Sensors and Actuators B 202 (2014) 286–293

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

journal homepage: www.elsevier.com/locate/snb

Detecting the stiffness and mass of biochemical adsorbates by a resonator sensor

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ARTICLE INFO

Article history:
Received 19 February 2014
Received in revised form 12 May 2014
Accepted 13 May 2014
Available online 24 May 2014

Keywords:
Resonator
Inverse problem
Mass
Stiffness
Material identification

ABSTRACT

The biochemical adsorption on a resonator sensor can result in the changes of both stiffness and mass. If the effect of stiffness is not considered, the resonator response will be wrongly interpreted. Determining the adsorbate stiffness and mass by the shifts of resonant frequency formulates an inverse problem. The inverse problem is solved by varying the adsorbate thickness and measuring the corresponding shifts of resonant frequencies. With the technique of solving the inverse problem, a micro/nanomechanical resonator can be used to identify what kind of material an adsorbate is, which is more than a mass resonator sensor.

1. Introduction

Micro/nanomechanical resonator provides a label-free, high throughput and rapid detection of biological and chemical molecules [1,2]. When a resonator structure is scaled down in size, the resonant frequency increases, which also leads to a higher sensitivity [3]. The micro/nanomechanical resonators with the capability of detecting the presence of a biomolecule [2], a cell [4], a virus [5], a protein [6] and a gold atom [7], have been developed. A recent record of sensitivity was achieved by a carbon nanotube (CNT) based nanomechanical resonator, which can detect the mass of a single proton [8]. The sensing mechanism of all above micro/nanomechanical resonators [1–8] is based on the following equation

$$\frac{\Delta\omega}{\omega_o} \approx -\frac{1}{2}\frac{\Delta m}{m}, \tag{1}$$

where ω_o is the circular resonant frequency without adsorption and $\Delta\omega$ is the resonant frequency shift due to adsorption; m is the (known) effective sensor mass and Δm is the (unknown) effective adsorbed mass. Once ω_o and $\Delta\omega$ are measured, Δm is uniquely determined by the above equation. The implicit assumption of Eq. (1) is that adsorption only induces the mass addition; the resonator based on Eq. (1) is a mass resonator sensor. However, the mass information only is insufficient to provide fundamental insights into the resonator-based molecular detection [9]. In general, the appropriate properties of a detected material including its mechanical properties as well as the mass must be considered when interpreting the resonator data [10]. A vivid example is that in their pioneering experiment, Ramos et al. [11] found that the adsorption of the *Escherichia coli* (*E. coli*) bacteria on a silicon resonator causes the increase of resonant frequency. According to Eq. (1), the mass addition due to adsorption can only decrease the resonant frequency. The increase of resonant frequency can only mean that the stiffness of the bacteria plays a more important or even a dominant role [11,12]. Similarly, the adsorption of organic molecules (alkanethiol) also causes the increase of resonant frequency [12]. Even for the resonant frequency decreasing cases, if the stiffness effect is not considered, the mass can be significantly underestimated [12,13]. Furthermore, in the adsorption tests of various proteins, it has also been found that the mass addition alone cannot explain the (anomalous) shifts of the resonant frequencies [14,15].

When adsorption occurs, the stiffness, mass and damping of the system change and the resonant frequency is given as follows [16]

$$\omega' = \sqrt{\frac{k+\Delta k}{m+\Delta m}}\sqrt{1-\frac{(C+\Delta C)^2}{4mk}}, \tag{2}$$

ω' is the circular resonant frequency after adsorption ($\Delta\omega = \omega' - \omega_o$). k, m and C are the effective spring stiffness, mass and damping of a resonator, respectively. Δk, Δm and ΔC are those corresponding changes due to adsorption. The mechanisms for the damping variation are rather complex and still unclear

