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Optical detection of brain activity using plasmonic ellipsometry technique

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ABSTRACT

In spite of the existence of many techniques in the field of neural signal recording and mapping, the realm for emergence of novel methods is still open. One of the novel methods that attracts the researchers' attention is neuroplasmonics which benefits from the voltage-sensitive plasmonics. However, this field faces two main ambiguities: the physical mechanism of voltage-sensitive sensing of plasmonics and second, the strength of recorded responses. In this paper, after replying briefly the first question, we go forward by proposing ellipsometry measurements as a strong and very sensitive characterization method for voltage-sensitive plasmonics. Here, the suggested parameter of effective delta (i.e. delta contrast) creates the opportunity to distinguish clearly the results of applying different voltages to biological solutions (i.e. Phosphate Buffer Solution and artificial Cerebrospinal Fluid) and brain tissue (i.e. cerebellum tissue). The strong response of effective delta for cerebellum tissue indicates that the stimulation of brain tissue via external potential redistributes the charges at the interface of metal and modulates its dielectric constant at Thomson-Fermi layer which subsequently, leads to the variation in surface plasmon resonance signal.

1. Introduction

Brain and its functions are one of the fundamental questions of human being and the knowledge about it may answer to biological and psychological origin of thought and existence concept besides helping to treat mental and physical diseases. With this goal, various neuroimaging and signal recording techniques are competing with each other to provide more precise recordings/mappings with less invasiveness like computed or axial tomography scanning (CT scan), electroencephalography (EEG), thermal imaging, event-related optical signal (EROS), magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), positron emission tomography (PET), single-photon emission computed tomography (SPECT), surface-plasmon resonance (SPR)-based and fiber-optic techniques [1–7]. However, the most challengeable part in all of these techniques is to record the activity of large neuron populations at arbitrary depth in brain tissues with less than cell spatial and millisecond temporal resolutions [8–11]. Consequently, this challenge states the demand for new neural recording techniques in the realm of electronics, magnetics, optics and so on. Neuroplasmonics is one of newborn optical techniques which uses SPR sensing for recording non-invasively the signals of neural tissue [12]. The basis of SPR sensing is the detection of a small reflective index or layer thickness changes [13–16]. Precisely speaking, in situ detecting of the neural activity is based on the small changes occurred in the cellular volume and the membrane-localized refractive index [16–24]. Neuroplasmonics benefits from real-time, label-free detection with high sensitivity and yields both qualitative and quantitative data about interactions occurring between the sensing layer and the biological sample [25–39]. This technique makes the study on individual neurons or connections possible by providing valuable data in vitro and in vivo with high spatial and temporal resolutions. Also, signals recorded by this technique do not encounter the interference of other mechanisms because the laser beam is wirelessly addressed to the recording spot [18,40]. Sensing methods based on neuroplasmonics can be divided into four main groups [12]. For interested readers, the main researches on neuroplasmonics are listed in Table 1. However, this field encounters two main ambiguities: how can the electrical signal of the brain modulate the optical signal? and how can the minor, negligible optical modulation originated from voltage applying become more distinguishable from background noises? In order to clarify the first ambiguity, we investigate and categorize the previously proposed modulation ori-

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Table 1
Main studies on Neuroplasmonics [12].

Main categories of Neuroplasmonics	References	Key parameters
Neuroplasmonics based on prism-based methods	Hyoungwon et al. [40]	Measurement method: *Reflection (SPR)* Input: *Laser 632.8 nm, applied voltage* Output: *Time resolved photodiode voltage* Chip: *Two spaced Au films* Biological sample: *Buffer solution* Stimulation type: *Electrical (Gold-coated plates)*
	Ae kim et al. [18]	Measurement method: *Reflection (SPR)* Input: *LD 635nm (5 mW), Fixed current* Output: *Time resolved RIU* Chip: *One Au film* Biological sample: *Sciatic nerve (Tissue)* Stimulation type: *Electrical (electrodes)*
	Choi et al. [20]	*Theoretical proofs in neuroplasmonics*
Neuroplasmonics based on the combination of SPR and fluorescence microscopy	Chikara et al. [43]	Measurement method: *Reflection (SPR and SP field-enhanced fluorescence)* Input: *Laser 632.8 nm* Output: *Reflectivity and fluorescence intensity vs incident angle* Chip: *4-layered grating of Cr/Ag/Cr/SiO2* Biological sample: *Cultured hippocampal nerve cells* No stimulation
	Choi et al. [44]	Measurement method: *Fluorescence microscopy* Input: *White light source* Output: *Microscope images of neuron cells* Chip: *Dielectric grating on Au film* Biological sample: *Neuron cell culture* No stimulation
Neuroplasmonics based on nanorods	Paviolo et al. [45,46]	Measurement method: *Epifluorescence microscopy* Input: *LD (780 nm)* Output: *neuron characteristics vs laser irradiance* Chip: *neural cells containing Au nanorods* Biological sample: *NG108-15 mouse neuroblastoma_rat glioma hybrid cells* No stimulation
	Eom et al. [47]	Measurement method: *Electrical recording* Input: *Pulsed NIR light (980nm LD)* Output: *Time resolved CNAP(mV)* Chip: *Gold NRs distributed in the vicinity of the plasma membrane of nerve tissues* Biological sample: *In-vivo Sciatic nerve (Tissue)* Stimulation type: *Optical (fiber-coupled LD)*
	Yoo et al. [48]	Measurement method: *Electrical recording* Input: *NIR laser (785 nm), applying voltage* Output: *Time-resolved electrical response* Chip: *MEA with a GNR-based interface* Biological sample: *Cultured hippocampal nerve cells* Stimulation and inhibition type: *Electrical stimulation and recording- Optical inhibition*
Neuroplasmonics based on plasmonic crystals	Le et al. [25]	Measurement method: *Plasmonic reflection imaging* Input: *Halogen light source* Output: *Image* Chip: *Nano-hole array* Biological sample: *Cell Culture of Aplysia californica Pedal Ganglion Neurons* No stimulation
	Zhang et al. [19,42]	Measurement method: *Scattering* Input: *LD (850 nm)* Output: *Time-resolved differential scattering signal* Chip: *Nanoparticle array* Biological sample: *Cultured rat hippocampal neurons* Stimulation type: *chemical*
	Dipalo et al. [49] Malerba et al.[50]	Measurement method: *Electrical recording, SERS* Input: *Laser 785 nm, 2 mW* Output: *Time-resolved electrical recording-SERS spectra: Intensity vs Raman shift* Chip: *Nanoantennas integrated with MEA* Biological sample: *Cultured rat hippocampal neurons* Stimulation type: *Electrical (electrodes)*

gins into three groups [18,20]: a) The change in refractive index of neuron. This phenomena is originated from structural changes like volume change and reorganization of axon membrane protein molecules. However, this phenomena cannot be the main origin due to showing monophasic changes and slow signal response. In other words, a time lag of 1–2 ms is required for 2–3 nm swelling of the axon. b) The change in refractive index of artificial cerebrospinal fluid (aCSF). This phenomena causes the order of 10^{-8} changes in sensing response which is negligible in comparison with experimental data that show the changes in order of 10^{-5} [20] c) The