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Editorial

Special Issue "Neurophotonics—Optics for the Brain"

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Abstract: Light-tissue interactions allow for a multitude of possibilities to sense; image; and impact the brain at molecular, cellular, and tissue levels. The application of optical techniques to neuronal tissue is the essence of neurophotonics, to which this Special Issue is dedicated. The eleven articles in this Special Issue are representative of the broad scope of this field and of the wide range of optical techniques that it encompasses. In more detail, the articles cover basic neuroscience, neuroanatomy, functional imaging, cerebral hemodynamics, brain development and aging, brain–computer interfaces, and therapeutic treatments. The optical techniques considered include various types of optical microscopy, optical coherence tomography, photoacoustic imaging, diffuse optical spectroscopy and imaging, photobiomodulation, and optogenetics.

Keywords: brain; functional near-infrared spectroscopy; photoacoustic imaging; optical coherence tomography; optical microscopy; photobiomodulation; optogenetics; neuroanatomy; functional connectivity; Brainsmatics

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1. Introduction

The term neurophotonics, or optics for the brain, refers to a broad range of applications of optical techniques in neuroscience, neuroimaging, and neuromodulation that are relevant for basic science, medical diagnostics, therapeutic treatment, and brain monitoring. The eleven articles in this Special Issue represent a good portion of the many facets of neurophotonics, including a variety of optical imaging techniques (microscopy and optical coherence tomography [1,2], photoacoustic imaging [3], diffuse optics [4–9]), optical control of specific neural populations (optogenetics) [10], and the therapeutic application of red/near-infrared light (photobiomodulation) [11]. To illustrate the power and far-reaching possibilities of neurophotonics, specific applications reported in this Special Issue include the visualization of large-scale neurodynamics at high spatio-temporal resolution [3]; whole-brain atlases at high resolution [1,2]; development of the infant brain [5]; assessment of mental workload [7]; characterization of cerebral hemodynamics [9]; measurable effects of brain aging [8]; development of innovative brain–computer interfaces (BCI) [6]; a review of diffuse optical imaging in cognitive and social sciences, functional studies, and medicine [4]; photobiomodulation for Alzheimer's disease [11]; and optogenetics as a therapeutic and rehabilitative tool [10]. Neurophotonics is a scientifically and technologically diverse field that can sense and interact with the brain at molecular, cellular, and tissue levels. It may rely on intrinsic tissue properties or take advantage of genetic engineering or the introduction of suitable fluorescent, absorbing, or voltage-sensitive agents. Applications range from tissue specimens and animal models to human subjects either at rest or freely moving in naturalistic environments.

2. Diffuse Optics and Functional Near-Infrared Spectroscopy (fNIRS)

Non-invasive diffuse optical methods for diagnostic, functional, and monitoring applications have been applied to the human brain since the early 1990s. Their major advantages are the safe, non-invasive applicability, including in infants and children; a sensitivity to cerebral hemodynamics and oxygenation; and the portability/wearability of the instrumentation. Limitations include a low spatial resolution that prevents studies at a cellular level, a limited penetration depth that restricts measurements to the most superficial brain cortex, and sensitivity to extracerebral tissue (scalp, skull, etc.) that may impact the specific sensitivity to the brain. A number of reviews have been devoted to the field, including a history review [12]; applications of continuous-wave (CW) [13], time-domain (TD) [14], frequency-domain (FD) [15], and wearable [16] functional near-infrared spectroscopy (fNIRS); perspectives [17]; and a bibliometric evaluation of publications in the field from 2000 to 2019 [18]. These review articles show how diffuse optics for the brain and fNIRS are very active and growing fields of research that permeate a large number of areas, including cerebral diagnostics, monitoring, neural development, functional imaging, mental states assessment, psychology research, hyperscanning, etc.

This Special Issue includes articles that describe a variety of fNIRS applications. Anna Blasi et al. present the unique and powerful application of fNIRS to the infant brain for neurocognitive development studies, including markers of compromised brain development, the role of socio-economic and environmental conditions, and global health aspects explored in low- and middle-income countries [5]. The state of the art of fNIRS is reviewed by Valentina Quaresima and Marco Ferrari, who consider basic and technological developments (see Table 1 in their article [4]) as well as applications in cognitive and social sciences, functional neuroimaging, and medical diagnostics (see Table 2 in their article [4]), including a critical perspective of future directions [4]. Functional imaging can be used to assess mental workload, as conducted by Kosar Khaksari et al. in an n-back working memory task [7], which can lead to the development of real-time feedback on brain states of a user for the development of novel implicit brain–computer interfaces (BCI), as discussed by Alexa Bosworth et al. [6]. Antonio Chiarelli et al. found that aging-related physiological and anatomical brain changes correlate with non-invasive optical measurements of the effective attenuation coefficient, which represents the collective absorption and scattering properties of extracerebral and cerebral tissue [8]. A study by Giles Blaney et al. targeted extracerebral and cerebral hemodynamics that are coherent with oscillations in systemic arterial blood pressure, finding evidence of blood-volume-dominated extracerebral hemodynamics vs. blood-flow-dominated cerebral hemodynamics [9].