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http://dx.doi.org/10.1016/j.snb.2014.05.059
0925-4005/

for micro/nanomechanical resonator [16,17]. When a resonator motion is measured in an experiment, C and ΔC can be extracted by the half-power method [18]. The reason for the mass change in an adsorption process is obvious. The stiffness change is mainly caused by two mechanisms: the adsorbate stiffness [11,12] and surface stress [19,20]. The adsorbate stiffness always increases the resonant frequency. Because surface stress can be either tensile or compressive [21,22], it can either increase or decrease the stiffness [19,23,24]. It is worth mentioning here that the heated debates on whether surface stress can be modelled as an axial load on a cantilever beam, which can thus change the stiffness, are still being exchanged [23,25,26]. However, in a clamped-clamped beam, there is no doubt that surface stress can result in the stiffness change [25,26]. There are other scenarios which can also cause the stiffness change. For example, because a coating polymer layer absorbs vapor molecules, which results in swelling and thus compressive force, the resonator stiffness decreases significantly [27]. In the forward problem in which Δk, Δm and ΔC are given, ω' is uniquely determined by Eq. (2). However, in the real application of a resonator, ω', k, m, C and ΔC are the (known) measured quantities; Δk and Δm are the two unknown quantities to be determined. For a given/measured ω', there are infinite combinations of Δk and Δm. Therefore, in order to characterize more properties of adsorbate, we encounter the following inverse problem in practice: *How to use the shifts of resonant frequencies to determine the stiffness and mass of adsorbate?* A similar inverse problem was also raised by Chen et al. [28]. Because of the formation of amalgamation in the mercury adsorption test [28,29] and the formation of hydride in the hydrogen adsorption test, the stiffness and mass of a micromechanical sensor often change together in those vapor adsorption tests and the inverse problem thus arises naturally. In contrast, in the mass resonator case, there is no such inverse problem because Δm is the only unknown variable, which is uniquely determined by the resonant frequency shift.

In Ramos' experiment [11], they counted the total *E. coli* bacteria number (about 4200) and calculated the mass; the bacteria stiffness was then obtained by curve-fitting, which in essence is still a forward problem. They changed the adsorption location to try to "uncouple" the effects of stiffness and mass of the bacteria [11]. As shown later in this study, the methods including shifting adsorption location, multiple resonant frequencies and changing the adsorption length can not be used to solve the inverse problem. By varying the adsorbate thickness and utilizing a geometric approximation, a solution method to the inverse problem is presented and its accuracy is also demonstrated. The advantages of solving the inverse can be the following two: (1) the application of a micro/nanomechanical resonator can be extended beyond mass sensing. (2) Because the stiffness and mass of adsorbate are among the most difficult quantities to be measured in the resonator application, our method, which only requires the measurement of the resonant frequency and adsorbate thickness, is expected to reduce extra experimental instruments and relieve some laborious efforts.

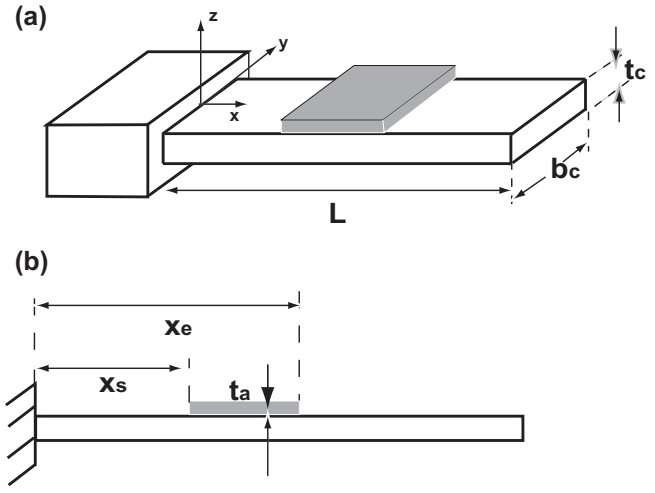

Fig. 1. (a) Schematic diagram of a cantilever resonator with molecules adsorbed on its surface and the coordinate system. E_c, E_a and ρ_c, ρ_a are the Young's moduli and densities of the resonator and adsorbed layer, respectively. l_c, b_c and t_c are the resonator length, width and thickness, respectively. (b) The adsorbed layer is (assumed) uniformly distributed from x_s to x_e with a thickness of t_a and a width of $b_a = b_c$.

