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Low coherence interferometer for sensing retardance change during neural activity

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***Abstract*—A variety of optical measurements, including retardance/birefringence change, have revealed transient optical and structural changes associated with action potential propagation. Those changes can be understood better by developing new techniques and improving the current approaches. To detect transient retardance changes in a stimulated nerve, we propose a differential phase technique utilizing two orthogonal polarization channels of a polarization-maintaining fiber based interferometer. The superior sensitivity of the system (10.4 pm) is promising to achieve a non-contact optical measurement of action potential propagation in reflection mode, and to study the transient retardance changes during neural activity.**

I. Introduction

Action potential (AP) propagation in nerve fibers is accompanied by temporary alterations in structural and optical properties of the fiber. The signs of neural activity (i.e. AP propagation) that can be detected optically include changes in absorption, birefringence, optical rotation, fluorescence, light scattering, and volume changes [1]. Biochemical and structural changes contributing to these signals may include molecular reorientations in the membrane, influx and outflux of ions, and change in axon diameter. Studying these changes with better optical techniques is expected to enhance understanding of the underlying biochemical processes during neural activity.

Cohen *et al.* demonstrated light scattering and birefringence changes during activity with nerve bundles from walking legs of crabs and squid giant axons [2]. Tasaki *et al.* reported fluorescence, scattering and birefringence changes with nerve trunks from the legs of lobsters and spider crabs, and with squid fin nerve [3]. Although these signals indicate optical and structural changes in the functioning nerve, the techniques utilized for the studies do not produce depth-resolved information about the activity.

Many studies reported in literature used a common optical setup to measure relative light intensity change ($\Delta I/I$), which was interpreted as a retardance change (ΔR) in the nerve with low retardance (R) during AP propagation, $\Delta R = 0.5R(\Delta I / I)$ [4]. The retardance is the product of birefringence and thickness. The optical setup employed for the measurement consisted of two crossed-polarizers, and the nerve under study was placed between these components at 45°. Because the detector was placed behind the nerve, this was a transmission-mode measurement [2, 3]. When probing the edge of the squid giant axon, ΔR in response to stimulation was calculated to be 0.56 pm [4]. Higher ΔR values have been reported for nerve bundles; i.e. 41 pm for pike olfactory nerve containing about 4 million axons with average diameter of 0.2 μm [5].

Optical interferomety exhibits high sensitivity and operate in reflection-mode. It offers depth-resolved information with the use of low-coherent light sources. Because the light source and detector are on the same side of the nerve, the interferometric techniques have the additional advantage of being less invasive than many other optical techniques.

In this paper, we propose a low coherence interferometer potentially capable of measuring retardance change during neural activity. The interferometer is constructed with polarization-maintaining (PM) fibers and PM fiber components, and differential-phase measurement between its orthogonal polarization states yields superior sensitivity. The potential of the system originates from its low noise floor, and the reflection- and transmission-mode cross-polarized light intensity changes measured in pike olfactory nerve besides the numbers reported in literature.

II. Cross-polarized intensity measurements

A. Method

The olfactory nerve is dissected from a freshly sacrificed northern pike (*Esox lucius*) under a dissection microscope, and kept immersed in pike saline during the experiment. The ends of the nerve are tied with silk threads for easy positioning of the nerve in a nerve chamber shown in Fig. 1(a). The chamber body is made from acrylic glass. Platinum electrodes are fixed to the body for electrical stimulation and recording. The groove and the reservoirs of the chamber keep the nerve in contact with pike saline. Petroleum jelly is used to form an electrical insulator between the electrodes. The optical measurement is made through a glass window between the recording electrodes. An isolated pulse stimulator was used to apply current pulses to create APs. The externally recorded compound AP was amplified by an AC differential amplifier, and recorded by a 12-bit data acquisition card simultaneously with the optical signals.

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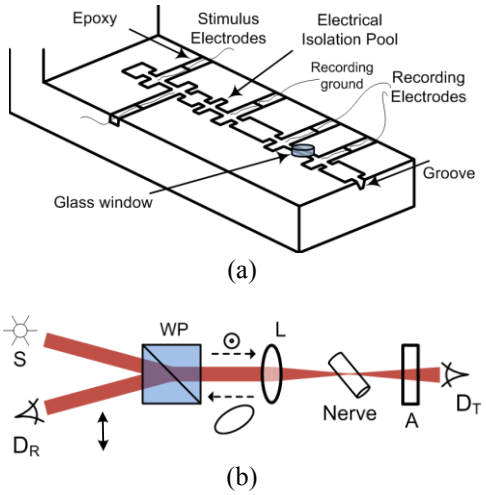


Fig. 1. (a) Nerve chamber, (b) Optical setup used to measure cross-polarized light intensities during AP propagation. S: light source, WP: Wollaston prism, A: analyzer, D_T: transmitted light detector, D_R: reflected light detector. Dotted arrows show direction of light.

