AN INTEGRATED FIBER-OPTIC MICROFLUIDIC DEVICE FOR DETECTION OF MULTICELLULAR ORGANISM MECHANICS

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ABSTRACT

A fiber-optic microfluidic device is developed to detect muscular force generated by a nematode worm. The device integrates a single mode (SM) emitting fiber cantilever, a multimode receiving fiber, and a sinusoidal microfluidic channel. The channel is open at multiple troughs and the SM fiber is horizontally placed adjacent to the channel. As a nematode worm swims through the channel, it contacts and deflects the SM fiber, causing to change optical coupling efficiency from the SM to the multimode fiber. The device is capable of detecting worm muscular forces at different troughs of the channel. Multiple force data can be used to verify each other, improving data accuracy and reliability. The minimal detectable muscular force of the device is 0.23 μN .

INTRODUCTION

Movement of multicellular organisms such as non-pathogenic nematode *Caenorhabditis elegans* exhibits a sinusoidal pattern, induced by contraction and local bending of cuticle [1]. Study of multicellular organism mechanics is critical for understanding how signals in the neuromuscular system give rise to behavior and how force-sensing organs and sensory neurons work [2]. While many excellent micro-electro-mechanical systems approaches have been developed for sorting, transferring, stimulating, phenotyping, imaging, and screening of *C.elegans* [3,4], study of multicellular organism mechanics has currently lagged far behind that of cell mechanics. Recently, a piezoresistive cantilever system was developed to analyze muscular force of *C.elegans* [5], but this microsystem was not able to detect dynamic force of a moving *C.elegans* nematode. The use of an array of polymeric micropillars overcome this problem [6], but a high resolution and fast speed microscope was required to record dynamic displacement of the pillars. Also, a strain gauge force microsensor was constructed from multiple layers of SU-8 and metal on quartz substrates [7], but substantial room exists for improving force detection resolution and reducing complexity in device structure and fabrication.

DEVICE DESIGN AND PRINCIPLE

Figure 1 presents the integrated fiber-optic microfluidic device for detecting muscular force generated by a nematode worm. A sinusoidal channel is designed wide enough to allow the worm to move freely, having a minimal physical constraints on the worm's natural movement. A SM optical fiber (10- μm diameter and 1-mm long) is horizontally placed adjacent to the sinusoidal channel. The SM fiber accepts input light at a wavelength of 1310 nm. One end of the SM fiber is anchored, while the other end is free to move. The central axis of the SM fiber is aligned with the central axis of a receiving multi-mode fiber (65- μm diameter) embedded in the device. Multiple troughs of the sine-wave channel provide multiple force detection points, where body contact of a worm with the SM fiber causes to displace the SM fiber away from its original position. This, in turn, reduces optical coupling efficiency from the SM fiber to the multi-mode fiber, and thus, decreasing the transmitted light power received by a detector. Thus, the device can detect muscular forces generated by the worm

at different locations along the SM fiber and at multiple time instances in a dynamic manner. These force data can be used to verify each other, largely improving data accuracy and reliability. Furthermore, the horizontal placement of the SM fiber allows us to take full advantage of the high aspect ratio of the fiber (~ 100), leading to a sensitive response of the fiber to a small force applied normal to the fiber.

Figure 2a shows simulated linear relationship between normal force F applied to the SM fiber at two different detection points of the device and vertical displacement Δx at the tip of the SM fiber. Figure 2b shows geometric change of the SM fiber under a normal force (9.16 μN) applied at the two detection points. In addition, finite-difference time-domain method is used to compute changes in normalized light intensity detected at the multi-mode fiber, as a function of Δx (Fig. 2c). By combining Figs. 2b and c, we build up a relationship between an applied normal force and a change in normalized light intensity detected.

Figure 1: Optical image of the fiber-optic microfluidic device for measuring force generation of a nematode worm.

Figure 2: (a) Simulated relationship between applied forces and deflections at the tip of the SM fiber. (b) Computed deflection of the SM fiber under 9.16 μN applied to the left and middle detection point. (c) Computed normalized optical intensity as a function of deflection at the free end of the SM fiber. (d) Computed force as a function of normalized optical intensity.

RESULTS AND DISCUSSION

Figure 3 describes device fabrication processes. Multiple detection regions are formed along the emitting fiber. Parasitic *Oesophagotomum dentatum* is used as a model nematode (approximately 20- μm diameter and 350- μm long).

