DESIGN OF OPTO-MECHANICAL MICRO TRANSCUCER FOR CELL CULTURE AND IN PLANE FORCE MEASUREMENT

Xiaoyu Zheng [1] and Xin Zhang[1]
[1]Department of Mechanical Engineering, Boston University, Boston, MA, 02215, USA

ABSTRACT
This paper presented a high sensitivit√ opto-mechanical transducer for real time cell culture and contractile force mapping on a chip. The contractile forces developed from cells to their extracellular matrix is crucial to understanding how cells regulate their ph√siological function to adapt to their living environment and cellular processes. The structure consists of micro fabricated pol√mer sensor arra√s that served as diffraction moiré grating lines and grids for supporting and culturing cells. Through carrier fringe anal√sis, the phase changes on moiré patterns with cell culture can provide real-time mapping of cell traction forces evolution without measuring the distortions on the substrates.

KEYWORDS
PDMS, OPTO-MECHANICAL, CELL TRATION FORCE

INTRODUCTION
Cells are complex entities in that they not only sense chemical cues, but also interact with their living environment mechanically for cell division, growth, phagocytosis, apoptosis, and migration. They respond to stimuli whose effects may be beneficial (e.g., in natural or engineered nutritive microenvironments) or harmful (e.g., in aging, stress, or injury) to human health [1-2]. These biomechano transductions, expressed in physical terms as cellular forces, usually ranged from pN to μ N, is critical in developing micro/nano implantable tissues and scaffolds, and sensors and medical devices that are able to sense and regulate the biophysical property of living cells, diagnostics of abnormal cellular and subcellular behaviors. We have previously demonstrated a method for cell traction force measurement based on optical moiré effect [3]. In summary, the employed interferometric moiré offers precise and high-resolution moiré mapping. This technique takes the advantage of moiré magnification effect by calculating the moiré fringe distortions and map into the distortions of polymeric periodic substrate. However, optical alignment added difficulty for achieving on-chip compact moiré system for real-time observation of cell contractility. In addition, the method used for retrieving force distribution was based on geometric fringe centering approach, which prevents further automation of the system into laboratory use. In this paper, we extend the moiré mapping mechanism to a versatile cell contraction force mapping transducer by the integration of two periodic substrates.

EXPERIMENT
The double layered device is made from two PDMS layers that are aligned to form a 3D chip, consisting of channels and reference gratings (top half) and pillars (bottom half); see Figure 1. The inlet channels are 370 μm in width, and the micropillars are 5 μm in diameter, double spaced. The pillar height depends on the thickness of the photoresist template, which is contingent upon the spin parameters used to coat the glass substrate. The layers are fabricated using photolithographic methods, although the specific steps are different for the channel and pillar components of the chip. This technique extends the moiré mapping mechanism to a versatile cell contraction force mapping transducer by the integration of two periodic substrates.

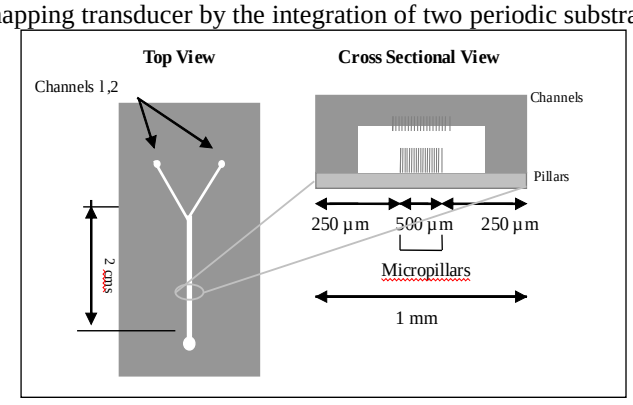

Figure 1. Design of opto-mechanical moiré transducer, top layer consists of reference gratings, bottom layer consists of micropillar array for contraction measurement.

The calibration of the system was performed by recording interference fringe patterns at successive sample

978-0-9798064-5-2/μTAS 2012/$20©12CBMS-0001

heating times and by repeated application of the Fourier-transform-based fringe pattern analysis method for phase retrieval (Figure 2). The fringe patterns were recorded at a temperature step increase ΔT=10 ºC, digitized into a 512 by 512 pixel array in the horizontal and vertical directions, and Fourier processed in order to compute the corresponding phase change. The calculated CTE agrees with existing literature values (310ppm/°C). Taking advantage of this linear relationship between phase and displacements field, the moiré fringes automatically serve as contour maps of distortion field caused by thermal heating without individually tracking and deriving the displacements.

The experimental setup for our compact 2D moiré mapping system includes an illumination source of 1.5-mW 633-nm He-Ne laser (Research Electro-Optics Inc.), a beam expander, a charge-coupled device (CCD) video camera (Pixelink 623), an inverted microscope (Nikon), a digital computer with MATLAB programs for automated moiré fringes analysis. The cell culturing substrate was sealed into a polycarbonate flow perfusion chamber with an internal volume of 30 mL. A cell culture media with cardiac myocytes were injected through the inlet of the perfusion chamber with the culturing substrate. Testing marks on the sidewalls were designed to locate the periodic features and relative orientation between the two substrates. The glass environmental chamber is maintained at 37.2 ºC with 5% CO2 concentration.