3. Photoacoustic Imaging (PAI)

Photoacoustic imaging (PAI) is a multi-modality technique that combines light and ultrasound to generate images based on optical contrast while exploiting the weaker scattering of ultrasound compared to light in biological tissue [19,20]. A distinct advantage of this technique is its unique flexibility that allows for the scalability of penetration depth, spatial resolution, field of view, and temporal resolution. In fact, PAI can achieve sub-micron to sub-millimeter resolutions at penetration depths of a few hundred microns to centimeters, respectively. The source of contrast in PAI is also versatile, as it may rely on endogenous chromophores as well as a variety of exogenous contrast agents that allow for the development of molecular PAI [21]. Non-invasive applications of PAI to the adult human brain are complicated by the strong optical scattering, ultrasound attenuation, and ultrasound distortion introduced by the scalp and adult skull, but preclinical animal brain models [22] and the infant brain [23] are successfully investigated with photoacoustic imaging.

The PAI article by Oleksiy Degtyaruk et al. in this Special Issue presents an approach to real-time imaging of neuronal activity in the whole mouse brain, collecting the fluorescence signal (centered at 525 nm) from a genetically encoded calcium indicator (GCaMP6f) excited at 488 nm [3]. The challenge presented by the strong absorption of blood at these visible wavelengths is tackled by intracardiac perfusion of the mouse brain with artificial cerebrospinal fluid to observe calcium dynamics deep in the mouse brain, thus paving the way for calcium indicator imaging with PAI [3].

4. Optical Microscopy and Optical Coherence Tomography (OCT)

A variety of optical microscopy techniques play a crucial role in neuroscience [24]: confocal microscopy, two-photon microscopy, light-sheet microscopy [25], super-resolution microscopy, coherent anti-Stokes Raman spectroscopy (CARS) microscopy, second-harmonic generation (SHG) and third-harmonic generation (THG) microscopy, optical coherence tomography [26,27], etc. Because of strong light scattering in brain tissue, optical microscopy can image only thin tissue layers, but deeper tissue and even whole brain imaging can be achieved by employing optical clearing techniques [28] or with physical sectioning by sequentially cutting or ablating tissue [29], as also conducted in serial block-face scanning electron microscopy (SBEM) [30].

In this Special Issue, Joël Lefebvre et al. review current efforts toward the creation of brain atlases at micron resolution by using serial block-face histology in conjunction with intrinsic contrast imaging techniques such as PAI, OCT, SHG, THG, and CARS microscopy [2]. The ability of optical clearing and mechanical sectioning methods, in conjunction with optical microscopy techniques, to generate high-resolution data for the entire brain at molecular and cellular levels is the basis for the scientific effort invested in the proposed brain-wide spatial informatics, named Brainsmatics, reported in the article by Hua Shi et al.

5. Photobiomodulation (PBM)

The application of low levels of red and near-infrared optical irradiance (energy per unit time per unit area) onto a tissue surface for beneficial effects (pain relief, enhancement of cell function, anti-inflammatory response, mitigation of pathological conditions, etc.) was introduced in the 1960s, and was indicated with various terms, including biostimulation and low-level laser therapy (LLLT), before settling on the current term of choice: photobiomodulation (PBM) [31]. The many tissues and conditions that PBM targets include the brain in animal studies, and areas such as ischemic stroke, traumatic brain injury, Alzheimer's disease, neurodegeneration, mental health conditions, etc. in clinical studies. [32].

In this Special Issue, Michael Hamblin reviews the involved chromophores, the photobiology, and mechanisms of PBM in the brain, and then focuses on Alzheimer's disease and dementia, discussing related PBM studies on animal models and human clinical trials [11].

6. Optogenetics

Optogenetics is a powerful neuroscience technique that allows for specific and temporally precise control of neural activity by selective optical excitation or inhibition of genetically engineered neurons that express light-sensitive proteins (opsins) [33]. Optogenetic approaches have revolutionized neurobiological and neuroscience research and found a multitude of applications, including developmental biology [34], studies on freely moving animals [35], psychiatric research [36], etc.

In this Special Issue, Elena Montagni et al. review the development of opsins as optogenetic actuators, approaches to light delivery that achieve desired spatio-temporal characteristics, optogenetic methods to study neural circuits and functional connectivity, and optogenetics as a potential therapeutic tool for neurodegenerative disease and stroke [10].

7. The Broad Scope and Impact of Neurophotonics

The articles in this Special Issue provide an overview, partial but certainly representative, of the exciting and far-reaching field of neurophotonics, which illustrates how light-tissue interactions can be exploited for sensing; imaging; and impacting brain tissue at molecular, cellular, and tissue levels. The scope of the application of neurophotonics is extremely broad, from basic neuroscience and neurobiology, to medical diagnostics, functional imaging, therapeutic treatments, brain–computer interfaces, etc. Neurophotonics is a fast growing field that is helping to advance our understanding of how the brain is structured and functions; how it develops and ages; how its health may be assessed, monitored, and potentially restored; and how its cognitive and mental states may be objectively determined.

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