COMPLEX MODULUS OF PDMS AND ITS APPLICATION IN CELLULAR FORCE MEASUREMES

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ABSTRACT
Cellular contraction is often accompanied by oscillatory motion of several Hz. Accurate force measurement using Polydimethylsiloxane (PDMS) micropillar based bio-transducers calls for the appropriate material characterization of PDMS in the frequency domain. In this work, the complex modulus of PDMS was measured using a dynamic nanoindentation technique. An improved method was developed to extract the complex modulus with the use of a flat punch indenter. The material properties of PDMS were further incorporated into a finite element model (FEM) to simulate the contraction force of cardiac myocytes.

KEYWORDS
Cardiac myocyte, cellular force, PDMS, micropillar, nanoindentation; Euler beam, Timoshenko beam, viscoelastic, complex modulus, frequency domain, Fourier series, Finite element analysis.

INTRODUCTION
Recently there is an increasing interest to use PDMS based micropillars as bio-transducers for cellular forces measurements due to their exceptional sensitivity (Fig. 1). The accuracy of these devices relies on appropriate material characterization of PDMS and modeling to convert the micropillar deformations into the corresponding forces. PDMS exhibits inherent viscoelastic behavior, which should be taken into account for accurate force conversion [1].

Cells often involve in cyclic motion, in which the viscoelastic properties in the frequency domain are needed for accurate force calculation. With the development of both instrumented nanoindentation and the associated analysis, dynamic nanoindentation has recently been used to characterize the viscoelastic properties of soft materials in the frequency domain. However, the accuracy of this measurement technique depends highly on the accurate characterizations of the dynamic response of the measurement system, the nanoindenter tip geometry, and an appropriate model for extracting the viscoelastic properties of a material. Herbert et al. used a single Voigt solid (a spring and a dashpot connected in parallel), which did not permit an instantaneous elastic response and finite contact damping [2]. Wright and Nix improved the method by modeling the sample as a standard linear solid [3]. The model incorporated only one relaxation time, therefore it is not sufficient to capture more complex viscoelastic behavior. The results for the storage and loss moduli as computed by the two methods were close to each other, with a difference of only ~3%. In this work, an improved model for complex modulus extraction was developed for the flat punch indenter. A general formulation is given so that this approach is applicable to all linear viscoelastic materials, thus removing all the constraints imposed by the previous methods. The complex modulus of PDMS measured at small scale will allow for more accurate cellular force measurements in the frequency domain.

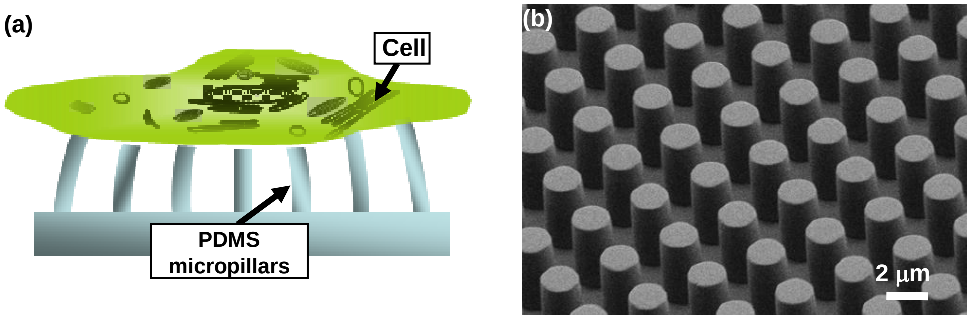

Fig.1: (a) Schematic illustration of PDMS micropillar-based cellular force transducer. (b) Scanning electron microscope (SEM) micrographs of high density micropillar arrays.

EXPERIMENT
PDMS samples were prepared by mixing the prepolymer Sylgard 184 (Dow Corning) with a curing agent at a volume ratio of 10:1, followed by degassing, and thermal curing at 65 ℃ for 90 min. The DNT tests were conducted on a G200 Nanoindenter system (Agilent), using a sapphire flat cylindrical punch indenter (Micro Star Tech.) with a diameter of 2.01 mm. The frequencies of the harmonic load were in the range of 1~45 Hz. The harmonic load was controlled such that the resulting amplitude of oscillatory displacement was maintained at 50 nm.

