bring out the contrast between hydrogen bonding and  $\pi-\pi$  interactions between them. It is important to understand these interactions in order to develop a specific receptor for a target gas like DNT.

**2. Experimental Setup. 2.1. 2D Cantilever Array and Optomechanical Readout.** Figure 1 shows the two-dimensional cantilever array. The fabrication process for the microcantilever array chip and the design of optical multiplexing are described in detail in previous publications.<sup>16</sup> The array contains 84 ( $14 \times 6$ ) individually addressable reaction wells, each of which contains multiple (4–6) cantilever sensors made of low-stress 0.5- $\mu\text{m}$ -thick  $\text{SiN}_x$  film, which was patterned to define cantilevers. Then, a 25-nm-thick gold film was thermally evaporated on the wafer with 5-nm-thick layer of chrome acting as an adhesive between the gold and the silicon nitride films. The gold film was patterned and bulk wet etching of silicon was carried out using KOH solution. Microcantilevers were then released in a critical point dryer. The response of multiple (4–6) cantilevers in each chamber can be averaged to increase the accuracy of measurements and show statistical variations. Each cantilever



**Figure 2.** Conceptual diagram of microcantilevers coated with benzene thiol receptors on the gold side and undergoing deflection due to interaction with aromatic gases.

has a rigid paddle structure at its end to provide a flat reflecting surface for optical diagnostics.

In order to simultaneously image multiple wells, it is necessary to construct a ray optics-based whole field illumination system. Briefly, a laser beam is expanded and reflected off the cantilever array chip. The flat paddles at the end of cantilevers produced spots on a CCD camera. By measuring the motion of each spot, it is possible to detect the deflection of cantilever beams in fashion similar to AFM system. The distance between the CCD and the cantilever array chip is directly proportional to the movement of the spot on CCD screen and inversely proportional to the intensity of the spot. The lower the distance, the closer the cantilever spots are to each other on the CCD screen, allowing more spots to be imaged by CCD. The increase in the movement and intensity of the spot improves the signal-to-noise ratio. Thus, adjustment of the distance between the cantilever chip and CCD not only determines the number of cantilevers being imaged but is also responsible for the good signal-to-noise ratio. Currently, 18 cantilevers can be tracked simultaneously. This number is limited primarily by the size of the CCD.

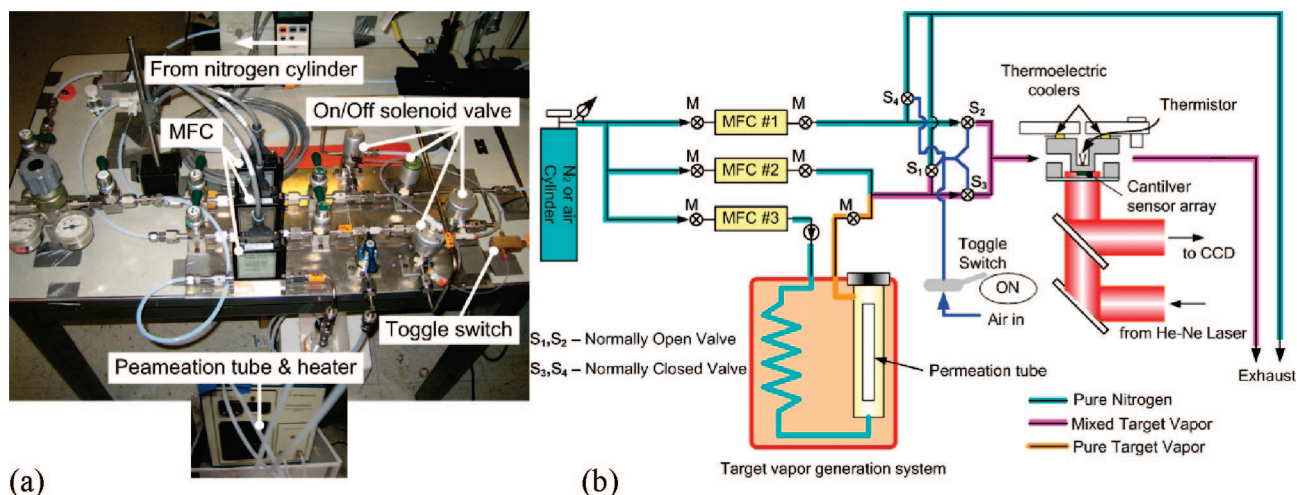
As mentioned earlier, cantilever sensors can detect the presence of chemical vapors at very low concentrations based on the surface-stress changes generated by the interactions between probe and vapor molecules on their surfaces (Figure 2).<sup>4,21</sup> Using Stoney's formula for surface-stress change,  $\Delta\sigma$ , the deflection at the end of a cantilever,  $\Delta h$ , can be expressed as<sup>23</sup>

$$\Delta h = \frac{3(1-\nu)L^2}{Et^2} \Delta\sigma \quad (1)$$

where  $L$  and  $t$  are length and thickness of the cantilever, respectively.  $E$  and  $\nu$  are Young's modulus and Poisson's ratio of the cantilever material.

