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# Microcantilever Sensors in Biological and Chemical Detections

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**Abstract:** Microcantilever sensors have attracted tremendous attention and numerous biological and chemical detections have been demonstrated. In comparison to conventional sensing techniques, the major advantages of microcantilevers include high sensitivity and quick response, direct detection (label free), low cost, versatility, array capability (small size and microfabricationable). The review covers the basic working principles and sensing mechanisms, the major types of microcantilevers, and the reported applications in biological and chemical detections. *Copyright © 2011 IFSA.*

**Keywords:** Microcantilever sensors, Biological and chemical detection, Detection sensitivity

## 1. Introduction

Biological and chemical sensors have recently become a major scientific interest with a wide variety of biomedical, environmental and homeland security applications. Especially after 9-11, there is an urgent need for highly sensitive sensors for rapid, real time, *in situ* biological and chemical warfare agent (CWA) detections both in the civilian and military environments.

After microcantilever was introduced as a novel sensing paradigm in the 90s, [1, 2] numerous sensing applications ranging from chemical, [3-15] physical, [2, 16-21] and biological and biomedical [22-57] areas have been demonstrated. For the chemical and biological detection, receptors were immobilized on the microcantilever surface to bind target chemical molecules, DNA, protein molecules, or bacteria. For example, Fig. 1 showed a Scanning Electron Micrograph (SEM) picture of a single *Escherichia coli (E. coli)* cell captured on an antibody immobilized silicon-based microcantilever after detection.[39] Binding of target species to the receptors on the microcantilever surface is detected by monitoring the tip bending displacement or the resonance frequency shift of microcantilever.

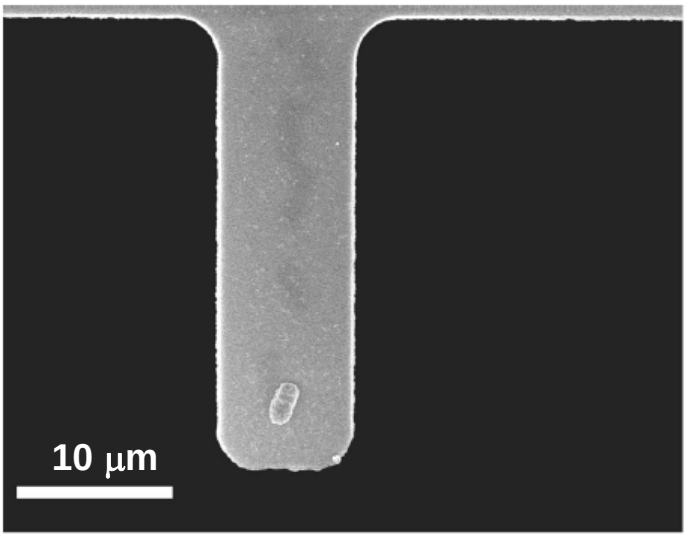



**Fig. 1.** A Scanning electron micrograph (SEM) micrograph of a single E. coli O157:H7 cell bound to the immobilized antibody layer on top of a silicon microcantilever [39].

## 2. Detection Schemes

Typically, for micocantilever sensors, two approaches are used to perform sensing and detection: 1) Dynamic (Resonance) method, and 2) Static (deflection) method.

### 2.1. Dynamic Sensing Method

The flexural resonance frequency (*f*) of an oscillating cantilever beam can be expressed as [58]:

$$f = \frac{1}{2\pi}\sqrt{\frac{k}{m_e}}, \tag{1}$$

where $k$ is the effective spring constant and $m_e$ is the effective mass at the tip of the cantilever. Assuming the effective spring constant ($k$) of the cantilever remains constant during the detection, and the effective mass $m_e$ can be obtained by approximating the cantilever as a point mass at the free end and for a rectangular cantilever is $m_e=0.236\ m$ where $m$ is the mass of the cantilever. [58-60] the adsorbed target species ($\Delta m$) can cause the resonance frequency shift Δf as

$$\frac{\Delta f}{f} = \frac{1}{2}\frac{\Delta m}{m_e} \tag{2}$$

Therefore, for example, when an *E. coli* cell was adsorbed on the cantilever as shown in Fig. 1, the resonance frequency shifted correspondingly (Fig. 2 (a)). Equation 2 implies that the frequency shift is linear to the loaded mass, and Fig. 2 (b) experimentally confirmed that the frequency shift is proportional to the captured cells.

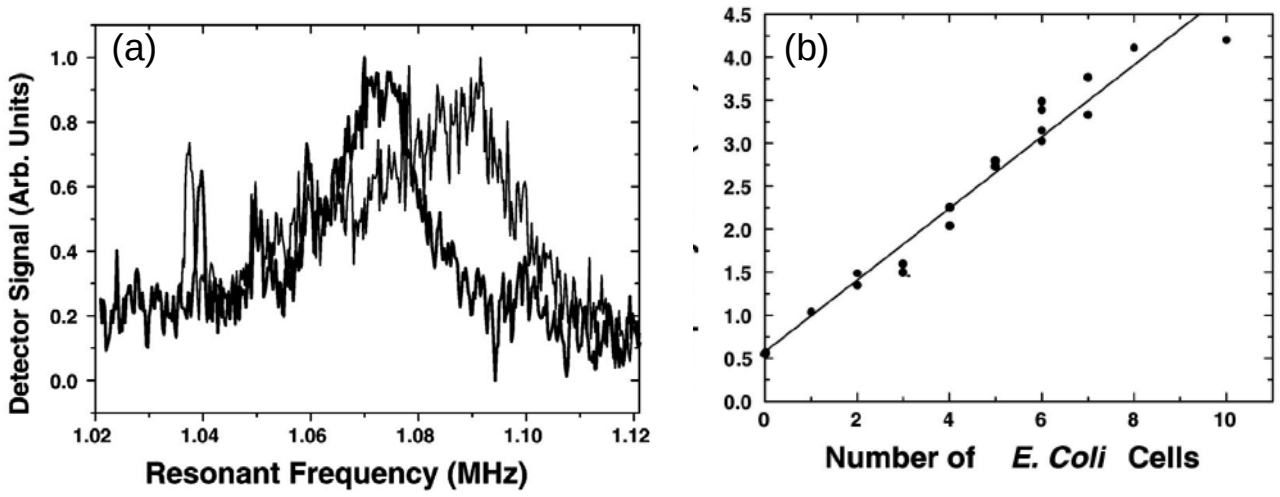



**Fig. 2.** The resonance frequency spectra of the cantilever before and after antibody immobilization and single cell attachment (a), and Measured frequency shift versus the number of bound E. coli cells (b) [39].

