Functional Near-Infrared Spectroscopy: Technology and Applications

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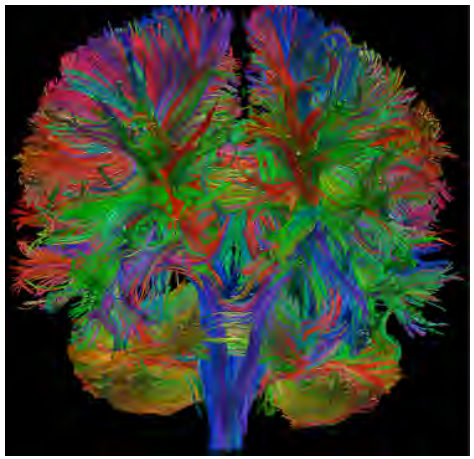
Outline

- Getting Started
- The NIRS Signal
- NIRS Technology and Capabilities
- Simple Experiments
- Going Forward

Connecting the dots….

Connectivity

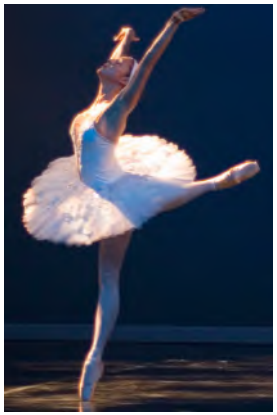


+

Neurochemistry

Bioelectric
(Hemodynamic)

Behavior



NIH Brain Initiative

Goal: → Hypothesis:

Achieve improved understanding of neural basis of behavior

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

*Inconvenient Truth

1 mm^3 brain tissue = 10e9 synaptic junctions

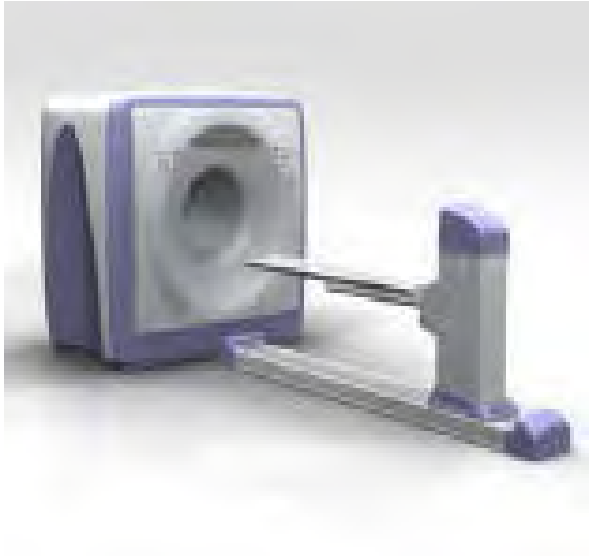
Current Neuroimaging Systems

Impressive Formats - Restricted Environments

Inappropriate for vulnerable populations

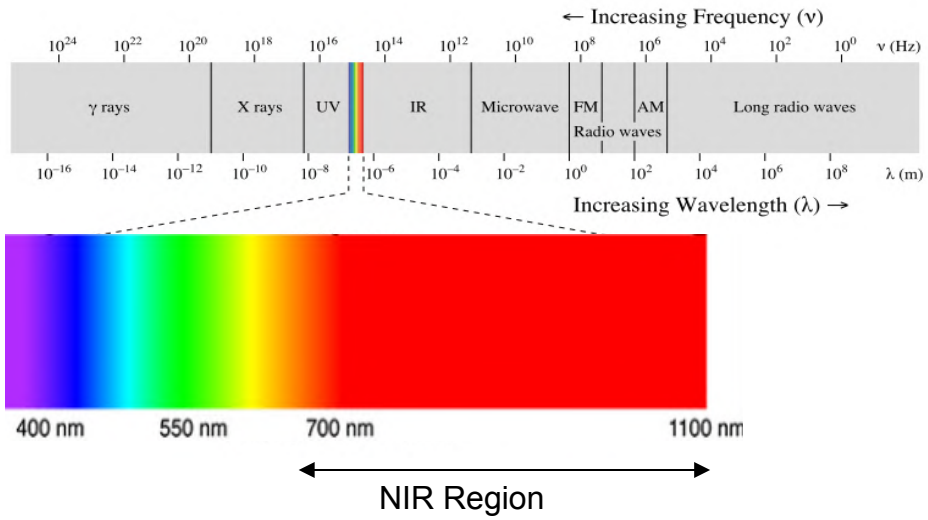
MEG

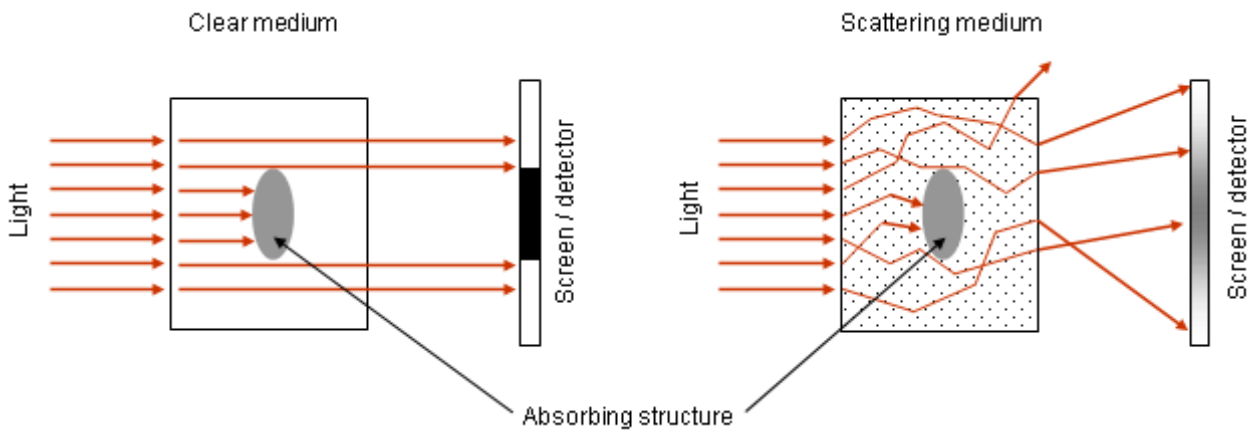
MRI



PET

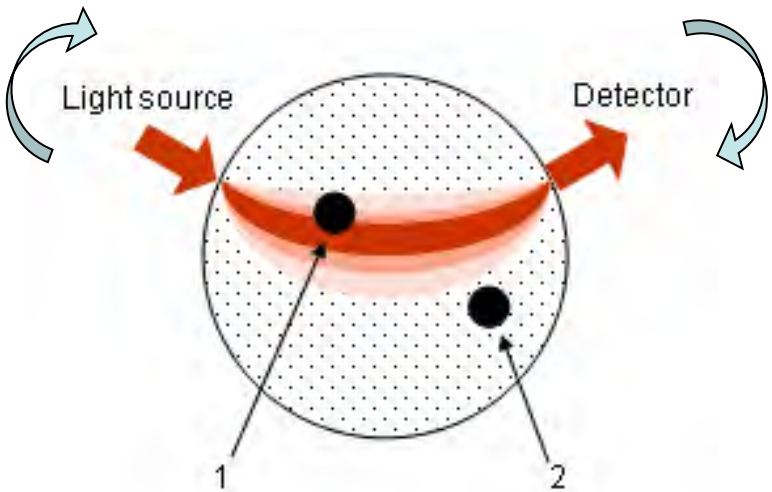
NIR Light Propagation in Tissue





Diffuse Imaging

Photon Transport in
Diffusing Media



Multi view measure

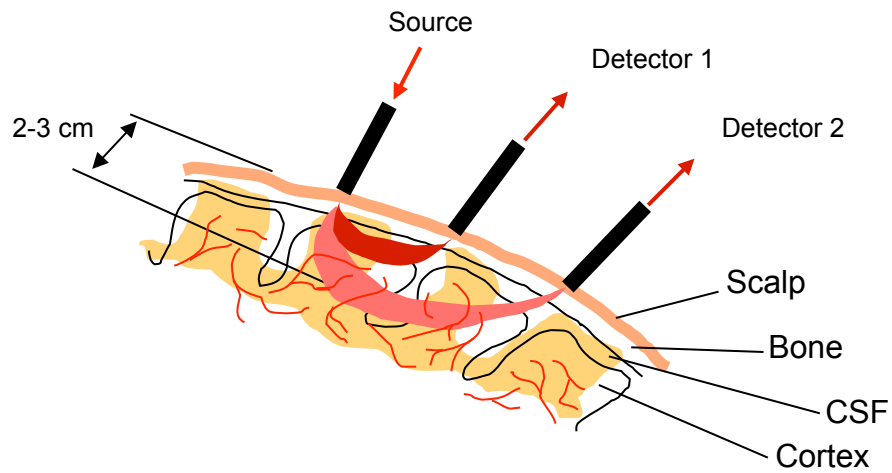
+

Tomographic inverse
solution

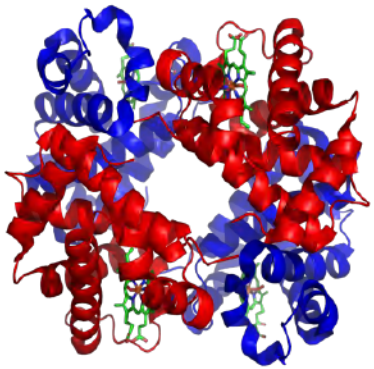
(Barbour, Aronson 1988)

$\Delta I/Io = \mathbf{W}\ \Delta x$

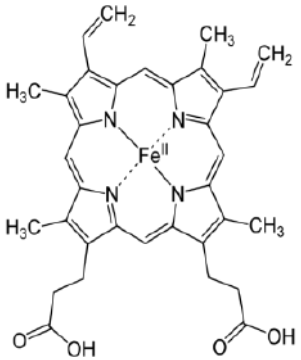
"Partial view" or back reflection geometry