Microcantilevers were calibrated by utilizing the thermal bimorph effect between adjacent gold and silicon nitride layers. The thermomechanical sensitivity of  $208 \pm 14$  nm/K for the 200- $\mu\text{m}$ -long cantilevers was observed and the surface stress sensitivity of  $24.5$  mJ/m<sup>2</sup>·K was estimated.<sup>16</sup>

**2.2. Target Vapor Generation System.** Because the concentration of DNT found around explosives is lower than normal ambient concentrations ( $\sim 100$  ppb), we have devel-



**Figure 3.** (a) Picture of very low vapor generation module and gas flow control module of chemical sensing setup. (b) Conceptual diagram of microcantilevers based sensing platform showing optical detection module, very low vapor generation module, gas flow control module, along with the flow paths.

oped a gas generation system that introduces very low concentrations (few ppb) of the target gas into the sensor chamber containing the cantilever array chip. Because cantilevers can be sensitive to changes in the flow rate of the gas, the chamber was attached to a constant flow rate gas generation system. The gas delivery system can also purge the chamber by introducing pure nitrogen gas.

The very low concentration target vapor generation system consisted of a permeation tube and the heater (Dynacalibrator-Model 190, VICI Inc.). The permeation tube was made up of polymer membranes containing the liquid or solid phase of the component compound. The heater was used to heat this permeation tube to a desired temperature (Trace Source Disposable Permeation Tube, KinTek Inc.), which produced predetermined very low concentrations (few ppb) of a target gas at the given temperature and nitrogen flow rate. The gas generation system also consisted of three mass flow controllers (0–200 sccm, accuracy  $\pm 1\%$ , Tylan Inc., calibrated by Coastal Instruments) with its controller (Type 247, MKS Inc.), manual on/off valves (M) to operate the gas lines, pneumatic toggle switch to control these valves, four solenoid valves (two normally open ( $S_1, S_2$ ) and other two normally closed ( $S_3, S_4$ ) valves) and Teflon tubes<sup>11</sup> (Figure 3a). As shown in Figure 3b, the toggle switch was used to flip between target vapor flow mode and the purge mode. In the target gas flow mode, target chemical gas flows into the chamber while nitrogen gas flows through the exhaust line. The target vapor can also be diluted by sending the nitrogen gas to the sensor chamber at the same time. In the purge mode, nitrogen gas is used to clean the sensor chamber. In the following experiments, we used separate permeation tubes for toluene and DNT. Because bimorph microcantilevers deflect because of the temperature change, we maintained the same temperature for the permeation tubes for both gases.

**3. Experimental Procedure.** In order to study the interactions between the gases and receptors, we carried out multiple experiments on receptor-coated microcantilevers exposed to

