**A NOVEL VERSATILE BIOMECHANO SENSOR FOR REAL TIME VASCULAR CELL CONTRACTILITY MAPPING**

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**ABSTRACT**

We herein describe a novel versatile biomechano-sensor for vascular cells contractility study. The chip consists of arrays of microfabricated structures and gratings confined within large sidewalls for cell alignment and cellular traction force measurement, resembling in-vivo environment. Since our approach requires neither the tracking/monitoring nor the visibility of each individual sensing unit, we anticipate that this method will increasingly find more applications for a variety of cell mechanics study. In this paper, we demonstrate the adaptation of the chip for cardiac myocyte and vascular smooth muscle cells (VSMCs) contractility mapping.

**KEYWORDS:** Vascular smooth muscle cells (VSMCs), Moiré, Cell contraction force

**INTRODUCTION**

Recently, micro and nano fabricated polymeric substrates have been introduced for measuring cell traction forces [1-2]. These methods introduce a local determination of the traction forces upon discretelized adhesion areas between the cells and their underlying polymeric substrates. In those techniques, the discrete displacement vectors are derived by tracking and monitoring deflections of each individual microstructure. However, these methods require intensive computation and expertise to track and derive the displacement fields. Moreover, with the fixed numerical aperture of the objective lens, the deflection or motion of individual sensing unit is often in the range of sub-micrometers. Tracking such deflection or motion of each individual high-density micro structure is time-consuming, and thus cannot meet the demands for real-time monitoring of cellular and subcellular behaviors. In this paper, we propose a novel optical moiré fringe mapping system for cell traction force measurements based on periodic polymeric substrates (PPS) which were designed and fabricated by us.

**THEORY**

The PDMS micropillar arrays were embedded between large sidewalls for cell alignment (Figure 1). A polycarbonate flow perfusion chamber is sealed under the chip. The same chip with imbedded pillars with aspect ratio of 1:3 was mounted on a rotational stage parallel to the first substrate. Diffraction moiré patterns can be generated by illuminating coherent beam via two parallel grating lines or grids. The
grating lines served as reference gratings for diffraction moiré pattern generation in (0,1,0) or (1,0,0) direction whereas 2D moiré fringes can be formed via two parallel imbedded pillars (Figure 1(b)).

EXPERIMENTAL

We investigated the regulated beating of aligned cardiac myocytes in response to ISO perfusion. Cardiac myocytes spread over along the channels and the myofibrillar proteins reorganize adapting to the local extracellular environment. The periodic pillars interact with grating lines on the reference chip to form moiré pattern that magnifies distortion along the longitudinal direction. The distortion of the moiré pattern was measured in its contractile and relaxation state, respectively. We then rotated the reference chip by an increment of 5° and measured the distortion of the moiré pattern and plotted on Figure 1. Via the magnification factor of the corresponding orientation, the deformation of the corresponding imbedded pillars was mapped. For relaxation and contraction, the real deformation on the imbedded pillars fall approximately on two different levels, suggesting good agreement between the moiré map and the corresponding pillar deformation map.

By translating the reference chip so that the two periodic pillar arrays serve as two parallel diffraction gratings, the moiré pattern will be in both (0,1) and (1,0) directions. We mapped the self spreading and contractility of human aortic smooth muscle cells (Ao184) in DMEM. As the VSMCs spread out, the moiré patterns changed (Figure 2) from regularly distributed to locally distorted, and further resembled a natural centrifugal pattern, revealing the concentric profile of the traction forces developed on the substrate (Figure 3). In contrast, after changing the media to DMEM without serum starting from the 12th hour, we observed a relative shrinking of the moiré pattern and the corresponding force evolution map is illustrated on Figure 3. The moiré fringes evolution in Figure 2 confirmed with that, by culturing VSMCs in serum, the cytoskeleton increases its stress state in medium containing serum until it is stressed and spread out, whereas in the absence of serum, the distortion area in the
moiré pattern decreased which corresponds to a decrease in the cell-substrate adhesion areas and the decrease in the cytoskeleton stress.

Figure 2. Moiré pattern evolutions in VSMCs culture for 0, 4, 8, 12, 18, 24 hours, respectively. From the 12th hour, the cells were deprived of serum.

CONCLUSIONS

We demonstrated that by characterizing the moiré pattern to the desired dimensions and orientations the diffracted moiré pattern introduces a real-time force evolution map of living cells cultured on the polymer periodic substrates. Such optical moiré system can be readily employed to study migration, morphology, motility and many other cell-substrate mechanical interactions on patterned polymer substrates.

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REFERENCES
