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Advancing Sensitivity in Measuring Cardiomyocyte Contraction Force through Single-crystal Silicon Strain Sensors

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***Abstract*[1]—Our proposed method involves the utilization of an SU-8 cantilever integrated with a single-crystal silicon strain sensor, which facilitates both miniaturization and accurate detection of cardiomyocytes contraction force. The single-crystal silicon strain sensor exhibits remarkable electrical stability and exceptional sensitivity, surpassing metal sensors by a factor of 17, while achieving force measurements below 0.02μN. Furthermore, the compatibility of SU-8 with photolithography techniques enables convenient miniaturization and large-scale production of the device. The proposed device was used to study the effect of verapamil and isoproterenol on the contractile properties of cardiomyocytes, demonstrating its potential as an early predictor of cardiotoxic compounds in analytical drug discovery.**

Keywords—cantilever; single-crystal silicon; strain sensor; cardiomyocytes; contraction force

I. Introduction

Cardiovascular disease (CVD) stands as the predominant global cause of mortality[1]. However, the approvals for CVD drugs have been considerably lower in recent years compared to oncology. While there are no studies comparing the development costs for CVD and oncology, it has been shown that clinical trials for CVD require larger trial sizes and longer lead times[2]. Consequently, early evaluation of cardiomyocyte side effects assumes paramount importance as it enables the identification of safe and effective drug candidates, thus enhancing the prospects of successful market introduction.

The patch clamp technique has long been regarded as the gold standard for assessing cardiotoxicity, enabling precise measurement of action potentials at the single cell[3]. Nevertheless, this technique is accompanied by technical complexities, invasiveness, and limitations in high throughput. To address the long-term and safe detection of CMs electrophysiological properties, microelectrode arrays (MEAs) have been widely used for detecting field potentials in cardiac tissue[4, 5]. However, the assessment of electrophysiological properties does not directly capture the mechanical contraction activity of cardiomyocytes. To overcome this limitation, culturing cardiomyocytes on cantilever and utilizing strain sensors to detect mechanical deformation induced by CMs contraction force have emerged as an attractive option[6-10]. Elastomers such as PDMS, PI, and SU-8 are commonly chosen to fabricate cantilevers, as they generate substantial strains and support cell culture[11]. Initially, PDMS cantilevers with metal strain sensors were developed due to their low stiffness and compatibility with cell culture. However, the limited strain coefficient of metal sensors restricts force resolution[6-8]. Lind et al. employed a 3D printing technique to fabricate a PDMS cantilever integrated with a CB:TPU strain sensor. Nevertheless, the manufacturing method-imposed constraints on the cantilever thickness and device sensitivity[9]. Crack sensors have garnered attention for their flexibility, durability, and mechanical sensitivity (exhibiting a 600 times higher signal-to-noise ratio than metal sensors). However, their unstable output characteristics render them less suitable for high-throughput screening applications[10].

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2020R1A5A8018367 and RS-2022-00165505)

II. Methods And Materials

A. Design and fabrication

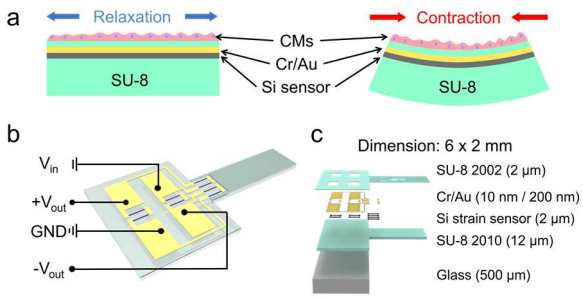

Fig. 1 The SU-8 cantilever integrated with a single crystal silicon strain sensor for cardiomyocytes contraction force measurement. (a) Working principle of the single crystal silicon strain sensor. The schematic (b) and design structure (c) of the SU-8 cantilever integrated with a single-crystal silicon strain sensor.