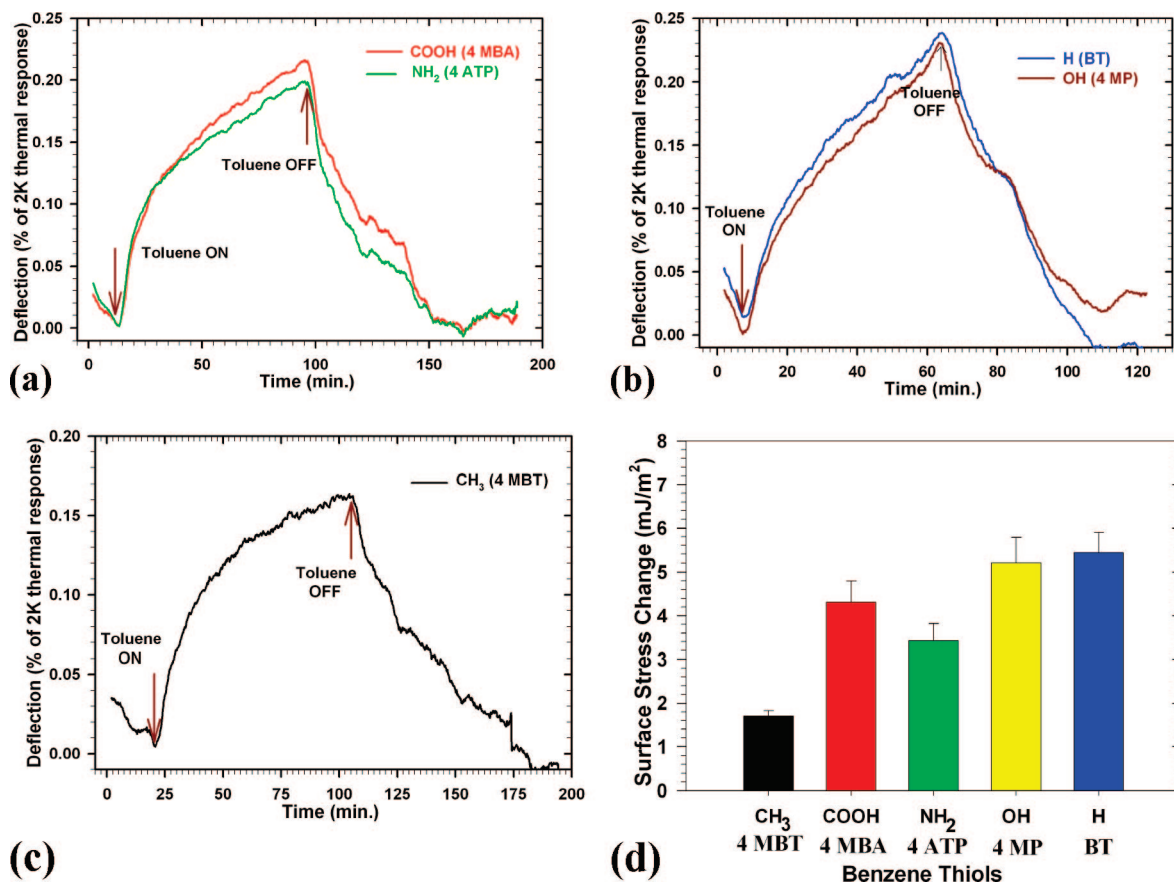
toluene and DNT gases. We used five types of benzene thiols having different end groups as receptors. Microcantilevers were coated with these thiols, and target gases were introduced in the sensor chamber. In this section, the receptor coating procedure, the thermal response, and chemical gas experiments are explained in details.

**3.1. Microcantilever Receptor Coating.** Several alkane thiols<sup>11,19</sup> and benzene thiols<sup>4,24</sup> have been used for cantilever-based sensors. In these experiments, we chose five benzene thiols with different functional end groups: (i) 4 methyl benzene thiol [4MBT,  $\text{SH}-\text{C}_6\text{H}_4-\text{CH}_3$ ]; (ii) 4 mercapto benzoic acid [4MBA,  $\text{SH}-\text{C}_6\text{H}_4-\text{COOH}$ ]; (iii) 4 amino thio phenol [4ATP,  $\text{SH}-\text{C}_6\text{H}_4-\text{NH}_3$ ]; (iv) 4 mercapto phenol [4MP,  $\text{SH}-\text{C}_6\text{H}_4-\text{OH}$ ]; (v) benzene thiol [BT,  $\text{SHC}_6\text{H}_4-\text{H}$ ] as the sensor coating layers. All of the receptors have a benzene ring with its  $\pi$ -electron cloud, although the electron distribution is expected to be altered in the presence of the different moieties on the fourth carbon atom. 4MBA is acidic in nature due to the presence of the  $-\text{COOH}$  group, which can dissociate into a  $-\text{COO}^-$  charged group.<sup>24</sup> 4MP and 4ATP have  $-\text{OH}$  and  $-\text{NH}_3$  end groups, respectively, which do not dissociate as easily, but can form hydrogen bonds with polar molecules. Similarly,  $-\text{CH}_3$  and  $-\text{H}$  end groups in the case of 4MBT and BT, respectively, are inert to polar molecules and can interact via van der Waals force, hydrophobic effect and  $\pi-\pi$  aromatic interaction. Also, only BT is a planar molecule.

Because each benzene thiol has a sulfur group at the end, they bind to the gold surface of the cantilever. Since the gold–thiol bond is almost covalent in nature, the receptor coating is quite stable, and forms a closely packed self-assembled monolayer, which allows transduction of surface stresses to the cantilever beam.

