An Electro-Optical Device For Early Diagnosis of Peripheral Neuropathy

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Abstract

We present an electro-optical device that measures near-infrared optical signals from peripheral nerves during electrical stimulation. Our previous studies have shown that these optical signals peak on a distinctly different timescale (~100 ms) as the fMRI BOLD signal due to systemic recruitment of blood flow (~3×5 s) and the fast scattering signal due to neuronal swelling during an action potential (~5 ms)[1]. The timescale difference signifies that the 100 ms optical signals are not originating directly from the nerve activation, but are a mediated response to neuronal activation. Our studies on the peripheral nerves provide some insight into the origins of the fast optical signalsØ also on the 100 ms timescaleØ measured in the brain. We have found that this optical signal is delayed in patients with diabetic neuropathy (average peak time of 230 ms) when compared to the optical signal measured in healthy subjects (average peak time of 160 ms), demonstrating the potential of our methods to be further developed into a diagnostic tool for early peripheral neuropathy.

Introduction

Increased cerebral blood flow due to neural activation has been studied extensively at the second time scale using the BOLD signal in fMRI [2] and using near-infrared spectroscopy [3]. There are also fast electrical signals (10-100ms) that can be detected in event related potential studies [4]. These electrical activities are correlated with a hemodynamic response to deliver metabolic supplies through neurovascular coupling.

Fast optical signal in membrane potential of neuron cell cultures

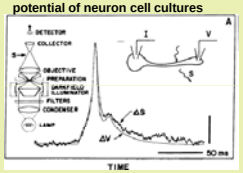


Fig. 1 [6]

Studies in neuron cell culture [5] (fig.1), brain stem surface of rats in vivo [6], and noninvasive measurements in the human brain [7,8,9] (figs3-5) have recorded fast optical signals around the same time scale (~10-100ms) as the post synaptic potential measured in the brain. However, the biophysical mechanism and the practical feasibility of measuring fast optical signals associated with brain activation through the intact human head are under debate.

Fast optical signal and electrical evoked response measured in rat brain stem surface

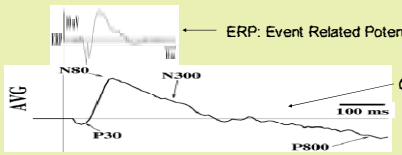


Fig. 2 from reference [7]

Fast optical signal in human brain

Visual stimulation

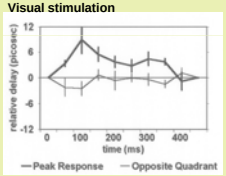


Fig. 3 from reference [8]

Median nerve stimulation

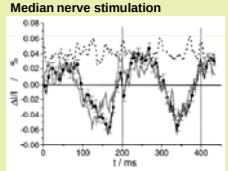


Fig. 4 from reference [9]

Motor Stimulation

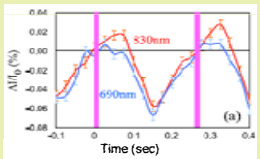
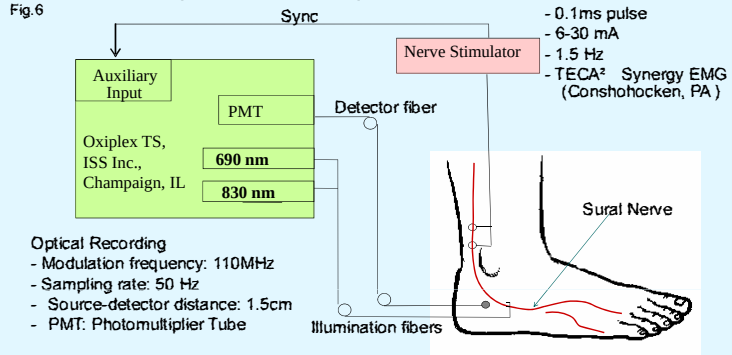


Fig. 5 from reference [10]

The peripheral nervous system provides a potentially simpler and more robust model to study the optical signals in response to electrical stimulation of selected nerves. The electric stimulation of the sural nerve provides a sensory nerve action potential (SNAP) a few milliseconds after stimulation pulse. We have studied the optical response associated with the electrical stimulation of the sural nerve.

