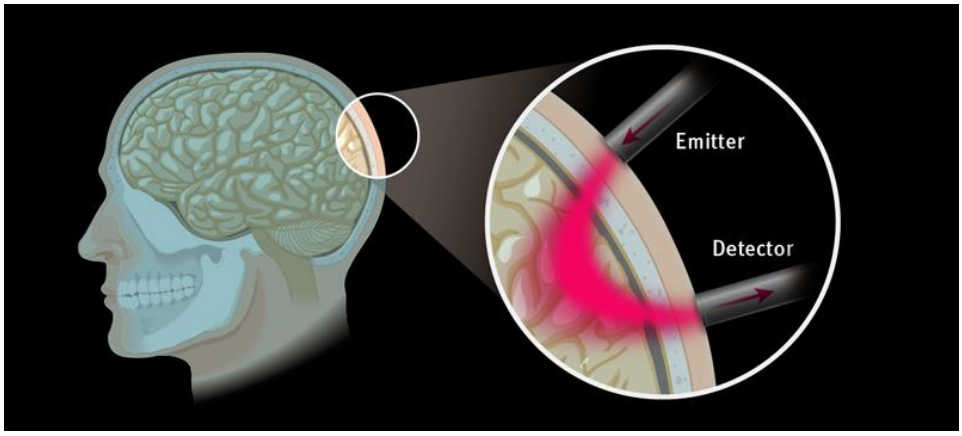
Imagent for fNIRS and EROS measurements

1. Brain imaging using Infrared Photons

Brain imaging techniques can be broadly classified in two groups. One group includes the techniques that have a good spatial resolution (up to 1-2 millimeters) but a poor temporal resolution, such as functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET). The second group includes techniques featuring an excellent temporal resolution (of the order of milliseconds) but providing a limited spatial information. This group includes the Event Related Brain Potential (ERP) and the Magneto-encephalography (MEG).

The ISS Imagent provides a balance between temporal (ERP, MEG) and spatial (fMRI, PET) resolution for the study of superficially located areas of human brain. The Imagent detects variations in the oxygenation levels of activated brain areas and provides a map of the areas where the changes occur. This working principle is based on the use of near infrared light for probing the cortical surface or imaging changes in the tissue hemodynamics.



2. Theory of Operation

The penetration depth of light in tissues is quite significant in the wavelength range from 650 nm to 900 nm. The main absorbers in this spectral region are oxy- and deoxy-hemoglobin. On a smaller scale, water, fat and cytochrome oxidase contribute to the partial absorption of the light.
For typical head tissue (skin/scalp, skull and cortical layer), with an absorption coefficient of $\mu_a = 0.1\ cm^{-1}$ and a reduced scattering coefficient $\mu_s' = 8\ cm^{-1}$, the maximum optical penetration can be estimated to be about 1-1.5 cm when a detector is placed at 3 cm from the source.
The penetration depth can be increased by increasing the distance between the source and the detector, although, eventually, the signal-to-noise ratio of the measurement deteriorates.

