In Vivo Optical Control of Spinal Cord and Muscle Function with Polymer Fiber Probesbes

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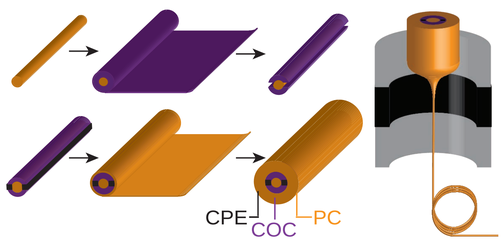
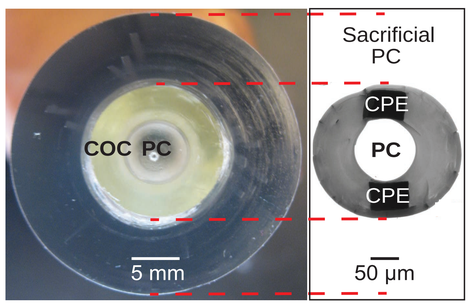
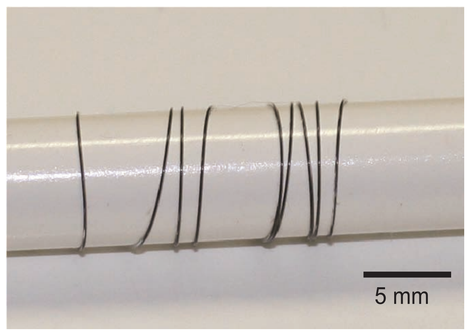
Introduction

Restoration of sensory and motor functions in paralyzed patients requires tools with simultaneous stimulating and recording functions. However, the flexible and fibrous geometry of spinal cord and the repeated deformation during normal motions really create technical barriers to have such tools. To address the technical challenges, we develop highly flexible fiber probes consisting entirely of polymers for combined optical stimulation and recording of neural activity. Combining with optogenetics, we apply the fiber probes in the spinal cords of the transgenic mices expressing the light sensitiveion channel, channelrhodopsin 2 (ChR2), and observe the neural activity and limb movements evoked by the optical stimulation.

Methods







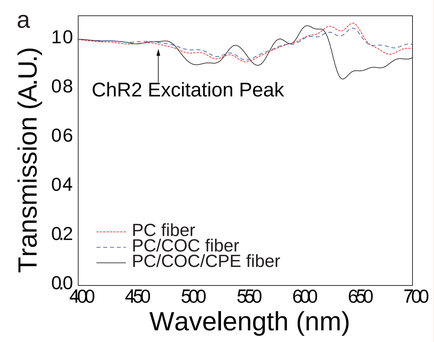
Thermal Drawing Process:

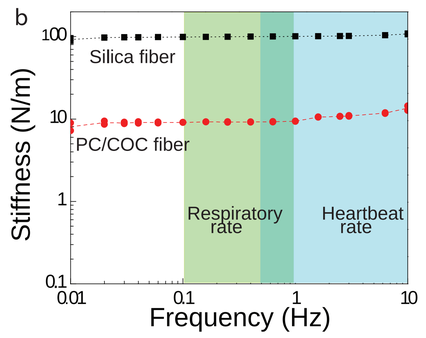
- processing multipule materials simultaneously (Fig. Upper Left and Table)
- creating arbitrarily long device with single process
- Gdraw donw ratio up to 100x (from cm to μm, Fig. Mid. and Bottom Left)

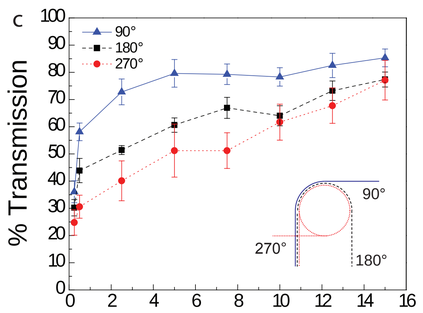
Material Characteristics:

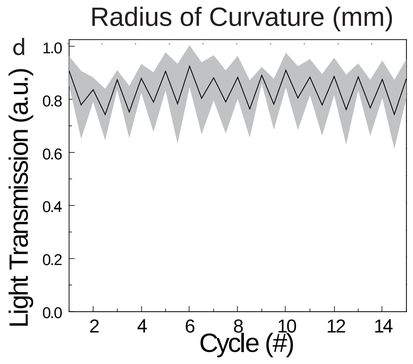
- transparent at λ = 473 nm (excitation peak of ChR2, Fig. a)
- >10x less stiff than silica fiber (Fig. b)
- functional at various bending angles and radii of curvature (Fig. c)
- performance of light transmission does not degrade after multiple cycles of bending (180 rad. of curvature =2.5 mm, Fig. d)

