Optical Neuroimaging

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***Abstract*—This article seeks to explore optical neuroimaging in brief and two major methods of the same. Optical imaging techniques are fast, portable, inexpensive, and provide excellent spatiotemporal resolution. There are significant advantages of optical methods, arising from the nature of light's interaction with animal tissue. Light provides excellent sensitivity to functional changes, either via intrinsic changes in absorption, fluorescence, or scattering. Oxy- and deoxy-hemoglobin (HbO_2 and HbR) act as chromophores.**

Two major methods of optical neuroimaging are Diffuse Optical Tomography (DOT) and functional Near-Infrared Spectroscopy (fNIRS). fNIRS is essentially a sparse array of sources and detectors that measure increases in HbO_2 and consequential decreases in HbR, thereby capturing blood flow volume/activity which is then mapped onto a 2-D topographical map of the brain. DOT can be considered an enhanced version of fNIRS, which produces 3-D Maps of higher resolution.

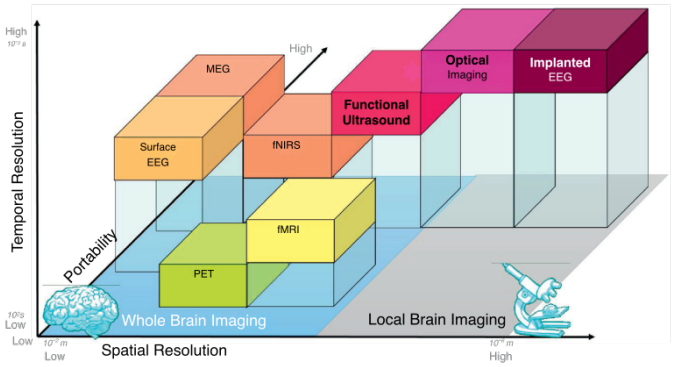

Fig. 1. Comparison of major Neuroimaging techniques [2]

I. Introduction

NEUROIMAGING refers to any experimental technique of imaging the brain and central nervous system of humans (and animals). Over the last many decades, tremendous progress has been made in the field of neuroimaging, contributing to much of today's understanding of the structure and function of the brain. Neuroimaging today is a key tool for neuroscientists to investigate the physiological basis of neurological diseases such as epilepsy, Alzheimer's, and stroke and the development of diagnostic methods, drugs, and treatments among many other applications [1].

There are several widely employed neuroimaging modalities including electroencephalography (EEG), magnetoencephalography (MEG), positron emission tomography (PET), single-positron emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI). Each of them employs a different method and is widely distinct but nevertheless, each has its own limitations.

Neuroimaging methods can be classified according to various parameters - invasive and non-invasive, structural and functional. Structural imaging deals with the structure of the brain and the diagnosis of large-scale intra-cranial images. It is generally used to detect injuries or tumors. Functional imaging on the other hand measures an aspect of the brain's function and is used to understand neuropsychology and cognitive neuroscience.

Traditionally, functional neuroimaging techniques are differentiated based on their spatiotemporal resolution. Spatial resolution refers to how accurately the measured activity (function) is localised within the brain and temporal resolution describes its ability to tell when exactly the activation happened. Fig. 1 depicts the major neuroimaging techniques on a 3-axis chart, temporal resolution, spatial resolution and portability.

II. Optical Neuroimaging

Noninvasive functional optical neuroimaging is an emerging field that has several major advantages in research as well as clinical use. One of the major advantages is that the subject need not maintain absolute stillness during observation unlike in EEG or other methods [3]. The equipment is also portable and compact, is a low-cost option, and is also highly safe [4].

The history of optical neuroimaging dates back to 1977 when Jöbsis first demonstrated "the feasibility of measuring blood and tissue oxygenation changes in the brain of a living organism by employing near-infrared (NIR) light" [5]. The near-infrared (NIR) spectrum is constituted by light of wavelength approximately 700-900 nm. NIR light provides several advantages for imaging tissues which will shortly be elaborated. Here, oxy- and deoxy-hemoglobin behave as chromophores.