Figure 3: Schematic of fabrication process for the device. (a) A PDMS open channel is formed using soft lithography technique. (b) A multi-mode fiber (CPC6, Corning) and a SM fiber (SMF-28, Corning) are pre-thinned down to 65 μm diameter using buffered hydrofluoric acid (HF) solution (49 wt%). They are then inserted into two aligning slots on two sides of the channel. (c) The channel is filled up with a precursor solution consisting of isobornyl acrylate (IBA), tetraethylene glycol dimethacrylate, and 2,2-dimethoxy-2-phenylacetophenone (weight ratio 32:1.7:1). (d) The mixture solution is polymerized under UV light to protect the fibers being etched in the following etching process. (e) Buffered HF solution (10%) is used to remove the cladding layer of the SM fiber. (f) The device is capped with a glass slide through oxygen plasma surface treatment.

Figure 4 shows time-lapse images for the bending emitting fiber ($\lambda = 1310 \text{ nm}$), as an *O. dentatum* nematode worm squeezes through the middle detection point (Fig. 1). The maximum deflection at the free end of the fiber caused by the worm movement is about 6.9 μm . The corresponding optical intensity change is 38.3 %, showing a good agreement with the simulation result (Fig. 2). The resulting force generated by the worm is 9.23 μN .

Figure 4: Time-lapse images as a worm interacts with the SM fiber at the middle detection point (see Fig. 1) during force measurement. (a) $t = 30 \text{ s}$, and (b) $t = 35 \text{ s}$.

Figure 5 shows that as the worm swims downstream, the tight interaction with the left detection point results in light intensity change of 90.4 %. The corresponding force signal is 8.94 μN , which is almost similar to the force signal obtained at the middle detection point, demonstrating a high reliability and validity of the present detection method. As shown in the optical measurement result, the background noise intensity is at a level of 2.5 % of the maximum optical signal. The minimal detectable force or the

sensing resolution of the device is determined by the signal-to-noise (S / N) ratio of the detector used, and is calculated as two times the noise floor intensity. A light intensity drop of 5 % from the maximum intensity corresponds to a deflection of 0.48 μm at the tip of the SM fiber and thus a normal force of 0.23 μN at the first detection point on the left and 0.64 μN at the second one in the middle of the device. We note in Fig. 2c that the light intensity is almost saturated at a low level of 3% of the maximum intensity when the SM fiber deflects beyond 25 μm from the horizontal direction. Thus, larger bending of the fiber caused by worm-fiber interactions cannot be detected. According to Fig. 2d, the detection range of the device is up to 12.31 μN and 33.53 μN at the first the second detection point of the channel.

Figure 5: Normalized light intensity received at the multi-mode fiber as a function of time. Two obvious dips demonstrate the significant influence of fiber deflection on reducing optical coupling efficiency from a SM to a multi-mode fiber. Light wavelength used here is 1310 nm.

CONCLUSION

The integrated fiber-optic microfluidic device offers a simple and effective scheme to measure muscular force of a nematode worm. The method does not involve using complex device structures or a microscopic imaging and recording system. This work can potentially be beneficial to better understand force-sensing organs and neurons of multicellular organisms.

REFERENCES

- [1] R. Waterston, "Genome sequence of the nematode *C. elegans*: A platform for investigating biology," Science vol. 282, 1998, pp. 2012-2018.
- [2] C. Cronin, J. Mendel, S. Mukhtar, Y.-M. Kim, R. Stirbl, J. Bruck, and P. Sternberg, "An automated system for measuring parameters of nematode sinusoidal movement," BMC Genetics vol. 6, 2005, pp. 1-19.
- [3] K.H. Chung, M.M. Crane, and H. Lu, "Automated on-chip rapid microscopy, phenotyping and sorting of *C. elegans*," Nat. Methods vol. 5, 2008, pp. 637-643.
- [4] N. Chronis, "Worm chips: Microtools for *C. elegans* biology," Lab Chip vol. 10, 2010, pp. 432-437.
- [5] S.-J. Park, M.B. Goodman and B.L. Pruitt, "Analysis of nematode mechanics by piezoresistive displacement clamp," PNAS vol. 44, 2007, pp. 17376-17381.
- [6] A. Ghanbari, V. Nock, W. Wang, R. Blaikie, J.G. Chase, X.Q. Chen, and C.E. Hann, "Force pattern characterization of *C. elegans* in motion," Proc. 15th International Conference on Mechatronics and Machine Vision in Practice, 2008, pp. 634-639.
- [7] J.C. Doll, N. Harjee, N. Klejwa, R. Kwon, S.M. Coulthard, B. Petzold, M.B. Goodman, and B.L. Pruitt, "SU-8 force sensing pillar arrays for biological measurements," Lab Chip vol. 9, 2009, pp. 1449-1454.