In order to coat the gold layer with thiols, we cleaned the microcantilevers in oxygen plasma for 2 min at 150 W. Then, the gold surface of microcantilevers was coated with thiols by injecting  $0.5\ \mu\text{L}$  volume of 5 mM solution of the thiolated receptor molecules dissolved in ethanol.<sup>25</sup> To achieve repeat-





**Figure 4.** (a–c) A typical set of real time deflection for microcantilevers exposed to very low concentration of toluene vapor (~50 ppb) from which the results presented in this paper were derived. Specifically, the data in this figure are part of the set used to derive the results reported in Figure 4d. Here, the gold side of microcantilevers was immobilized with 4 MBA and 4 ATP in a, BT and 4 MP in b, and 4 MBT in c. (d) Steady-state deflection for microcantilevers when exposed to very low concentration of toluene vapor (~50 ppb). Cantilevers were functionalized by benzene thiols with 5 different end groups.

ability of results, physically adsorbed thiolated receptors were washed off in the CPD (critical point drying) process. This also helped to avoid the stiction of cantilevers.

Although humidity and water vapor can play an important role in target–receptor interactions, these can significantly complicate the experiments and any inferences. Hence, to simplify our study, we have eliminated the presence of water vapor in our experiments, and we will leave the role of water vapor for a future study. After placing the immobilized chip inside the sensor chamber, the entire system was purged with nitrogen for 24 h to reduce the relative humidity level to almost 0%. Then the spots reflected from microcantilevers are located on CCD by adjusting the optics.

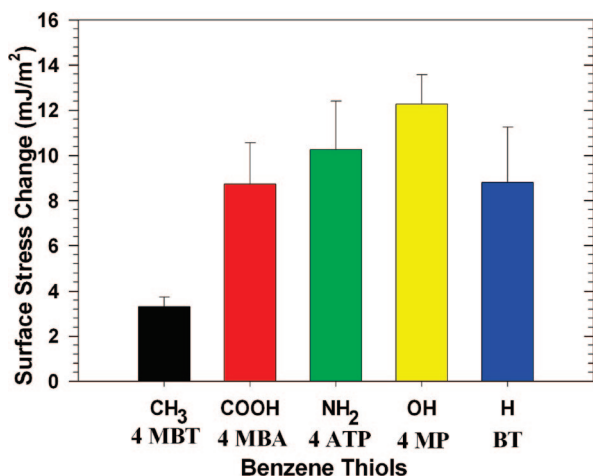
**3.2. Thermal Calibration.** In order to compare the response of different cantilevers, they were calibrated with their temperature response.<sup>11</sup> The chip temperature was increased by 2 °C with the thermoelectric cooler attached to the chamber. The step response of cantilever to a known change in the temperature was then used to calculate the actual deflection of cantilever in subsequent chemical interactions.<sup>16</sup> This also helped us to image more than 3 wells (18 cantilevers) at different intervals of time.

After the thermal response, nitrogen gas flow was cut off and toluene gas was introduced into the chamber. The response to toluene gas for all five thiol-based receptors was

then observed. After the mechanical response saturated, toluene gas was switched off from the chamber and nitrogen was introduced to purge the system. Similarly, after placing the DNT permeation tube, the gas was flown into the chamber and the response of microcantilevers was observed in the real time.

**4. Results and Discussions.** Figure 4a–c show the real-time representative deflection data for microcantilevers coated with 4MBA and 4ATP, 4MP and BT, 4MBT respectively normalized by the thermal response, whereas Figure 4d shows the steady-state deflections for exposing toluene gas at very low concentration (~50 ppb) to receptors with all five end groups. As seen from this data, the deflection of cantilevers reaches its equilibrium state within 120 min. The average deflection of cantilevers is much higher for BT than that for 4MBT, with that for the other benzene thiols lying in between. It should also be noted that 4MP has a higher response than 4MBA. The maximum surface stress experienced by cantilevers was around 6 mJ/m<sup>2</sup>.

One should note that when benzene thiols are introduced onto the Au surface they form packed monolayers and produce repulsive interactions that bend the cantilever downward with the Au on the top surface. Hence, tensile stresses are generated in the Au film. One would expect that



**Figure 5.** Steady-state deflection for microcantilevers when exposed to very low concentrations of DNT vapor ( $\sim 50$  ppb). Cantilevers were functionalized by benzenethiols with five different end groups.

when exposed to toluene vapor, the toluene molecules would intersperse in the benzene thiols and stack up, and thereby produce even larger repulsive forces as shown in Figure 6a. However, the cantilevers always bent upward with the Au layer on top, which implies that the tensile stress was reduced. This suggested that the presence of toluene led to produced attractive interactions or decreased the repulsive interactions between receptor molecules attached the Au surface.

