Functional Near-Infrared Spectroscopy: Technology and Applications

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Outline

• Getting Started
• The NIRS Signal
• NIRS Technology and Capabilities
• Simple Experiments
• Going Forward
Connecting the dots...
Goal: Achieve improved understanding of neural basis of behavior

Hypothesis: Macroscale sensing is capable of providing meaningful insights* into functional elements of behavior

*Inconvenient Truth

1 mm$^3$ brain tissue = 10e9 synaptic junctions
Current Neuroimaging Systems

Impressive Formats - Restricted Environments

Inappropriate for vulnerable populations

MEG  MRI  PET
NIR Light Propagation in Tissue

NIR Region

Clear medium

Screen/detector

Absorbing structure

Scattering medium

Screen/detector

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Diffuse Imaging

“Partial view” or back reflection geometry

Photon Transport in Diffusing Media

Multi view measure + Tomographic inverse solution

(Barbour, Aronson 1988)

\[ \frac{\Delta I}{I_0} = W \Delta x \]
Functional Imaging with NIRS

• Background tissue contrast
  • Hb and other heme containing proteins
  • Lipid
  • H₂O
  • Light scattering: power, amplitude

Hemoglobin
Protoporphyrin IX

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• Spatial resolution of neuro-activation within the mm-to-cm range (depends on probe density)

• Excellent sensitivity to Hb and HbO

• Excellent sampling rate (several Hz to 60Hz+)

• Measures top 1cm of cortex

• Greatest light transmission is on forehead (prefrontal) due to lack of hair, supporting vascular structure, and sinuses
The NIRS Signal

Neural activation → Metabolic demand → Increased blood flow → Increase in oxy-hemoglobin → Wash-out of deoxy-hemoglobin

Stimulation period

Most Significant Activation Response

fNIRS

fMRI

z-scored activation changes

seconds

MRI
NIRS

fNIRS

fMRI

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Jan Mehnert, OHBM Annual Meeting, 2010

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Vascular Tree:
- Arteries  $\sim$1Hz
- Veins  $\sim$0.25Hz
- Microvessels  $\sim$0.01-0.15 Hz
  - Largest cross sectional area-
    Primary source Hb signal

Hboxy: Responsive to arteriolar activity
Hbdeoxy: Responsive to venule activity

Other factors: Lymph vessels modulated at similar frequencies as microvessels.
- Light scatter changes can mimic Hb signal.
• **NIRS technology offers:**
  - Compact, low cost sensing hardware
  - Noninvasive, continuous measures
  - Highly configurable and scalable platforms
  - Information-rich sensing data

• BOLD-like response *without* the magnet
• Source localization >> EEG
• Minimal sensitivity to movement artifacts
NIRS Technology and Capabilities
Development Timeline

2000

2004

2012 Hyperscanning

2013 Mobile Studies
Technology-Application Space

Wearable NIRS

NIRS-TMS
NIRS-MRI
NIRS-EEG

Hyperscanning

Optional Fiber Based Illumination
Optional Fiber Based Detection

Environment

Low Density
64 channels

NIRSport™
NIRScout™
NIRScout™ Tandem™

NIRScout™
NIRScout™
NIRScout™ Tandem™

NIRScoutX™
NIRScoutX™
NIRScoutX™ Tandem™

High Density
>3000 channels

Neonatal
Sensory
Learning / ADHD
Intensive Care/TBI
Neuromarketing
Rehab
Sports Med.

Cognition
BCI
Communication
Neurovascular coupling
Group Activity

Epilepsy
Neuro-Modulation

Applications

Technology-Application Space

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System-Subject Permutations

Standard Setup
Single system/single subject
Standard Channel Count
ex: 1 x 16S-16D System

Single Subject Tandem Setup
Two Systems/Single Subject
Double Channel Count
ex: 2 x 16S-16D Systems
- Effectively 32S-32D

Hyperscanning Setup
Single System/Two Subjects
2 x Half Channel Count
ex: 32S-32D System (NIRScoutX)
- Effectively 16S-16D per subject