Activity in human brain can be measured with the help of physiological dynamics and biomarker fluctuations that occur during neurological processes. When a part of the brain is active, the firing of neurons in that part gives rise to spikes of varying electrical field potentials. This results in a considerable rise in glucose consumption and local blood flow, which raises the amount of oxygen available. This is reflected in the local concentration levels of oxygenated hemoglobin (HbO_2), deoxygenated hemoglobin (HbR), and total hemoglobin (HbT) [6]. See fig. 2.

Thus, by exploiting the optical properties of these biomarkers to measure the change in their concentration and detectors placed in multiple measurement sites simultaneously, the results are displayed in a topographical map.

The two methods for analyzing noninvasive optical neuroimaging data in humans are Functional Near Infrared Spectroscopy (fNIRS) (also known as Optical Topography) and Diffuse Optical Tomography (DOT).

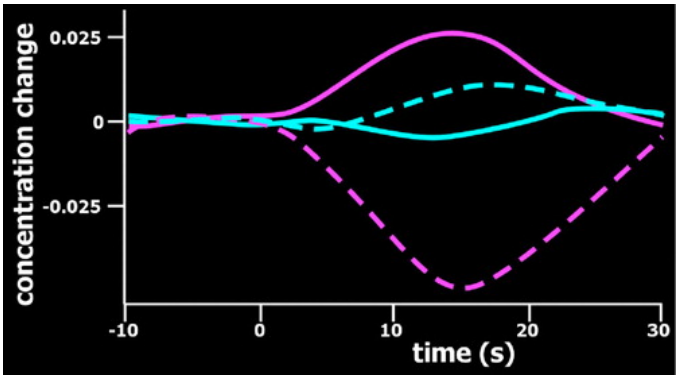

Fig. 2. Concentration change during brain activation [4]

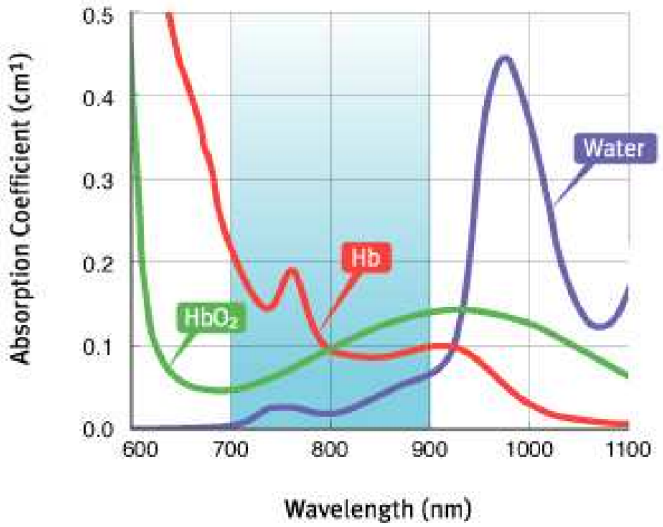

Fig. 3. Absorption Characteristics of Tissue [9]

III. Light-Tissue Interactions

Light interacts with biological tissues in three main ways - absorption, scattering, and fluorescence. However, it has been observed that for the purposes of the study of the concerned imaging methods, fluorescence contributes significantly lesser, and hence the focus shall be only on absorption and scattering.

A. Absorption

The main absorbers of near-infrared (NIR) light in tissues are oxy-hemoglobin, deoxy-hemoglobin, and water. Hemoglobin (Hb) here is a chromophore, that is, it absorbs light at a specific frequency to impart colour.

Absorption can be quantified using the absorption coefficient μ_a (in mm^{-1}) which is the reciprocal of the Mean Absorption Length, the average distance travelled by a photon before it gets absorbed in the medium. It is representative of the probability that a photon is absorbed by the medium per unit path length [7].

The absorption coefficient is a function of wavelength and the relation is given by (1) [8]:

$$\mu_a = \sum_{i=1}^{N} \varepsilon_i(\lambda_i) C_i \tag{1}$$

where, ε is the extinction coefficient and C is the concentration summed for N chromophores.