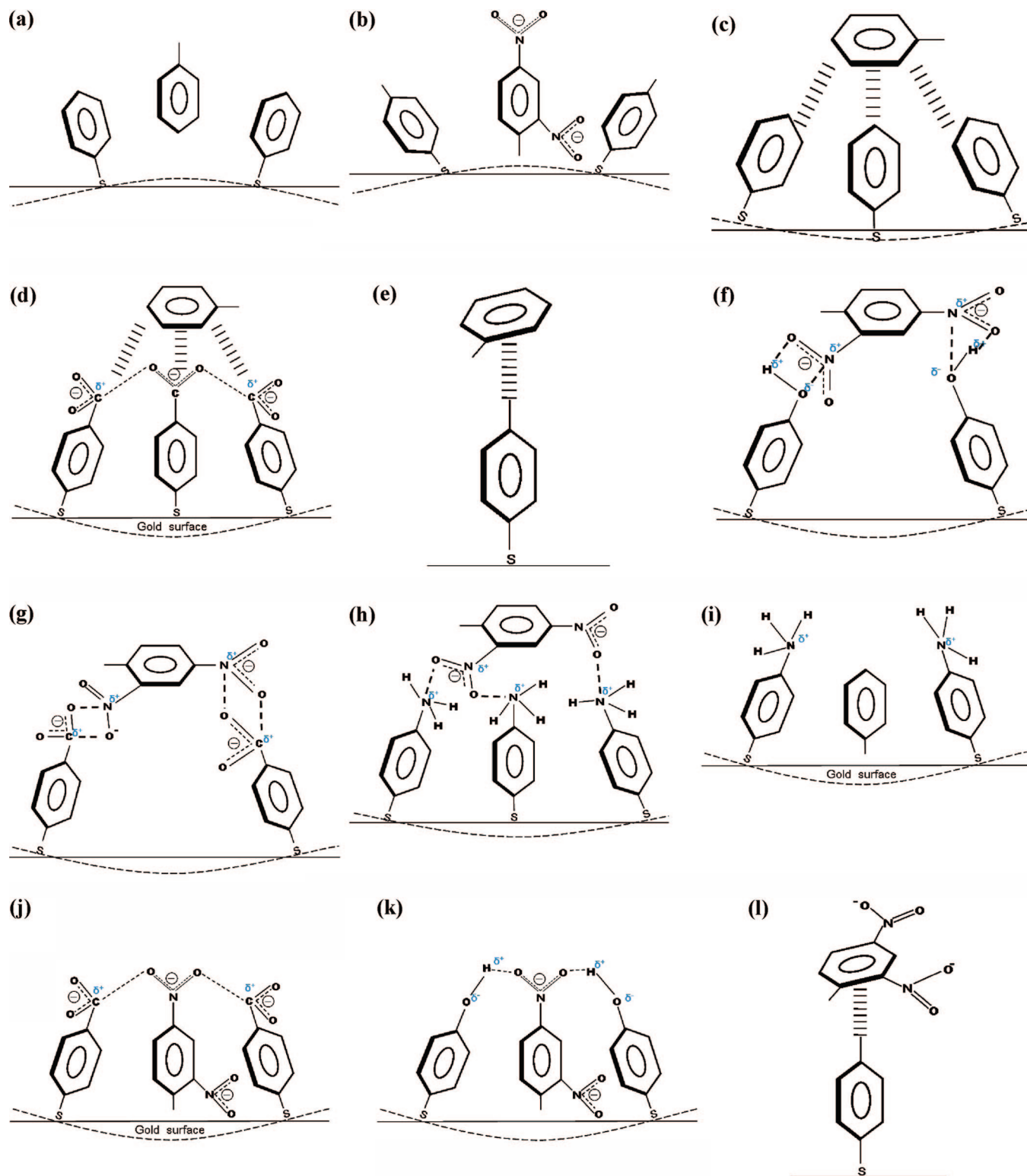
Figure 5 shows the response of microcantilevers coated with benzene thiol receptors to DNT. It is observed that the maximum response is obtained from 4MP, whereas the minimum response is again observed for 4MBT. The signal from 4MBA and 4ATP is higher than or equal to that of BT. It should be noted that both 4MP and 4ATP give higher signals than 4MBA even though 4MBA is frequently chosen as a receptor for the detection of nitroaromatic compounds.<sup>24</sup>