## 2.2. Scaling Law Based on Mass Loading Model

As a sensing platform, mass sensitivity is one of the most important criteria of the microcantilever. From Eq. 2, the resonance frequency shift of the cantilever will change if foreign mass attaches to the sensor. The mass sensitivity (Δm/Δf) can be defined as mass change (Δm) during detection over the measured resonance frequency shift (Δf). It depicts the capability of the response of the microcantilever to the loaded mass (target). The smaller the value, the more sensitive the sensor is. In 2002, Dr. J. W. Yi et al. reported both experimental and theoretical investigations of the resonance frequency change and the mass sensitivity of a piezoelectric unimorph cantilever due to the mass loaded at the tip of the cantilever [60]. Theoretically, based on the mass loading model, i.e., assuming the spring constant is constant, and once the effective Young's modulus and effective density of the cantilever is fixed, i.e., by maintaining the same layer thickness fractions, the mass sensitivity of a cantilever follows the scaling law [60]

$$\frac{\Delta m}{\Delta f_n} \propto \frac{L^3 w}{\nu_n^2}, \tag{3}$$

where $\Delta m$, $\Delta f_n$, $L$, $w$, and $\nu_n$ are the loaded mass, resonance frequency shift of the *n-th* flexural mode, length, width, and *n-th* mode eigen value of the cantilever, respectively. This indicated that the mass sensitivity of the cantilever can be improved via miniaturization, i.e., if the length and width were shrunk 10 times, the mass sensitivity can be increased by 10,000 times.

Experimentally, they examined the cantilevers composed of a lead zirconate titanate (PZT) layer and a stainless steel layer, and the length of the cantilevers varied from 4.4 mm to 13.7 mm. In Fig. 3, the result of the first-mode resonance frequency shifts, $\Delta f$, versus the loaded mass, $\Delta m$, for the cantilevers were shown with various lengths. The slopes are the mass sensitivities of the cantilevers. It's clear that the shorter cantilever has higher mass detection sensitivity.

The normalization in Fig. 4 validated the scaling law depicted by Eq. 3. This model was validated by numerous publications on biological or chemical detection using microcantilevers [34, 38-40, 61, 62].

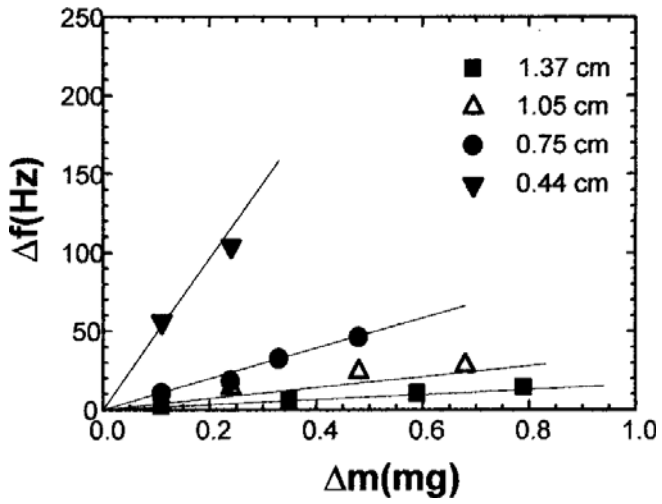



**Fig. 3.** Δ*f* versus Δ*m* of a cantilever 0.4 cm in width and 1.37 cm, 1.05 cm, 0.75 cm, and 0.44 cm in length [60].

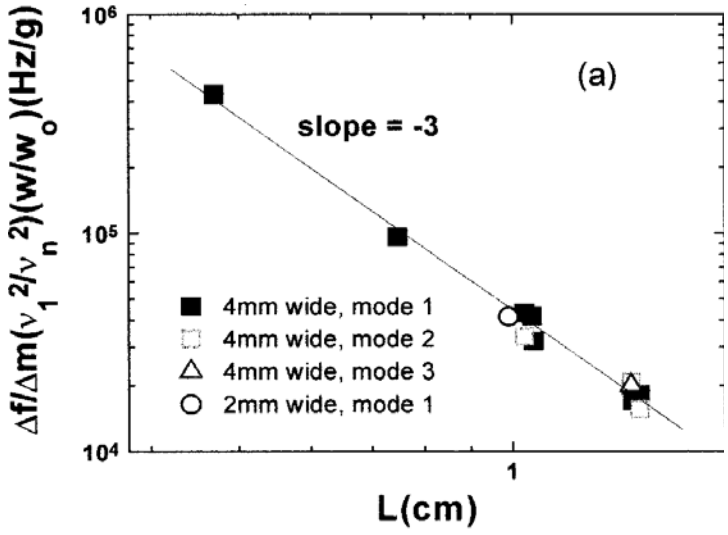



**Fig. 4.** $(\Delta f_n/\Delta m)(\nu_1^2/\nu_n^2)(w/w_0)$ versus $L$ on a double logarithmic plot [60].

## 2.3. Adsorption Induced Surface Stress

Adsorption-induced surface stress has been reported and characterized in a wide range of adsorption systems both in air and in liquid such as adsorption of molecule [11, 54, 63-66], polymer [67], ions [4, 21] biological antigen, [43] protein [44, 45], and DNA [31, 68]. The adsorption induced surface stress arises from the molecular interactions which are universal and mainly originate from the following sources:

1) Intermolecular forces of attraction and repulsion. An example was illustrated in Fig. 5 - a schematic of the adsorption process of gas molecule to adsorbent layer from the vapor phase. The gas molecules adsorb to the adsorbent immobilized on cantilever surface, and upon adsorption the molecules pack with an average spacing $d_a$ which is less than the equilibrium intermolecular spacing ($d_0$) of the gas molecules in the ambient. Hence, once the gas molecules absorb on the cantilever, the cantilever surface will want to expand to increase the intermolecular spacing and a tensile surface stress is present as a result of adsorption.

2) The electrostatic force. Typically, this kind of force is present for biological species because normally antigen, cell, protein, or DNA is charged in liquid. Once they adsorb on the sensor surface, electrostatic force is present because of the charges they carry.

3) Steric force. This force is typically present between polymer-covered surfaces or in solutions containing non-adsorbing polymer can modulate interparticle forces, producing an additional steric repulsive force or an attractive depletion force between them [69].

