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17-20 April 2016

Hotel Matsushima Taikanso & L-Park Sendai, Miyagi, Japan

Editorial Design: Compass Two-One

Sunday 17 April

	IEEE-NEMS2016 & iCAN'16		IEEE-NEMS2016 Technical Tour
	Studio Hall, L-Park Sendai	Gallery Hall, L-Park Sendai	Tohoku University
9:00	**Registration (NEMS2016) (9:10-)**		
10:00	**Premium Tutorial by Prof. Masayoshi Esashi** (9:30-12:30)	Registration (iCAN'16) (9:30-10:30)	
11:00		Exhibition (iCAN'16) (10:30-13:30)	
12:00			
13:00	Presentation of Applications (iCAN'16) (13:00-16:10)		
14:00			**Technical Tour (NEMS2016)** (14:00-17:30) ①Jun-ichi Nishizawa Memorial Research Center ②Department of Engineering ③Micro/Nano-Machining Research and Education Center
15:00			
16:00			
17:00	Award Ceremony (iCAN'16) (17:30-18:30)		
18:00			
18:30-20:00		**NEMS2016 & iCAN'16 Joint Reception** (18:30-20:00)	

Monday 18 April

Hotel Matsushima Taikanso

	Room A (Fuji)	Room B1-2 (Chiyo1+Chiyo2)	Room B3 (Chiyo3)	Room C (Hagi)	Room D (Tokiwa)	Room E (Suehiro)
8:30-9:30		Registration				
9:30-9:40	Grand Opening					
9:40-10:30	Plenary 1 Prof. Neto					
	Break		Break			
10:50-12:25	**A1L-A** Micro-fluidics and Nano-fluidics 1		**A1L-B** Integration & Systems	**A1L-C** Nanometrics 1	**A1L-D** Nano-biology and Informatics	**A1L-E** Molecular Robotics Session I (*)
	Lunch		Lunch			
13:25-15:00	**A2L-A** CM Ho Best Paper Award Session	Exhibition (10:30-17:15)	**A2L-B** NEMS/MEMS Fabrication	**A2L-C** Graphene and Related Materials (13:25-15:15)	**A2L-D** Biomedical Micro/Nano devices	**A2L-E** Molecular Robotics Session II (*)
	Break		Break			
15:20-16:55	**A3L-A** Micro-fluidics and Nano-fluidics 4		**A3L-B** NEMS/MEMS 1	**A3L-C** Conference Paper Award Session (15:35-16:35)	**A3L-D** Nano Scale Fabrication	**A3L-E** Molecular Robotics Session III (*)
	Break		Break			
17:15-19:05		**A4P-B** Poster Session				
19:05-21:05	Banquet (Banquet Room:TENKAI)					

(* International Symposium on Molecular Robotics) Co-sponsored by KAKENHI Molecular Robotics)

Tuesday 19 April

Hotel Matsushima Taikanso

	Room A (Fuji)	Room B1-2 (Chiyo1+Chiyo2)	Room B3 (Chiyo3)	Room C (Hagi)	Room D (Tokiwa)	Room E (Suehiro)
8:00-8:35		Registration				
8:35-9:25	Plenary Prof. Ayazi					
	Break		Break			
9:45-11:00	**B1L-A** Tactile Devices and Systems	Exhibition (9:25-12:20)	**B1L-B** Advanced Micro/Nano Fabrication Technologies 1	**B1L-C** Nanoscale Robotics, Assembly, and Automation	**B1L-D** Micro-fluidics and Nano-fluidics 2	**B1L-E** Metamaterial Special Session 1 (**)
	Break		Break			
11:20-12:20	**B2L-A** Piezoelectric MSMS		**B2L-B** Advanced Micro/Nano Fabrication Technologies 2	**B2L-C** Nano-biology and Cell	**B2L-D** Molecular Sensors 1	**B2L-E** Metamaterial Special Session 2 (**) (11:10-12:25)
	Lunch					
13:20-15:10		**B3P-B** Poster Session /Exhibit Inspection				
15:10-16:45	**B4L-A** NEMS/MEMS 2		**B4L-B** Fabrication of Organic Materials	**B4L-C** Student Paper Award Session	**B4L-D** 2D Materials and Their Application (15:10-17:00)	**B4L-E** Nanophotonics/ Microoptics 1