Material	Polycarbonate (PC)	Cyclic Olefin Copolymer (COC)	Conductive Polyethylene (CPE)
Transition Temperature (^{0}C)	145 (T_g)	158 (T_g)	120 (T_m)
Refractive index	1.58	1.52	N/A
Conductivity	N/A	N/A	~10^3 S/m
Function	Waveguide	Cladding	Electrode







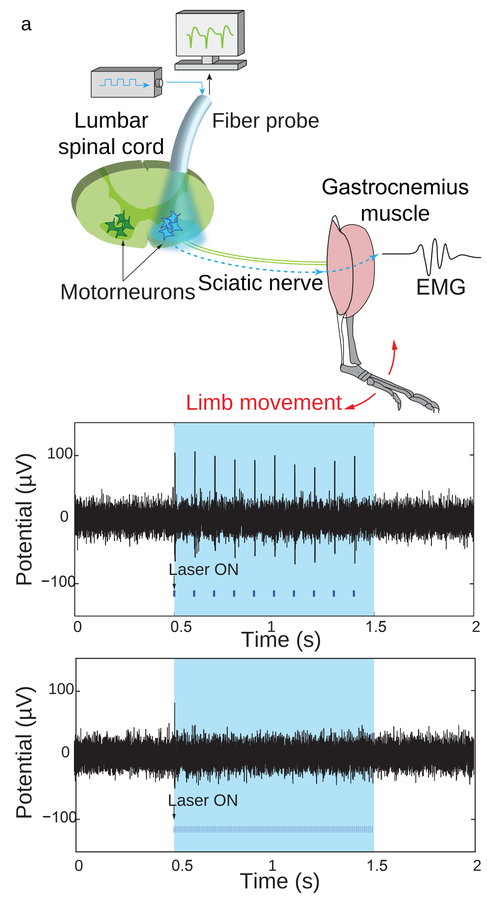


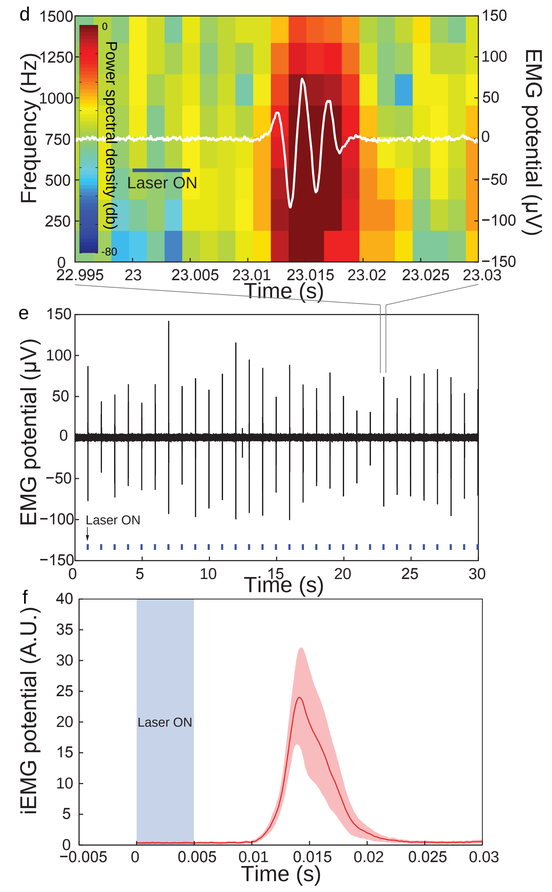
Results

The fiber probes were applied in the lumbar spinal cord of transgenic Thy1-ChR2-YFP mice expressing ChR2 across the excitatory nervous system (Fig. a).

Neural activity was robustly evoked by laser pulses (473 nm, 32 mW/mm^2, 5 ms pulse width, 10 Hz, 1 s epochs, 5 s interval) and recorded within the same device (Fig. b). Stimulation at 100 Hz was done to confirm the physiological nature of the optically evoked activity (Fig. c).

EMG was performed to quantify the optically evoked muscle activity recordings during 120 s of 1 Hz optical stimulation with 5 ms pulse width (Fig. 5d and e). The average envelopes of the EMG waveforms across trials were temporally correlated to laser pulses with a time delay of 10.6±2.3 ms (mean ± s.d.) (Fig. f).





Conclusions

- We successfully applied a fiber drawing process to a materials set consisting exclusively of polymers for simultaneous optical stimulation and electrical neural recording in the spinal cord in vivo.

- Our fiber probes exhibit low optical losses and maintain their functionality at deformation angles up to 270°, radii of curvature as small as 500 μm, and following repeated loading.

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