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Keynote Paper

Multiscale modeling of nano-biosensors

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ABSTRACT

Ultrasensitive nano-biosensor related research is a vital and rapidly developing field owing to its potential social and economic impact. Chemo-bio-mechanical phenomena in biosensing offer an enticing opportunity for researchers in the field of computational mechanics to investigate these phenomena with methodologies that have not previously been exploited and to furthermore provide new insight for designing next-generation ultrasensitive nano-biosensors. In this paper, some recent advances on predicting macroscopic response of microcantilevers through the microscopic fidelity of molecular interactions are highlighted. Detailed surface stress calculations were performed in a representative volume using first principles density functional theory (DFT) calculations. A multiscale method that couples microscopic surface stress calculations with finite element method (FEM) was developed to analyze the global deformation and stress fields of the microcantilever. Self-assembled monolayer (SAM) adsorption on Au(111) surface of the microcantilever was studied to demonstrate the applicability of the method. The multiscale modeling scheme provides quantitative analysis of the displacement and stress fields and can be used to predict the response of nanomechanical sensors subjected to complex molecular adsorption.

1. INTRODUCTION

Ultrasensitive nano-biosensor related research has received a great attention recently owing to its potential social and economic impact. Microcantilevers and nanowires have been suggested as the next-generation sensing devices to detect disease in an early stage (Heath et al. 2009). The microcantilever is highly portable and supports label-free molecular recognition measurement with an ultra-high sensitivity. With the advance of the micro/nano electromechanical systems (MEMS/NEMS) technology, variously shaped microcantilevers can be now routinely fabricated in batches. Figure 1 shows a scanning electron micrograph (SEM) of a V-shaped microcantilever fabricated in-house using the MEMS/NEMS technology.

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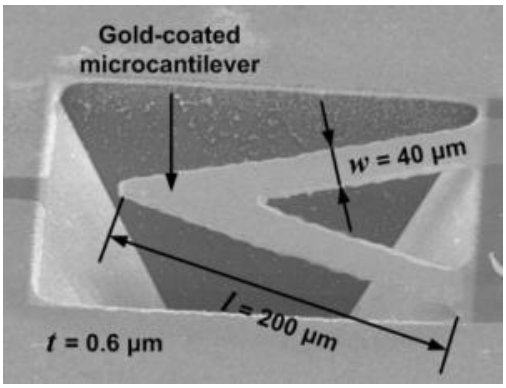


Fig. 1 Scanning electron micrograph of a gold-coated microcantilever fabricated in-house using MEMS/NEMS technology.

The microcantilever has been widely used to detect biomolecules (such as DNA and proteins associated with cancer or other diseases), chemicals (such as explosives and glucose), and ionic species (such as calcium ions). It is thus rather surprising to note that the theoretical description and predictive modeling of these devices are not well developed, and lag behind advances in fabrication and applications (Chen et al. 2013a, Chen et al. 2013b, Chen et al. 2011, Shih et al. 2013, Yen et al. 2013). In this paper, some recent advances on predicting macroscopic response of microcantilevers through the microscopic fidelity of molecular interactions are highlighted. The multiscale modeling scheme provides quantitative analysis of the displacement and stress fields and can be used to predict the response of nanomechanical sensors subjected to complex molecular adsorption.

2. MULTISCALE METHODOLOGY

We shall briefly describe the underlying multiscale methodology and detailed derivations can be found in Shih (2013). At its simplest, the key components of biosensors consist of a sensing layer, a transducer and a recorder (Fig. 2). The sensing layer is normally a receptor which can bind or interact with a target analyte molecule. The transducer transforms the signals and the recorder is a read-out system. For example, microcantilever biosensors can translate bio-recognition events into mechanical motion ranging from a few to hundreds of nanometers. The theoretical modeling challenge thus lies in how to couple molecular interactions with a continuum description.

We assume weak coupling existed between sensing layer and transducer for the microcantilever. Therefore, detailed calculations between analytes and bioreceptors need to be performed to capture the proper molecular interactions. We thus need to perform detailed first principles density functional theory (DFT) calculations and

classical molecular dynamics (MD) simulations. However, since weak coupling is asserted between sensing layer and transducer, it is possible to perform DFT or MD calculations in a representative volume at the microscopic level and use this information to solve the desirable macroscopic response with finite element (FE) analysis (Fig. 3).