(** Cooperation with IEEJ (code:E) Investigating R&D Committee on Applications of Metamaterials and Plasmonics to Optical and Electronic Devices)

Wednesday 20 April

Hotel Matsushima Taikanso

	Room A (Fuji)	Room B1 (Chiyo 1)	Room B3 (Chiyo3)	Room C (Hagi)	Room D (Tokiwa)	Room E (Suehiro)
8:30-8:55		Registration				
8:55-9:20	Special Talk Prof. Takata					
	Break					
9:30-10:55	**C1L-A** Bio & Medical Devices	**C1L-F** Micro/Nanomechanics and instrumentation 1	**C1L-B** Fabrication of Functional Materials	**C1L-C** Molecular Sensors 2	**C1L-D** Nanocarbon based Devices and Systems 1	**C1L-E** Nanophotonics/ Microoptics 2 (9:30-11:00)
	Break					
11:10-12:35	**C2L-A** Micro-fluidics and Nano-fluidics 3	**C2L-F** Micro/Nanomechanics and instrumentation 2	**C2L-B** Application of Nano/Micro Structures	**C2L-C** MEMS with Molecular Sensor	**C2L-D** Nanocarbon based Devices and Systems 2	**C2L-E** Nanophotonics/ Microoptics 3
	Break					
12:45-13:00	Award Ceremony & Closing					

C2L-C
MEMS with moleculer sensor
11:10 AM - 12:35 PM, April 20, 2016 Room C (HAGI, 1F)
Zhuqing Wang, Tohoku University (Chair)

Paper ID : C2L-C-1 (#1128)

INVITED TALK
Enhancements of Biosensor's Sensitivity
Congo Tak Shing Ching
National Chi Nan University, Taiwan
In the past 20 years, many researches focused on the development of biosensors in order to make them act as a tool for analysis. For example, biosensor is widely used nowadays in clinical diagnosis, environmental monitoring, food safety surveillance and so forth. And, many researches focused on the enhancement of the biosensor's sensitivity. In fact, there are so many approaches to enhance the biosensor's sensitivity, such as by the use of electron-transfer mediators, bimetallic materials, bienzymes, nanowire and etc. In this presentation, the use of sensor array and microfluidic & interdigitated microelectrode on the enhancements of biosensor's sensitivity will be presented.
Keywords - Biosensor, Sensitivity, Signal-to-Noise Ratio

Paper ID : C2L-C-2 (#1139)

Dual-Aptamer Assay for C-Reactive Protein Detection by Using Field-Effect Transistors on an Integrated Microfluidic System
Wei-Chieh Kao, Chia-Ho Chu, Wen-Hsin Chang, Yu-Lin Wang, Gwo-Bin Lee
National Tsing Hua University, Taiwan
Rapid diagnosis of C-reactive protein (CRP) is crucial for preventing cardiovascular diseases because it is a well-known biomarker of cardiovascular diseases. This study presents a dual-aptamer assay for detection of CRP, which is a critical indicator for cardiovascular diseases, by using field-effect transistors (FET). This is the first time that two aptamers, were used to form a sandwich assay such that the CRP concentration could be detected by FET. In addition to electric signals from the FET device, fluorescent signals were also used to confirm this assay. Experimental results revealed that the first aptamer (1st aptamer) and the second aptamer (2nd aptamer) could be specifically binded with target CRP. Furthermore, the microfluidic chip integrated with FET can be reused if the binded CRP and 2nd aptamer was eluted. Besides, in order to prevent the interference material like protein, cells and any nonspecific molecules from adhering onto the gate region of the FET device even after immobilization of 1st aptamer, we used the blocking agent named ethanolamine to prevent nonspecific adhesion, and the results confirmed that blocking using ethanolamine has a good congruence.
Keywords - C-reactive protein, AlGaN HEMT-based FET, dual-aptamer, sandwich assay, ethanolamine, microfluidic