Two Subject Tandem Setup
Two Systems/Two Subjects
2 x Standard Channel Count
ex: 2 x 16S-16D Systems
- Effectively 1 x 16S-16D per subject

Multi-Subject Tandem-Hyperscanning Setup
Two Systems/Four (or more) Subjects
2*2 (or more) x Half Channel Count
ex: 4 subjects on 2 x 32S-32D Systems (2 x NIRScoutX)
- Effectively 16S-16D per subject
Subject-Environment Domains

- Infant - Adult
- Interacting groups
- Mother-child learning
**Principal Attributes for Sensing Hardware**

**Optical Detection**

Programmable gain control

- Dynamic range – 10e9
- Sensors: SiPD, APD
- Up to 5 cm S-D Separation

**Multidistance**

up to 2048 channels

**Programmable Source Control**

- One source – 62 Hz,
- Two sources – 31 Hz…
- Multisite parallel illumination

**Illumination**

- Dual Source e.g., 1,9; 2,10,…
- LED (2λ), 760, 850 nm
- Laser (up to 8 λ), 680-1050 nm
Software – Instrument Control & Recording

• NIRStar
  – Real-time cortical viewing
  – Real-time data streams
  – Real-time block averages
  – Hyperscanning
  – Optode position registration
  – BCI/Neurofeedback
Software – NIRStar – Real-Time Block averages
Favorable Attributes of NIR Optical Measures

- Highly sensitive detection
- Brilliant, non-damaging light sources
- Fast response; well suited for functional studies
- Easily configurable for wearable studies
- Economical technology
Integrated Solutions

Software
- NIRStim
- NIRStar
- SDK
- nirsLAB

Hardware
- NIRScout
- Head Gear
- NIRSport
- LED-Laser

Subjects
- Infant
- Adult
- Child
- Groups

Environments
- Mobile
- Remote
- Hyper scanning
- Tandem

3rd Party
- EEG
- fMRI
- tDCS
- Eye Tracking
Parameter Space for Behavioral Assessment

Environment | Subject | Tools | Goal
---|---|---|---
Virtual Reality | Active | Complementary Technologies | Performance Enhancement*
Ambulating | Individual - Group | fNIRS | Anxiety Abatement
Quiescent | Tasks | Signal Analysis | Disease Detection
Sleep | | | Treatment Guidance

Modifiers (Stress level, Distractors)

- EEG
- tDCS
- Eye Tracking
- fNIRS
- TDCS
- EEG
- Event Related Connectivity
- Machine Learning
- BCI

*Honing Skills
Athletic, Decision Making, Language, Attention, Learning and Memory

Excludes fMRI, MEG

Biofeedback

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Wally: “We scan by way of **optical tomography**, white light pinpoints pulse along the entire length of the headgear and re-read after absorption through their brain tissue. We see their thoughts … we see what they see”
Information Content of NIRS
Information Content of NIRS Measures

- Background tissue contrast
  - Hb, Lipid, H$_2$O, light scattering: power, amplitude.
- Neurovascular coupling
  - Event Related: BOLD signal
- Connectivity
- Co-Variational States
- Modeling Studies
Mechanisms of Neurovascular Coupling

Stimulus

DeoxyHb

OxyHb

Vascular Endothelium

Astrocyte

Neuron

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• Time variations in Hb signal

\[ Hb_{deoxy} + Hb_{oxy} = Hb_{total} \]

\[ Hb_{deoxy} - Hb_{oxy} = Ext_{eff} \]

\[ \frac{Hb_{oxy}}{Hb_{total}} = HbO_2Sat \]

Supply – Demand Balance

Autoregulation
Controlling Influences on Hb Dynamics

- Local metabolic feedback
  - Effects Hb, HbO, Hbtot
- Systemic modulation (autonomic)
- Hb is a strong biological buffer:
  - Binds NO, bicarbonate, peroxides

Coupled dynamical system
• Different preferred states, sensitive to prevailing conditions
• Unequal path-dependent transition probabilities
• Different time constants
Hb State Transitions

(+)

Hb Oxy

(+)