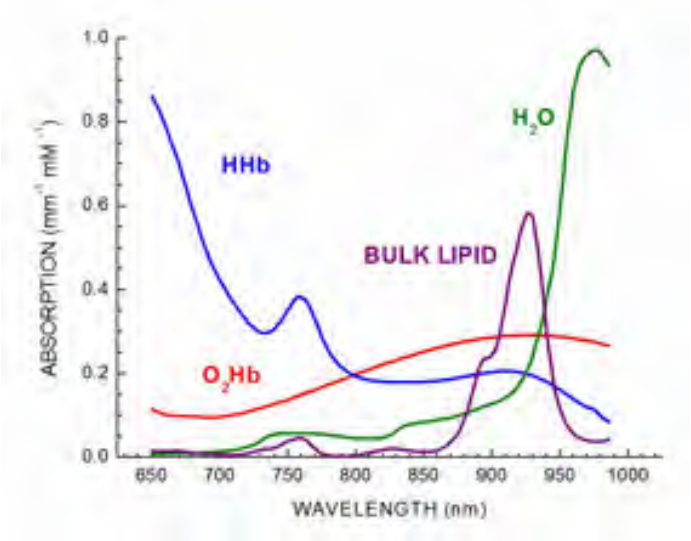
Functional Imaging with NIRS



Hemoglobin



Protoporphyrin IX

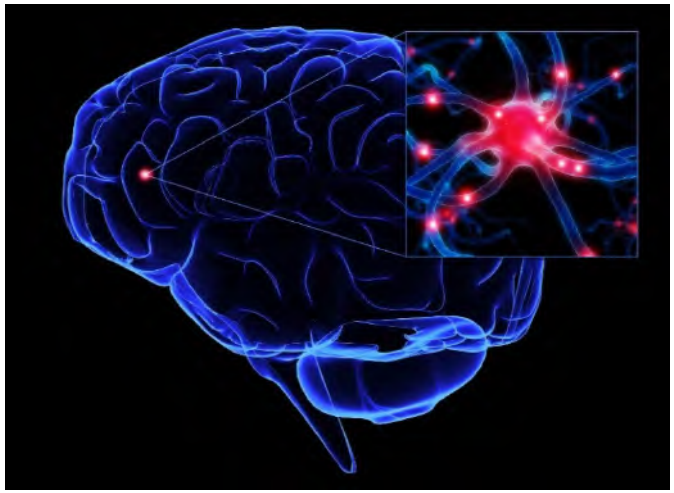


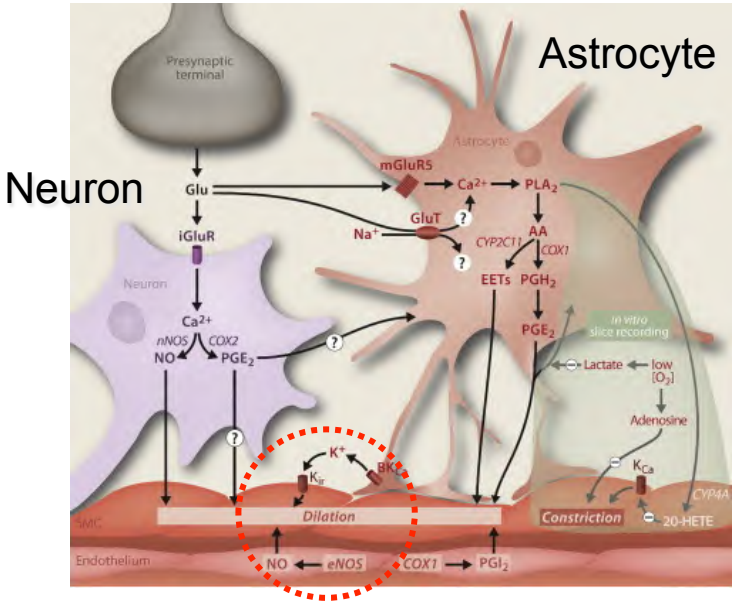
- Background tissue contrast
  - Hb and other heme containing proteins
  - Lipid
  - H_2O
  - Light scattering: power, amplitude

Physical and Biological Properties of NIRS

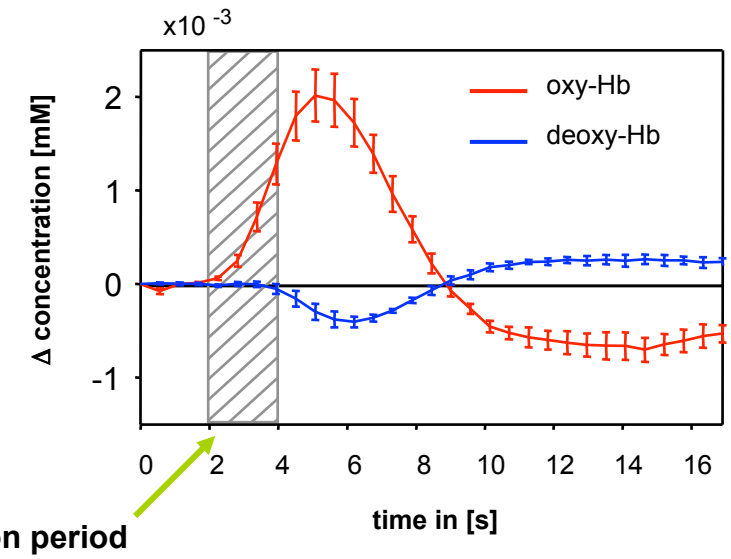
- Spatial resolution of neuro-activation within the mm-to-cm range (depends on probe density)
- Excellent sensitivity to Hb and HbO
- Excellent sampling rate (several Hz to 60Hz+)
- Measures top 1cm of cortex
- Greatest light transmission is on forehead (prefrontal) due to lack of hair, supporting vascular structure, and sinuses

The NIRS Signal





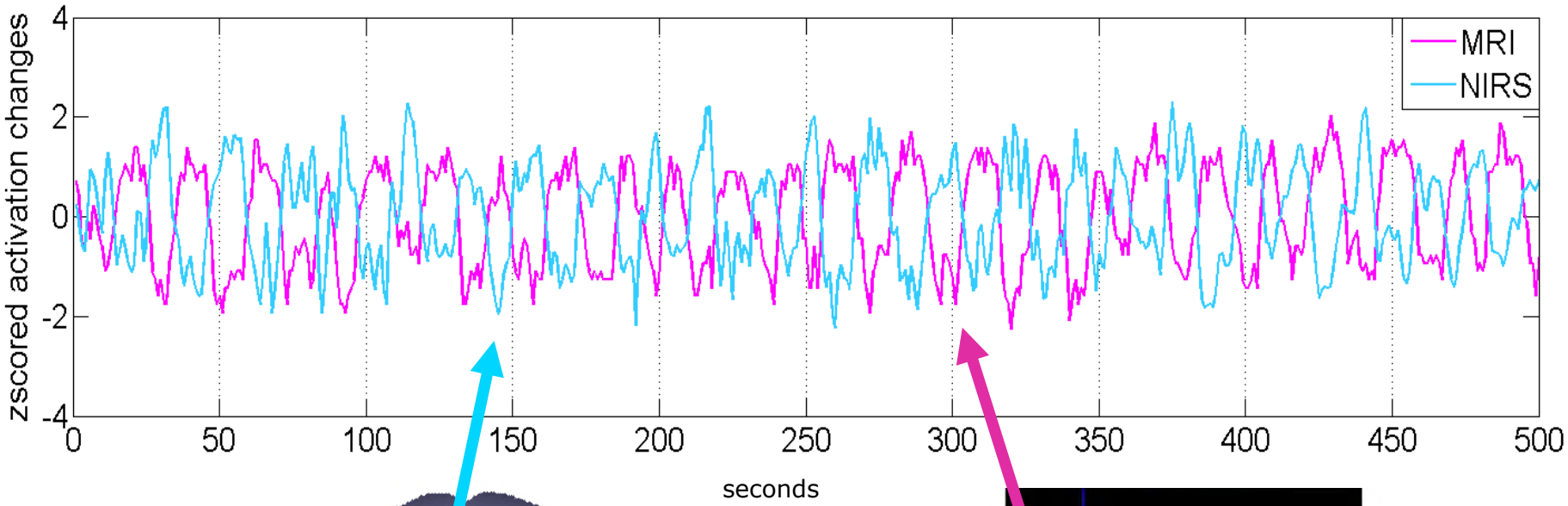
Vascular Endothelium



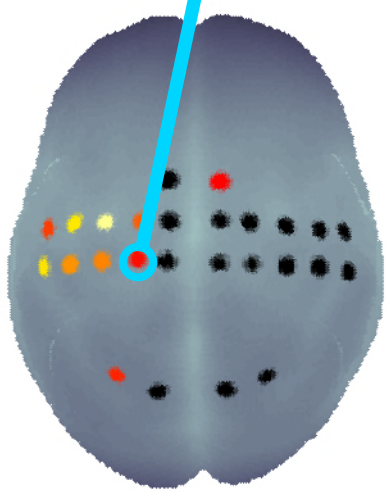
Neural activation
↓
Metabolic demand
↓
Increased blood flow
↓
Increase in oxy-hemoglobin
↓
Wash-out of deoxy-hemoglobin

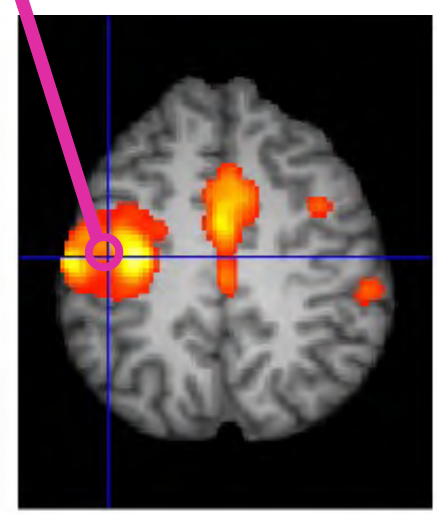
Kohl M ,.. , Dirnagl U. Phys. Med. Bio. 2000

Most Significant Activation Response



fNIRS





fMRI

The Hemoglobin Signal

Vascular Tree:

- Arteries ~1Hz
- Veins ~0.25Hz
- Microvessels ~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.