Paper ID : C2L-C-3 (#1157)

Miniaturized Electrochemical Sensor Modified with Aptamers for Rapid Norovirus Detection
Nan Wang{2}, Masaaki Kitajima{3}, Kalaivani Mani{3}, Elgar Kanhere{2}, Andrew Whittle{1}, Michael Triantafyllou{1}, Jianmin Miao{2}
{1}Massachusetts Institute of Technology, United States; {2}Nanyang Technological University, Singapore; {3}Singapore-MIT Alliance for Research and Technology, Singapore
This paper presents a miniaturized electrochemical sensor fabricated by means of MEMS (microelectromechanical systems) techniques, which utilizes aptamers as recognition elements for simple, sensitive and rapid detection of murine norovirus (MNV). The novelty of this work is to integrate micro fabrication technology with aptamers to develop miniaturized and portable electrochemical sensors for environmental monitoring of microbial pathogen. The binding capability between aptamers and on-

chip sensing electrodes is investigated and the performance of proposed MEMS electrochemical aptasensor in terms of sensor responses to different titers of MNVs is characterized.

Keywords - MEMS Electrochemical Sensor, Miniaturized Aptasensor, Murine Norovirus Detection

Paper ID : C2L-C-4 (#1245)

An Array of Micropatterned SU-8 Cantilevers for Drug-Screening Applications

Jong Yun Kim, Dong-Weon Lee
Chonnam National University, Korea, South

This paper describe the utilization of microgrooves-integrated SU-8 cantilever arrays for biosensors which analyze the changes of the contraction force and beating frequency of cardiomyocytes in real time in an in vitro environment. The surface- patterned SU-8 cantilevers were manufactured using a conventional photolithography. The longitudinally patterned- microgrooves enhanced the contraction force of cardiomyocytes by 2.7 times, which was due to the alignment of cardiomyocytes on the Su-8 cantilever. The displacement of the SU-8 cantilever by contraction of cardiomyocytes was maximized around day 8. After the preliminary experiments, Isoproterenol and Verapamil were used to understand the physiology of cardiomyocytes regarding drug toxicity. The contraction force was 30% and beating frequency was increased 200% faster for 1microM Isoproterenol and respectively decreased 56% and 42% slower for 500nM Verapamil. The proposed SU-8 cantilever arrays with a laser vibrometer based measurement systems can be expected to the novel drug toxicity screening system in future.

Keywords - Cardiomyocytes, SU-8 cantilever, Laser vibrometer, Contraction force, Drug screening

Paper ID : C2L-C-5 (#1057)

An Integrated Microfluidic System for Antibiotic Resistance Gene Identification Capable Differentiating Live and Dead of Vancomycinresistant Enterococcus

Wen-Hsin Chang{4}, Sung-Yi Yang{1}, Yi-Cheng Lin{1}, Chih-Hung Wang{4}, Huey-Ling You{2}, Jiunn-Jong Wu{3}, Mel S. Lee{2}, Gwo-Bin Lee{4}
{1}Jabil Circuit Inc., Ltd., Taiwan; {2}Kaohsiung Chang Gung Memorial Hospital, Taiwan; {3}National Cheng Kung University / National Yang-Ming University, Taiwan; {4}National Tsing Hua University, Taiwan

This study presents an integrated microfluidic system which can identify vancomycin resistant gene (VanA) from live hetero-bacteria automatically. In this study, a new approach to diagnose VanA gene from live hetero-bacteria by using ethidium monoazide (EMA) and loop-mediated isothermal amplification (LAMP) was proposed and its feasibility was tested and verified. In addition, an integrated microfluidic system including a microfluidic chip and a control system was also demonstrated. The experimental results showed that the proposed system can detect VanA gene from live Enterococcus successfully with a detection limit of 10 colony formation units (CFU) within 1 hour including sample pre-treatment process. This is the first time that an integrated microfluidic system was demonstrated to diagnose VanA gene from live bacteria by LAMP. With its high sensitivity, the proposed system might be promising to verify antibiotic resistance genes from live hetero-bacteria which cannot be achieved by using the existing diagnostic methods.

