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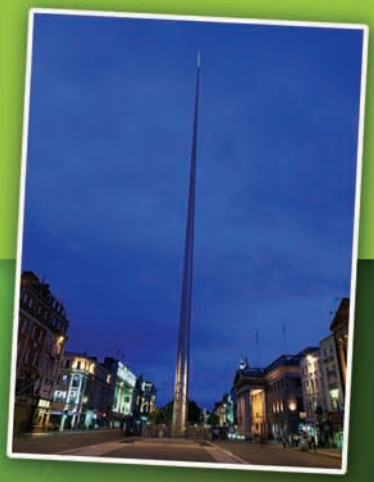

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Biosensors

M156h **BIOLOGICAL ASSAYS PERFORMED ON SUSPENDED DROPLETS**
R. Hernández-Pérez[1], H. Fan[2], and J.L. García-Cordero[1]
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M157h **DISCRIMINATION OF DROPLETS CONTAINING SINGLE CULTURED FILAMENTOUS FUNGAL CELL USING IMPEDANCE SPECTROSCOPY**
N. Sobahi, J. Dai, W.-B. Shim, and A. Han
Texas A&M University, USA

M158h **ELECTRICAL STIMULATOR-INTEGRATED PDMS DIAPHRAGM SENSOR FOR DRUG-INDUCED CARDIAC TOXICITY SCREENING**
Y.J. Jeong, B.-K. Lee, and D.W. Lee
Chonnam National University, KOREA

M159h **GRAPHENE SENSORS FOR DETECTION OF ESCHERICHIA COLI O157:H7**
S. Sando and T. Cui
University of Minnesota, USA

M160h **INTEGRATED PERISTALTIC PUMP FOR PROBING A BIOFILM ONLINE MONITORING SYSTEM**
K. Sachsenheimer, J. Bruchmann, T. Schwartz, and B.E. Rapp
Karlsruhe Institute of Technology (KIT), GERMANY

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J.-R. Lee[1], D.J. Bechstein[1], C.C. Ooi[1], A. Patel[2], R.S. Gaster[1,3], E. Ng[1], L.C. Gonzalez[2], and S.X. Wang[1]
[1]*Stanford University, USA,* [2]*Genentech Inc., USA, and* [3]*Harvard University, USA*

M162h **MULTIPLEXED RESISTIVE PULSE SENSING OF CELLS USING ARBITRARY PULSE SEQUENCES**
R. Liu, N. Wang, C.-H. Chu, and A.F. Sarioglu
Georgia Institute of Technology, USA

M163h **ON-WAFER QUARTZ BASED BROADBAND DIELECTRIC SPECTROSCOPY FOR μL BIOLOGICAL LIQUIDS UP TO 50 GHZ**
J. Bao, S. Liu, I. Ocket, and B. Nauwelaers
KU Leuven, BELGIUM

M164h **QUANTUM DOT-FULLERENE BASED MOLECULAR BEACONS FOR HIGHLY SENSITIVE DNA DETECTION**
Y. Liu, A. Kannegulla, and L.-J. Cheng
Oregon State University, USA

M165h **SINGLE PARTICLES ANALYSIS USING A NANOPORE TRAPPING METHOD**
A. Arima, M. Tsutsui, M. Taniguchi, and T. Kawai
Osaka University, JAPAN

ELECTRICAL STIMULATOR-INTEGRATED PDMS DIAPHRAGM SENSOR FOR DRUG-INDUCED CARDIAC TOXICITY SCREENING

Y.J. Jeong, B.-K. Lee, and D.W. Lee
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ABSTRACT

Herein, we describe in detail the fabrication and evaluation of diaphragm based bio-sensor for cardiac toxicity screening applications. The diaphragm is made by a biocompatible, flexible and optically transparent-polydimethylsiloxane (PDMS) material. The diaphragm sensor can monitor the mechanical physiology of the electrically synchronized cardiomyocytes under the drug effect. The μgrooves structure are formed on the surface of diaphragm sensor to increase the mechanical deformation of the sensor using the alignment of the cardiomyocytes. Further, the gold electrode patterned for external electrical stimulation to bring out the constant synchronous of the cardiomyocytes. The displacement of the diaphragm resulting from the contraction force of cardiomyocytes is measured through the laser displacement sensor. The typical cardiovascular drug, verapamil was selected as treatment agent to test the performance of the biosensor.