Although the exact mechanism is not yet completely understood, we attempt to explain the effects of various weak interactions on the mechanical signal. There are few interactions that are especially important:  $\pi$ - $\pi$  stacking interaction, hydrogen bonding, and dipole-dipole interaction. Consider a closely packed monolayer of receptor molecules bound to the cantilever through the strong Au-thiol bond. Because there are aromatic rings in both the target and the receptor, a possible configuration is when the aromatic ring of the target molecule is sandwiched between those the adjacent receptor molecules through  $\pi$ - $\pi$  stacking interaction. This will most likely lead to repulsion between strands due to the steric hindrance. It is also possible that an interaction of an end group of benzene thiols with the side chain of a gas molecule causes adjacent thiol molecules to move away from each other. Both of these would induce the tensile stress in the gold film, leading to the downward deflection of the cantilevers as shown in Figure 6a and b. However, this is the opposite of what is observed; that is, in reality, the cantilevers bend upward with Au on top. If there was any space for an aromatic ring to be sandwiched between two neighbors, then one could also argue that because the

Au-thiol bond is so strong, a receptor molecule rather than a target molecule would have been accommodated since the former is accompanied by the free-energy gain of the Au-thiol bond. Hence, it is highly unlikely that aromatic rings of the target molecule are sandwiched between the receptor molecules unless there are defects in the self-assembled monolayer (see later).

In case of toluene gas, it has a benzene ring with a nonpolar group ( $-\text{CH}_3$ ) side chain. As a result, it is incapable of forming a hydrogen bond or participating in dipole-dipole interactions with any polar end groups of benzene thiols. However, the toluene molecule can interact via  $\pi$ - $\pi$  interactions with the benzene ring of thiols. Among various thiols, it is likely that the planar BT molecule forms the strongest  $\pi$ - $\pi$  interaction with toluene molecule because the relatively bulky end groups ( $-\text{COOH}$ ,  $-\text{OH}$ ,  $-\text{NH}_2$ ) can prevent toluene from forming equally strong interactions with 4MBA, 4MP, and 4ATP molecules, respectively. The data in Figure 4d suggests this, and the BT-toluene interaction is shown in Figure 6c. It should be noted that  $\pi$ - $\pi$  interactions are attractive in nature. In the case of 4MBA, 4MP, and 4ATP, the toluene molecule might screen electrostatic repulsion among  $-\text{COO}^-$ ,  $-\text{O}^-$ , and  $-\text{NH}_3^+$  species, respectively. As a result of these interactions, a toluene molecule can bring adjacent thiol molecules closer to each other, which would lead to a compressive stress in the gold film, as conceptualized in Figure 6d. In the case of 4MBT, the relatively low deflection can be explained on the basis of the  $\text{CH}$ - $\pi$  interaction<sup>26</sup> with a relatively bigger end group ( $-\text{CH}_3$ ) as compared to BT. Here, one toluene molecule would most likely interact with a single 4MBT molecule as shown in Figure 6e.

In the case of DNT gas, it is seen that benzene thiols having polar end groups (4MBA, 4MP, and 4ATP), which are capable of forming hydrogen bonds,<sup>14</sup> show the maximum change in the deflection. DNT has two  $-\text{NO}_2$  groups, which are capable of forming multiple hydrogen bonds due to the electronegative oxygen atom. Also, different end groups of benzene thiols have different degrees of polarity. In the case of 4MP and 4ATP, the  $-\text{OH}$  end group can form stronger hydrogen bond than the  $-\text{NH}_2$  group because of the higher electronegativity of oxygen when compared to nitrogen (leading to the more polar nature of the end group). The  $-\text{NO}_2$  group of DNT also exhibits a dipole, which can interact with those observed in the end groups of 4MBA, 4MP, and 4ATP. Among end groups, the difference in electronegativities of adjacent atoms is highest for the  $-\text{OH}$  group and lowest for the  $-\text{NH}_2$  group with that for the  $-\text{COOH}$  lying in between. As a result, the dipole-dipole interaction between  $-\text{NO}_2$  groups of DNT and end groups of benzene thiols should be strongest for 4MP, medium for 4MBA, and weakest for 4ATP. BT and 4MBT do not exhibit any dipole. The trend might be partially explained on the basis of lone pairs of end groups, which also play an important role in  $\pi$ - $\pi$  interactions. In the case of 4MP, two lone pairs of electrons of oxygen atom overlap with the delocalized  $\pi$  electrons of the benzene ring. The donation of lone pairs into the ring increases the density of  $\pi$  electrons