Keywords - vancomycin resistant gene, microfluidics, live hetero-bacteria,loop-mediated isothermal amplification

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An Array of Micropatterned SU-8 Cantilevers for Drug-screening Applications

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***Abstract*—This paper describe the utilization of microgrooves-integrated SU-8 cantilever arrays for biosensors which analyze the changes of the contraction force and beating frequency of cardiomyocytes in real time in an *in vitro* environment. The surface-patterned SU-8 cantilevers were manufactured using a conventional photolithography. The longitudinally patterned-microgrooves enhanced the contraction force of cardiomyocytes by 2.5 times, which was due to the alignment of cardiomyocytes on the Su-8 cantilever. The displacement of the SU-8 cantilever by contraction of cardiomyocytes was maximized around day 8. After the preliminary experiments, Isoproterenol and Verapamil were used to understand the physiology of cardiomyocytes regarding drug toxicity. The contraction force was increased 30 % higher and beating frequency was also increased 200 % faster for 1μM Isoproterenol and decreased 56 % lower and 42 % slower for 500nM Verapamil. The proposed SU-8 cantilever arrays with a laser vibrometer based measurement systems can be expected to the novel drug toxicity screening system in future.**

Keywords—Cardiomyocytes; SU-8 cantilever; Laser vibrometer; Contraction force; Drug screening

I. INTRODUCTION

In recent years, abnormal symptoms such as arrhythmia due to drug side effects have occurred frequently, so various studies have been conducted to identify the reasons [1]. One of the electric physiological measurements is patch-clamp, which uses pipettes with integrated electrodes, and assesses drug toxicity by measuring changes in potassium ions of cardiomyocytes [2]. However, it is conducted with single cardiomyocytes so assessment of tissue unit is not convenient, and much time and cost are consumed for drug tests. To solve these drawbacks, a number of methods to observe physiology related to the heart's contraction force directly have been attempted. As a typical method, using micropost and cantilever has neen proposed [3-6]. However, since it analyzes displacements using optical microscope images as in the method using microposts, it is difficult to measure in real time or micro-displacements less than several micrometers. Furthermore, polydimethylsiloxane (PDMS) is mostly used as the material of microposts or cantilevers, and it is difficult to achieve miniaturization and mass production. In this study, an SU-8 cantilever displacement measurement system consisting of a laser vibrometer and a micro motorized stage was fabricated and through this system, changes in contractibility were measured according to the cultured day *in vitro*. A sensor having high sensitivity integrated to the purposed SU-8 cantilever arrays is expected to be used in a variety of fields related to high-speed screening.

II. MATERIALS AND METHODS

A. Measurement system for contraction force of cardiomyocytes

To measure the contraction force of cardiomyocytes cultured on the SU-8 cantilever, a laser vibrometer-based micro-displacement measurement system was designed and fabricated. This system measured cantilever displacement and beating frequency in relation to the contractile forces of cardiomyocytes while a laser was irradiated on the reflective plate of the cantilever using a position sensitive photodiode (PSPD) sensor. As shown in Figure 1, the cantilever displacement measurement system consisted of a laser vibrometer that measured micro-displacements, a table-top incubator that maintained well plate temperature, and a motorized stage that measured various samples very quickly. All devices used in the measurement system were controlled via a single program by LabVIEW and could measure SU-8 cantilever arrays rapidly because they used high-precision motor-driven stages. Furthermore, the proposed system could measure displacements and beating frequencies of the SU-8 cantilever precisely with a nano-scale unit. The contraction force of cardiomyocytes can be calculated by substituting measured cantilever displacement, which can be estimated, in a theoretical equation.