We developed an improved model to extract the complex modulus without involving constitutive model of material. The viscoelastic behavior under a time-harmonic loading condition was analyzed using a hereditary integral operator [1]. After some lengthy derivations, the resulting storage modulus E' and loss modulus E'' can be obtained from the magnitude and phase information of input harmonic force and output displacement.

$$E'(\omega) = \frac{1-\nu^2}{2R}\frac{\Delta P_0}{\Delta h_0}\cos\phi\,, \qquad E"(\omega) = \frac{1-\nu^2}{2R}\frac{\Delta P_0}{\Delta h_0}\sin\phi \tag{1}$$

where ν is the Poisson's ratio of the test material, R is the radius of indenter, ΔP_0 is the amplitude of harmonic load, Δh_0 is the amplitude of harmonic displacement, and ϕ is the phase between the load and displacement. The expression essentially agrees with Herbert et al.'s formulas in the case of the circular flat punch indenter [2]. The advantage of our method is that there is no linear constitutive model used in derivation, therefore the frequency-dependent viscoelastic behavior is precisely captured without assumptions. Since flat punch indenter tip is used in this work, the measurement results are sensitive to the mounting conditions associated with the small angle between the tip end and the sample surface. Therefore it is important to identify the full contact region. It is seen that pre-compression depth has a strong effect on the storage modulus. At small depths (2.5 - 20 μm), the partial contact due to the tip tilting results in the lower modulus; at larger depths (70 - 100 μm), the increase is most likely induced by the large strain applied on the PDMS which violates the small deformation assumption in linear viscoelasticity. The modulus in the vicinity of 50 μm depth is comparable to previous report by Conte and Jardret [4], and our own measurement in the time domain [1]. Therefore we conclude that this is the "full contact" region for the 2.01 mm diameter flat punch indenter tip.

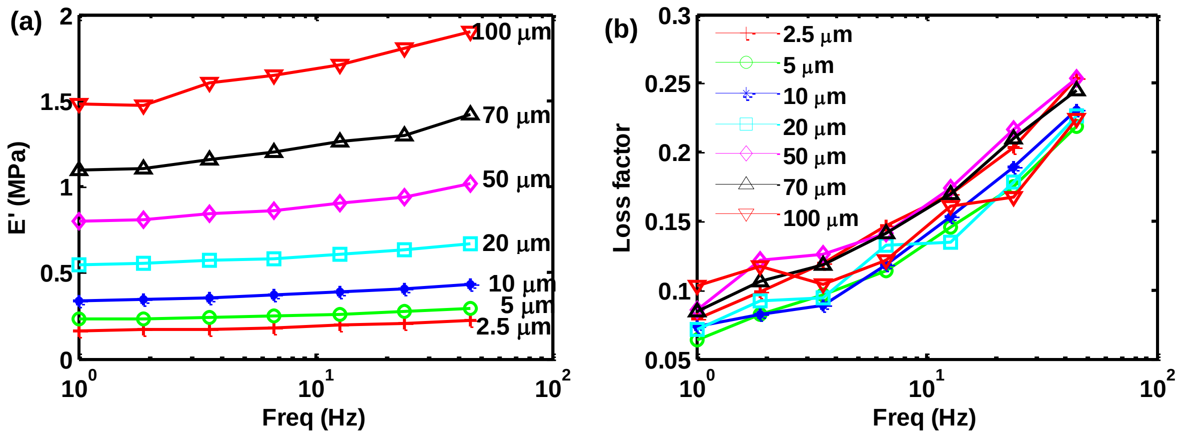

Fig. 2: Frequency-dependent (a) storage modulus and (b) loss factor of PDMS under various pre-compressions.

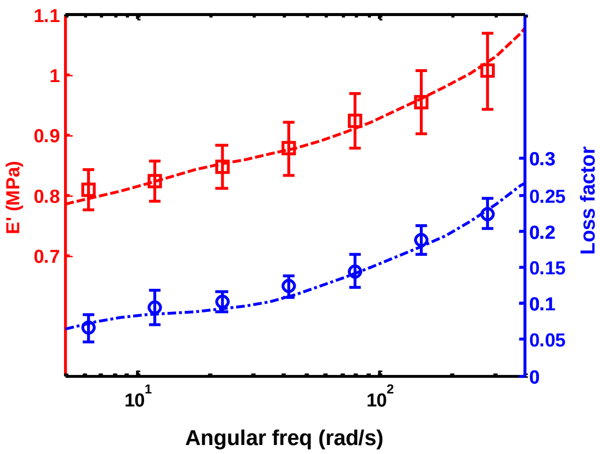

Fig. 3: The experimental data (marker with errorbar) and generalized Maxwell model fitting (dashed lines) for both the storage modulus and loss factor.