2. Model development

Fig. 1(a) is a schematic of a cantilever beam with an adsorbate layer ranging from x_s to x_e. The governing equation is thus divided into three domains as follows [11,12]

$$\begin{cases} m\dfrac{\partial^2 w_1}{\partial t^2} + D\dfrac{\partial^4 w_1}{\partial x^4} = 0, & 0 \le x \le x_s \\ (m+\Delta m)\dfrac{\partial^2 w_2}{\partial t^2} + (D+\Delta D)\dfrac{\partial^4 w_2}{\partial x^4} = 0, & x_s \le x \le x_e \\ m\dfrac{\partial^2 w_3}{\partial t^2} + D\dfrac{\partial^4 w_3}{\partial x^4} = 0, & x_e \le x \le L \end{cases} \tag{3}$$

where w_i (i = 1, 2, 3) is the beam deflection in different domains and L is the beam length; m is the beam mass per unit length and $m = \rho_c b_c t_c$ (ρ_c, b_c and t_c are the mass density, width and thickness of the beam, respectively). Δm is the mass per unit length of the adsorbate layer and $\Delta m = \rho_a b_a t_a$ (ρ_a, b_a and t_a are the mass density, width and thickness of the adsorbate layer, respectively). $D = E_c b_c t_c^3/12$ is the beam bending stiffness and E_c is the beam Young's modulus. ΔD is the stiffness change due to the adsorbate layer, which is given as the following [11,12]

$$\Delta D = \frac{b_c}{12}\frac{E_c^2 t_c^4 + E_a^2 t_a^4 + 2E_c E_a(2t_c^2 + 3t_c t_a + 2t_a^2)}{E_c t_c + E_a t_a} - D. \tag{4}$$

Here E_a is the Young's modulus of the adsorbate layer, which is assumed to have the same width as that of the beam. Here the stiffness change due to surface stress is not considered. Because the surface of the silicon resonator is not functionalized, the surface stress induced by the adsorbate materials as discussed in this study is very small [11,12]. Surface stress is the sensing mechanism for many receptor-based sensors [21,22]. However, the receptor–ligand binding is highly selective for identifying an adsorbate/ligand; the challenges for developing robust and stable recognition methods through functionalized coatings (i.e., the receptor materials) and even interpreting the responses of receptor-based sensor still remain [30]. The development for the receptor-less or receptor-free sensors, which bypass the chemistry of receptor–ligand binding and capitalize on the intrinsic material properties of adsorbate, has been called for [30]. Here the mass density (related with mass) and Young's modulus (related with stiffness) are the intrinsic material properties, which can be used to identify the material of an adsorbate.

By introducing $\xi = x/L$, $\tau = \sqrt{EI/(mL^4)}t$ and $W = w/L$ [23,24], Eq. (3) is nondimensionalized as follows

$$\begin{cases} \dfrac{\partial^2 W_1}{\partial \tau^2} + \dfrac{\partial^4 W_1}{\partial \xi^4} = 0, & 0 \le \xi \le \xi_s \\ (1+\beta)\dfrac{\partial^2 W_2}{\partial \tau^2} + (1+\alpha)\dfrac{\partial^4 W_2}{\partial \xi^4} = 0, & \xi_s \le \xi \le \xi_e \\ \dfrac{\partial^2 W_3}{\partial \tau^2} + \dfrac{\partial^4 W_3}{\partial \xi^4} = 0, & \xi_e \le \xi \le 1 \end{cases} \tag{5}$$