B. Cell culture

Ventricles were harvested from one-day old neonatal Sprague-Dawley rats. Cardiomyocytes were digested with 0.4 $mgmL^{-1}$ of collagenase and 0.6 $mgmL^{-1}$ of pancreatin mixed solution from ventricular tissue. The digested solution was separated into cardiomyocyte and fibroblast layers using percoll. The separated layers were pre-plated to prepare high purity cardiomyocytes. Cardiomyocytes were cultured on the

SU-8 cantilever with a density of 1000/mm^2 and media consisting was 67 % Dulbecco's modified Eagle medium (DMEM, LONZA), 17 % Heparin sodium salt from porcine intestinal mucosa (M199, Sigma-Aldrich), 10 % Horse serum (HS, Sigma-Aldrich), 5 % fetal bovine serum (FBS, Sigma-Aldrich), and 1 % penicillin streptomycin (P/S, Sigma-Aldrich). Cardiomyocytes were cultured in an incubator that maintained 37 ℃ and CO_2 at 5 %, and the culture solution was replaced every three days. Cardiomyocytes start beating cultured after 24 hours and synchronization proceed after 48 hours.

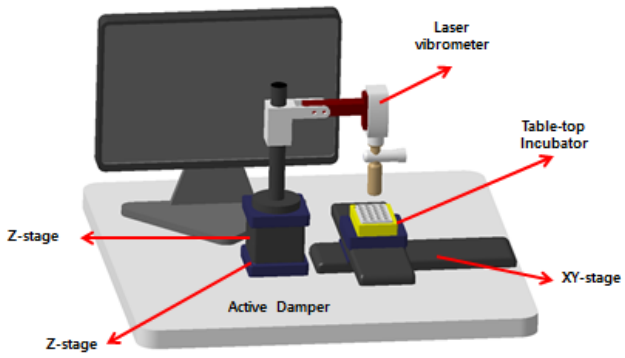

Fig. 1. Schematic of contraction force of cardiomyocytes measurement system.

III. Results

A. Characterization of SU-8 cantilever array

Figure 2 show optical images of Fabricated SU-8 catilever array. Each SU-8 cantilever was 4000 μm length, 2000 μm width, and 20 μm thickness. Each μgroove integrated on a cantilever was 0.8 μm deep and 3 μm wide, and the gap between μgrooves was 3 μm. To measure contraction force of cardiomyocytes, two different type of SU-8 cantilever with and without μgrooves were used. First 1ml of fibronectin (corning) was coated on the SU-8 cantilever for 1hour at room temperature. And then SU-8 cantilever was washed with PBS for removing the left of fibronectin solution.

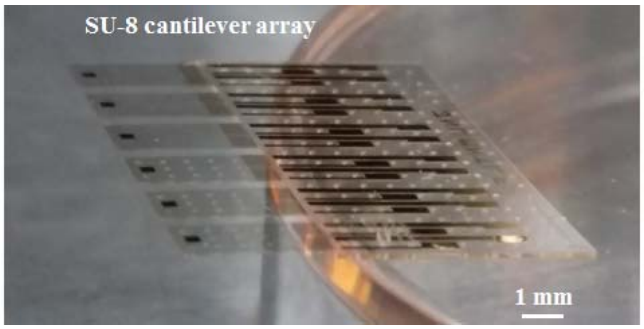

Fig. 2. Fabricated SU-8 cantilever array

B. Preparation of cardiomyocytes and geometric effects on cell alignment

Figure 3 show the characteristics of cardiomyocytes grown on SU-8 with and without μgrooves. Optical image shows cardiomyocytes were alignment along the μgrooves direction and cantilever length direction was caused contraction force. Especially, after 48 hours later made more contraction force due to the beginning of synchronization. We also optimized a pitch distance by employing various microgrooves with pitches ranging from 1 μm to 10 μm and a depth of about 1 μm. In case of SU-8 cantilever without μgrooves cardiomyocytes were grown isotropic, SU-8 cantilever with μgrooves cardiomyocytes were aligned along the μgrooves direction and grown anisotropic.