Summary

- 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

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Development Timeline

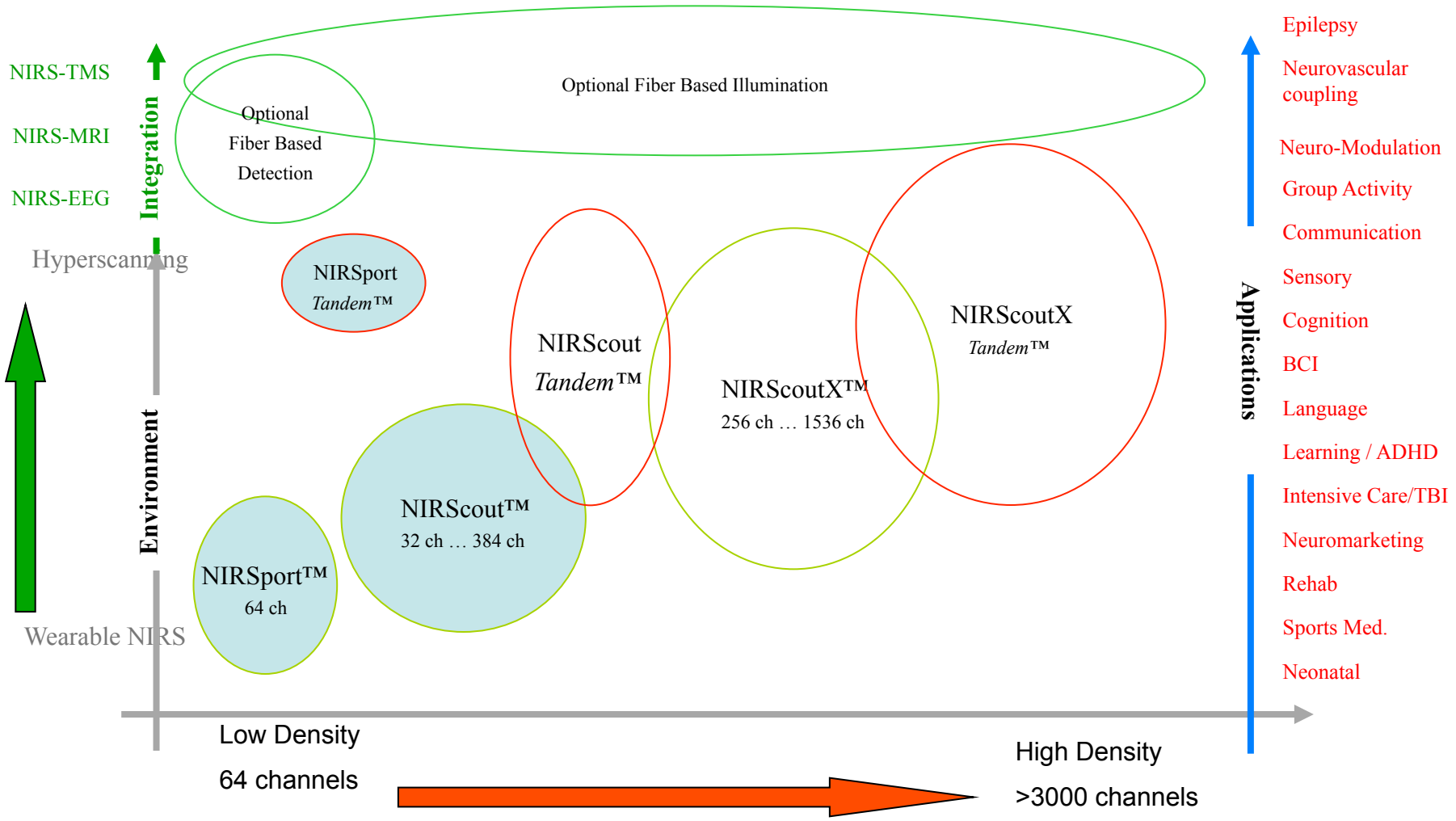
2000

2004

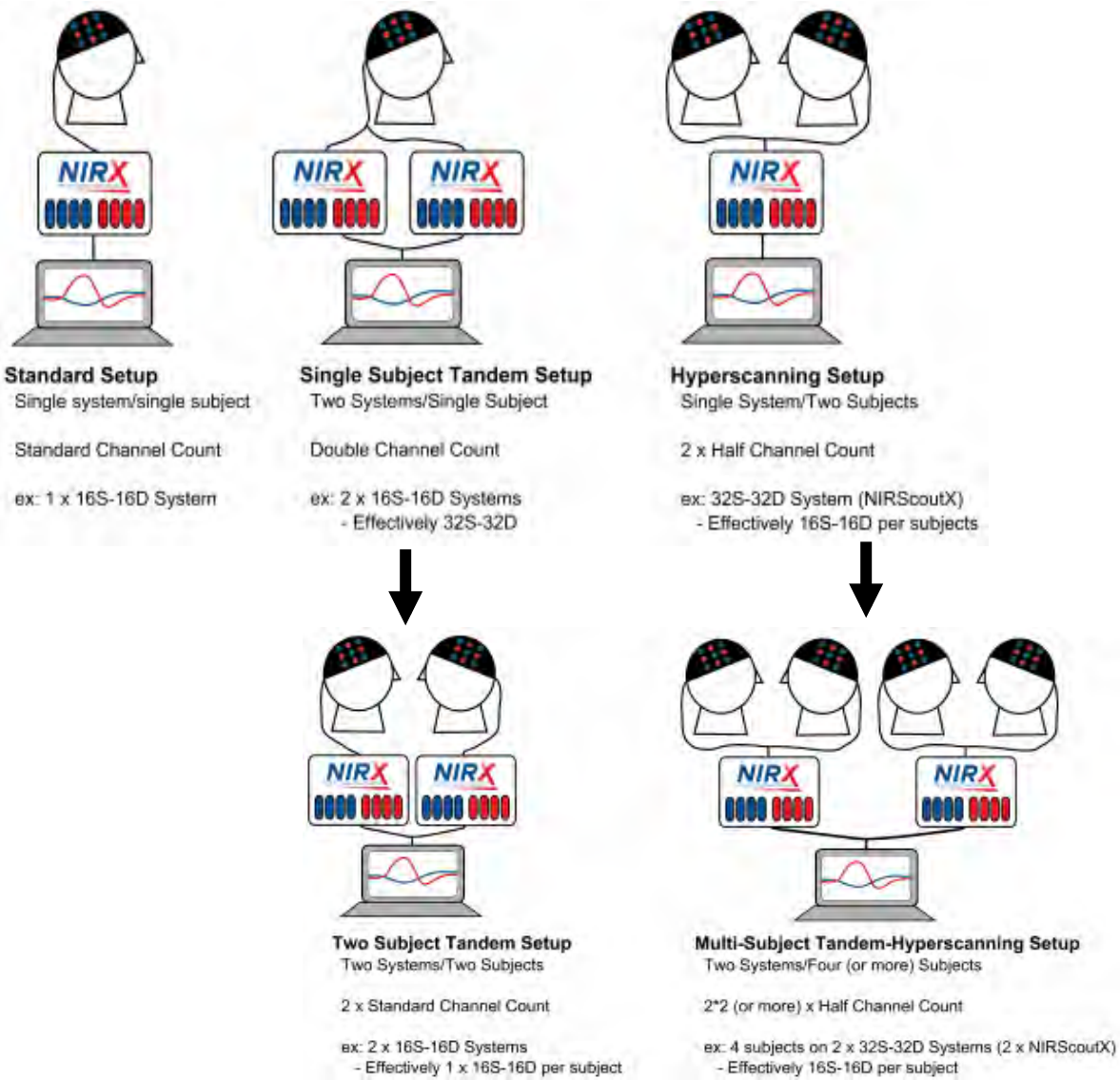
2012 **Hyperscanning**

2013 **Mobile Studies**

Technology-Application Space



System-Subject Permutations



Subject-Environment Domains

Infant - Adult

Interacting groups

Mother-child learning

Principal Attributes for Sensing Hardware

Optical Detection

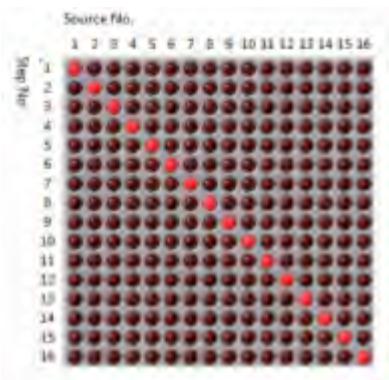
Programmable gain control

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

Multidistance
up to **2048** channels

Illumination

LED (2λ), 760, 850 nm
Laser (up to 8 λ),
680-1050 nm



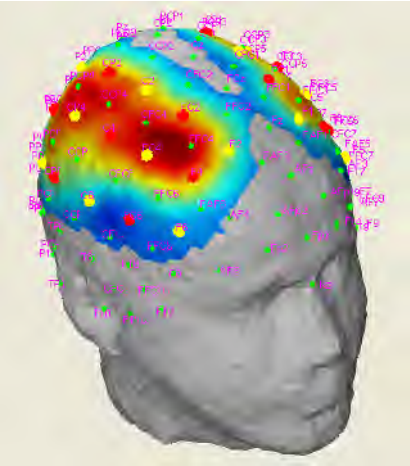
Programmable Source Control

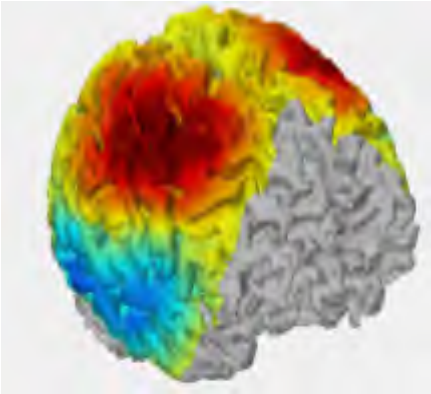
- One source – 62 Hz,
- Two sources – 31 Hz…
- Multisite parallel illumination