Fig. 3 shows the absorption characteristics for water, Hb, and HbO_2. It is clear that at shorter wavelengths, absorption by hemoglobin is dominant and at longer wavelengths, absorption by water is dominant. The optical penetration depth is limited in these ranges. Thus, it is in the Near-Infrared (NIR) window, from $700\ nm$ to $900\ nm$ that the absorption is minimum. This region known by different names like 'optical window', 'therapeutic window', or 'medical spectral window' allows light to penetrate deep into tissue thereby allowing non-invasive procedures. In the NIR, μ_a for tissues ranges from 0.02 to $0.30\ cm^{-1}$ and the photon mean absorption length ranges between about 3 and $50\ cm$ [8].

B. Scattering

The scattering phenomenon is mainly guided by the relative sizes of the scattering particles and the wavelength of light. In tissues, cellular organelles behave as the scattering particles and their sizes are in comparable dimensions with the wavelength of NIR spectrum. Also, it may be noted that their refractive index is close to that of the surrounding extracellular liquid, hence the scattering direction is largely in the forward direction.

Analogous to the absorption coefficient, the scattering coefficient can be defined as:

$$\mu_s = \rho_s \sigma_s \tag{2}$$

where ρ_s is the volume density of the scatterers in the medium, and $_s$ is the scattering cross-section. μ_s is the probability of a photon getting scattered per unit path length and its reciprocal gives us the scattering length, which is the average path length between two consecutive scattering events [7] The scattering coefficient in tissues is ranges from 2 to $20\ cm^{-1}$, clearly scattering is 100 times more probable than absorption [8].

Light gets scattered more as it penetrates further into the tissues. It has been observed that they follow a 'banana-shaped' curved path. In general, the depth is about a third of the distance between the source and detector [4]. Some studies also show that it can be half the source-detector distance [10].

Any optical imaging setup consists of a set of sources that emit light and another set of detectors. The amount of photons absorbed by tissue and scattered back to the detector is indicative of a change in the concentration of oxyhemoglobin or deoxyhemoglobin.

IV. Functional Near Infrared Spectroscopy - fNIRS

Noninvasive NIRS was initially used to examine brain oxygenation experimentally and therapeutically, as described by Professor Frans Jöbsis's seminal work, the first in vivo near-infrared (NIR) spectroscopy. Later, it was also used in muscle oxidative metabolism and since 1993, multichannel NIRS

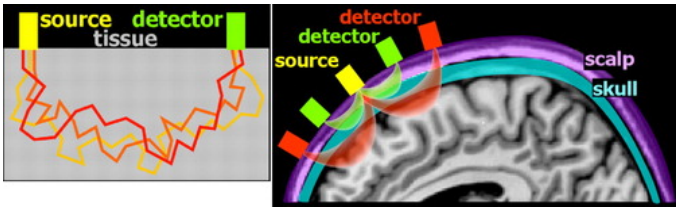

Fig. 4. Scattering in Tissue [4]

devices have been used extensively to study the functional activity of the adult human cerebral cortex [11].

The apparatus of a simple fNIRS (also known as Optical Topography - OT) system is as follows. An optode (fiber-optic bundles) connects the light source to the subject's head. A second optode is positioned 2–7 cm from the first to capture the scattered light coming out from the tissue. A photomultiplier or a CCD camera may be connected to the detector optode [12].

The relative changes in concentration of Hb, HbO_2 and HbR can be calculated using the modified Beer-Lambert law which quantifies the attenuation in light [12]:

$$A = log\ \frac{I}{I_o} = \epsilon \times\ c \times\ d \times\ B\ +\ G \tag{3}$$

where, I_o is the incident light, I is the measured light, ϵ is the extinction coefficient (which is a function of wavelength), c is the substance concentration, B is the differential path length factor (DPF) and G is the signal loss due to scattering.

Assuming that the DPF and d are known and remain constant,

$$\Delta(A) = \epsilon\ \cdot\ \Delta(C)\ \cdot\ d\ \cdot\ DPF \tag{4}$$

In order to distinguish between the changes in Hb and HbO_2, two wavelengths are used simultaneously, one above the isosbestic point and the other below it (the wavelength at which the absorptivity of Hb and HbO_2 are equal, around 800 nm).