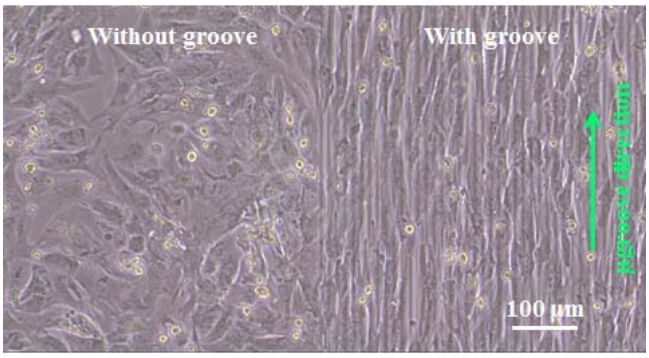

Fig. 3. Formation of confluent cardiac cell monolayer on cantilever.

C. Contraction Force of Cardiomyocytes

The beating of cardiomyocytes started at 24 hours after cell cultivation, and synchronization between cardiomyocytes was conducted at 48 hours after cultivation. The cell contraction force using SU-8 cantilever was evaluated from 96 hours to 10 days after cell cultivation at intervals of 24 hours. Figure 4 shows the displacement of SU-8 cantilever over the cell cultivation time. The test result showed that both the SU-8 cantilevers, with or without μgrooves, had the largest contraction force on the 8th day after cell cultivation. In particular, for the SU-8 cantilever with μgrooves, the contraction force was approximately 2.5 times that of the cantilever without μgrooves. This was because cardiomyocytes aligned in one direction along the μgrooves, thereby contracted anisotropically as shown in the optical microscope images. It is expected that the increased contraction force can increase the sensitivity of the SU-8 cantilever sensor in drug toxicity evaluation.

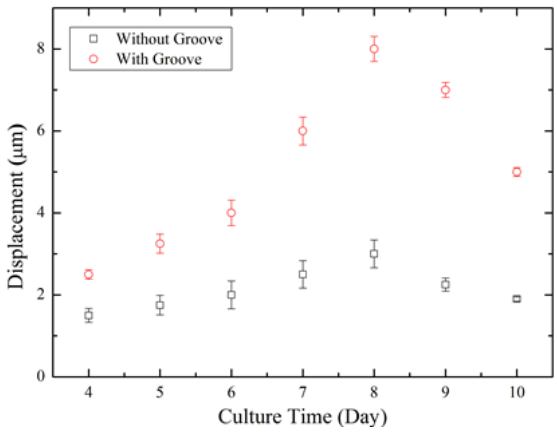

Fig. 4. Change in cantilever displacement from day 4 to day 10.

D. Change in contraction force with respect to drug treatment

A stock solution of Isoproterenol (Calbiochem), Verapamil (Sigma-Aldrich) was prepared by melting in ethanol and dimethyl sulfoxide (DMSO, Sigma-Aldrich) for cell cultivation and stored in a refrigerator whose temperature was maintained at 4°C. A wide range of concentrations of the drug were made by controlling the amount of ethanol, and all drugs used in the test did not exceed their ethanol concentration over 0.1 % [4]. Prior to the drug test, changes in the physiology of cardiomyocytes due to ethanol concentration used for the stock solution fabrication were verified.

To measure the reproducible contraction force of cardiomyocytes, the size of SU-8 cantilever, cardiomyocytes seeding density, and drug processing time were made constant. In the drug test, Isoproterenol, which increased the contraction force of cardiomyocytes, Verapamil, which decreased the contraction force of cardiomyocytes were used. Isoproterenol was injected on day 9 after cell cultivation, and Verapamil was injected on day 6 after cell cultivation. Changes in the contraction force and beating frequency of cardiomyocytes due to drug concentration were measured immediately after drug injection. In the test, the μgroove-integrated SU-8 cantilever was used.

Changes in the physiology of cardiomyocytes with regard to Isoproterenol (0.2, 0.5, 1, 2 μM), which was a β-adrenalin agent, Verapamil (50, 100, 200, 500 nM), which was a Ca^{2+} channel inhibitor are shown in Figures 5-6. Figure 4 (a-c) shows the physiology of cardiomyocytes according to the concentration of Isoproterenol. Displacement of SU-8 cantilever was increased 30% and beating frequency was faster 200% when injected 1μM, such as figure 5-a. The normalized displacement test result is shown in Figure 5-b. As shown in Fig. 5-c heart rate can be obtained the same result.