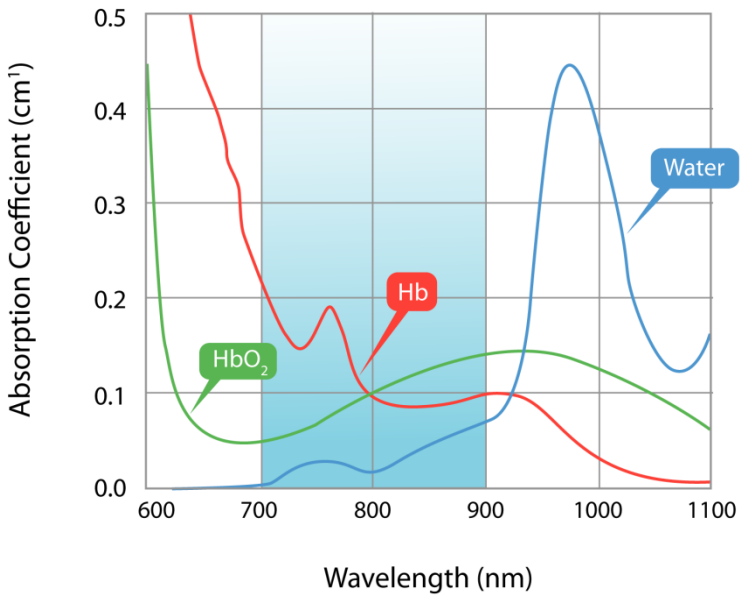


Figure 2. The absorption spectra of major absorbers (Oxygenated Hemoglobin, De-Oxygenated Hemoglobin, and Water) in the region 600-1100 nm.

Frequency Domain NIRS

The standard light sources used in the Imagent emit light at wavelengths of 690 nm and 830 nm (an equal amount of light sources at each wavelength is provided). The light sources used by the ISS Imagent are modulated at an RF frequency of 110 MHz. This means that the light intensity is not constant but varies with time. Mathematically, the light source intensity as a function of time is expressed as:

$$I_0 = I_{DC_0} + I_{AC_0} \sin(2\pi ft - \Phi_0)$$

where:

I_0	=	source intensity
I_{DC_0}	=	average component of the light source intensity
I_{AC_0}	=	alternating component of the light intensity
f	=	modulation frequency
Φ_0	=	phase of the light source

As seen in the above equation, the light source intensity has three critical elements, the constant DC component, the alternating AC component, and the phase component. The excitation light is displayed in Figure 3 by the blue line. The light that traversed the tissue is collected by fiber bundles, which divert it to the light detectors (photomultiplier tubes). The three components of the detected signal are measured: the DC, AC and the phase of the photon density wave. After traversing the tissue, the light has a lower modulation (ratio AC/DC) than the excitation light and, moreover, it is delayed, or has a phase shift (red line) with respect to the excitation light.

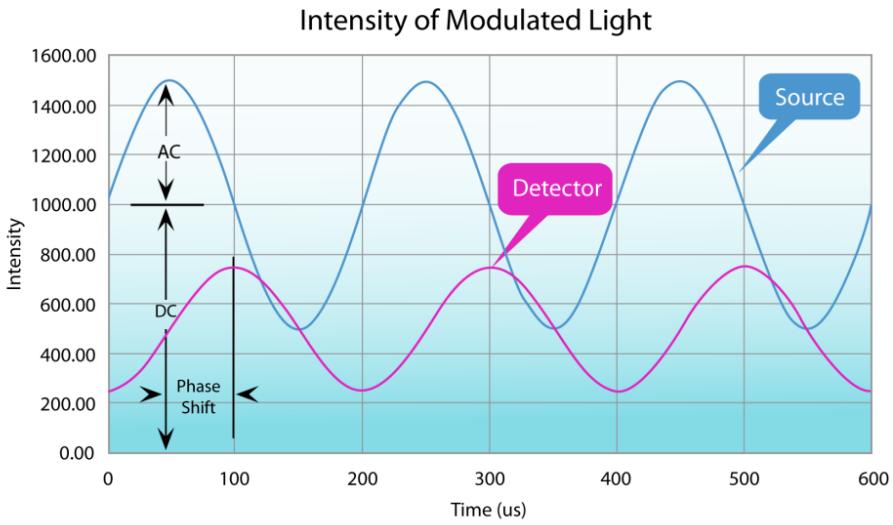


Figure 3. The light source modulation parameters are shown. AC is the amplitude of the modulation. DC is the average intensity. The phase shift between the two signals is also shown.

The use of the AC and phase components, contrary to the DC component of the signal, assures that the room light does not interfere with the measurement. Additionally, modulated light penetrates the tissue at a deeper depth than non-modulated light.

Multiplexing the light sources

The light sources in Imagent are grouped in banks of eight units; in one bank, four laser diodes emit at 690 nm and the remaining four lasers emit at 830 nm. The light is delivered to the tissue by fiber optics, which are typically paired (for carrying the two wavelengths) although for some measurements it is convenient to use them at a single wavelength. The fibers are arranged in a geometrical pattern (montage) selected by the researcher that includes the fiber bundles that bring back the light to the detectors. The different source-detector distances allow for the researcher to probe different depths in the same region, as well as an estimate of the scattering and absorption coefficient in the region.