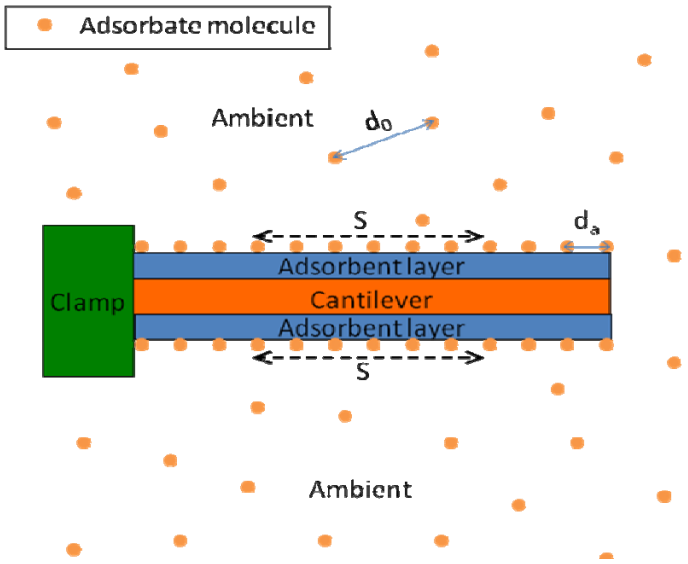



**Fig. 5.** A schematic of adsorption induced surface stress on cantilever.

It was observed that when surface stress is present, the resonance frequency of the microcantilever also shifted and this frequency shift could not be explained by mass loading model described in Section 2.2. The stress effect in cantilever was first reported in 1975. Lagowski et al. from Massachusetts Institute of Technology first observed the natural frequency shift of a fresh etched GaAs cantilever plate due to surface stress induced by adsorption/desorption of gas molecules [70]. Since 90s, the silicon-based microcantilever had become a hot research topic as a sensing platform for a wide range of chemical and biological detections. Observations of the stress effect of the silicon microcantilever in both gaseous and in liquid detections were reported [6, 21, 63]. It was found that for silicon-based microcantilever, the enhancement in frequency shift due to stress effect could be 10 times larger than predicted by the mass loading model [21, 64]. Some researchers argued [63, 71] that the spring constant of the cantilever could change when adsorption induced stress is present. Therefore, the resonance frequency shift would follow

$$\frac{\Delta f}{f} = \frac{1}{2}\left(\frac{\Delta k}{k} - \frac{\Delta m}{m_e}\right), \tag{4}$$

where Δf, Δk, and Δm is the frequency shift, spring constant change, and mass change due to adsorption.

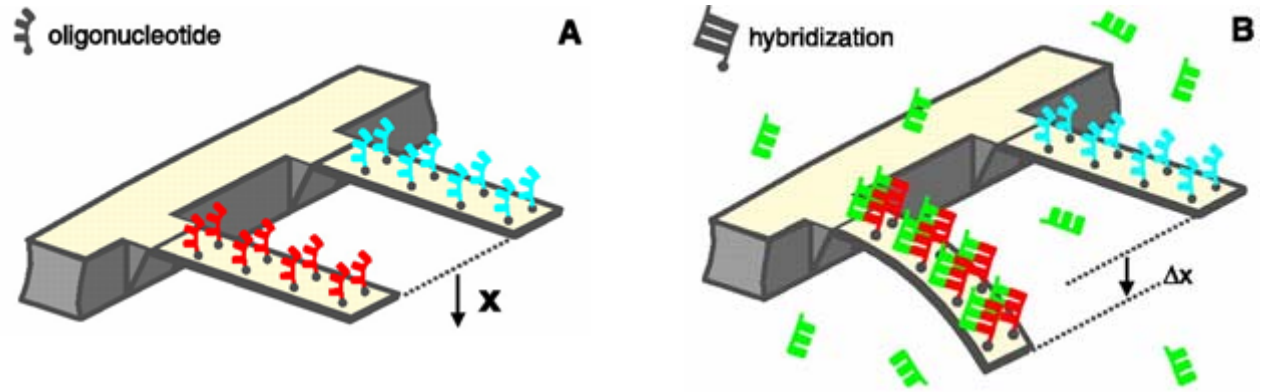
## 2.4. Static Sensing Method

Because of the universality of the adsorption induced stress, another way of detecting molecular adsorption is by measuring the tip deflection of the cantilever due to adsorption stress. In order to

generate bending or deflection, only one side of the cantilever is functionalized or two sides are functionalized differently [4, 6, 11, 21, 31, 64, 65]. Therefore, one of its sides is relatively passive, whereas the other exhibits high affinity to the targeted analyte. As a result, upon adsorption, depending on the nature of the bonding of the target species, the cantilever can bend up or down because the induced stresses are unequal on two sides. For example, Fig. 6 illustrated the deflection of a cantilever due to the hybridization (adsorption) of DNAs. In this case, only one side of the cantilever was functionalized with receptors. Upon adsorption, the deflection (Δx) of the cantilever can be measured. The adsorption induced surface stress can be quantified using Stoney's Equation [72]:

$$\Delta x = \frac{3L^2(1-\nu)}{Yt^2}\Delta S,$$

where L, t, ν, and Y are the length, thickness, Poisson's ratio, and Young's modulus of the cantilever, and ΔS is the differential surface stress of the two surfaces.




(a) (b)

**Fig. 6**. Scheme illustrating the hybridization experiment. Each cantilever is functionalized on one side with a different oligonucleotide base sequence (red or blue). (a) The differential signal is set to zero (before detection). (b) After injection of the first complementary oligonucleotide (green), hybridization occurs on the cantilever that provides the matching sequence (red), increasing the differential signal $\Delta x$ [65].

In general, sophisticated optical instruments are needed to measure the tip displacement while the resonance frequency measurement can be done by electrical means and thereby can be easily deployable.

## 3. Applications of Microcantilever Sensors in Biological and Chemical Detections

Based on the operation mechanisms and materials, microcantilevers can be classified into silicon-based, piezoresistive, capacitive, magnetoresistive, and piezoelectric microcantilevers.

### 3.1. Silicon-based Microcantilever Sensor

Silicon-based microcantilever has been widely used in Atomic Force Microscopy (AFM) and has been demonstrated as a versatile sensing platform in a wide range of areas [2, 4, 6-11, 13, 27, 30, 35, 37-42, 51, 52, 54, 57, 64, 73-77]. It has several advantages over the conventional analytical techniques in

terms of high sensitivity, label-free, quick response, and array capability. With the development of silicon-based microfabrication and most recently developed nanofabrication, the mass sensitivity of the cantilever has been boosted significantly.

In 2001, Illic, et al from Cornell University reported single *Escherichia coli* (*E. coli*) cell detection [39]. The cantilevers they used are 5 or 10 μm wide, and 15 or 25 μm long (one of the cantilevers was shown in Fig. 1). The binding of a single *E. coli* cell caused 4.7 kHz shift in resonance frequency (see Fig. 2 (a)) and the detection was performed in air which was not *in situ*. The mass sensitivity of the cantilevers was $1.4\times10^{-16}$ g/Hz.

In 2004, Gupta, et al from Purdue University reported single vaccinia virus detection using arrays of silicon microcantilevers with nanoscale thickness (Fig. 7) [34]. The dimensions of the fabricated cantilever were in the range of 4-5 μm in length, 1-2 μm in width and 20-30 nm in thickness. The resonance frequency of the cantilever was in the 1-2 MHz range with quality factor of around 5-7. After loading of a single virus particle, there was 60 kHz decease in the resonance frequency (Fig. 8) and the mass sensitivity was $1.6\times10^{-19}$ g/Hz.