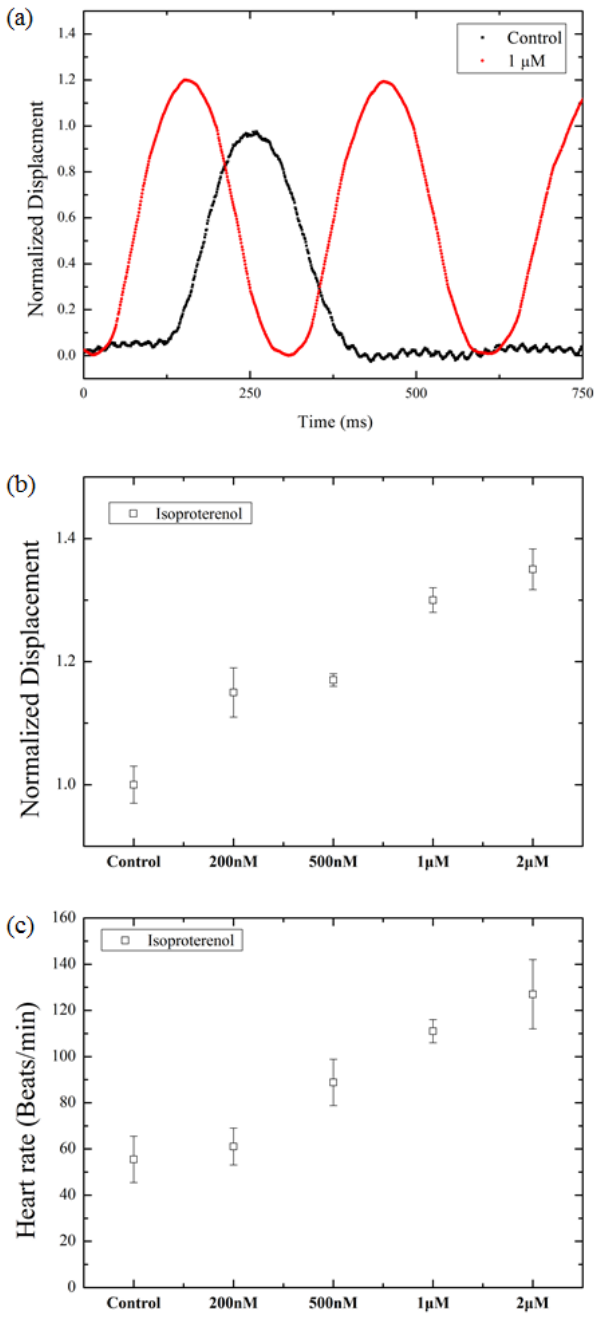

Fig. 5. Mechanical response of cardiomyocytes to Isoproterenol; (a) changes in cantilever displacement as a function of time after treatment with 1 μM Isoproterenol, (b) cantilever displacement as a function of drug concentration, (c) heart rate in accordance with various concentrations of drug.

Figure 6 (a-c) shows cardiomyocytes physiology according to the concentration of Verapamil. Approximately at 500nM concentration of Verapamil cardiomyocytes contraction force was reduced by half, after the new media change was confirmed to retain normal state again. Figure 6-a shows SU-8 cantilever displacement and beating frequency change according to the Verapamil 500nM. The result of experiment shows in figure 6-a, during one cycle cardiomyocytes

contractile time was not significant but beating frequency changed significantly. Figure 6-b and 6-c is a result of cardiomyocytes contraction force and beating frequency change according to concentration of Verapamil.