Table 1: Fitting parameters for the generalized Maxwell model of the complex modulus

τ_j (sec)	λ_j (Hz)	E_j (kPa)
10	0.1	2.2×10^{-11}
1	1	18.4
0.1	10	94.1
0.01	100	119.1
0.001	1000	742.3

The complex modulus data measured at discrete frequencies can be interpolated to a frequency-dependent function using the generalized Maxwell model

$$E(t) = E_\infty + \sum_{j=1}^{N} E_j e^{-\lambda_j t} \tag{2}$$

where E_∞, E_j are relaxation coefficients, λ_j are the reciprocals of relaxation times (τ_j) and N is the number of exponential terms in the Prony series. Using the half-sided Fourier transform, the complex modulus $E(\omega)$ can be obtained from the relaxation modulus $E(t)$

$$E(\omega) = i\omega \int_0^\infty E(t)e^{-i\omega t}dt = \left(E_\infty + \sum_{j=1}^{N} \frac{E_j\omega^2}{\lambda_j^2 + \omega^2}\right) + i\left(\sum_{j=1}^{N} \frac{E_j\lambda_j\omega}{\lambda_j^2 + \omega^2}\right) \quad (3)$$

Nonlinear least squares curve fitting method was performed to obtain the coefficients and relaxation times using both the storage modulus and loss factor. The fitting results are plotted in Fig. 3 and Table 1.

DISCUSSION

The complex modulus of PDMS was further incorporated into FEM to calculate the cellular contraction force. The cellular contraction displacements from Zhao and Zhang's previous testing on cardiac myocytes were used [5]. Since the cells responded to the isoproterenol perfusion very strongly, we chose 3 min and 7 min after the stimulation as two cases. The regularly periodic contraction was converted to Fourier series, and the interpolations agree well with the experimental data.

The cellular force was simulated by FEM using ABAQUS. The enlarged root and notched sidewall of micropillar was modeled using 3D elements C3D10. The Fourier series of displacement and complex modulus from previous analysis were incorporated into the FEM. The calculated forces are plotted in Fig. 4. The force responses follow the similar cyclic patterns as the contraction displacements. The magnitude of forces for 3 min and 7 min cases are 15.9 nN and 10.8 nN, respectively. These values are significantly less (approximately 75%) than the calculated forces from Zhao and Zhang's report. Based on these results, it is seen that the effects of viscoelastic properties and appropriate beam model are very important in the calculation of cellular contraction forces using PDMS micropillar sensor arrays. The advantage of FEA analysis is that it can seamlessly incorporate the complex material properties, structure geometry and boundary conditions, thus providing accurate results on the cellular contraction forces.

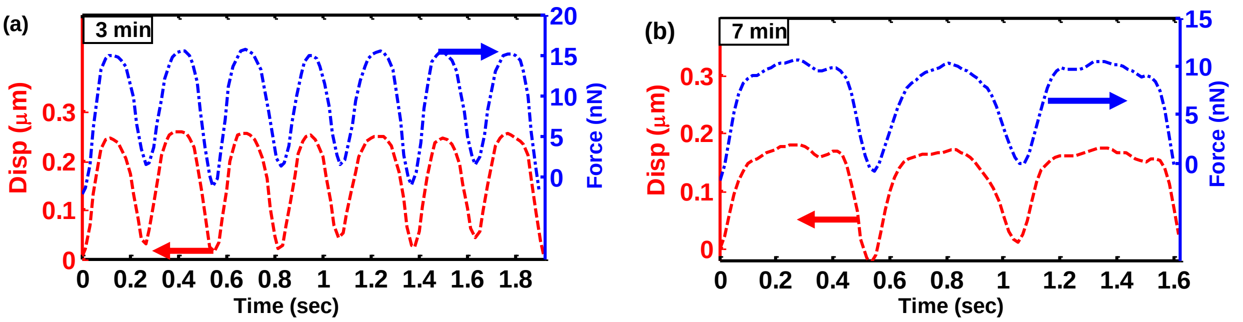

Fig. 4: Displacement (red dashed-line) and force (blue dash-dot line) curves for both (a) 3 min and (b) 7 min cases.

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REFERENCES

[1] P. Du, I-K Lin, H. Lu and X. Zhang, *Extension of the beam theory for polymer bio-transducers with low aspect ratios and viscoelastic characteristics*, J. Micromech. Microeng., vol 20, pp. 095016, (2010).

[2] E. G. Herbert, W. C. Oliver, and G. M. Pharr, *Nanoindentation and the dynamic characterization of viscoelastic solids*, J. Phys. D: Appl. Phys., vol. 41, pp. 074021, (2008).

[3] W. J. Wright and W. D. Nix, *Storage and loss stiffnesses and moduli as determined by dynamic nanoindentation*, J. Mater. Res., vol. 24, pp. 863-871, (2009).

[4] N. Conte, V. Jardret, *Frequency Specific Characterization of Very Soft Polymeric Materials Using Nanoindentation Testing*, Proc. Mater. Res. Soc., vol. 710, pp. DD.7.10, (2001).

[5] Y. Zhao and X. Zhang, *Cellular mechanics study in cardiac myocytes using PDMS pillars array*, Sens. Actua. A-Phys., vol. 125, pp. 398, (2005).

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