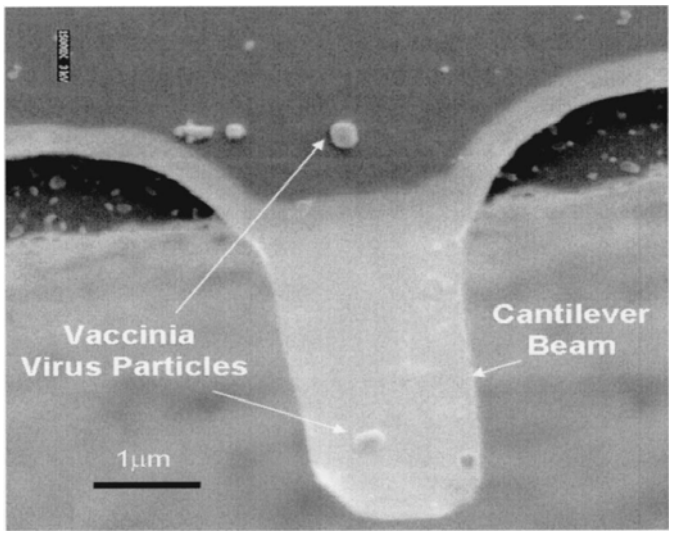



**Fig. 7.** Scanning electron micrograph showing a cantilever beam with a single vaccinia virus particle. The cantilever beam has planar dimensions of length, L=4 μm, and width, W=1.8 μm [34].

In 2005, Ilic et al. from Cornell University demonstrated single DNA detection in vacuum using a cantilever fabricated from 90 nm thick low-pressure chemical vapor deposited low-stress silicon nitride [40]. The lengths of the cantilevers were between 3.5-5 μm (Fig. 9 (a) and (b)). To localize binding site, they formed the cantilever with nanoscale gold dots (see Fig. 9 (c)) at precise locations to act as spatially and chemically discriminant binding sites to selectively capture disulfide modified 1578 base pair long double-stranded deoxyribonucleic acid (dsDNA) molecules ($m_{DNA}$=999 kDaltons). Fig. 10 showed the frequency shift corresponding to a single dsDNA molecule bonding. The mass sensitivity of the cantilever was as high as $5\times10^{-21}$ g/Hz and better than attogram ($10^{-18}$ g) mass detection was demonstrated.

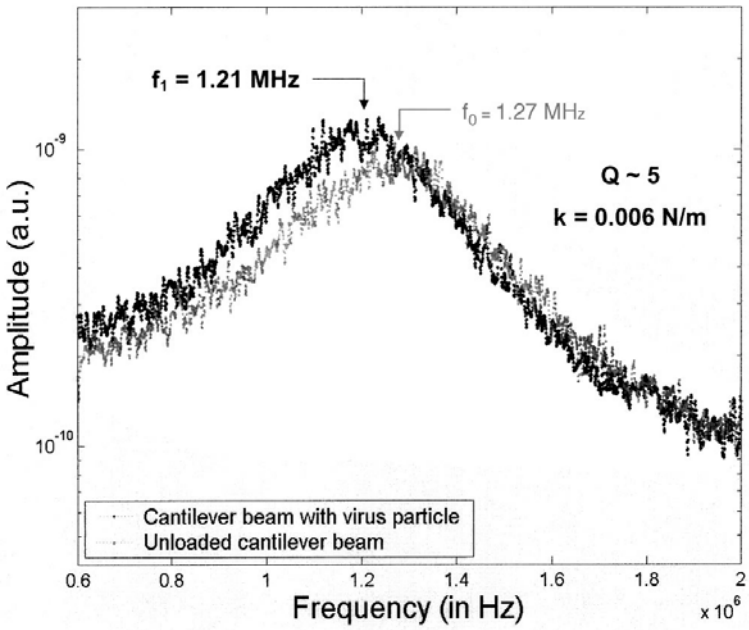



**Fig. 8.** Plot of resonant frequency shift after loading of a single virus particle [34].

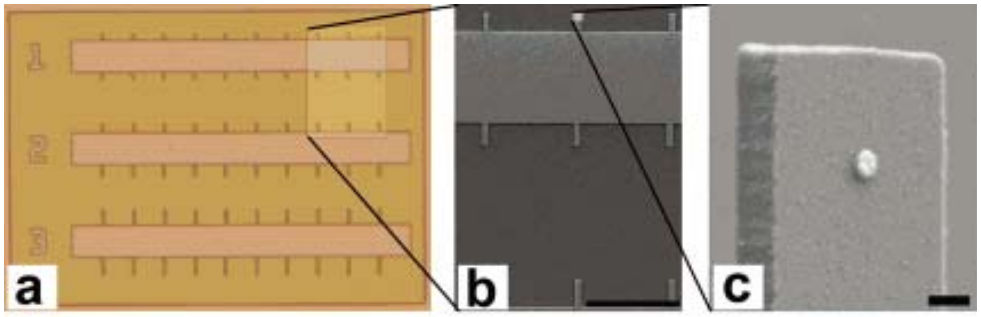



**Fig. 9.** (a) Optical micrograph showing arrays of cantilevers of varying lengths. (b) Zoomed-in scanning electron microscope (SEM) image. (c) Oblique angle SEM image of the 90 nm thick silicon nitride cantilever with a 40 nm circular Au aperture centered 300 nm away from the free end. Scale bar corresponds to 100 nm [40].

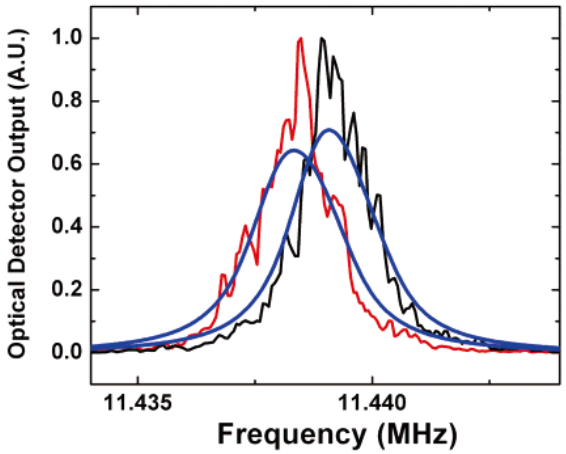



**Fig. 10.** Frequency spectra before (black) and after (red) the binding events show a frequency shift due to a single dsDNA molecule bound to the Au surface of the cantilever [40].

In 2006, Yang et al from California Institute of Technology demonstrated zeptogram ($10^{-21}$ g) scale mass sensing in high vacuum using a doubly clamped micocantilver beams (Fig. 11). The dimensions of the beam were 2.3 mm long, 150 nm wide, and 70 nm thick and the resonance frequency was around 190 MHz. As shown in Fig. 11, a minute, calibrated, highly controlled flux of Xe atoms or $N_2$ molecules is delivered to the device surface by a mechanically shuttered gas nozzle within the apparatus. Fig. 12 showed the frequency shift upon deposition of the $N_2$ molecules. The mass detection sensitivity of the device was as high as $8.6\times10^{-22}$ g/Hz and the best mass resolution corresponds to 7 zg, equivalent to an individual 4 kDa molecule.