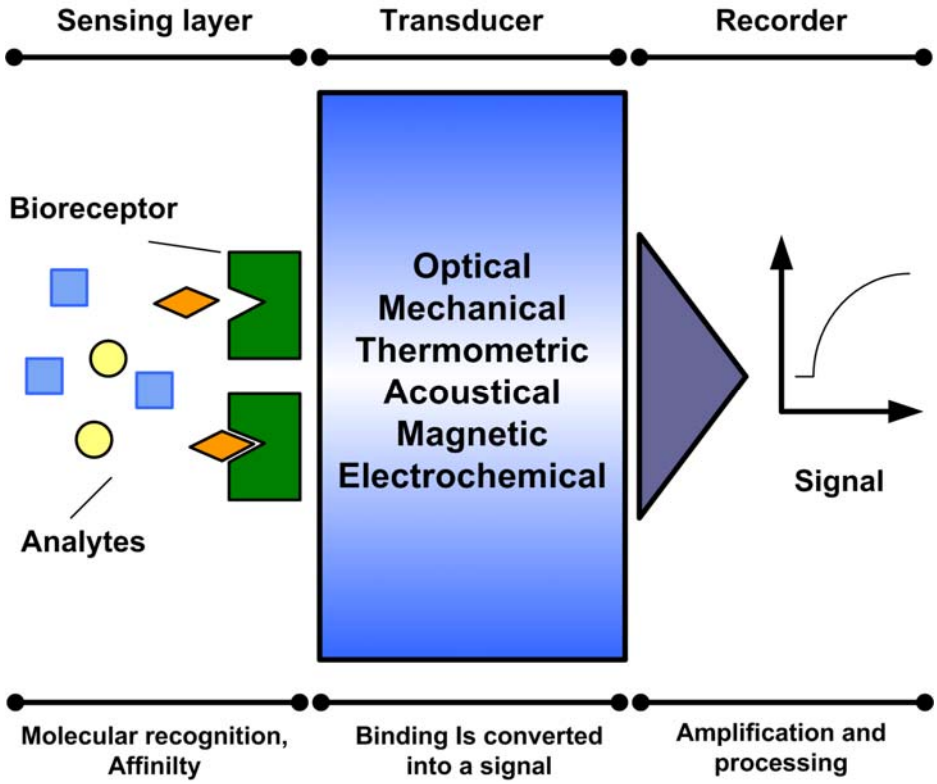


Fig. 2 Three key components of biosensors: a sensing layer for molecular recognition, a transducer for signal translation, and a recorder for processing.

	Micro-scale		Macro-scale
Phenomenon	Molecular adsorption	→	Sensor deformation
Analysis method	Density functional theory	→	Finite element method
Output	Adsorption configuration, Local stress	→	Sensor deflection, Global stress

Fig. 3 Multiscale scale methodology: phenomenon, method and output at micro- and macro-scales.

3. RESULTS AND DISCUSSION

Alkanethiolate adsorption on a gold surface forms a self-assembled monolayer (SAM) and is often used as the backbone of the sensing layer for microcantilevers. During alkanethiolate adsorption on gold surface, the overall surface stress comes from two types of interactions: chain-chain interactions and surface charge redistribution. Interactions between the alkyl chains of alkanethiolates on gold surfaces are attractive, as described by van der Waals or London dispersion forces, and generate tensile surface stress. Surface charge redistribution arising from alkanethiolate adsorption on Au(111) usually produces compressive surface stress.

To quantitatively analyze the surface stress contributions from chain-chain interactions and surface charge redistribution, we performed DFT calculations with a recently developed fully nonlocal van der Waals density functional (vdW-DF). The vdW-DF was proposed to rectify the problem of inadequate description of London dispersion interactions for traditional DFT functionals within the local density approximation (LDA) or semi-local generalized gradient approximation (GGA). This functional has shown great promise in the study of molecular adsorption on substrates.

The optimized methanethiolate and ethanethiolate configurations on Au(111) surface for vdW-DF are shown in Fig. 4. The adsorption-induced surface stresses of various alkyl chains of alkanethiolates were calculated. The principal surface stresses g_{11} and g_{22} (N/m) of the clean and alkanethiolate-covered $\sqrt{3}\times\sqrt{3}$ R30°Au(111) surfaces for vdW-DF are listed in Table 1. The clean Au(111) surfaces have isotropic tensile stresses of 3.02 N/m. Anisotropic surface stresses after alkanethiolates adsorbed onto Au surface were found.