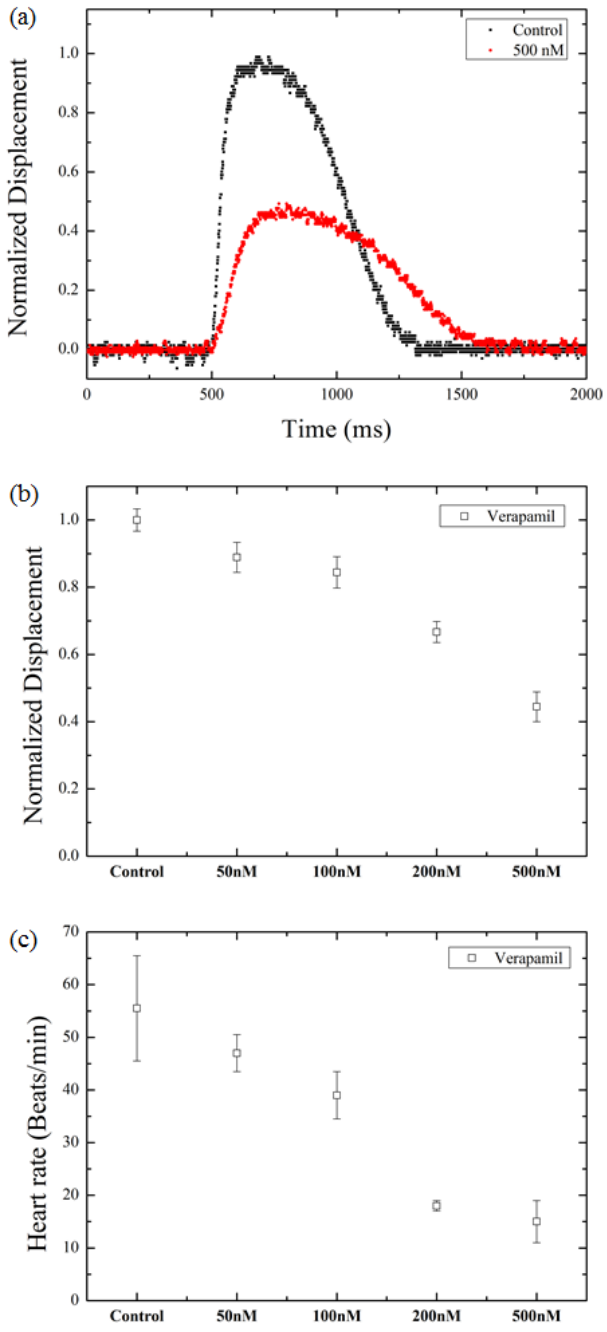

Fig. 6. Mechanical response of cardiomyocytes to Verapamil; (a) changes in cantilever displacement as a function of time after treatment with 500nM Verapamil, (b) cantilever displacement as a function of drug concentration, (c) heart rate in accordance with various concentrations of drug.

IV. CONCLUSION

In this paper we used SU-8 cantilever with μgroove patterns and laser vibrometer system to measure cardiomyocytes contraction force change due to drug treatment *in vitro*. Various SU-8 cantilever with and without μgrooves were produced to confirmed the effect on contraction force of the three-dimensional surface structures on cardiomyocytes, it optimized the structure of μgrooves to maximize the contraction force of cardiomyocytes. SU-8 cantilever was fabricated by using the semiconductor process and has the advantage of miniaturization and mass production is possible. The experimental results show that maximum contraction force of cardiomyocytes in response the culture day, occurred in two different types of SU-8 cantilever were all day 8. The maximum contraction force of cardiomyocytes was 2.5 times enhanced in cantilever with μgrooves compared to the cantilever without μgrooves. This is because the grooves in accordance with the pattern having a three-dimensional shaped cardiomyocytes that were aligned and growth in groove direction. The cardiomyocytes were cultured on SU-8 cantilever that groove had been integrated; various concentrations of Isoproterenol, Verapamil, we analyzed the characteristics of cardiomyocytes with drug treatment. The contraction force was increased 30 % higher and beating frequency was also increased 200 % faster for 1μM Isoproterenol and decreased 56 % lower and 42 % slower for 500nM Verapamil. The proposed SU-8 cantilever arrays with a laser vibrometer based measurement systems can be expected to the novel drug toxicity screening system in future.

ACKNOWLEDGMENT

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