KEYWORDS: Diaphragm, Polydimethylsiloxane, Mechanical Physiology, Cardiomyocyte

INTRODUCTION

Cell-based biosensor is an effective method to achieve a drug preclinical assessing. The in vitro cell-based biosensor method can effectively reflect the pharmacological effects in a short period of time as compared to in vivo animal method. Cardiomyocytes are subjected to mechanical stress periodically, therefore the pharmacological study on mechanical properties of cardiomyocytes is an important part for the drug preclinical assessing. Over the years several research have been carried out to quantitatively measure the contractile force of cardiomyocytes to the stimulus of the drug. In continuations of those great efforts, herein we proposes the use of a PDMS diaphragm structure to characterize the contraction force of cardiomyocytes. In order to electrically synchronize the beating of cardiomyocytes in a younger Sprague-Dawley rat the gold electrode integrated into PDMS diaphragm sensor.

EXPERIMENTAL RESULTS

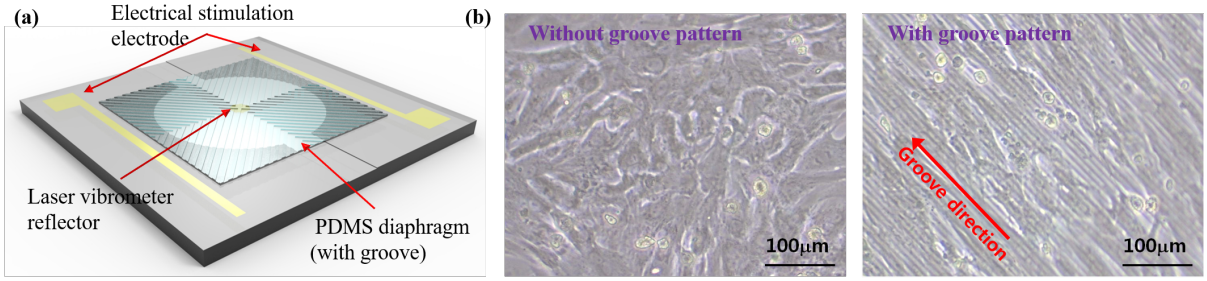

Figure. 1: (a). Schematic illustration of the PDMS diaphragm sensor; (b). Optical microscope images of the cardiomyocytes cultured on with and without μgrooves PDMS diaphragm sensor.

Fabricated stimulator-integrated PDMS diaphragm sensor device is schematically illustrated in Fig. 1(a). The length, width, and thickness of the diaphragm sensor sizes are kept at 19mm(l) × 19mm(w) ×500μm(h), diaphragm diameter is 10mm and the distance between the electrical stimulation electrode is 13mm. Subsequently, the μgroove structures (1μm thick, 3μm line and spaces) are formed on the PDMS diaphragm. A glass body with electrical stimulation electrodes is used for the synchronized beating rate of cardiomyocytes [1]. The mechanical deformation of the diaphragm sensor is measured through the laser based displacement sensor.

A heart is aseptically isolated from a Sprague-Dawley rat . The separated ventricles are washed by using ADS buffer solution, then single cardiomyocytes were acquired through enzyme solution and pre-plating. The acquired cardiomyocytes are then seeded onto the both unpatterned and μ patterned PDMS diaphragm. Figure 1(b) shows the optical microscope images of the cardiomyocytes cultured on PDMS diaphragms with and without μgrooves. The cardiomyocytes cultured on the unpatterned

PDMS diaphragm were grown isotropically. Whereas in the μpatterned PDMS diaphragm, the cultured cardiomyocytes respond to the μpattern features and aligned, grew along the grooves direction. The displacement of the diaphragm caused by the contractile force of cardiomyocytes is measured by using a laser based displacement sensor. After the cell culture, the maximum displacement of the μpatterned PDMS diaphragm and the un-patterned PDMS diaphragm sensor is observed on day 9. The μpatterned PDMS diaphragm sensor shows the maximum displacement which is ~310% higher than the unpatterned PDMS diaphragm sensor. The beating condition of cardiomyocytes is controlled through the external electrical stimulation by using square monophasic pulses (2ms duration, 0.5 Hz, 2V amplitude). Figure 2(a) shows the displacement of the μpatterned PDMS diaphragm sensor before and after electrical stimulations.