Figure 1 provides a comprehensive depiction of the structural composition and dimensional specifications of the SU-8 cantilever integrated with a single crystal silicon strain sensor. Accurate quantification of the cardiomyocytes contractile behaviors requires precise measurement of the SU-8 cantilever deformation during long-term culture or

drug screening tests (Figure 1a). Here, the strain sensor, consisting of single crystal silicon resistors, is incorporated into the SU-8 cantilever to measure the deformation of cantilever which caused by cardiomyocytes contractile behavior. After, the change in resistance is converted into a change in output voltage using a Wheatstone bridge (W.B.) circuit (Figure 1b). By measuring the change in output voltage enables the detection of alterations in cardiomyocytes contraction force, as well as the analysis of cardiomyocytes beat rate and duration time. The dimensional specifications of the proposed device are presented in Figure 1c.

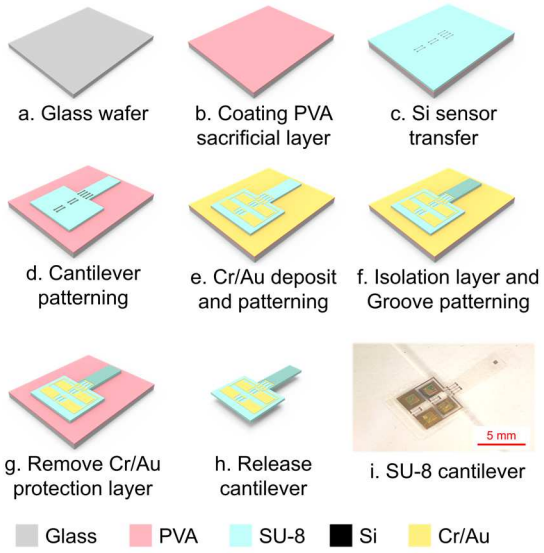

Fig. 2 Fabrication process flow and optical images of the device.

Figure 2 illustrates the fabrication process for the SU-8 cantilever that is integrated with a single crystal silicon strain sensor. In the fabrication process, a layer of polyvinyl alcohol (PVA) was spin-coated onto a glass wafer and baked at 115°C as a sacrificial layer. Next, a 10 µm layer of SU-8 3010 was spin-coated and patterned using UV lithography to create the SU-8 cantilevers. Silicon sensors were subsequently transferred to the cantilever surface using an additional 2 µm layer of SU-8 2002 adhesion[12]. Using an electron beam evaporator, a thin film of chromium (Cr) and gold (Au) was deposited on the cantilever at a deposition rate of 1 Å/s and a pressure below 5×10^{-6} Torr. Before metal deposition, the native oxide layer on the silicon sensors was removed using a BOE solution treatment for 10 seconds. AZ-GXR-601 photoresist and wet etching were used to achieve metal patterning, with separate etchants for Au and Cr. The metal layer covering the PVA layer remains in place to protect it. The isolation layer was created by applying a 2 µm layer of SU-8 2002 onto the device using spin-coating. In order to promote cell maturation, microgrooves with a width of 3 µm were patterned on the device using UV lithography. Subsequently, the metal layer covering the PVA layer was removed using etchant. Next, the PVA sacrificial layer was dissolved in deionized water to release the SU-8 cantilever. Lastly, the cantilever was affixed to a glass substrate using epoxy glue.

B. Cell culture

All animal experiments were performed following protocols approved by the Animal Ethics Committee of Chonnam National University in accordance with the Principles of Laboratory Animal Care and specific national laws (license number: CNU IACUC-YB-2022-29). Cardiomyocytes were isolated from one day old neonatal rats (Sprague-Dawley, SD), which follows a standard isolation method. To increase cardiomyocyte adhesion, each cantilever was coated with fibronectin (50 g ml^{-1}, Corning) for 1 h. Finally, cardiomyocytes were cultured at a density of 1000 mm^{-2} on the SU-8 cantilever. Cardiomyocytes were cultured in a conventional incubator. After 24 h, cardiomyocytes began contracting and synchronizing after 48 h.