There are three techniques of fNIRS based on the type of illumination used [13]:

- Continuous wave (CW)
- Frequency domain
- Time-domain

CW NIRS instruments are the earliest and most commonly used. They employ light sources with a constant frequency and amplitude and a photomultiplier, photodiode or an avalanche photodiode detector is used as a detector. It is simple and cost-effective.

Frequency domain instruments on the other hand use modulated white light sources, laser diodes, or LEDs as sources. They use either a photon counting detector or a gain-modulated area detector to assess the attenuation, phase shift (ϕ), and modulation depth (M) of the light at the detector. They accurately separate the absorption and scattering effects.

Time domain instruments utilize a semiconductor or solid-state laser to generate ultrashort NIR pulses in the order of picoseconds. For detecting the attenuation, synchroscan streak camera or a time-correlated single photon counting is used in which a photon counting detector detects and sorts the received photons by their time of arrival. The major advantages of are their spatial resolution and penetration depth.

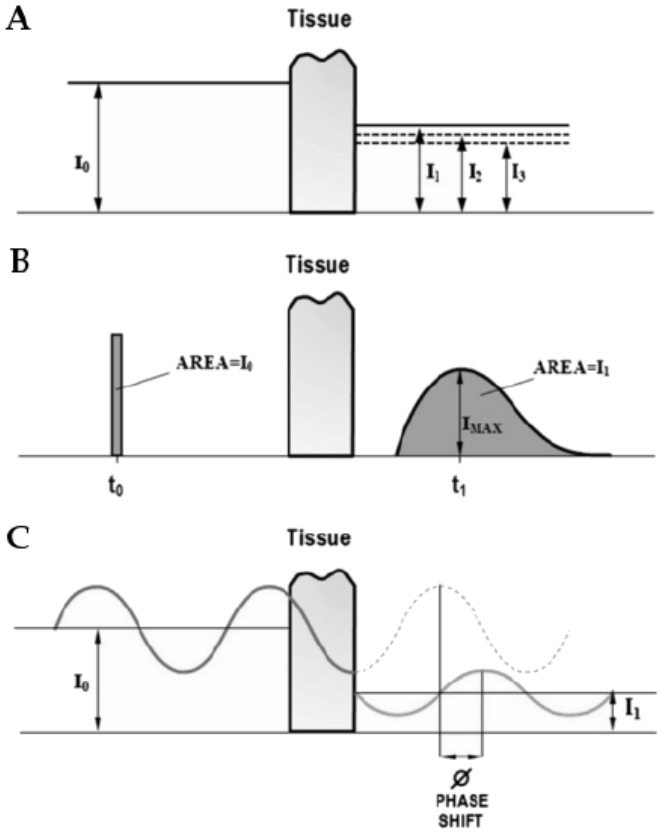

Fig. 5. Schematic representation of fNIRS modalities [13]

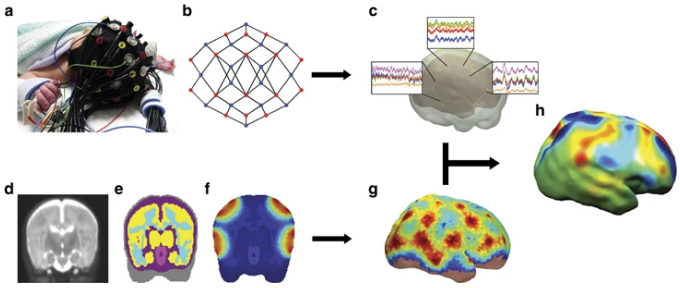

Fig. 6. Schematic representation of DOT: (a) DOT headgear, (b) schematic array representation of the gear, (c) Measured signals mapped by location, (d)(e) structural mapping, (f)(g) behavior of light in tissue and at channel location, (h) reconstructed image [14]

Fig. 5 is a schematic representation of all three types.