Hb Deoxy

(+)

Hb Total

(-)

Hb Oxy

(-)

Hb Deoxy

(-)

Hb Total

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## Covariations of Hemoglobin States

<table>
<thead>
<tr>
<th>Hemoglobin State</th>
<th>State 1</th>
<th>State 2</th>
<th>State 3</th>
<th>State 4</th>
<th>State 5</th>
<th>State 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Hb}_{\text{oxy}} )</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>( \text{Hb}_{\text{deoxy}} )</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>( \text{Hb}_{\text{tot}} )</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>( \text{Balanced} )</td>
<td>Balanced</td>
<td>Uncomp. oxygen debt</td>
<td>Comp. oxygen debt</td>
<td>Balanced</td>
<td>Uncomp. oxygen excess</td>
<td>Comp. oxygen excess</td>
</tr>
</tbody>
</table>
### Individual Hb States

**Hb\textsubscript{oxy}**

**Hb\textsubscript{deoxy}**

**Hb\textsubscript{total}**

---

### Covariational Hb States

<table>
<thead>
<tr>
<th>State</th>
<th>Hb\textsubscript{oxy}</th>
<th>Hb\textsubscript{deoxy}</th>
<th>Hb\textsubscript{total}</th>
<th>Time Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Image" /></td>
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<td>2</td>
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<td><img src="image5.png" alt="Image" /></td>
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<td><img src="image8.png" alt="Image" /></td>
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<tr>
<td>4</td>
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<tr>
<td>5</td>
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<td><img src="image15.png" alt="Image" /></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image16.png" alt="Image" /></td>
<td><img src="image17.png" alt="Image" /></td>
<td><img src="image18.png" alt="Image" /></td>
<td></td>
</tr>
</tbody>
</table>

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40 mm Hg

NIRS Array

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Spatial Dependence of Covariational Response

ROIs sharing similar Hb state $t_1 \ldots t_n$
Resting State Behavior is Tissue Specific

Breast

Muscle

Brain

Hb States

V_1, V_2, V_3, ..., V_n
Vascular Autoregulation: Rat seizure model

Seizure model:
Administration of 4-Aminopyridine

Experimental data from: Ma et al., Weill Cornell Medical College, unpublished data.
Hb Response to Seizure

Hemodynamic response to seizure

Hb state response to seizure
Hb state response to seizure

CCD Image

Hb state map at time frame 501

Temporal state fraction during an acute seizure (time frames: 300-700)
Input: HbO, Hb, Hbtot spatial time series maps

Output:

- Spatial dependence of preferred states
  - 18 spatial maps
- Transition Probabilities
  - 30 possible transitions
- State Time Constants
  - 6 spatial maps
Benefits of Co-Variational Measures

• Spatiotemporal features of state transitions are stable and task dependent.

• Provides wealth of information for use of classification schemes (LDA).
Questions?
Walkthrough of Process Control

NIRStar
- Sensor Registration
- Instrument Setup
- Task Definition

NIRStim
- Event Recording
- Data Editing

nirsLAB*
- Hb State Computation
- Topography

NIRS-BBCI*
- Cap Setup
- Brain Comp. Interface
- Connectivity-DCM, GC

NAVI*
- Stat. Para. Mapping

*http://www.nitrc.org/projects/fnirs_downstate
Dedicated neoprene headbands
Probes for infants/newborns
OPTICAL COUPLING SOLUTION

External Detector Unit
External Source Unit

TMS/fMRI Fiber Solution

6 mm profile
fNIRS/fMRI – Concurrent Measurements

Magnet Room

LED-to-Fiber Coupler

~2 m

Detection Fiber Optics (7+m)

LED Driving Current
Stimulus Presentation System:
- Hardware
- Stimulus Software

Digital Interface:
- LPT (parallel) Port
- Data Acquisition Card
- 3rd Party Interface

PC Bus

Trigger Cable (4 or 8 lines)

Trigger Splitter (optional)

EEG Amp

NIRStar records:
- NIRS Data
- Event markers

USB

NIRS Measurement

• Subject

Stimulation:
- Visual
- Auditory
- Tactile
  etc.