C. Simulation Analysis

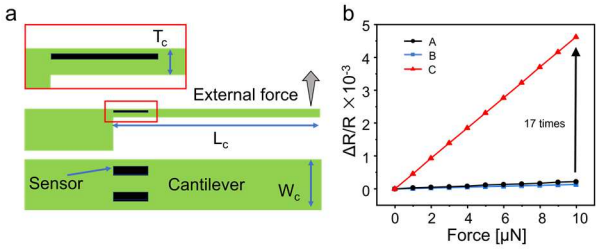

Fig. 3 (a) The cantilever model used for FEA testing. (b) Comparation of the force sensitivity between different models.

The theoretical study was tested with COMSOL Multiphysics software for simulation. A schematic of the model used in the simulation analysis is shown in Figure 3a. A fixed constraint was applied to the fixed end of the cantilever during the analysis. Even though, in reality, the cardiomyocyte exerts a homogeneous stress on the cantilever surface, a vertically upward traction force was applied to the free end of the cantilever to facilitate subsequent comparison with the results of the performance tests. The performance of the cantilever is greatly influenced by the material properties, especially Young's modulus. To demonstrate the superior characteristics of the SU-8 cantilever integrated with a monocrystalline silicon strain transducer, a comparative analysis of three different combinations was conducted, with specific parameters detailed in Table 1.

TABLE I. PARAMETERS OF THE SIMULATION MODEL

No.	*Cantilever*		*Sensor*	
	Type	*Dimension (L*W*T)*	*Type*	*Dimension (L*W*T)*
A	SU-8	6000*2000*16 (µm)	Au	800*30*0.2 (µm)
B	Si		Si	800*50*0.1 (µm)
C	SU-8		Si	800*50*2 (µm)

The force sensitivity of different models is compared in Figure 3b. Quantification of force sensitivity is achieved by comparing the resistance change of different models experiencing the same load force. Force sensitivity is described by the following equation:

$$S_f = (\Delta R/R)/F$$

In this equation, S_f represents the change in sensor resistance, and F represents the force loaded onto the free end of the cantilever. The comparison of force sensitivity among the three models found that the SU-8 cantilever integrated with a monocrystalline silicon sensor is 17 times more sensitive than the gold strain sensor.

III. Result And Siscussion

A. Characterization of the silicon strain sensor

The change in resistance (ΔR) and voltage (ΔV) across the W.B. circuit were investigated as the primary sensor characteristics, with the displacement applied to the cantilever as the variable parameter. The displacement that is applied on the cantilever is used as a variable parameter. The test uses a PZT driver to drive a cantilever and generate a displacement signal at the free end of the cantilever. the PZT driver is controlled by a function generator and a

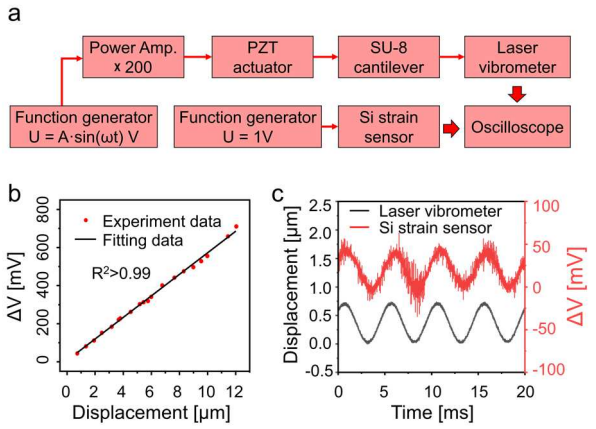

Fig. 4 (a) PZT test system for testing silicon sensor characteristics. (b) Linear plot of the change in resistance with respect to the displacement. (c) The variation curve of the output voltage with a displacement of 0.6 μm and a frequency of 200 Hz.

power amplifier, and the drive voltage is gradually increased from 20 V to 160 V. The characteristics of the strain transducer are evaluated based on the output electrical signals and the displacement (Figure 4a).