In general, the advantages of the silicon based microcantilever over the conventional analytical techniques are high sensitivity, low cost, label free, low analyte requirement (in μl), and quick response [78]. However, the main challenge for silicon cantilever is in liquid detection capability, i.e., the quality of the resonance peak is too low to use in liquid. For the recently developed ultrasensitive cantilevers, they are unable to sustain the damping in air, therefore, high vacuum ($10^{-6}$ Torr or higher) is necessary to perform sensing [37, 40, 57, 61].

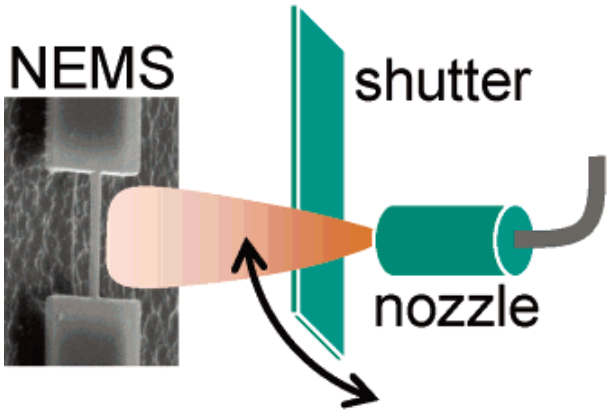



**Fig. 11.** Experimental configuration. A gas nozzle with a 100 μm aperture provides a controlled flux of atoms or molecules. The flux is gated by a mechanical shutter to provide calibrated, pulsed mass accretions upon the NEMS device [57].

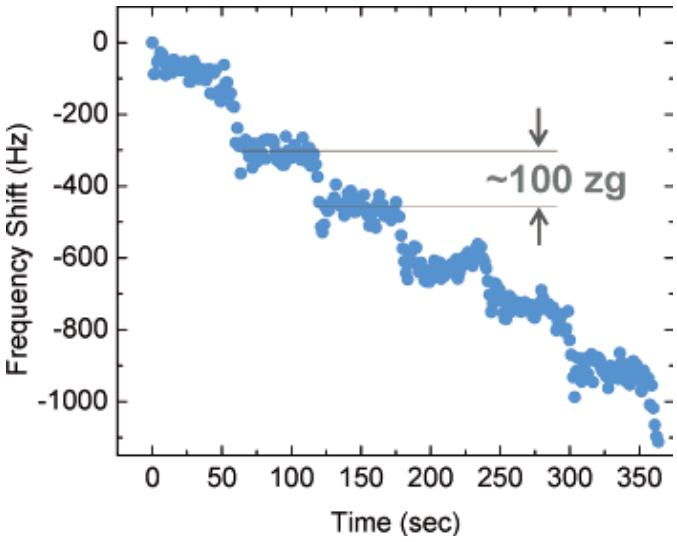



**Fig. 12.** *Real time* zeptogram-scale mass sensing experiment. Sequential mass depositions are executed *in situ* upon the 190 MHz device within a cryogenic ultrahigh vacuum apparatus [57].

### 3.2. Piezoresistive Microcantilever Sensor

Typically, optical method is adopted to detect the static deflection or dynamic vibration of silicon based microcantilever. Alternatively, piezoresistive read-out method can be used. Piezoresistive method is based on the changes observed in the electrical resistance of the material of the cantilever as a consequence of a surface-stress change [79-82]. This method involves the embedding of a piezoresistive material near the top surface of the cantilever during fabrication to record the stress change occurring at the surface of the cantilever. Fig. 13 shows a schematic of a piezoresistive cantilever. Piezoresistive elements fabricated onto or into cantilevers comprise either semiconductor or metallic strain gauges [83].

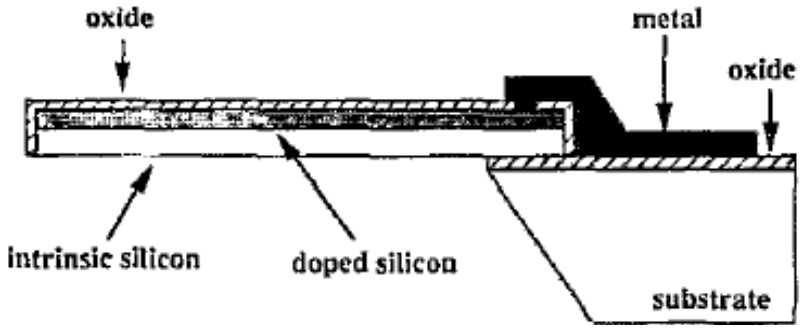



**Fig. 13.** Schematic drawing of the cross section of a piezoresistive cantilever (doped silicon is piezoresistive layer) [79].

As the microcantilever deflects, it undergoes a stress change that will create strain to the piezoresistor, thereby causing a change in resistance. The relative change in resistance as function of applied strain can be written as: [80, 81].

$$\frac{\Delta R}{R} = K_l \delta_l K_t \delta_t$$

where K denotes the Gage Factor, which is a material parameter, and δ is the strain in the material and R is the resistance. The subscripts l and t refer to the longitudinal and the transversal part of the Gage Factor. The piezoresistor material in the beam must be localized as close to one surface of the cantilever as possible for maximum strain/sensitivity.

The piezoresistive cantilever beam can be measured by Wheatstone Bridge circuit as shown in Fig. 14 [78, 80, 81].

The resistance of the variable resistance arm ($R_0$+$\Delta R$) in the above figure can be determined by using the common Voltage divider formula and is shown as below:

$$\Delta V = V_0 \left\{ \frac{R_2}{R_1 + R_2} - \frac{R_3}{R_0 + \Delta R + R_3} \right\} \Rightarrow R_0 + \Delta R = R_3 \left\{ \frac{V_0 (R_1 + R_2)}{R_2 V_0 - \Delta V (R_1 + R_2)} - 1 \right\}$$

Numerous physical, chemical and biomedical applications have been demonstrated using piezoresistive microcantilevers including calorimetry [84], humidity sensing [73], TNT detection [85], C-reactive protein detection [86], *Salmonella enterica* detection [87], *Vaccinia* virus detection [88] and allergy check [89].