• Response
Figure 7-10. Graphical specification of detector locations.

Figure 7-12. Specification of arbitrary probe locations.
Instrument Setup

- Tandem
- Instrument 1
- Instrument 2
- SDK
- Hyperscan
- S-D Layout/Registration
- Triggers - NIRStim

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Tandem mode

- Two identical instruments (any model)
- Channel number doubled
- Integration in software, seamless operation as one instrument

NIRSport Tandem Setup (pictured left) for 16-source and 16-detector measurements

NIRScout Extended Tandem Setup (pictured right) for a maximum of 128-source and 64-detector measurements
NIRScout Extended 8-bit Trigger OUTPUT

Direct, programmable digital (TTL) control of other systems

EEG

EMG

Brain stimulation (TMS, etc.)
NIRS Instrumentation Highlights

• Comprehensive:
  - Wearable → Large-scale/High-density
  - Wide range of accessories

• Scalable:
  - Upgradeable, Tandem Mode
  - Hyperscanning

• Integrated:
  - Experimental control (Trigger I/O)
  - Single cross-platform control software
  - Multi-modal ready (EEG, fMRI, TMS, …)
Task Definition: NIRStim

Define Trials

Trial Sequence

Parameters:
- ID:
- Name:
- Type:
- Marker:
- Duration:
- Jitter:
- Color:
- Del:

Trial Sequence:
- Trials ID:
- Reps:
- Order:
Beer-Lambert Analysis

\[ \frac{I}{I_0} = e^{-lec} \]

- \( l \) = pathlength
- \( e \) = ext. coeff.
- \( c \) = conc.
SPM Analysis

Figure 3: Plot of HRF Parameter Specification

- Specify basis function: hrf
- Parameter: 6 16 1 1 6 0 32

Convolved Model(s)

Model 1

- Time Frame: 500, 1000, 1500, 2000

Convolved Design Matrix

- Design Matrix

t-score

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**nirsBCI: BBCI toolbox + nirsLAB**

**Experiment:** Left and right finger tapping

Source (red) and detector (blue) layout

Event (left and right finger tapping) markers
nirs Signals: \( \text{oxyHb and deoxyHb} \)

DeoxyHb changes during finger tapping (block-averaged)

Brain (left) and head (below) surface mapping (block-averaged deoxyHb)
**BBCI toolbox:** (publicly available under [http://www.bbcide/toolbox/](http://www.bbcide/toolbox/)) was designed to perform advanced offline analyses of neuronal data; online framework for data processing and classification*.

**Classification algorithm:** Regularized Linear Discriminant Analysis (RLDA)

A hyperplane which separates two classes: the “circles” and the “crosses”

nirs Signals (deoxyHb) → BBCI toolbox: training and classifying

Classifier accuracy is estimated by cross-validation

Classifier accuracy based on spatial feature

Classifier accuracy based on temporal feature
BCI Performance Improvement: EEG+HbO

Fazli et al, Neuroimg. 2011
Optical Activity

Barbour et al., "A programmable laboratory testbed ..., “
Effective Connectivity

Dynamic Causal Modeling

Dynamic perturbation $u(t)$
Structural perturbation $b_{23}$
For example:

\[
T(t) = \text{ctHb}\left\{\phi^{(a)}\left[1 + v^{(a)}(t)\right] + F^{(c)}\phi^{(c)}\left[1 + v^{(c)}(t)\right] + \phi^{(v)}\left[1 + v^{(v)}(t)\right]\right\},
\]

\[
S_{BOLD}(t) = \left(\phi^{(a)} + \phi^{(c)} + \phi^{(v)}\right) \left[3.4 \left(1 - \frac{D(t)}{D_0}\right) - \frac{\left(1 - S^{(a)}\right)v^{(a)}(t) + \left(1 - S^{(c)}\right)v^{(c)}(t) + \left(1 - S^{(v)}\right)v^{(v)}(t)}{3 - S^{(a)} - \left\langle S^{(c)}\right\rangle - S^{(v)}}\right].
\]