Dual Source
e.g., 1,9; 2,10, …

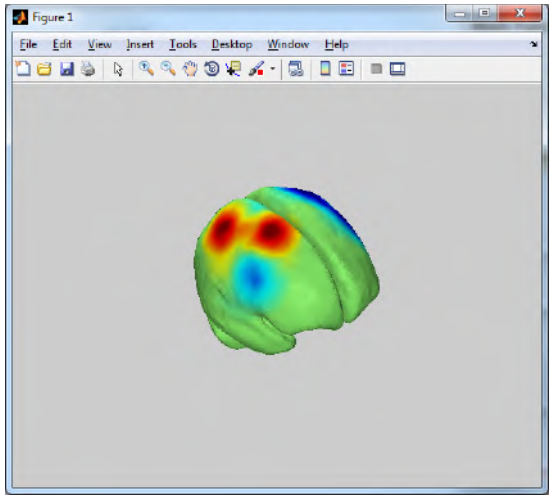
System Control Software

Software – Instrument Control & Recording

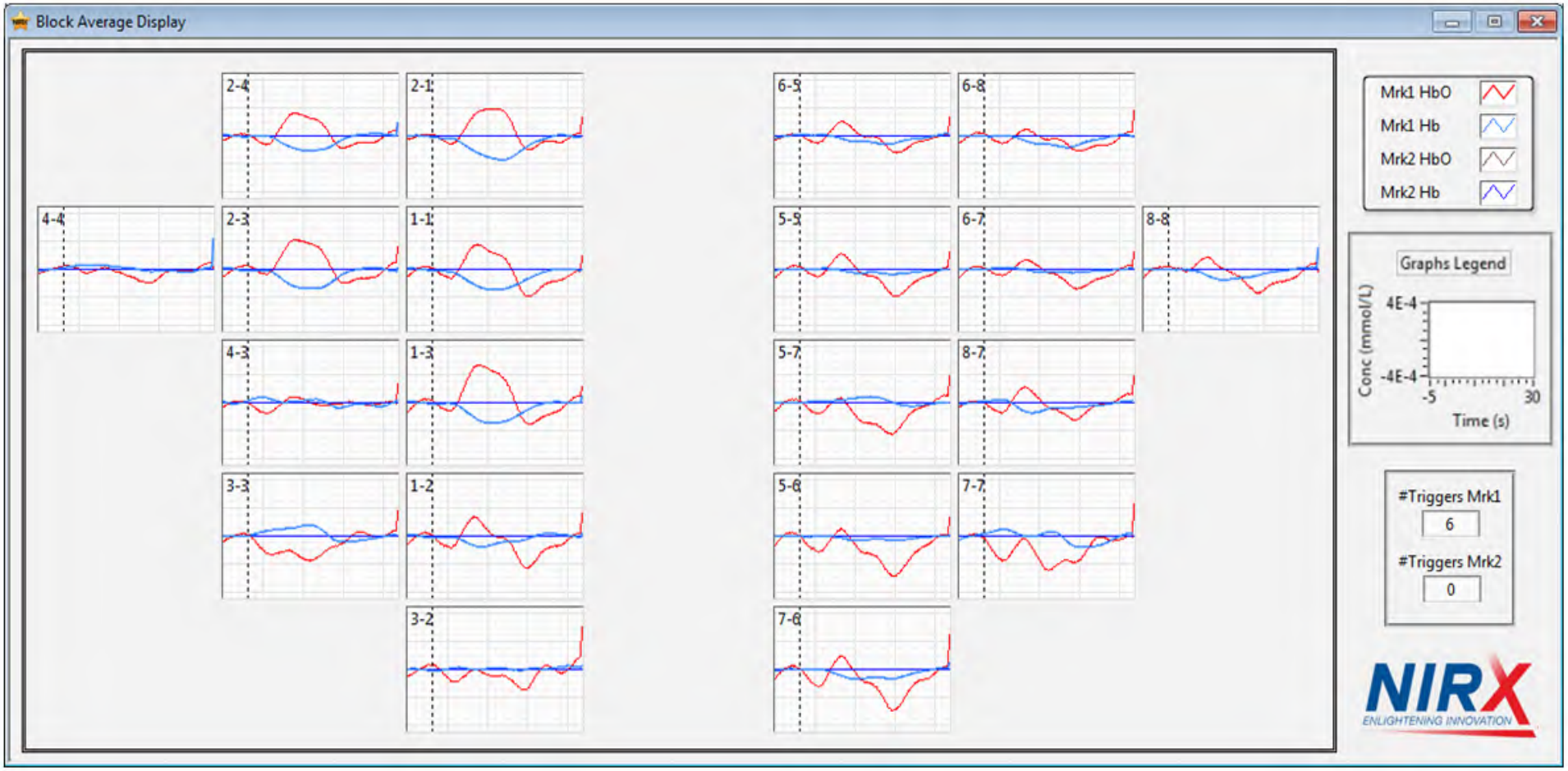




- **NIRStar**
  - Real-time cortical viewing
  - Real-time data streams
  - Real-time block averages
  - Hyperscanning
  - Optode position registration
  - BCI/Neurofeedback



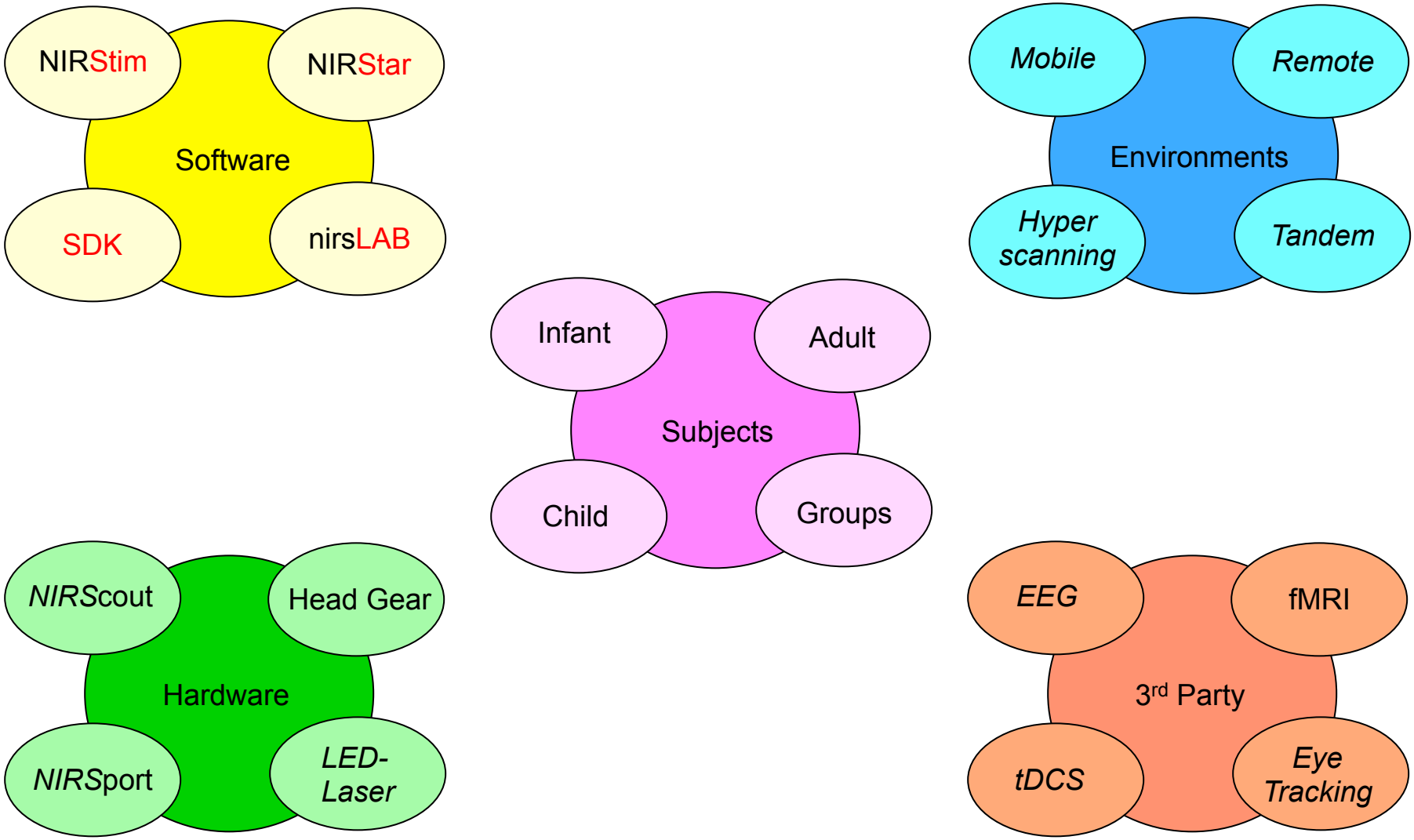
Software – NIRStar – Real-Time Block averages



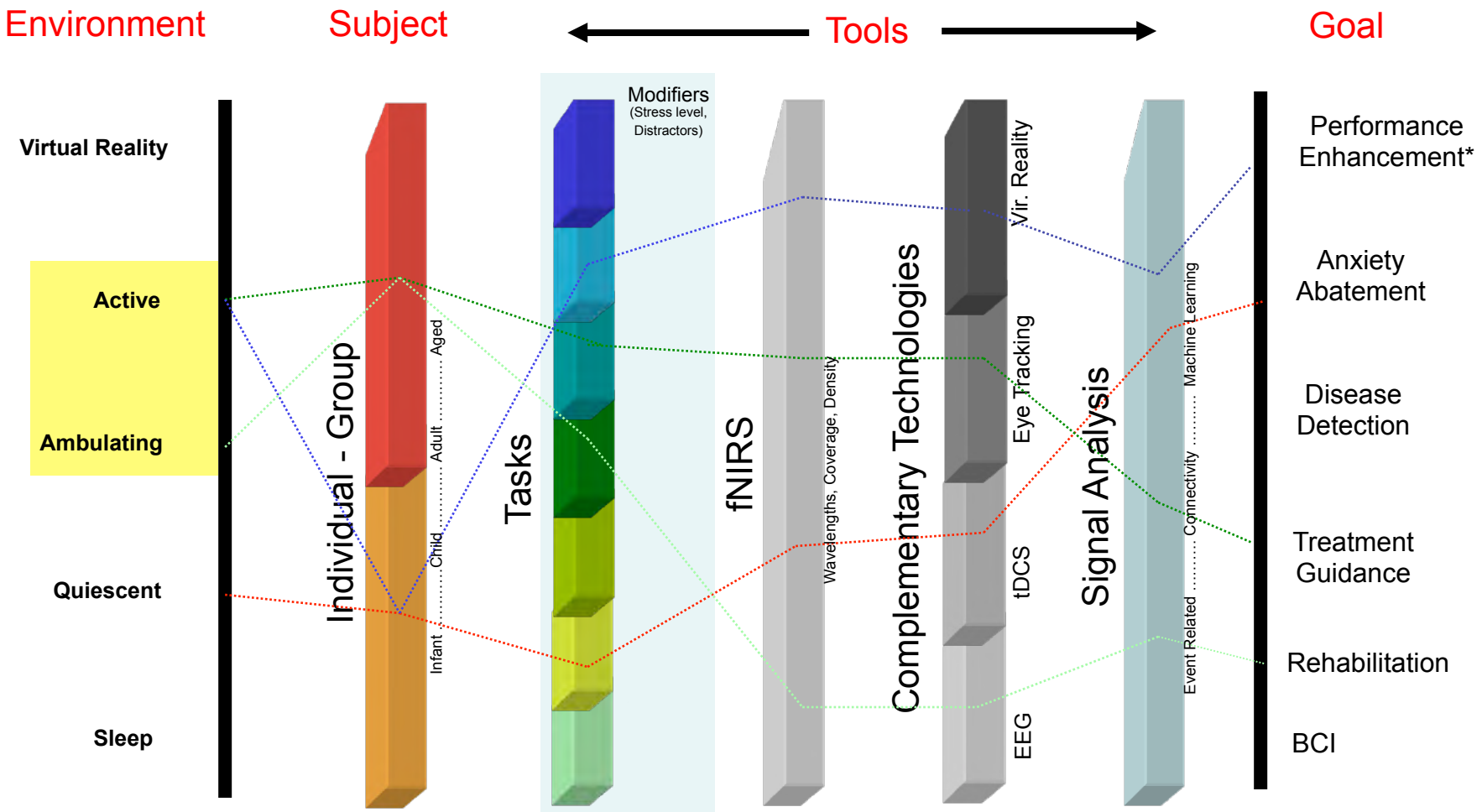
Favorable Attributes of NIR Optical Measures