Sural Nerve Experimental Setup

Fig.6

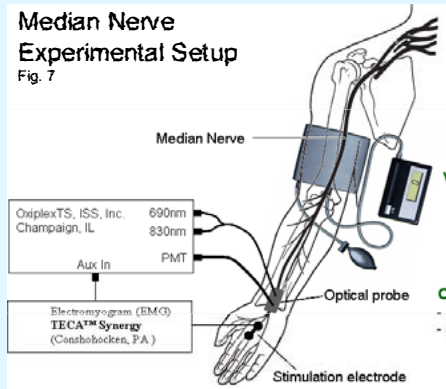


Electrical Stimulation
- 0.1ms pulse
- 6-30 mA
- 1.5 Hz
- TECA² Synergy EMG (Conshohocken, PA)

Optical Recording
- Modulation frequency: 110MHz
- Sampling rate: 50 Hz
- Source-detector distance: 1.5cm
- PMT: Photomultiplier Tube

Median Nerve Experimental Setup

Fig. 7

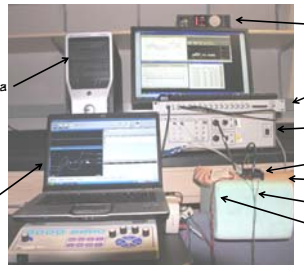


Vascular occlusion at upper arm
Venous occlusion - 40 mmHg
Arterial occlusion - 220 mmHg

Optical measurements
- Sampling rate: 25 Hz (40ms per point)
- Source-detector distance: 1.5cm

Nerve stimulation
- Pulse duration: 0.1 ms
- Repetition frequency: 1.5 Hz

Fig. 8 Picture of actual experimental setup



Results

Fig .9 A typical negative optical response (above) and its corresponding sensory nerve action potential (below) showing the difference in timescales between the electrical and optical signals.

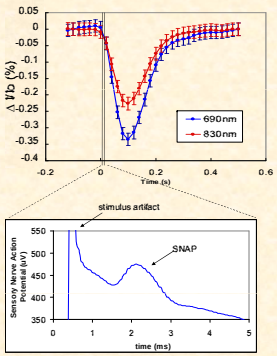


Fig. 10 Real time optical response showing optical response to each single stimulation

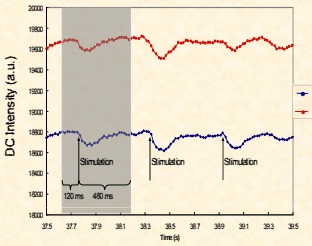
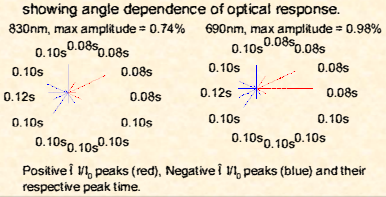


Fig.11 Normalized peak amplitudes of 690nm (right) and 830nm (left) obtained using the 360Äprobe, showing angle dependence of optical response.



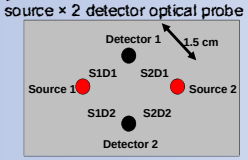
Positive Î I/I$_0$ peaks (red), Negative Î I/I$_0$ peaks (blue) and their respective peak time.

Conclusion

We have non-invasively measured optical responses due to electrical stimulation of peripheral nerves on the order of 0.1% change in intensity. The signals have been characterized using temporal, spatial and angle dependent analysis in an effort to develop an early diagnostic tool for diabetic neuropathy.

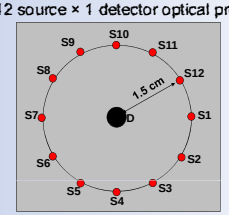
Current Optical Probes

Fig. 12
2 source × 2 detector optical probe



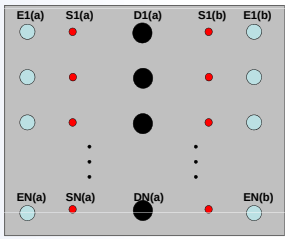
- 4 source×detector pairs
- S×D distance = 1.5 cm
- 25 Hz Data acquisition collecting all 4 areas at one time

Fig. 13 360©angular discrimination
12 source × 1 detector optical probe



- 12 source×detector pairs
- 30©angles
- S×D distance = 1.5 cm
- S_i-S_{i+1} distance = 0.9 cm
- 50 Hz Data acquisition collecting one angle at a time

Fig. 14 Future Development



- N source× N detector pairs
- Customized for measurement area size
- Multi-Distance Measurements
- 50+ Hz Data acquisition collecting all positions at one time
- Recording electrode integration for co-localized electro-optical measurements

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