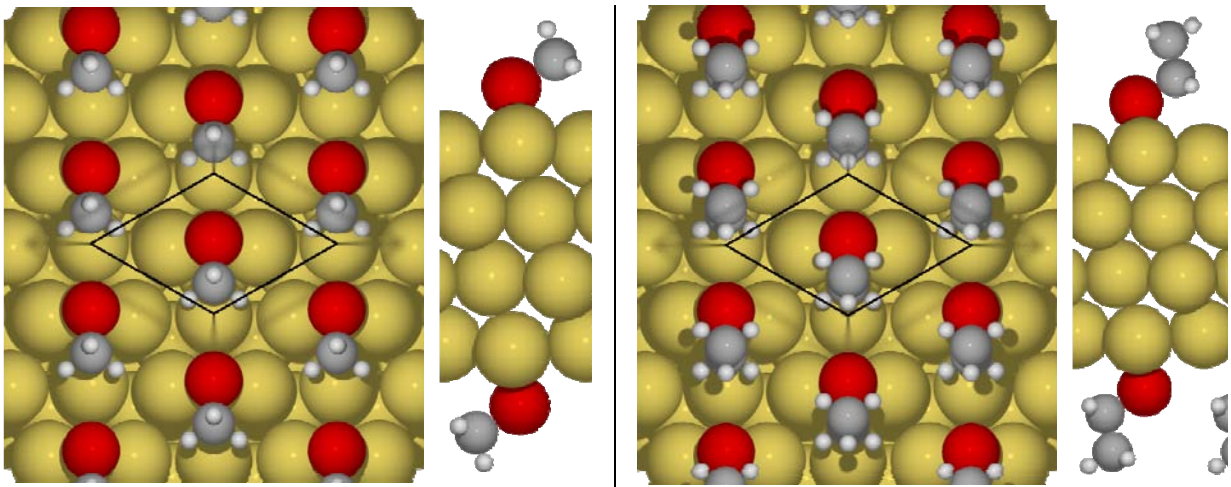


Fig. 4 Optimized alkanethiolate configurations on Au(111) surface from vdW-DF. Top and side views of (a) methanethiolate and (b) ethanethiolate.

Table 1 Calculated principal surface stresses g_{11} and g_{22} (N/m) of the clean and alkanethiolate-covered Au(111) surfaces for vdW-DF.

Adsorption configuration	g_{11}	g_{22}
Clean	3.02	3.02
Methanethiolate-covered	1.72	0.59
Ethanethiolate-covered	2.01	0.85
Propanethiolate-covered	2.28	0.86
Butanethiolate-covered	2.61	1.23
Pentanethiolate-covered	2.92	1.27
Hexanethiolate-covered	3.30	1.48

The surface stress obtained from DFT calculations of alkanethiolate on the gold surface was applied in the FEM analysis, which was carried out in a commercial finite element software ABAQUS. A shell/solid modeling technique was adapted in our finite element models of the microcantilever in order to maintain the accuracy of the full 3D solid element solution with the computational efficiency of a shell finite element model. The microcantilever was modeled by using 3D quadratic solid element type C3D20R, while the alkanethiolate self-assembled monolayer adsorption on Au(111) was modeled by using 3D quadratic shell element type S8R. The thickness of the shell section is the same as the distance between the center of gold slab and the last carbon in the chain tail of the optimized alkanethiolate in DFT unit cell along the slab surface normal. The surface stress obtained from DFT was applied as initial stress in the surface section along surface plane.

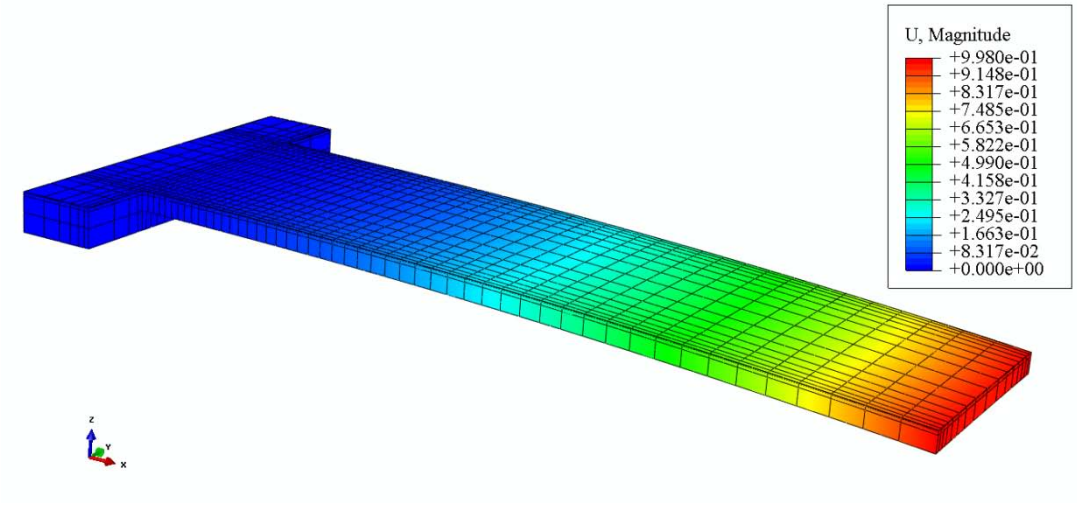
It should be noted that the surface stress distribution on the real Au surface of the microcantilever is rather complex. Surface roughness and grain morphologies of the Au thin film on the top surface both affect the true surface stress distribution. Therefore, an assumption of random distribution of the surface stress was made by sampling an angle randomly distributed from 0 to 180 degrees. The angle was then used to convert the principal stresses into normal stress components and shear stress components in each shell element. A surface-to-surface TIE modeling technique in ABAQUS was used to attach the shell section to the top surface of the solid section.