Figure 4b shows a robust linear relationship between the applied displacement and the resistivity change rate of the sensor, where the resistivity change rates at 10 μm and 100 μm displacements are 1.33×10^{-4} and 12.38×10^{-4}, respectively. When the applied load is gradually removed, the silicon sensor returns to the initial state without significant hysteresis. Comparing the experimental data with the simulated data, we determined that the actual GF and force sensitivity of the sensor were 89.04 and 0.43 μN^{-1}, respectively. These values were in agreement with the target values of 93.65 and 0.46 μN^{-1}. The effectiveness of the system is further demonstrated in Figure 4c, which shows the corresponding change in sensor output voltage for small displacements (0.6 μm) measured by the laser vibrometer. Even at the displacements of 0.6μm, the change in output voltage is still significant at (45.34 ± 11.72) mV, which, when converted to the same applied force, allows the device to detect external forces as low as 0.02μN. This significant change in output voltage highlights the excellent sensitivity of the system, which outperforms noisy signals and provides reliable detection and measurement capability.

B. Drug dose response

To evaluate the efficacy of the device for drug screening, we tested two clinically recognized drugs, Verapamil and Isoproterenol, which affect the excitation-contraction coupling process and modulate the contractile behavior of CMs. Verapamil is a calcium channel blocker. It causes a decrease in the amplitude and rate of cell contraction. Figure 5a illustrates the changes in output voltage resulting from CMs treated with different concentrations of verapamil. It is evident that the relative contraction force and beat rate of CMs gradually and significantly decrease with increasing concentrations of the verapamil. Isoproterenol, a sympathomimetic drug, exhibits effects on cardiomyocytes by enhancing the influx and release of calcium ions. This action leads to a positive inotropic effect, resulting in increased contractility and volatility. In Figure 5b, we observe the output voltage changes induced by the CMs contraction force after

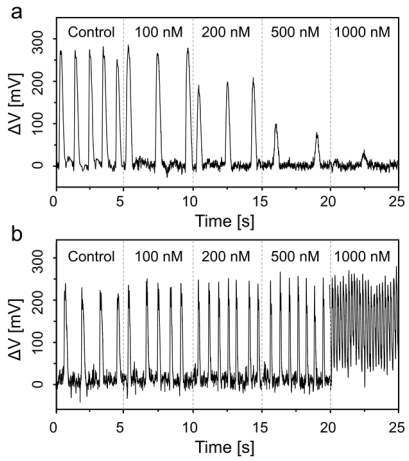

Fig. 5 Effect of (a) Verapamil and (b) Isoproterenol on the contractility of cultured cardiomyocytes

treatment with isoproterenol. As the concentration of isoproterenol increases, the contractile force and beating rate of cardiomyocytes exhibit a gradual increase. At a concentration of 1000 nM, cardiomyocytes demonstrate signs of tachycardia. This is consistent with the previously reported conclusion[14].

IV. Conclusion

Replacing the conventional metal strain sensor with a single crystal silicon strain sensor, we significantly improve the sensitivity of cardiomyocyte contraction force detection. The experimental results demonstrate the responsiveness of the single crystal silicon strain sensor, capable of detecting small forces below 0.02 μN, with a force sensitivity nearly 17 times higher than that of metal sensors. We quantify the effects of verapamil and isoproterenol on the contractile properties of cardiomyocytes using the proposed integrated SU-8 cantilever.

REFERENCES

[1] G. A. Roth, G. A. Mensah, and V. Fuster, "The global burden of cardiovascular diseases and risks: a compass for global action," J. Am. Coll. Cardiol., vol. 76(25), pp. 2980-2981, December 2020.

[2] M. Abdelsayed, E. J. Kort, S. Jovinge, and M. Mercola, "Repurposing drugs to treat cardiovascular disease in the era of precision medicine," Nat. Rev. Cardiol., vol. 19(11), pp. 751-764, November 2022.