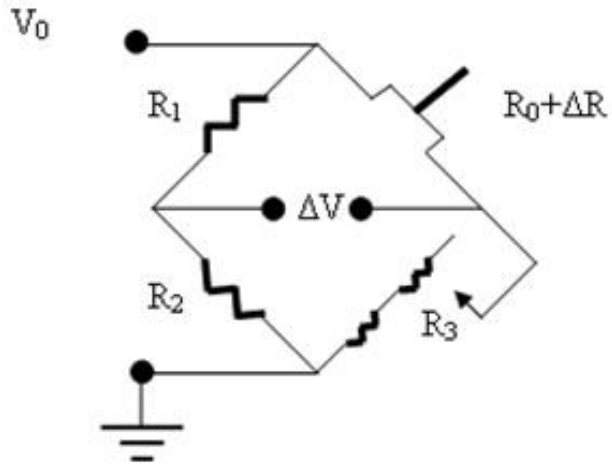



**Fig. 14.** The Wheatstone Bridge Circuit used for the piezoresistive microcantilever [78].

In general, the advantage of piezoresistive cantilever is that the read-out electronics can be integrated onto the chip containing the cantilever array and it is unaffected by light-absorbing or scattering components in the analyte stream. Because current is flowing through the cantilevers while measurements are being made, local heating can occur and it is a major problem for practical applications, although it can be managed by changing the amount of current flowing through the resistive layer [55]. Other drawbacks to this technique are thermal, electronic, and conductance fluctuation noise, thermal drifts, nonlinearity in piezoresponse, and poor sensitivity [90]. In addition, a piezoresistor has to be embedded in the cantilever, therefore, fabrication of such a cantilever with a composite structure is more complicated.

### 3.3. Capacitive Microcantilever Sensor

Capacitive cantilever acts as one of the parallel plates of a capacitor [91, 92]. Fig. 15 showed a schematic of a capacitive microcantilever system [93]. As the cantilever deflection takes place due to the adsorption of the analyte, the distance between the two plates changes and this changes the capacitance of the system.

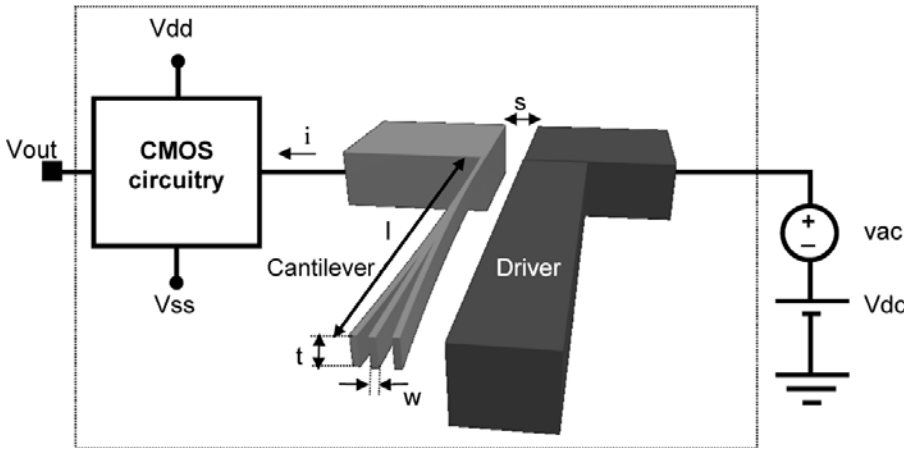



**Fig. 15.** Schematic drawing of the capacitive microcantilever system based on a laterally vibrating cantilever (s direction) electrostatically excited and with capacitive readout [93].

The advantage of capacitive detection is the simplicity of the associated electronics [94] and it is highly sensitive and provides absolute displacement. However, this technique is not one of the most commonly used because of a number of limitations [83]. To accurately record cantilever deflection, the dielectric material between the conductive plates must be constant throughout the experiment. The presence of analyte within the gap often changes its effective dielectric constant. In addition, although the capacitive cantilevers can be integrated onto a microchip [93-95] scaling down the size of the capacitive cantilever will lower its overall sensitivity because the capacitance of a capacitor is directly proportional to its surface area.

Capacitive cantilever is mainly used for gaseous phase chemical sensing since it does not work in electrolyte solutions due to the faradic currents between the capacitive plates. For gas sensing, Amirola and co-workers [96, 97] used capacitive detection of gaseous molecules and found the limit of detection to be 50 ppm for toluene and 10 ppm for octane. Britton Jr. and co-workers demonstrated hydrogen detection using their capacitive cantilever array and the detection limit of the hydrogen was as low as 100 ppm [94] Verd and co-workers report mass resolution for their specific capacitive cantilever system is on the order of $10^{-18}$ g [93].

### 3.4. Magnetostrictive Microcantilever Sensor

Recently, a research group from Auburn University developed magnetostrictive microcantilever (MSMC) as a sensing platform [98-101]. MSMS consists of two layers - one is active (magnetostrictive) and the other is inactive. MSMC is actuated remotely using a magnetic field. Due to the magnetic nature, the vibration of the microcantilever results in an emission of a magnetic signal, which is sensed remotely using a pickup coil. Figs. 16 (a)-(d) illustrated the operation mechanism of the MEMS: [101] the length of the active layer in an MSMC would be changed with a magnetic field due to the magnetostrictive effect. Therefore, an applied magnetic field on an MSMC (Fig. 16 (a)) would lead to a length difference between the active and inactive layers, which would bend the MSMC since the active and inactive layers are bonded together. Therefore, a time-varying magnetic field would make an MSMC bending vibration as shown in Fig. 16 (b)**.** Due to the magnetic nature of the magnetostrictive alloy, the bending vibration of an MSMC would emit a magnetic signal, which can be measured using a pick-up coil (see Fig. 16 (c)). If the time-varying magnetic field is a sine wave, the bending vibration of an MSMC would also be a sine function of time. The amplitude of the bending vibration of an MSMC changes with the amplitude and frequency of the magnetic field. Additionally, there would be a phase difference between the driving magnetic field and the bending vibration. If an ac magnetic field is swept over a frequency range with constant amplitude, as shown in Fig. 16 (a), the amplitude of the bending vibration of the MSMC would change with the frequency as shown in Fig. 16 (d).

Since there is no physical connection between the MSMC and the integration device, this is the principal advantage of MSMCs over other microcantilevers [99, 100]. Another advantage of MSMC is the capability of operation in liquid. Real time in liquid biological detections of yeast cells [99], *Salmonella typhimurium* [101], and *Bacillus anthracis* spores [98] were demonstrated.

### 3.5. Piezoelectric Microcantilever Sensor

A typical Piezoelectric Microcantilever sensor (PEMS) consists of a piezoelectric layer bonded to a nonpiezoelectric layer (Fig. 17). Because of the converse piezoelectric effect, when an AC voltage is applied to the thickness direction of the piezoelectric layer, it will elongate or shrink along the length and width directions due to its piezoelectric characteristics. However, the nonpiezoelectric layer does

not deform thereby constraining the movement of the piezoelectric layer and resulting in the alternative bending (vibration) of the cantilever structure. PEMS was originally developed to overcome the complexity of the force detector of the conventional non-contact AFM [102, 103]. Comparing to the silicon-based microcantilever, PEMS has several advantages: 1. PEMS can self-excite and self-sense, i.e., the exciting can be performed by applying an AC field on the piezoelectric layer and the sensing can be achieved by monitoring the phase angle change; 2. PEMS can withstand high environmental damping and it can operate in liquid; 3. The detection scheme is all electric and the system can be easily made portable (Lab-On-A-Chip).