Each light source is turned ON/OFF by the computer in a sequence determined by the operator to ensure that the signal emitted by each source is correctly identified by the detectors. Typically, the ON time for a light source is about 20 ms - although a longer or shorter time can be selected – and the entire cycle for eight light sources takes 160 ms. This is the measurement time for characterizing the hemodynamics changes occurring in a region.

Three modes of operation are selectable through the software and reported in Table I (for the Imagent with 64 sources and 8 detectors). The instrument is versatile as it allows the researcher, when required, to utilize a smaller number of light sources and probe a region in a shorter time.

Operation mode	No. of sources simultaneously ON	Typical cycle time * (ms)	Typical max cycle time *EROS* (ms)	Description
Switch-8	8	160 or less	16 or less	Each of the 4 laser boards has one LD ON for 20 ms. The signal is collected simultaneously on 4 detector channels. Since 4 light sources are on simultaneously, they must be positioned far apart from one another.
Switch-16	4	320 or less	32 or less	Only 2 LDs are ON simultaneously. The signal is collected simultaneously on 4 detector channels. The probes can be positioned closer together as fewer light sources are on simultaneously.
Switch-32	2	320 or less	64 or less	In this mode of operation, the cycle time is long, but 1 light source is ON. More positions can be probed closer together.

Table I. Mode of operation for Imagent 64/8

Fast Signals and Slow Signals

For the detection of fast signals – signals related to neuronal activation - one wavelength only is typically utilized. In this mode of operation, it is feasible to have a readout time of less than 20 ms.

3. fNIRS Applications

As an example we report the case of a probe applied on the head of a volunteer in the position indicated in Figure 3 (left side of the head in the motor cortex area). The subject was asked to begin or stop performing a finger-motion (palm squeezing) exercise using the right hand. The squeezing rhythm (1.5 Hz) was maintained by means of a metronome. Exercise epochs typically had stimulation/relaxation periods of 20/20 s, 20/13 s and 17/10 s, and each consisted of 10 periods.

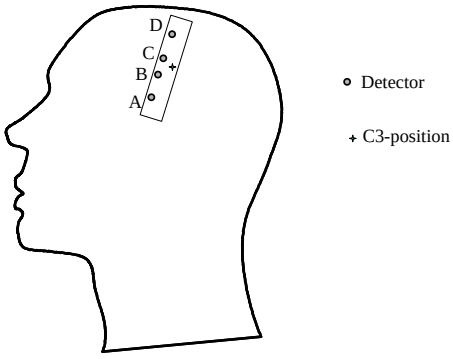


Figure 3. Position of the optical probe on the head

Figure 4 below shows the hemodynamics fluctuations measured in source-detector pairs A7 and D15.