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

Integrated Solutions



Parameter Space for Behavioral Assessment



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

Excludes fMRI, MEG

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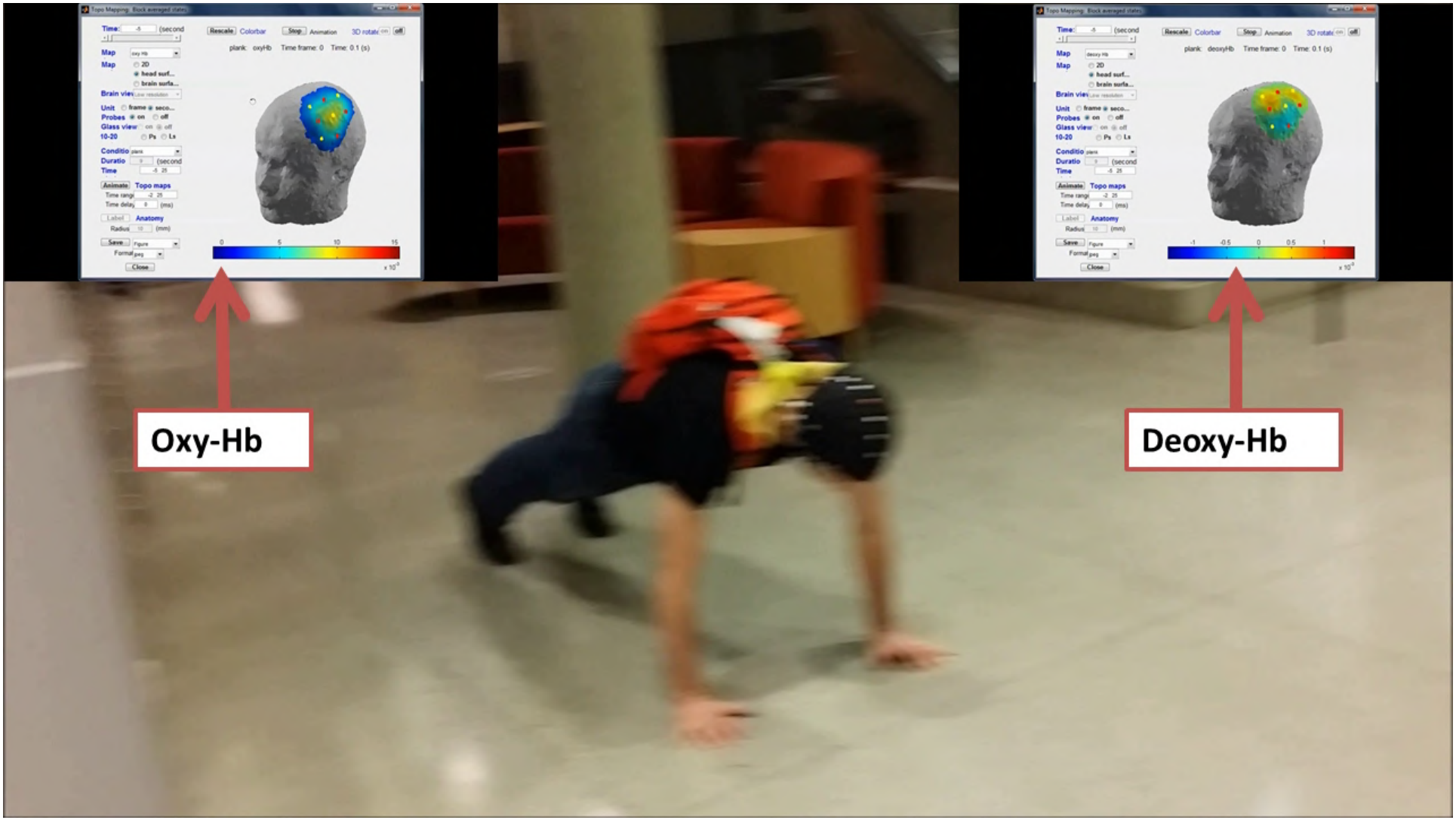
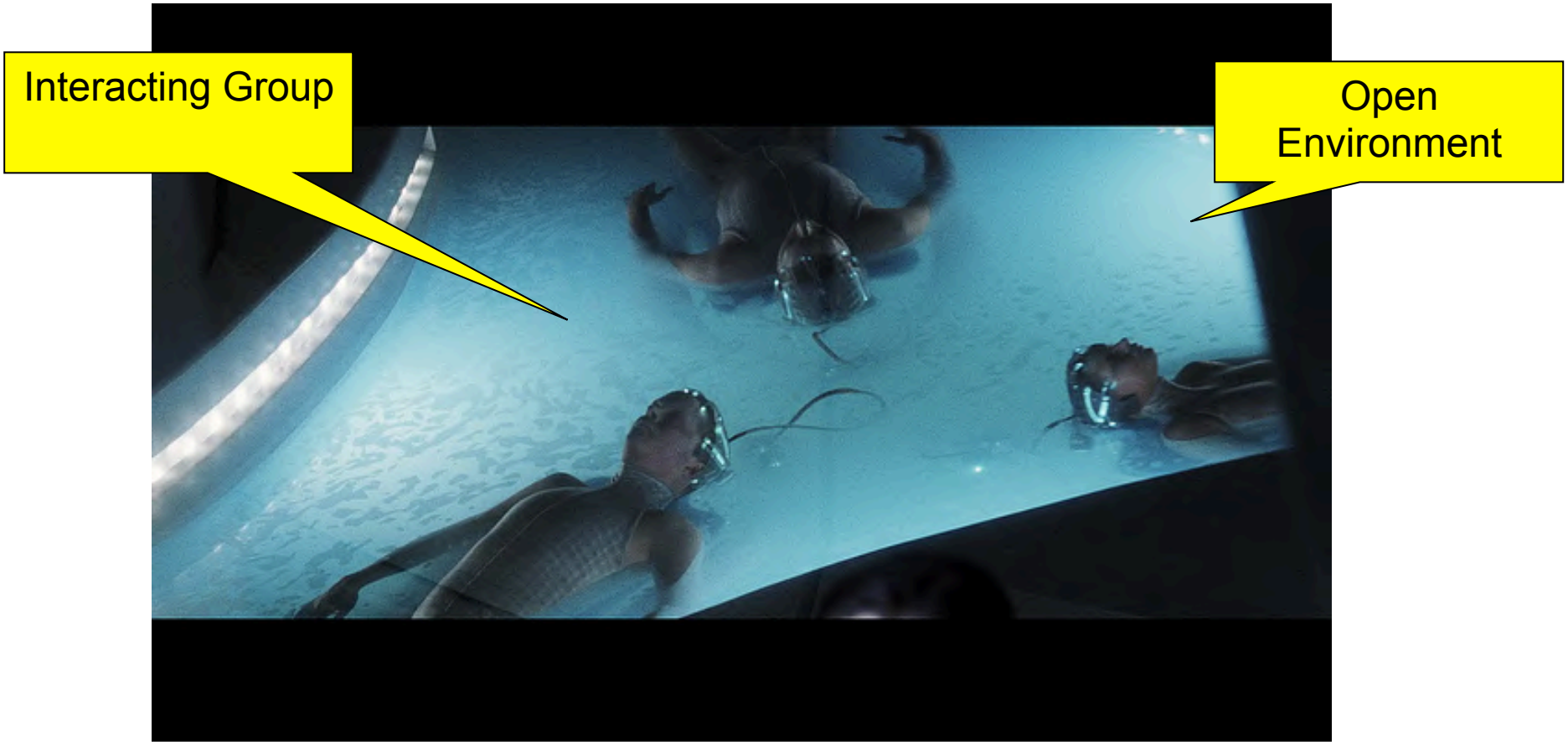

Oxy-Hb
Deoxy-Hb

Minority Report 2002



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

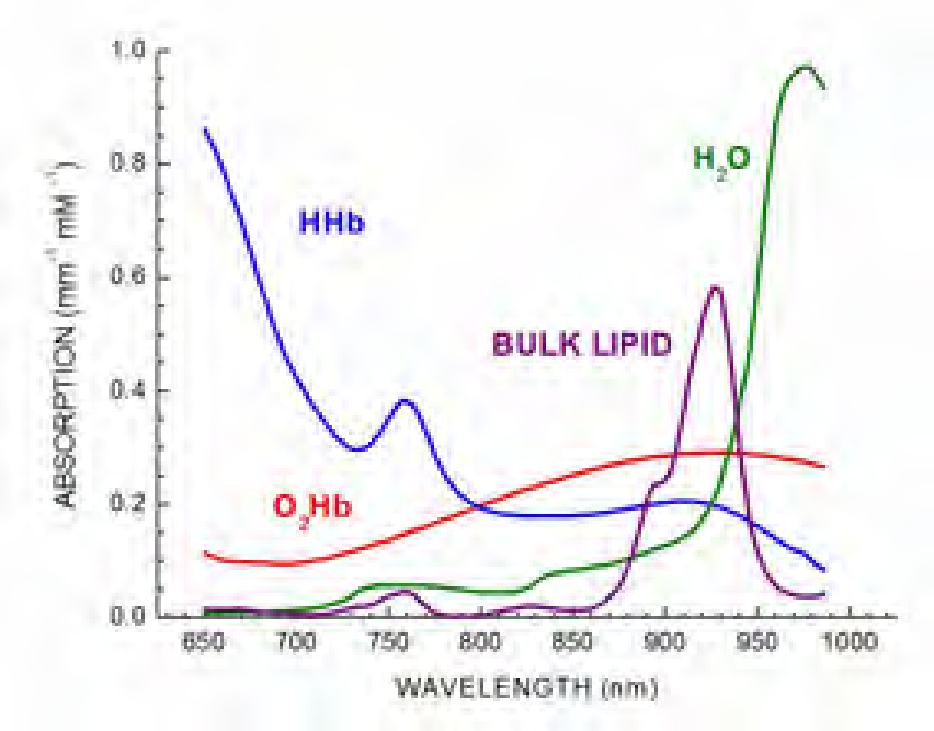
- Background tissue contrast

  -Hb, Lipid, H_2O,light scattering: power, amplitude.