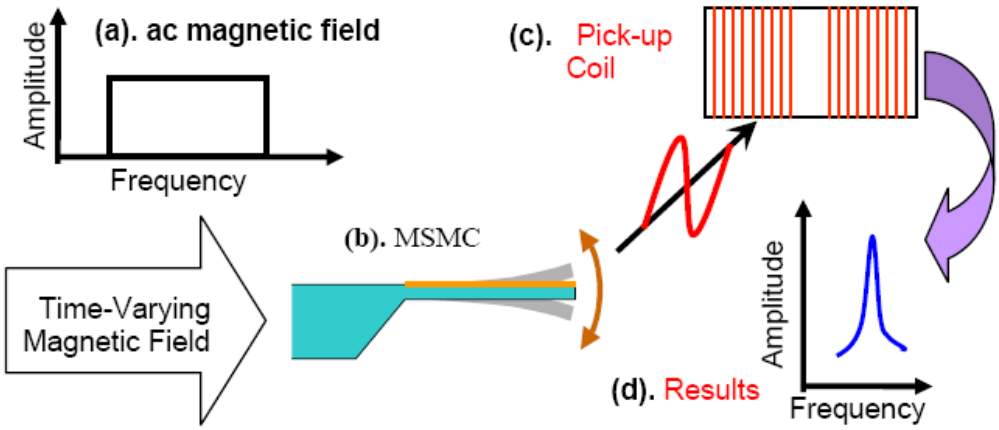



**Fig. 16.** Schematic illustration of the principle of MSMC as a transducer for biosensors [101].

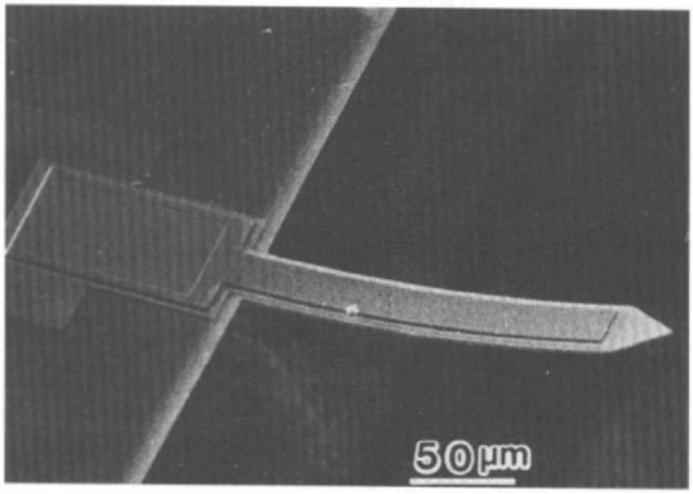



**Fig. 17.** A SEM micrograph of a ZnO/$SiO_2$ piezoelectric microcantilever [102].

Recently, PEMS has become a very hot research focus and various physical [16, 104-106] chemical [3, 66, 107-111] and biological [22-26, 43-45, 47, 48, 68, 112-117] sensing applications have been demonstrated using PEMS.

In 2001, Shih et al. performed simultaneous liquid viscosity and density determination using lead zirconate titanate (PZT)/stainless steel cantilever. Their study indicated that the viscosity and the density of a liquid can be determined simultaneously by measuring resonance frequency and peak width. In 2002, Yi et al. demonstrated real time *in situ* in liquid yeast cells detection using PZT/stainless steel microcantilever [22]. The peak height of the PEMS was not reduced much when

immersed in water and the quality factor (Q) almost remained the same as that in air (Fig. 18). This study demonstrated PEMS as a power sensing platform for real time in liquid detection which is a big hurdle for Si-based microcantilevers.

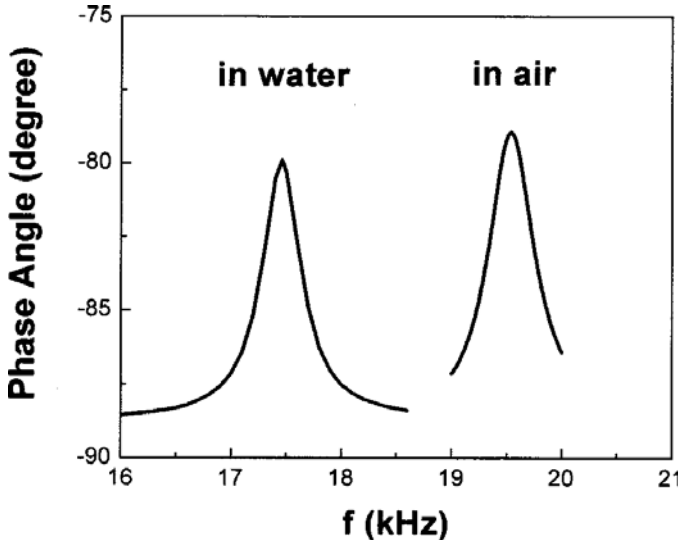



**Fig. 18.** Phase angle vs. frequency of cantilever both in air (right) and in water (left) [60].

Since 2004, Lee et al. fabricated PZT/$SiN_x$ PEMS via microfabrication (Fig. 19) and various biological detections of prostate-specific antigen (PSA) [43, 112], C-reactive protein [44, 45, 116], myoglobin [113], protein kinase [115], and aptamer [68] were demonstrated. However, because the ions in the liquid would cause 'short-circuit' between the two electrodes of the piezoelectric layer, most of the above detections were performed *ex situ* [43-45, 68, 113].

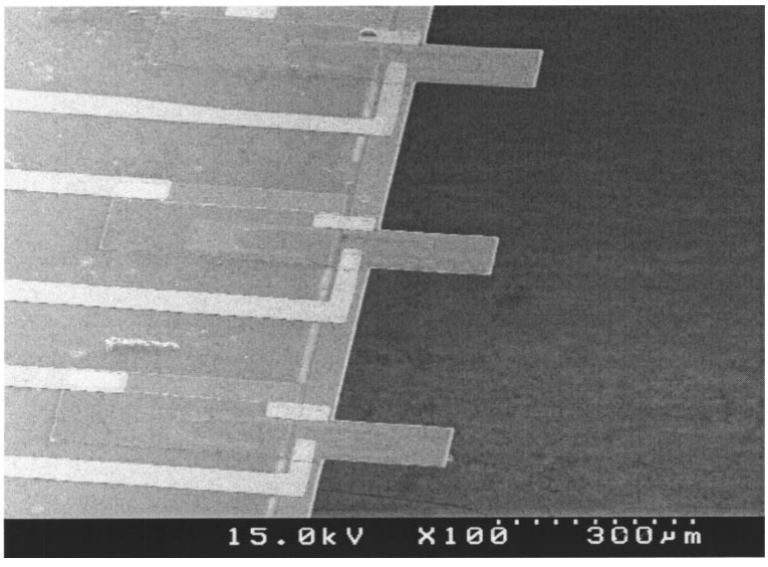



**Fig. 19.** A SEM photograph of the micromachined PZT cantilever arrays designed for simultaneous self-actuating and sensing [44].