The vertical displacement U and longitudinal stress S_{11} distribution in the silicon nitride layer of the microcantilever is shown in Fig. 5. Not surprisingly, the stress in the supporting block is relatively small compare to those in the microcantilever part, where we found the tensile (compressive) stress occurred on the upper (bottom) surface the silicon nitride layer because of the overall compressive surface stress in the shell section. The longitudinal stresses concentrate near the corners of the microcantilever closed to the supporting block, as shown in the inset of Fig. 5.

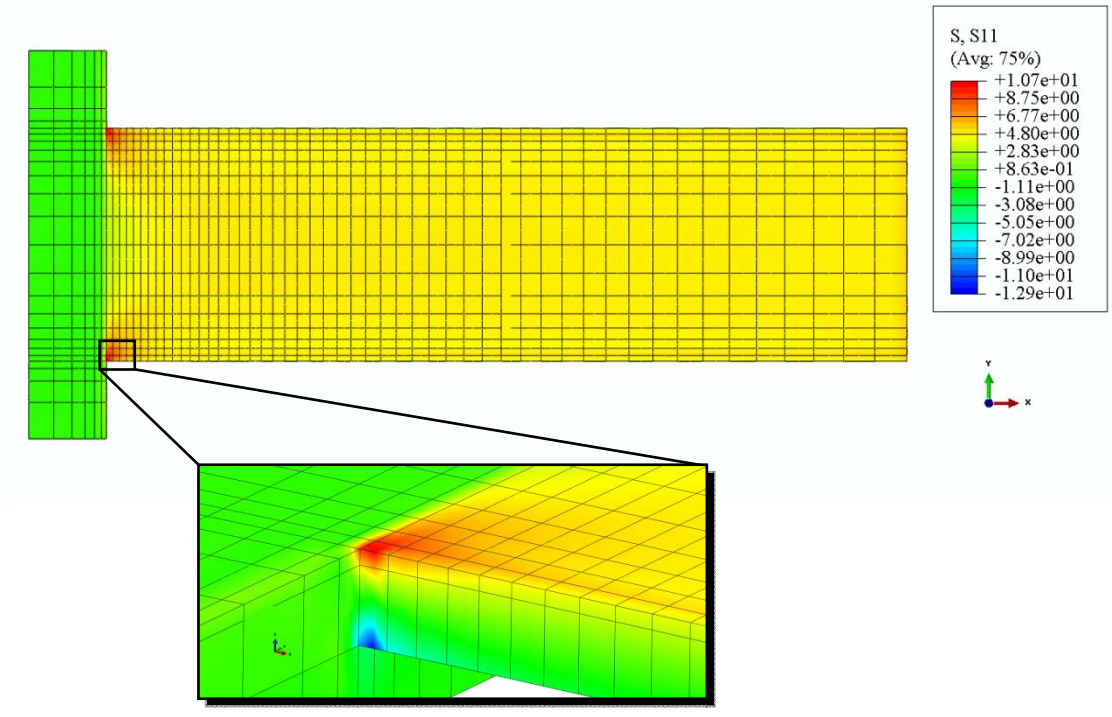
4. CONCLUSIONS

A multiscale method that couples microscopic surface stress calculations with finite element method (FEM) was developed to analyze the global deformation and stress fields of the microcantilever. Self-assembled monolayer (SAM) adsorption on Au(111)

surface of the microcantilever was studied to demonstrate the applicability of the method. The multiscale modeling scheme provides quantitative analysis of the displacement and stress fields and can be used to predict the response of nanomechanical sensors subjected to complex molecular adsorption.



(a)



(b)

Fig. 5 Vertical displacement and longitudinal stress distribution in the silicon nitride layer of the microcantilever.

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