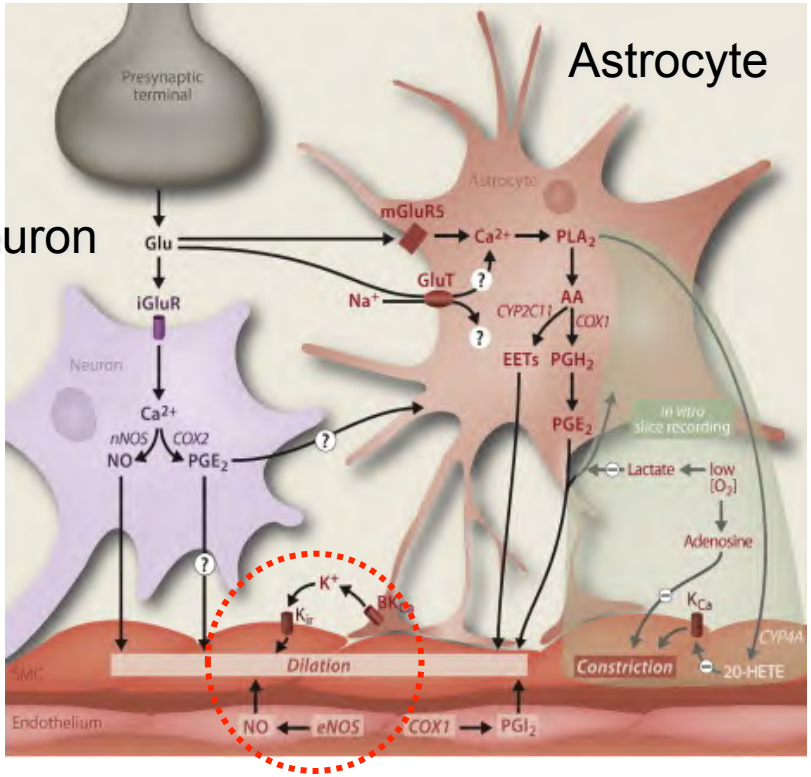
- **Neurovascular coupling**

  -Event Related: BOLD signal

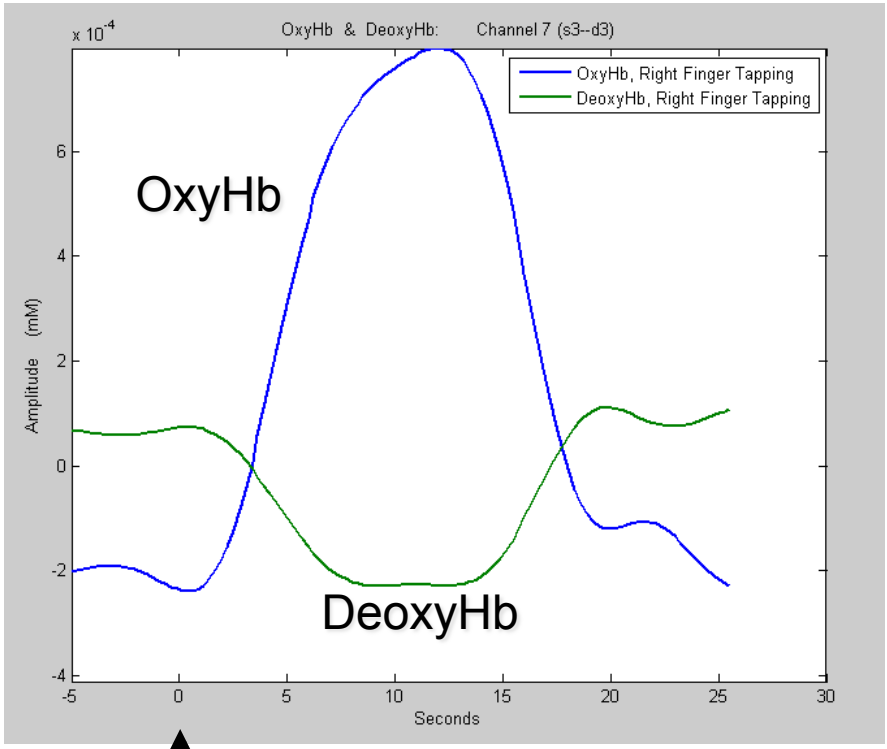
- **Connectivity**
- **Co-Variational States**
- **Modeling Studies**



Mechanisms of Neurovascular Coupling



Vascular Endothelium



Stimulus

Information Content of NIRS

- Time variations in Hb signal

$$Hb_{deoxy} + Hb_{oxy} = Hb_{total}$$

$$Hb_{deoxy} - Hb_{oxy} = Ext_{eff}$$

$$Hb_{oxy}/Hb_{total} = HbO_2Sat$$

Supply – Demand Balance

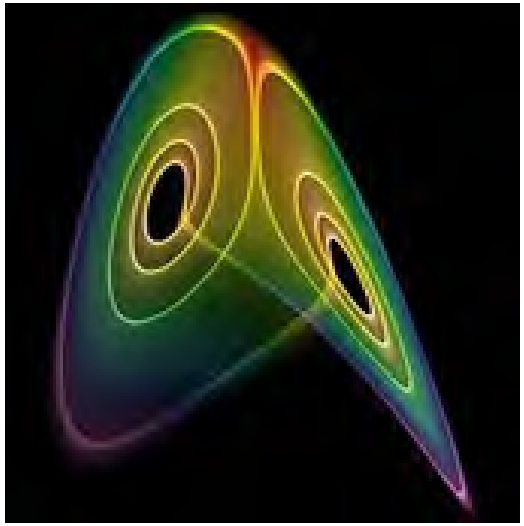
↓

Autoregulation

Controlling Influences on Hb Dynamics

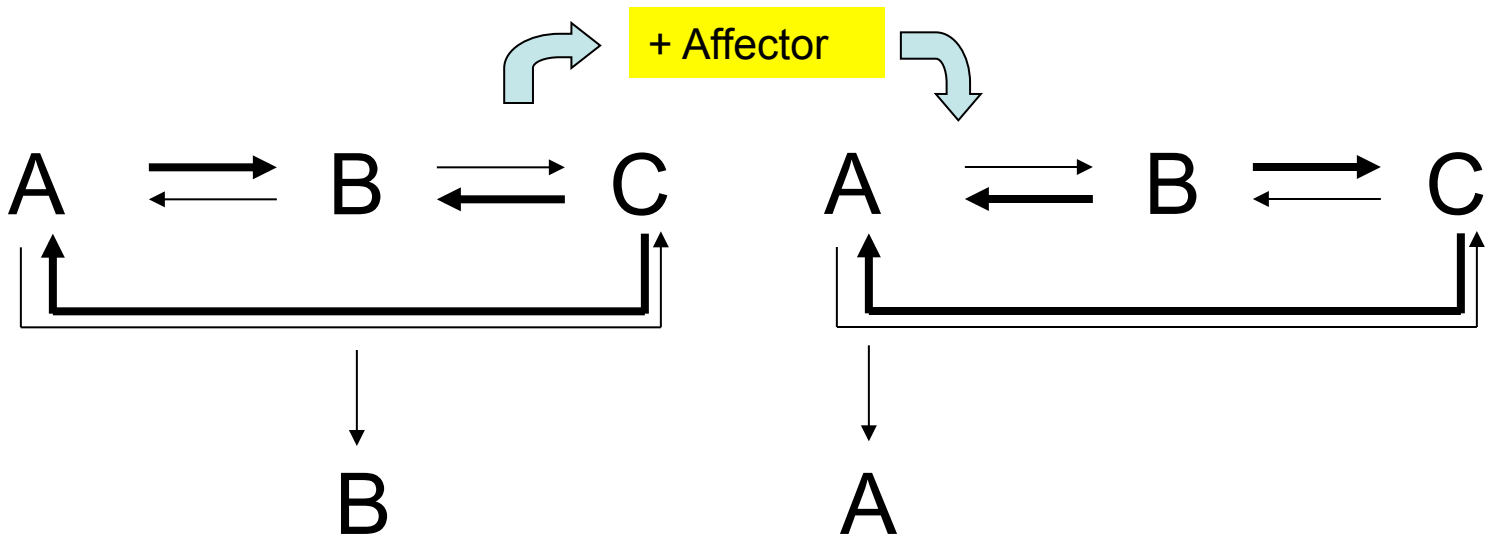
- Local metabolic feedback
  - Effects Hb, HbO, Hbtot
- Systemic modulation (autonomic)
- Hb is a strong biological buffer:
  - Binds NO, bicarbonate, peroxides

∴ Coupled dynamical system

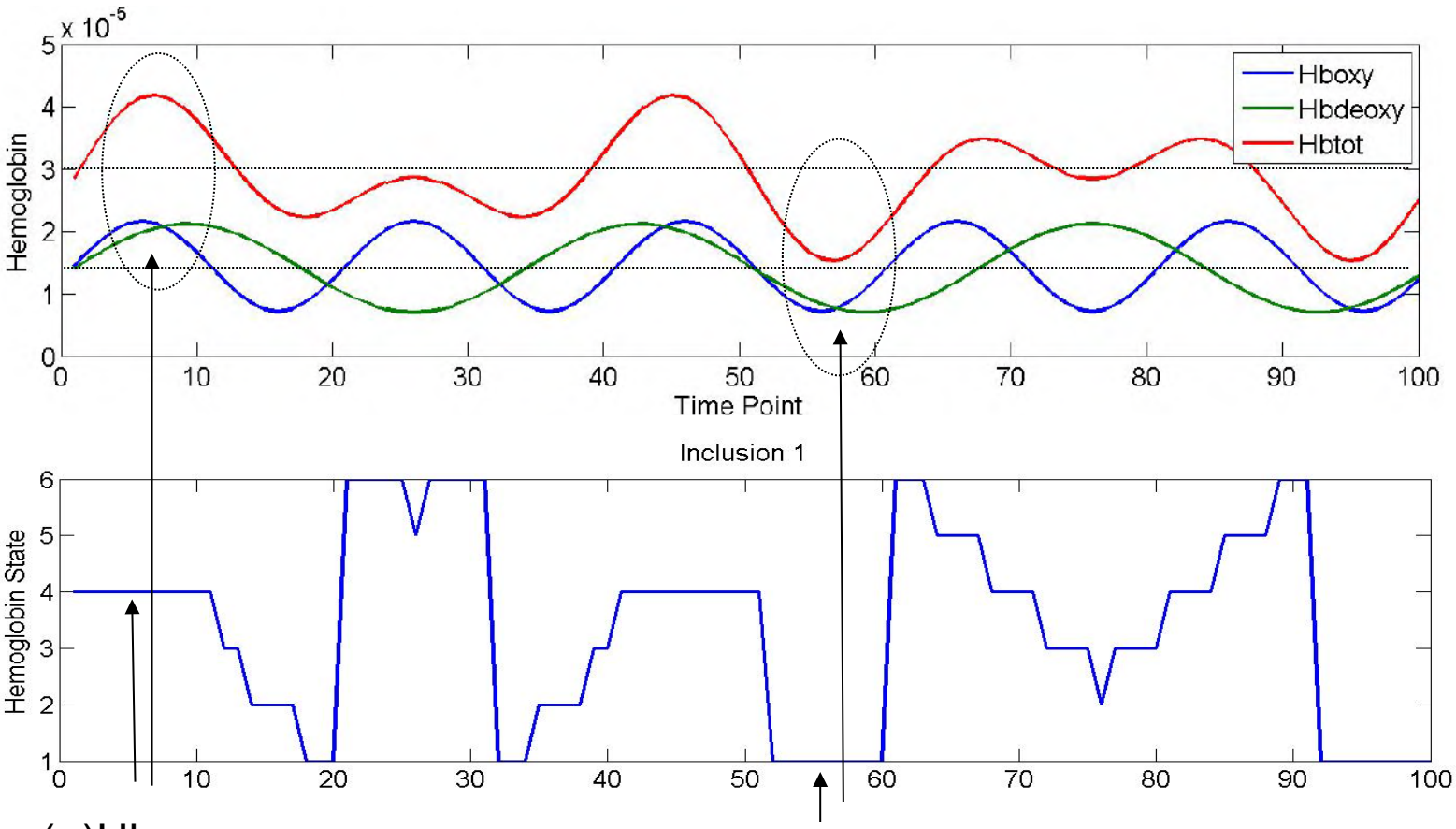


Properties of Coupled Dynamical Systems

- Different preferred states, sensitive to prevailing conditions
- Unequal path-dependent transition probabilities
- Different time constants