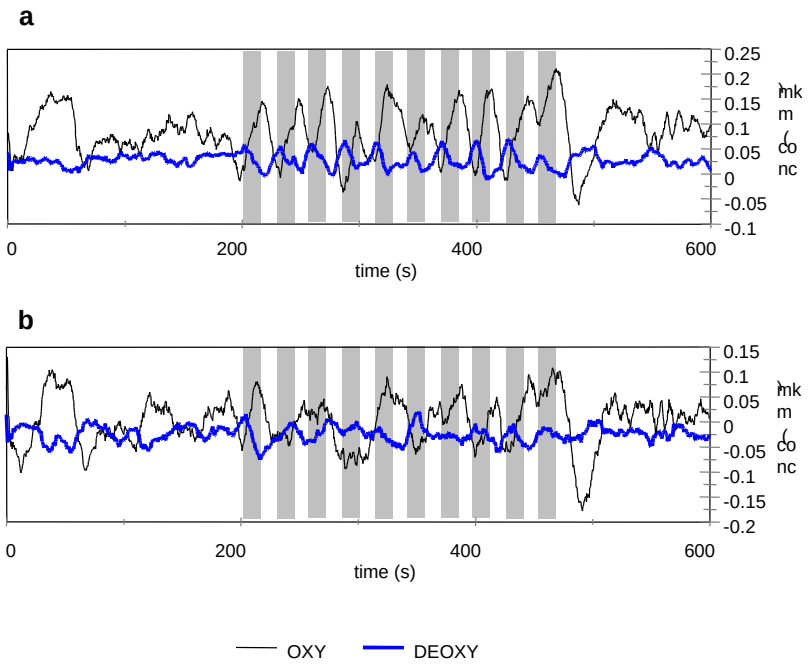


Figure 4. Hemodynamics fluctuation measured in source–detector pairs A7 (a) and D15 (b)

Figure 4a shows that, during the stimulation, the oxy-hemoglobin concentration, [HbO_2], increases and the deoxy-hemoglobin concentration, [Hb], decreases, and during the relaxation, there is a recovery toward the baseline level. This pattern of hemodynamic changes during the exercise is obviously different from the one observed at rest.

Figure 4b displays the signal detected at location D15: at this location there is no significant difference between the fluctuation patterns at rest and during exercise (the full scale of Fig. 4a is 0.25, while the full scale of the plot of Fig. 4b is 0.15).

4. EROS Applications

Event Related Optical Signal is an fNIRS technique that, instead of using changes in absorption due to the hemodynamics to infer the cognitive response to the stimulus, processes the information carried by the scattering component of the optical signal that probes the cerebral cortex. It is speculated that the changes in the signal are due to the changes in the shape of glia and neurons that are associated with neuron firing (which may be due to the movements of water and ions through the membrane) or to changes in the optical parameters of the membrane itself through the activation. As EROS does not use the changes in absorption due to the hemodynamics, it is a more direct measurement of the cellular activity; it is capable of localizing the brain activity within millimeters with a time scale of a milliseconds. The Imagent configuration used for EROS detection usually features one excitation wavelength only (830nm is preferred as it has a better efficiency penetration in the tissue than the 690 nm) and the fibers are not paired. Two parameters are measured:

(1.) the amount of light emitted by the source that reaches the detector;

(2.) the phase delay (or time delay) of the photons that reach the detector.

The event-related measures are recorded by synchronizing the recording to the stimulus presentation. Most often the EROS signal elicited by a given stimulus is analyzed with respect to a pre-stimulus baseline, recorded right before the stimulus presentation. To date most EROS studies have utilized a multiple subject paradigm, these studies included careful measurement of optical sensor locations to allow inter-subject comparisons and averaging.

Specifications

Light sources	Laser diodes emitting at 690±7 nm; 830±7 nm
Light detectors	Photomultiplier tubes
No. of light sources	Starting at 16, up to 128
No. of detectors	Starting at 2, up to 16; by adding a second computer, up to 48
Modulation frequency	110 MHz
Emitting fibers	400µm-diameter; NA=0.56;
Collecting fibers	Bundle, 3mm-diameter
Fiber length	typical: 2.5 m; for MRI applications: up to 10m
Imagent To Computer Cable Maximum Rated Length	Normally 3 meters; up to 10m by special order
Computer	Windows7, 4 GB RAM, 64-bit
Power	110/240 V, 50/60 Hz; 250 W
Operating Temperature***	5°C to 40°C
Relative Humidity	80% up to 31°C decreasing linearly to 50% at 40°C

*** The Imagent is safe for operation over the entire range of temperature. Maximum accuracy of the output measurement requires minimum drift in ambient temperature after calibration

ISS and ISS Medical are ISO 9001:2000 and ISO13485 certified.
The Imagent is covered by CE-mark for Class I

For more information please call (217) 359-8681

or visit our website at **www.iss.com**

1602 Newton Drive
Champaign, Illinois 61822 USA
Telephone: (217) 359-8681
Fax: (217) 359-7879
Email: iss@iss.com