**Figure 6.** Representative conceptual diagram of possible molecular interactions between (a) toluene and BT leading to the tensile stress in the gold film, (b) DNT and 4 MBT (tensile stress in gold film), (c) toluene and BT (compressive stress in the gold film), (d) toluene and 4MBA (compressive stress in the gold film), (e) toluene and 4 MBT, leading to negligible compressive stress in the gold film, (f) DNT and 4 MP (compressive stress in the gold film), (g) DNT and 4 MBA (compressive stress in the gold film), (h) DNT and 4 ATP (compressive stress in the gold film), (i) toluene and 4 ATP (compressive stress in the gold film) at SAM grain boundaries, (j) DNT and 4 MBA (compressive stress in the gold film) at SAM grain boundaries, (k) DNT and 4 MP (compressive stress in the gold film) at SAM grain boundaries, (l) DNT and 4 MBT leading to negligible compressive stress in the gold film.

around the ring. Hence, 4MP can interact more readily through  $\pi$ - $\pi$  interaction than 4ATP, which has a nitrogen atom carrying a single lone pair and 4MBA, which has a

carbon atom without any lone pair to donate. As a result, the microcantilever coated with 4MP is expected to experience more surface stress than 4ATP and 4MBA due to  $\pi$ - $\pi$



interactions. Also, it should be noted that the  $-\text{COOH}$  group is bigger in size than the  $-\text{NH}_2$  or the  $-\text{OH}$  group. Bulkier groups can prevent strong  $\pi-\pi$  interactions because of steric hindrance. The higher positive charge of the carbon atom surrounded by two oxygen atoms in the  $-\text{COOH}$  group of 4MBA reduces the density of the  $\pi$  electron on the benzene ring, thus reducing the  $\pi-\pi$  interaction with the DNT molecule. Hence, a DNT molecule can bring adjacent thiol molecules closer to each other via  $\pi-\pi$  interactions and hydrogen bonds, which would lead to a compressive stress in the gold film as shown in Figure 6f–h.

The discussion so far has focused on a self-assembled monolayer of benzene thiol derivatives as receptors, where it is assumed that the Au–thiol bond combined by  $\pi-\pi$  stacking interaction between adjacent receptors forms a packed monolayer. However, it is possible that one may encounter some kinetic traps whereby the monolayer is divided into domains or grains. Grain boundaries would then be defects where such close packing between adjacent receptor molecules may not exist. Here, those toluene and DNT molecules, which are present in the grain boundary region of the thiol self-assembled monolayer (SAM), can be sandwiched between the adjacent receptor molecules. It is then possible for the toluene molecule, present in the SAM grain boundary region, to attract nearby thiol molecules belonging to adjacent grains via  $\pi-\pi$  interaction as shown schematically in Figure 6i. This would result in an upward deflection of the cantilevers. In the case of DNT molecules, they can generate attractive forces between adjacent receptor molecules via  $\pi-\pi$  interaction and hydrogen bonding as represented in Figure 6j and 6k. As a result, these interactions lead to further increase in the compressive stress in the gold film. As expected, 4MBT does not show a considerable change in the deflection to DNT gas compared to toluene gas because of the inability of its  $-\text{CH}_3$  end group to form a hydrogen bond as shown in Figure 6l.

**5. Conclusions.** We have utilized a 2D multiplexed cantilever sensor to detect interactions of very low concentrations of target gases with specific receptors. Using this microsensor platform, we performed chemical-sensing experiments using toluene and DNT as target vapors with five benzene thiols as simple receptors. These experiments first demonstrated that microcantilevers are sensitive enough to mechanically detect the presence of vapors of benzene derivatives at very low concentrations ( $\sim 50$  ppb). Second, the interaction of vapors with the receptors can be studied and quantified. It is observed that weak chemical interactions such as those involving  $\pi-\pi$  interactions, dipole–dipole, or hydrogen bond lead to the deflection of cantilevers in the range of tens of nanometers. Aromatic compounds like toluene and DNT interact with benzene thiols via  $\pi-\pi$  interactions whereas polar end groups ( $-\text{NO}_2$ ) of DNT also interact with polar end groups of benzene thiols such as the  $-\text{OH}$  group via hydrogen bonds and dipole–dipole interactions. Gas molecules bring receptor molecules closer to each