[3] A. O. Verkerk, G. A. Marchal, J. G. Zegers, M. Kawasaki, A. H. Driessen, C. A. Remme, ... and R. Wilders, "Patch-clamp recordings of action potentials from human atrial myocytes: Optimization through dynamic clamp," Front. Pharmacol., vol. 12, pp. 649414, April 2021.

[4] A. Natarajan, M. Stancescu, V. Dhir, C. Armstrong, F. Sommerhage, J. J. Hickman, and P. Molnar, "Patterned Cardiomyocytes on microelectrode arrays as a functional, high information content drug screening platform," Biomaterials, vol. 32(18), pp. 4267-4274, June 2011.

[5] P. P. Kanade, N. E. Oyunbaatar, A. Shanmugasundaram, Y. J. Jeong, E. S. Kim, B. K. Lee, and D. W. Lee, "MEA-integrated cantilever platform for comparison of real-time change in electrophysiology and contractility of cardiomyocytes to drugs," Biosens. Bioelectron., vol. 216, pp. 114675, November, 2022.

[6] J. U. Lind, M. Yadid, I. Perkins, B. B. O'Connor, F. Eweje, C. O. Chantre, ... and K. K. Parker, Cardiac microphysiological devices with flexible thin-film sensors for higher-throughput drug screening. Lab Chip, vol. 17(21), pp. 3692-3703, 2017.

[7] D. S. Kim, Y. J. Jeong, B. K. Lee, A. Shanmugasundaram, and D. W. Lee, "Piezoresistive sensor-integrated PDMS cantilever: A new class of device for measuring the drug-induced changes in the mechanical activity of Cardiomyocytes", Sens. Actuators B Chem., vol. 240, pp. 566-572, March 2017.

[8] D. S. Kim, Y. J. Jeong, A. Shanmugasundaram, N. E. Oyunbaatar, J. Park, E. S. Kim, ... and D. W. Lee, "64 PI/PDMS hybrid cantilever arrays with an integrated strain sensor for a high-throughput drug toxicity screening application," Biosens. Bioelectron., vol. 190, pp. 113380, October 2021.

[9] J. U. Lind, T. A. Busbee, A. D. Valentine, F. S. Pasqualini, H. Yuan, M. Yadid, ... and K. K. Parker, "Instrumented cardiac microphysiological devices via multimaterial three-dimensional printing," Nat. Mater., vol. 16(3), pp. 303-308, March 2017.

[10] D. S. Kim, Y. W. Choi, A. Shanmugasundaram, Y. J. Jeong, J. Park, N. E. Oyunbaatar, ... and D. W. Lee, "Highly durable crack sensor integrated with silicone rubber cantilever for measuring cardiac contractility," Nat. Commun., vol. 11(1), pp. 535, January 2020.

[11] W. J. Polacheck, and C. S. Chen, "Measuring cell-generated forces: a guide to the available tools," Nat. Methods, vol. 13(5), pp. 415-423, May 2016.

[12] W. Cao, G. Liu, J. Miao, G. Zhang, J. Cui, Y. Yang, ... and R. Wang, "Batch Transfer Printing of Small-Size Silicon Nano-Films with Flat Stamp." Micromachines., vol. 12(10), pp.1255, October 2021

[13] J. Park, J. Ryu, S. K. Choi, E. Seo, J. M. Cha, S. Ryu, ... and S. H. Lee, "Real-time measurement of the contractile forces of self-organized Cardiomyocytes on hybrid biopolymer microcantilevers," Anal. Chem., vol. 77(20), pp. 6571-6580, October 2005.

[14] L. Wang, X. Xu, J. Chen, W. Su, F. Zhang, A. Li, C. Li, C. Xu, and Y. Sun, "Crack sensing of cardiomyocyte contractility with high sensitivity and stability." ACS Nano., vol. 16(8), pp.12645-12655. July 2022.