Figure 1(b) shows the optical setup used in the experiment. Two milliwatts of light from a super-luminescent diode (center wavelength: 856 nm; bandwidth: 32 nm) enters to a Wollaston prism at the prism's divergence angle; so that the prism transmits linearly polarized light. An achromatic lens (focal length: 35 mm) focuses the beam to a 36 µm spot on the olfactory nerve. The nerve is placed at 45˚ with respect to the incoming polarization state. A cross-polarizer (analyzer) is aligned behind the nerve to minimize the light intensity detected by a large area detector (D_T). Light backscattered/reflected from the nerve is collected by the same focusing lens and split into two orthogonal linear components by the WP. The cross-polarized component is detected by the detector D_R.

B. Results

Figure 2 shows the compound AP (a), and the cross-polarized light intensity changes ($\Delta I/I$) in transmission (b) and reflection geometries (c). The stimulus (2 mA, 5 ms) is presented at the beginning of the recording. Fifty records are averaged for each trace to improve the signal to noise ratio. The traces have a bandwidth of 150 Hz. The minute intensity changes clearly correspond to the AP arrival to the optical measurement area. The transmission mode intensity change we measured is comparable to the value (1.7×10^{-3}) reported in literature [5]. The scale bar for the $\Delta I/I$ measurement in reflection geometry, Fig. 2 (c), may be inaccurate, because reflection of source light from the front surface of WP was not taken into account for the dc (I) measurement.

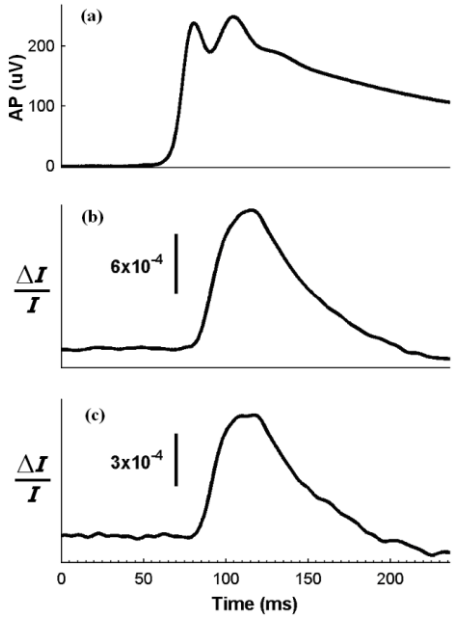


Fig. 2. Compound AP of an olfactory nerve of pike (a), and cross-polarized intensity changes in transmission (b) and reflection (c) geometries

III. Low-coherence interferometer

A. Setup

The interferometer is illustrated in Fig 3. The input arm is illuminated by a superluminescent diode with an average power of 5 mW, a gaussian spectrum centered at 856 nm, and a full-width half-maximum bandwidth of 32 nm. The free-space isolator is rotated 45˚ from the slow axis of the PM fiber, equally coupling the linearly polarized light in the orthogonal channels of the PM fiber. The PM fiber segment in the input, due to its birefringence, creates two decorr-elated and linearly polarized states traveling in the fast and slow channels of the PM fiber. A 2×2 PM coupler directs 30% and 70% of the incoming light into the sample and reference arms, respectively.

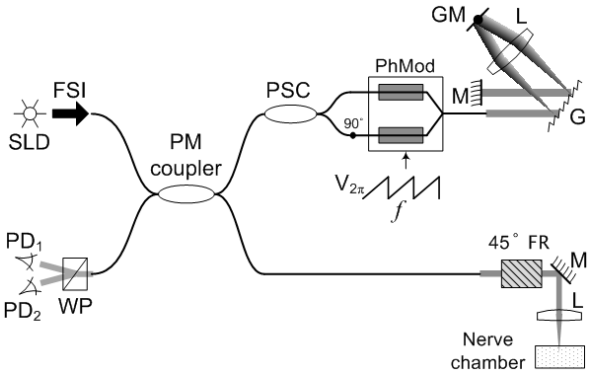


Fig. 3. Schematic diagram of the interferometer. SLD – Super-luminscent diode, FSI – free-space isolator, PSC – polarization splitter/combiner, PhMod – phase modulator, G – grating, L – lens, GM – galvanometer mirror, M – mirror, FR – Faraday rotator