Figure 3(a)-(f) illustrates fringe processing schemes for retrieving the lateral deformation on cardiac myocytes. Figure 3(a) estimates the background non-uniform intensity by a combination of dilation and erosion. Dilation enlarges the edges of bright objects and erodes dark ones while erosion erodes the edges of bright objects, and enlarges dark ones. Figure 3(b) illustrates the constructed elements by following a combination of dilation and closing by a 2X2 square elements of the image. Subtracting the image of Figure 3(b) from Figure 3(a) will give the final moiré fringes with background element removed (Figure 3(c)). Fringe will be enhanced by low pass filter

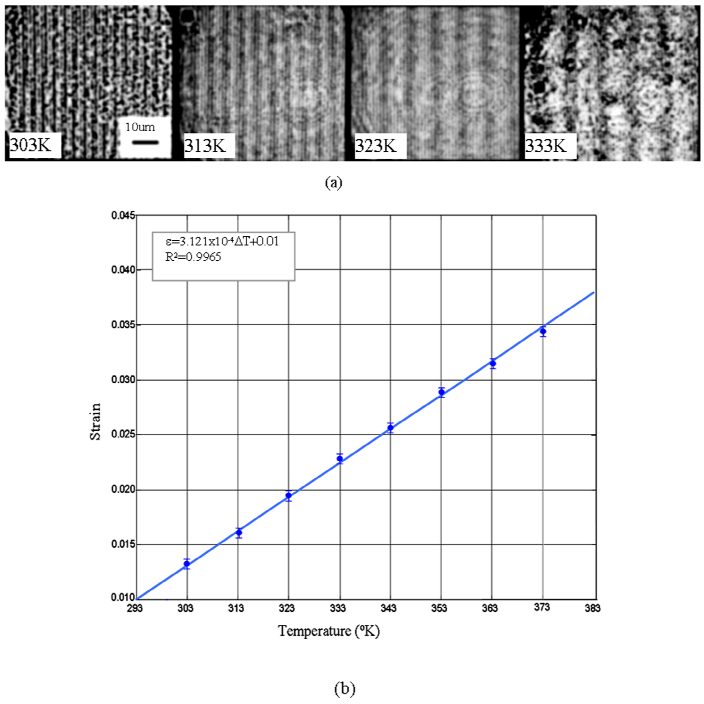

Figure 2. Calibration of moiré fringes by iso-thermal heating of PDMS substrate.

and compared with reference fringe prior to cell contraction. The final deformed fringe was shown in Figure 3(f) which serves as direct contours of cell contractions exerted on periodic substrate.

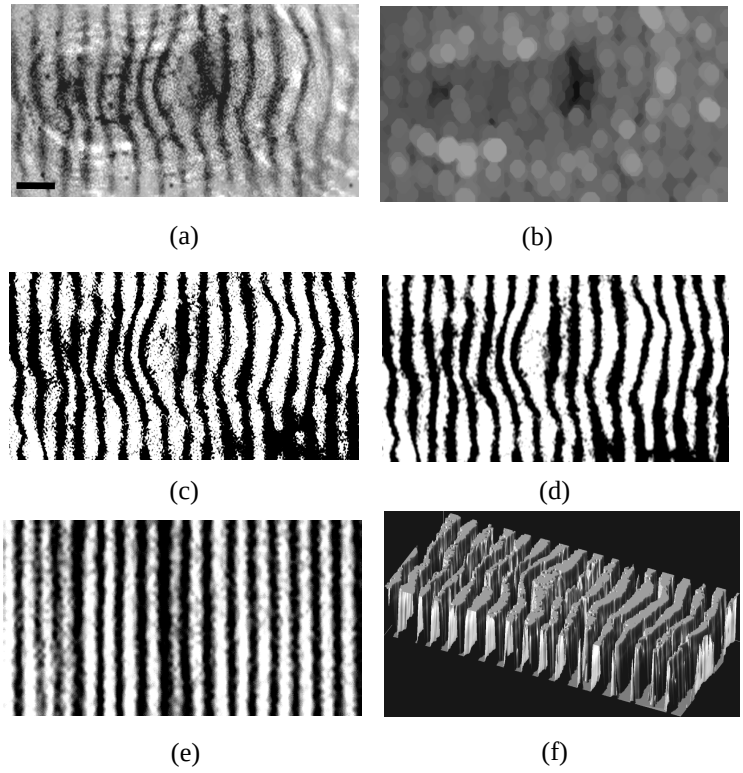

Figure 3. (a)-(f) Fringe Processing scheme of cardiac myocytes contraction and isolation of deformed fringes. Scale bar represents 8 μm.

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ACKNOWLEDGEMENT

The authors would like to acknowledge CMMI-0826191 and ECCS-0901702 for performing this work.

CONTACT

Xiaoyu Zheng, raynexzheng@gmail.com; Xin Zhang, xinz@bu.edu