other via these  $\pi-\pi$  interactions with adjacent molecules as suggested by the upward movement of the cantilevers with the gold layer on top. These gas molecules also have the potential to screen repulsive interactions between the  $-\text{COOH}$ , the  $-\text{OH}$ , and the  $-\text{NH}_2$  end groups of receptor molecules not only by changing the permittivity but also by forming hydrogen bonds and dipole–dipole interactions with them. It is observed that 4ATP is a better receptor group than 4MBA for improving the selectivity of the response of cantilevers to DNT.

To detect DNT at very low concentrations and in the presence of other nitroaromatic compounds, these highly sensitive microcantilevers need to be coated with DNT specific receptors. One way to ensure such specificity is to develop a synthetic receptor carrying multiple functional groups that can form hydrogen bonds with both  $-\text{NO}_2$  groups of DNT and interact with its aromatic ring via  $\pi-\pi$  interaction at the same time. We have recently developed such receptors for DNT and TNT molecules.<sup>18</sup> The microcantilever platform, being a multiplexed platform, can be used to screen the best receptor out of many such potential DNT receptor candidates.

**Acknowledgment.** We thank Dr. Thomas Thundat of Oak Ridge National Laboratory. We also thank the Microfabrication Laboratory, University of California, Berkeley, for providing microfabrication facilities. This work was partly supported by Center of Integrated Nanomechanical Systems (COINS) at University of California, Berkeley, the National Science Foundation under Grant No. 0425914 and Department of Energy.

## References

- (1) Huang, X. J. *Sens. Actuators, B: Chem.* **2003**, *96*, 630–635.
- (2) Mlsna, T. E. *Sens. Actuators, B: Chem.* **2006**, *116*, 192–201.
- (3) Yamazoe, N.; Miura, N. *Sens. Actuators, B: Chem.* **1994**, *20*, 95–102.
- (4) Pinnaduwa, L. A. *Appl. Phys. Lett.* **2003**, *83*, 1471–1473.
- (5) Collins, P. G. *Science* **2000**, *287*, 1801–1804.
- (6) Yangnt, J. S.; Swager, T. N. *J. Am. Chem. Soc.* **1998**, *120*, 11864–11873.
- (7) Lechuga, L. M. *J. Electrochem. Soc.* **1991**, *138*, 159–162.
- (8) Eklov, T.; Lundstrom, I. *Anal. Chem.* **1999**, *71*, 3544–3550.
- (9) Grate, J. W. *Anal. Chem.* **1993**, *65*, 1868–1881.
- (10) Hagleitner, C. *Nature* **2001**, *414*, 293–296.
- (11) Lim, S. H. *Sens. Actuators, B: Chem.* **2006**, *119*, 466–474.
- (12) Ren, K. *Anal. Chim. Acta* **1994**, *286*, 197–203.
- (13) Yokoyama, K.; Ebisawa, F. *Anal. Chem.* **1993**, *65*, 673–677.
- (14) Pasquinet, E. *J. Colloid Interface Sci.* **2004**, *272*, 21–27.
- (15) Staii, C.; Johnson, A. T. *Nano Lett.* **2005**, *5*, 1774–1778.
- (16) Yue, M. *J. Microelectromech. Syst.* **2004**, *13*, 290–299.
- (17) Rakow, N. A.; Suslick, K. S. *Nature* **2000**, *406*, 710–713.
- (18) Jaworski, J. W. *Langmuir* **2008**, *24*, 4938–4943.
- (19) Berger, R. *Science* **1997**, *276*, 2021–2024.
- (20) Biswal, S. L. *Anal. Chem.* **2006**, *78*, 7104–7109.
- (21) Pinnaduwa, L. A. *Sens. Actuators, B: Chem.* **2004**, *99*, 223–229.
- (22) Rose, A. *Nature* **2005**, *434*, 876–879.
- (23) Stoney, G. G. *Proc. R. Soc. London, Ser. A* **1909**, *82*, 172–175.
- (24) Zuo, G. *Nanotechnology* **2007**, *18*, Art. No. 255501.
- (25) Bietsch, A. *Nanotechnology* **2004**, *15*, 873–880.
- (26) Nishio, M. *Tetrahedron* **1995**, *51*, 8665.

NL080829S