Hb State Transitions



(+)HbOxy
(+)HbDeoxy
(+) HbTotal

(-)HbOxy
(-)HbDeoxy
(-) HbTotal

Covariations of Hemoglobin States

Hemoglobin State	State 1	State 2	State 3	State 4	State 5	State 6
Hb_{oxy}	-	-	-	+	+	+
Hb_{deoxy}	-	+	+	+	-	-
Hb_{tot}	-	-	+	+	+	-
	Balanced	Uncomp. oxygen debt	Comp. oxygen debt	Balanced	Uncomp. oxygen excess	Comp. oxygen excess

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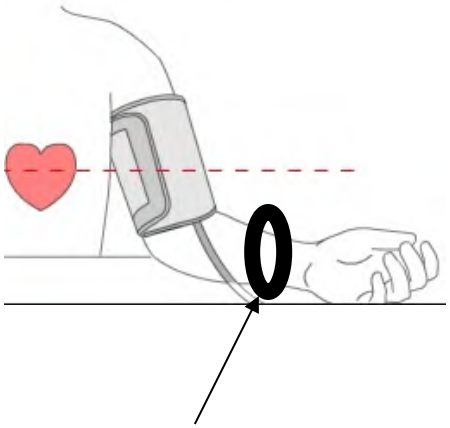
Individual Hb States

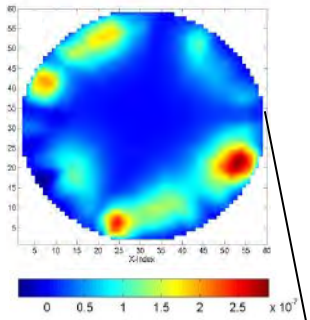
Covariational Hb States

40 mm Hg

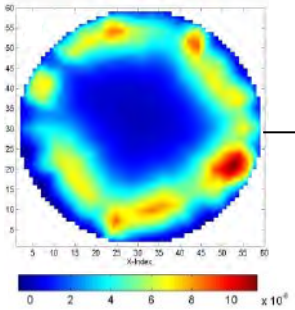


NIRS Array

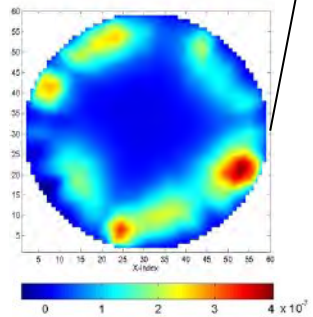
Hb_{oxy}

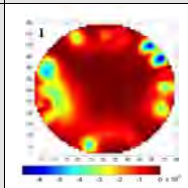
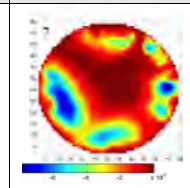
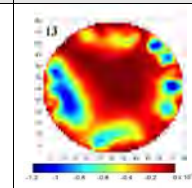
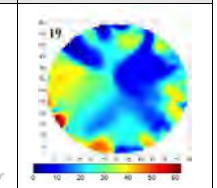
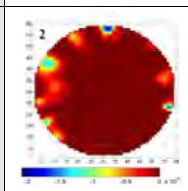
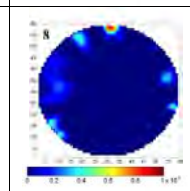
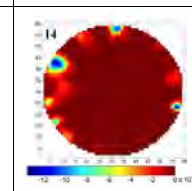
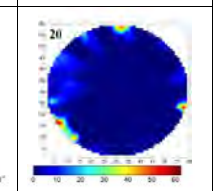
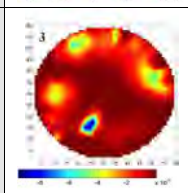
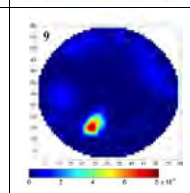
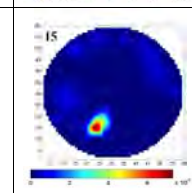
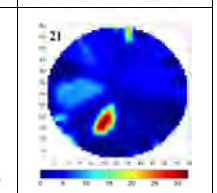
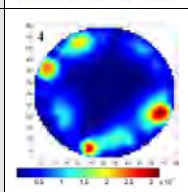
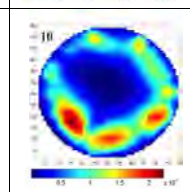
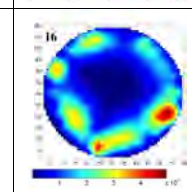
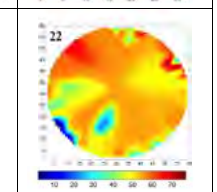
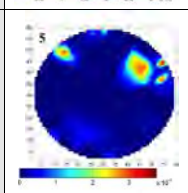
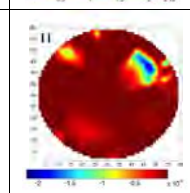
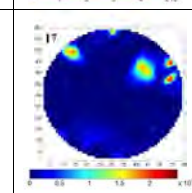
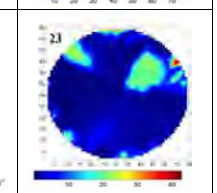
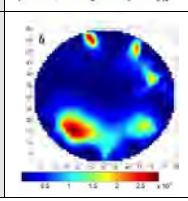
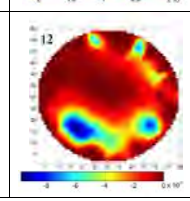
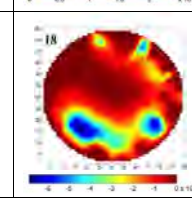
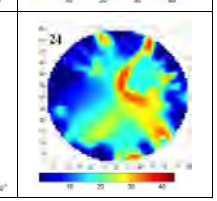


Hb_{deoxy}

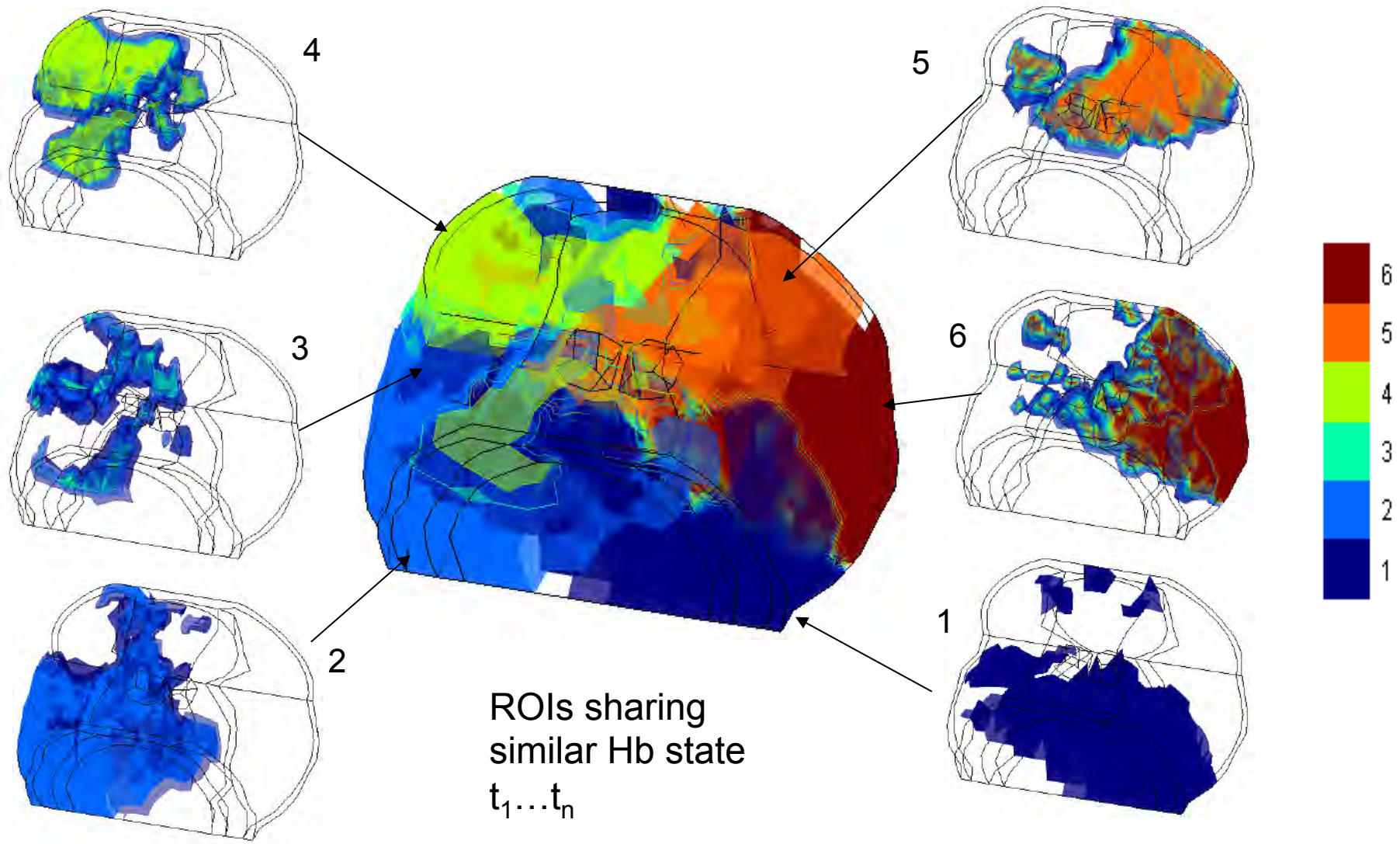


Hb_{total}



State	Hb_{Oxy}	Hb_{Deoxy}	Hb_{Total}	Time Fraction
1				
2				
3				
4				
5				
6				

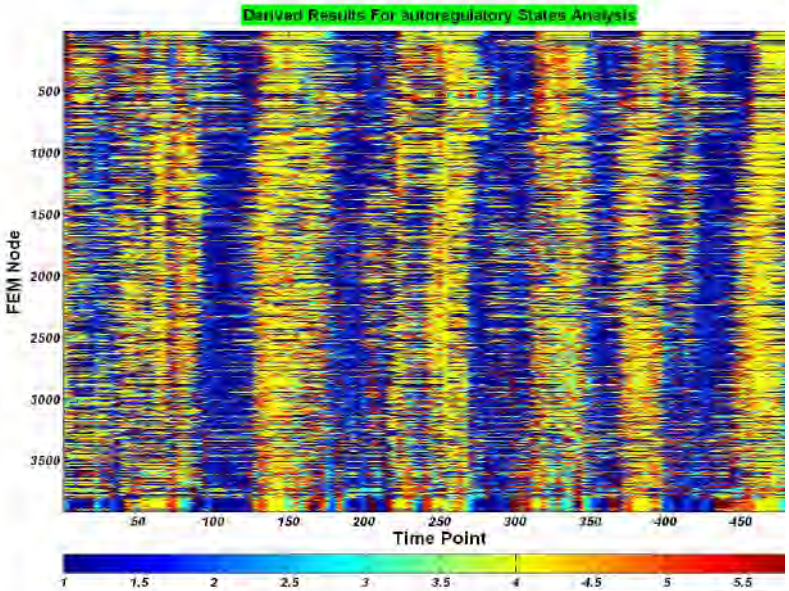
Spatial Dependence of Covariational Response