V. Diffuse Optical Tomography - DOT

Diffuse Optical Tomography can be considered an extension of fNIRS, which produces 3-D Maps of higher resolution by exploiting multiple (overlapping) source-detector channels of varying lengths. This makes it possible to get depth information [14]. Fig. 6 is a schematic representation of the working of a DOT system.

While DOT images can be reconstructed with CW, TD, as well as FD measurements, time domain measurements provide

more data for image reconstructions [15].

The reconstruction of 3D images is done using mathematical algorithms, popularly known as the forward and inverse problems.

The forward problem determines how light moves through the tissue and how the reemissions are reflected outward. The inverse problem seeks to calculate the optical property distribution that minimises the discrepancies between actual and measured data [16].

The quality of a DOT image depends upon the number of channels taken into consideration for the reconstruction. Generally, commercial devices use about 10-20 source-detector pairs [14]. However, they produce images of very low resolution and increasing the number of source-detector pairs will lead to prohibitive computation and storage requirements.

To further improve image quality, high-density DOT (HD-DOT) use a dense array with the closest source-detector (nearest neighbour) distance of 15 mm.

VI. Design Challenges

Optoelectronic design for fNIRS and DOT systems presents many challenges. The most important are the light budget, the detection and amplification strategy, and encoding/decoding strategies [6].

Light Budget: The choice of possible wavelengths determines the cross-talk between channels and also the separation of absorption and scattering characteristics. Further, LEDs emit photons over a relatively broad band when compared to Laser Diodes (LD) but LDs are typically not available at as many wavelengths as LEDs. Thus wavelength optimization is crucial in the design of optical neuroimaging systems [17].

Detection and amplification: It is observed that the output power of light varies over about six orders of magnitude as the source-detector distance varies from 2-7 cm (Fig 7). Also, it is important to have a very high signal-to-noise ratio (SNR) as changes in concentration due to activation-related brain function are only a few percent. To address these requirements, avalanche photodiodes (APD) are used. They allow a range of over 10^7 and SNR of > 100 [6].

VII. Application

Optical neuroimaging is widely used in basic neuroscience research and applications like brain-computer interfaces (BCI), neuroergonomics, and cognitive neuroscience. There are several important applications in the field of neurology namely, Alzheimer's disease, dementia, depression, epilepsy, parkinson's disease, post-neuro surgery disfunctions, rehabilitation, stroke recovery etc. fNIRS and DOT are also used in psychiatric and psychological settings [18].

VIII. Conclusion

With several benefits for application in psychiatric research, noninvasive optical imaging is an innovative and intriguing new technique of functional neuroimaging. Its uniqueness includes the capacity to conduct research in a variety of environments and with subject populations that cannot tolerate confinement or loud noises. Further, research in optical neuroimaging is in its early phases and has a long way to go. It is promising as a tool for the assessment, monitoring, and treatment of psychiatric disorders.

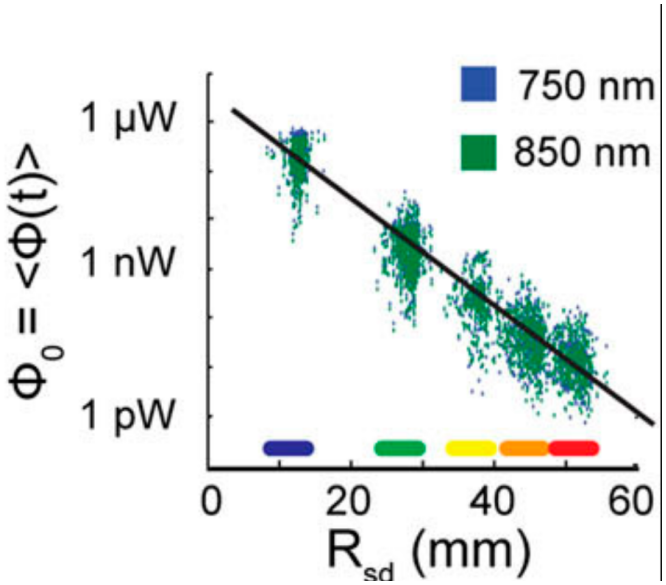

Fig. 7. Output power as a function of SD distance [6]

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