The typical cardiovascular drugs, Verapamil is a calcium channel inhibitor and prevents the calcium influence into the cell, thereby decreasing the contraction force of the cardiomyocytes. To evaluate the effect drug treatment on the contraction force of cardiomyocytes, different concentrations of verapamil (100 nM, 500 nM, and 1 μM) were added into the culture medium. As displayed in Fig. 2(b) the displacement of the μpatterned diaphragm sensors decreases with increasing the concentration of Verapamil. The displacement of the diaphragm decreased ~51.3% compared to the control state at a concentration of 1μM verapamil. This could be attributed to the serious side effects of drugs on cardiomyocytes over a certain level of concentration. The preliminary experimental results clearly showed that the fabricated μpatterned diaphragm cardiomyocyte biosensor can verify the drug side effects through beating status of the cardiomyocytes.

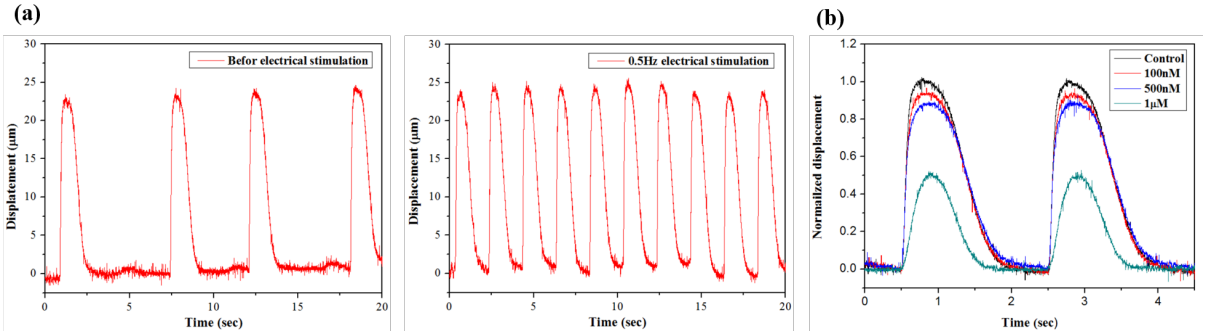

Figure 2: (a) real time displacement measurement of the PDMS diaphragm sensor at day 9 before and after electrical stimulations; (b) normalized displacement of PDMS diaphragm toward different concentration of Verapamil.

CONCLUSION

In this study, we present a PDMS diaphragm based cardiomyocyte biosensor for quantitatively measure the contraction force of cardiomyocytes in real time. The feasibility of the fabricated biosensor were demonstrated by measuring the changes in the mechanical physiology of electrically synchronized cardiomyocytes under the different concentration of Verapamil. The mechanical deformation of the PDMS diaphragm decreases with increasing the Verapamil concentrations. The preliminary mechanical physiology test results proved that the fabricated PDMS diaphragm sensor can effectively evaluate the drug side effects through beating status of the cardiomyocytes in the short term and in the long term.

ACKNOWLEDGEMENTS

This work was supported by the International Collaborative R&D Program through a KIAT grant funded by the MOTIE (N0000894) and the National Research Foundation (NRF) grant (Nos. 2015R1A2A2A05001405).

REFERENCES

[1] N. Tandon, C. Cannizzaro, P. H. G. Chao, R. Maidhof, “Electrical stimulation systems for cardiac tissue engineering” Nature Protocols, 4, 155-173, 2009.

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