In the reference arm, the polarization states are separated by means of a fiber-based polarization splitter/combiner. Since the TE axis of the lithium niobate ($LiNbO_3$) phase modulator is aligned with the slow channel of the PM fiber, the polarization state in the fast axis must be coupled into the slow channel; which is achieved by a 90˚ splice. The phase modulator corresponding with either of the channels is

driven by a sawtooth waveform with voltage amplitude $V_{2\pi}$ and frequency *f*. After recombining in the Y-connection of the modulator, light is transmitted in the rapid scanning optical delay line (RSOD), which matches the dispersion in the reference with that of the sample arm [6]. The RSOD can also provide rapid scanning of the optical path length for depth-resolved imaging of the samples. Polarization states coupled back into the fiber are equally split in the phase modulator. As a result, cross-coupled terms utilized by our system are modulated by $V_{2\pi}$, and travel exactly the same round-trip optical path. An alternative operation of the reference arm has been reported for frequency multiplexed polarization-sensitive OCT [7].

In the sample arm, the cross-coupled linear polarization states are utilized by using a 45˚ Faraday rotator. This non-reciprocal magneto-optical device rotates each polarization state a total of 90˚ in double pass. Consequently, the cross-coupled states travel the same optical path in the sample arm. The nerve's axis will be aligned with any of the incident polarization states.

Light will be focused on the reflector underneath the nerve bundle. Returning light will interfere with the corresponding states of the reference arm. With a stationary RSOD galvanometer mirror, the sinusoidal interference patterns on the orthogonal channels of the PM fiber are created by the $LiNbO_3$ phase modulator. The orthogonal states are split in the detection arm by a Wollaston prism, and transmitted to corresponding detectors. Interference patterns modulated at *f* are digitized; and phase information on each channel is retrieved by computing the angle between the fringe signal and its Hilbert transform. The phase difference ($\Delta\phi$) is converted to the change in retardance, $\Delta R = \lambda_0.\Delta\phi/4\pi$.

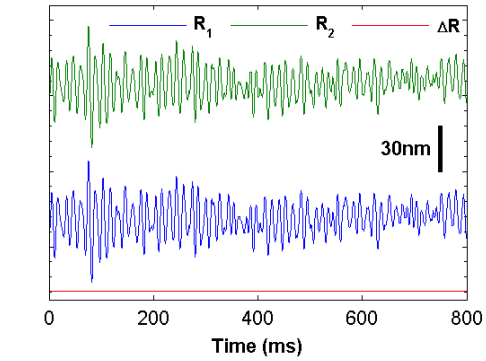
B. *System characterization*

To evaluate the sensitivity of the system, we used a glass wedge surface as the sample. Two hundred microwatts of light are focused on the wedge's surface using a 30 mm lens. Fringes modulated at 5 kHz are amplified and band-pass filtered before being digitized using a 12-bit data acquisition card at 250 kSamples/s.

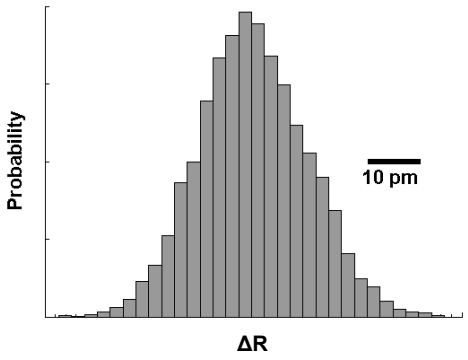
Figure 4(a) shows noise floor of retardance data with a bandwidth of 1kHz. The large variation (standard deviation of 11.5 nm) common for both channels (R_1 and R_2) is effectively rejected. The standard deviation of the noise on ΔR was measured as 10.4 pm, yielding a common mode noise rejection of 30 dB. Normal distribution of noise is shown in Fig 4(b). The measured sensitivity for ΔR corresponds to 12 millionth of a wave (λ_0=856 nm), which suggests enough sensitivity to measure ΔR in the pike olfactory nerve (41 pm) during activity.

IV. Conclusion

We presented a phase-sensitive low-coherence interferometer utilizing polarization channels of PM-fibers. The common optical path for polarization states in each of the sample and reference arms yielded an improved common mode noise rejection. The preliminary results indicate the potential of the system to detect retardance changes during neural activity. The olfactory nerve of northern pike, which produced cross-polarized intensity changes in reflection and transmission modes, can be a good model for studying depth-resolved neural activity.



(a)



(b)

Fig. 5. (a) Retardance noise on the two channels (R_1 and R_2), and their difference, (b) probability distribution of ΔR

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