In 2005, selective nerve gas simulant Dimethyl methylphosphonate detection has been demonstrated using PZT/stainless steel PEMS array [3]. In this study, three PEMSs were coated with different

adsorbents and the response of each PEMS/adsorbent generated a unique pattern to DMMP. Meanwhile, *in situ* real time *Salmonella typhimurium* detection in liquid was demonstrated using PZT/Gold coated glass PEMS [23, 24]. The detection was achieved without insulating by partially dipping the sensor in the liquid at nodal point [23, 59] or at controlled humidity [24]. In 2006, Shen et al. fabricated PZT/$SiO_2$ PEMS with a 60×25 μm PZT/$SiO_2$ section and a 24×20 μm $SiO_2$ extension (Fig. 20) and mass sensitivity was $1\times10^{-15}$ g/Hz calibrated by quartz crystal microbalance (QCM) in humidity detection.

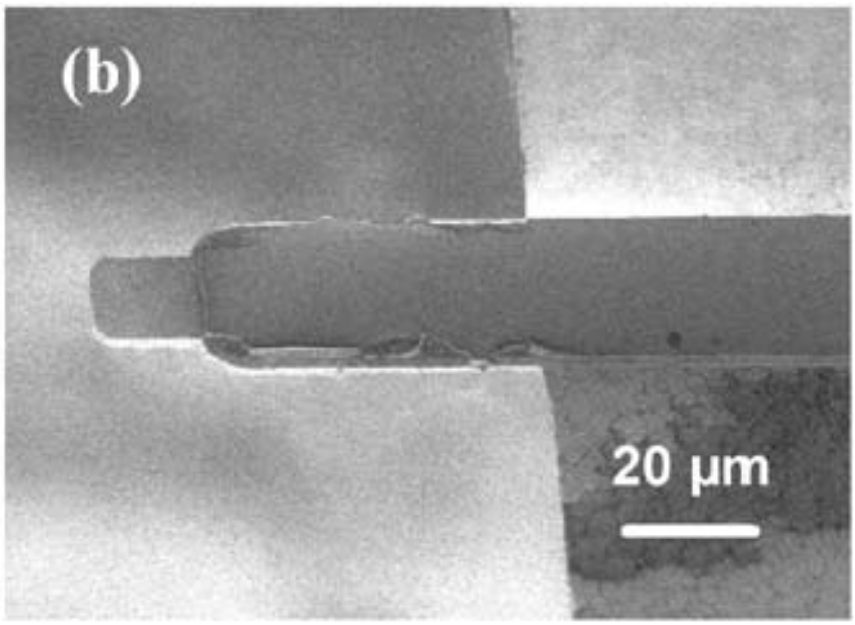



**Fig. 20.** A SEM micrograph of the PEMS with a 60×25 μm PZT/$SiO_2$ section and a 24×20 μm $SiO_2$ extension [66].

In 2006, Capobianco et al. invented a novel insulation scheme [25, 26] for PEMS which enabled the PEMS to be fully immersed in conductive solution. Since then, various *in situ* in liquid biological detections of *Escherichia coli* [25], single chain variable fragment (scFv) protein [26], and *Bacillus anthracis* spores [47, 48] were demonstrated using insulated lead magnesium niobate-lead titanate (PMN-PT)/Metal PEMS.

Interestingly, stress effect was observed and reported in a wide range of biological and chemical detections using PEMS [3, 16, 22, 24-26, 43, 44, 47, 48, 66, 104, 111]. Quantitatively, the enhancement observed in PEMS in both gaseous and aqueous detection was 100-200 times larger than predicted by the mass loading model, and was 10-50 times larger than the enhancement in the silicon-based microcantilever (see Table 1). It could be concluded that the two-order-of-magnitude enhancement would be a unique feature and advantage of the PEMS and a wide range of biological and chemical detections using PEMS showed dominant stress effect. The most recent study [111] showed this enhancement in frequency shift of a PEMS is a result of Young's modulus change in piezoelectric layer induced by surface stress. Furthermore, it is shown that the resonance frequency shift can be enhanced by applying a DC bias electric field to the piezoelectric layer during detection and 1000 times enhancement has been demonstrated for humidity detection [118].

**Table 1.** Enhancement due to stress effect comparing to the mass loading model of the microcantilever sensors reported in the literature.

| Cantilever | Detection system | Enhancement* | Reference |
|---|---|---|---|
| Silicon Nitride | *E. coli* detection | No | [39] |
| Silicon | Virus detection | No | [34] |
| Silicon | Mercury detection | ~4 times | [64] |
| Silicon Nitride | Na+ adsorption | 10 times | [21] |
| PZT/$SiO_2$/$SiN_x$ | C-protein detection | 100-120 times | [44, 45] |
| PZT/$SiO_2$/$SiN_x$ | PSA detection | 100-200 times | [43, 112] |
| PZT/$SiO_2$ | Humidity detection | 100 times | [66] |
| PZT/Glass | Salmonella cells detection | 100-200 times | [23, 24] |

*Enhancement in frequency shift in comparison to prediction by mass loading model.

## 4. Conclusions

Microcantilevers have several advantages over the conventional sensing techniques such as optical or fluorescence-based sensors, chemiresistive sensors, Quartz crystal microbalance (QCM), or surface acoustic wave (SAW0 devices in terms of high sensitivity, label free, versatility, array capability, and quick response. Single cell [39], single virus [34] and single DNA [40] detection have been demonstrated and single molecule [57] detection could be possible in the near future.

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**Sensors & Transducers Journal**

# Guide for Contributors

## Aims and Scope

*Sensors & Transducers Journal (ISSN 1726-5479)* provides an advanced forum for the science and technology of physical, chemical sensors and biosensors. It publishes state-of-the-art reviews, regular research and application specific papers, short notes, letters to Editor and sensors related books reviews as well as academic, practical and commercial information of interest to its readership. Because of it is a peer reviewed international journal, papers rapidly published in *Sensors & Transducers Journal* will receive a very high publicity. The journal is published monthly as twelve issues per year by International Frequency Sensor Association (IFSA). In additional, some special sponsored and conference issues published annually. *Sensors & Transducers Journal* is indexed and abstracted very quickly by Chemical Abstracts, IndexCopernicus Journals Master List, Open J-Gate, Google Scholar, etc. Since 2011 the journal is covered and indexed (including a Scopus, Embase, Engineering Village and Reaxys) in Elsevier products.

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Contributions are invited on all aspects of research, development and application of the science and technology of sensors, transducers and sensor instrumentations. Topics include, but are not restricted to:

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- Sensor instrumentation;
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