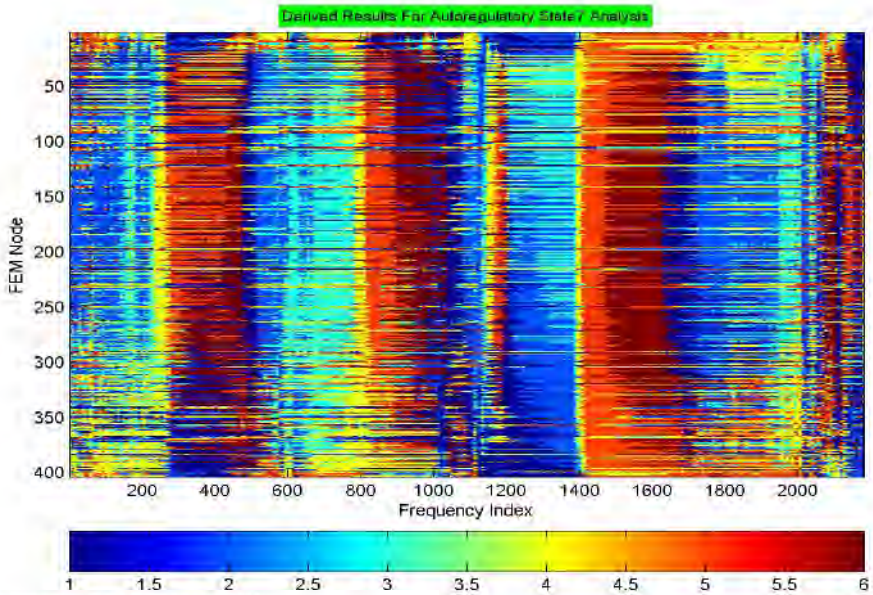
ROIs sharing similar Hb state $t_1 \ldots t_n$

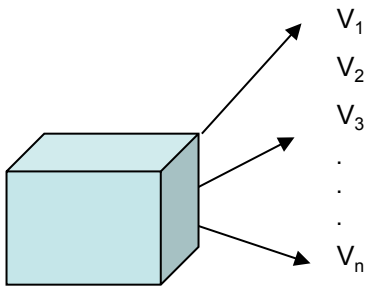
Resting State Behavior is Tissue Specific

Breast

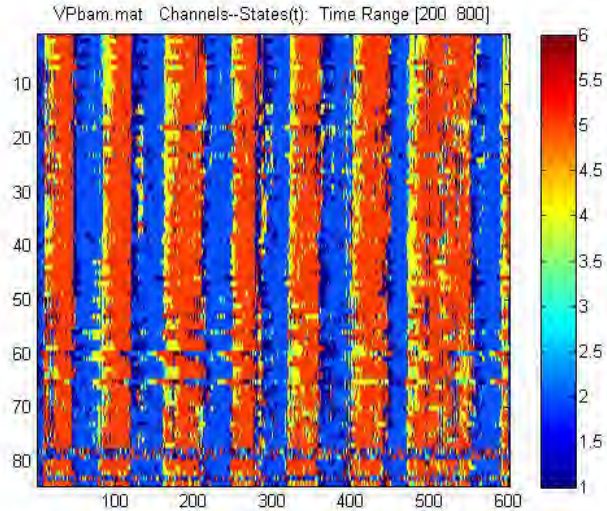


Muscle





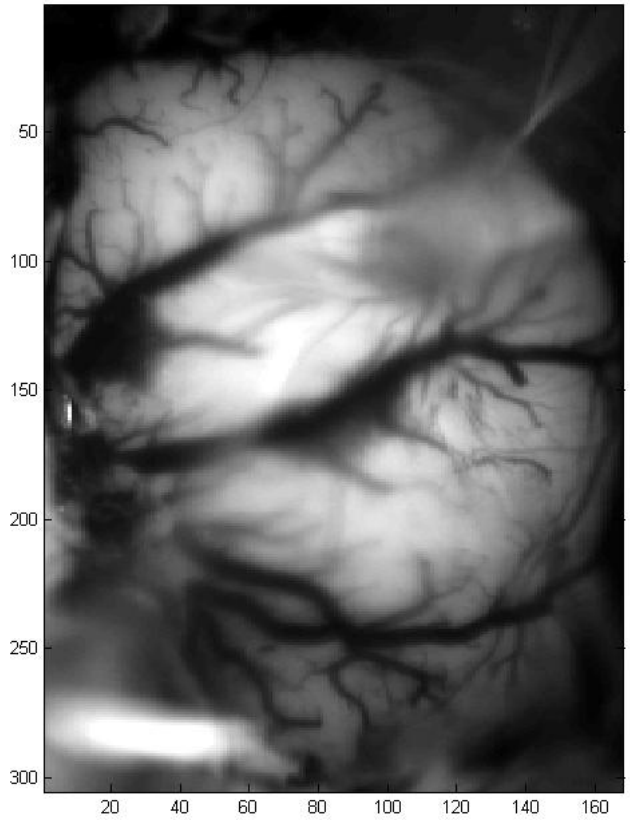
Brain



Hb States

Vascular Autoregulation: Rat seizure model

CCD image of
exposed rat brain



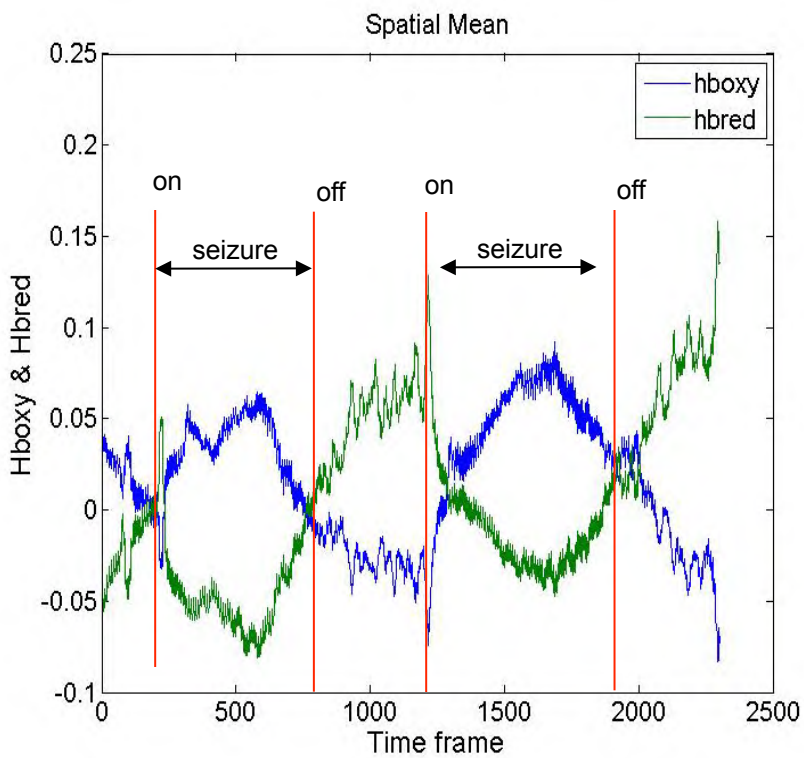
Seizure model:

Administration of 4-Aminopyridine

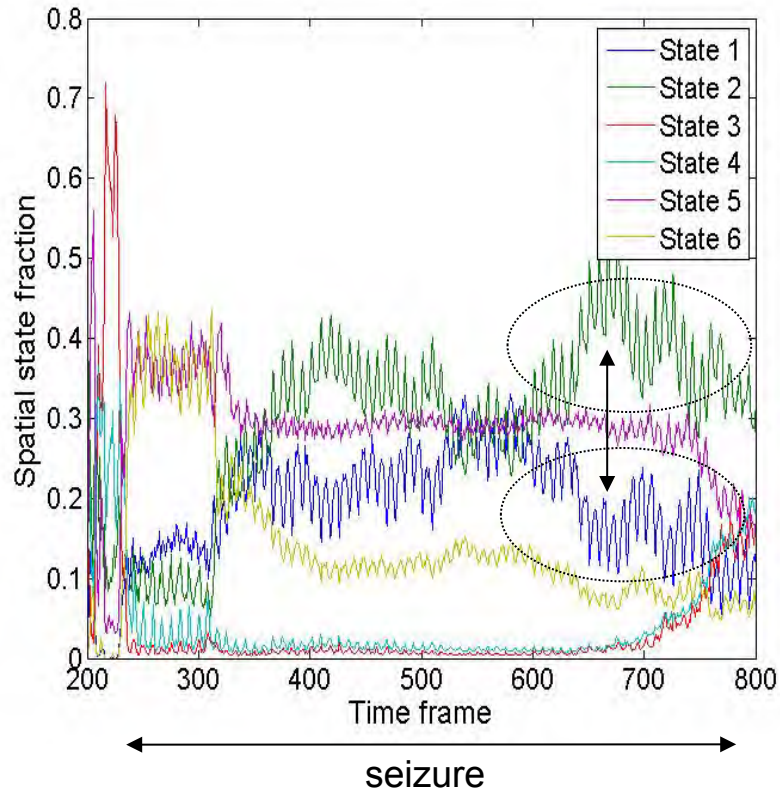
Experimental data from: Ma et al., Weill Cornell Medical College, unpublished data.

Hb Response to Seizure

Hemdoynamic response to seizure

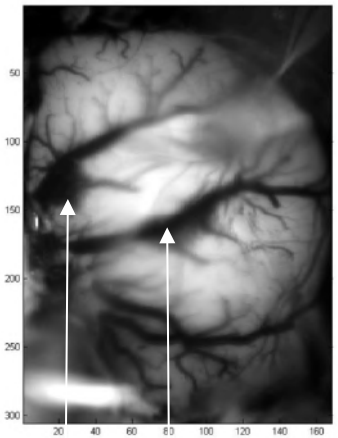


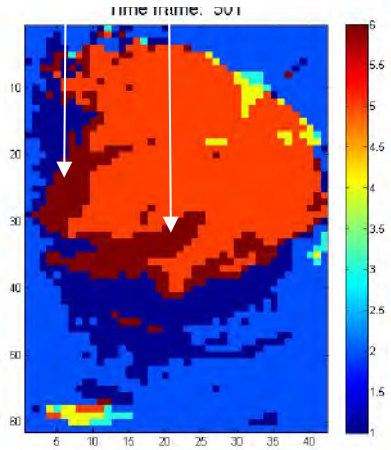
Hb state response to seizure



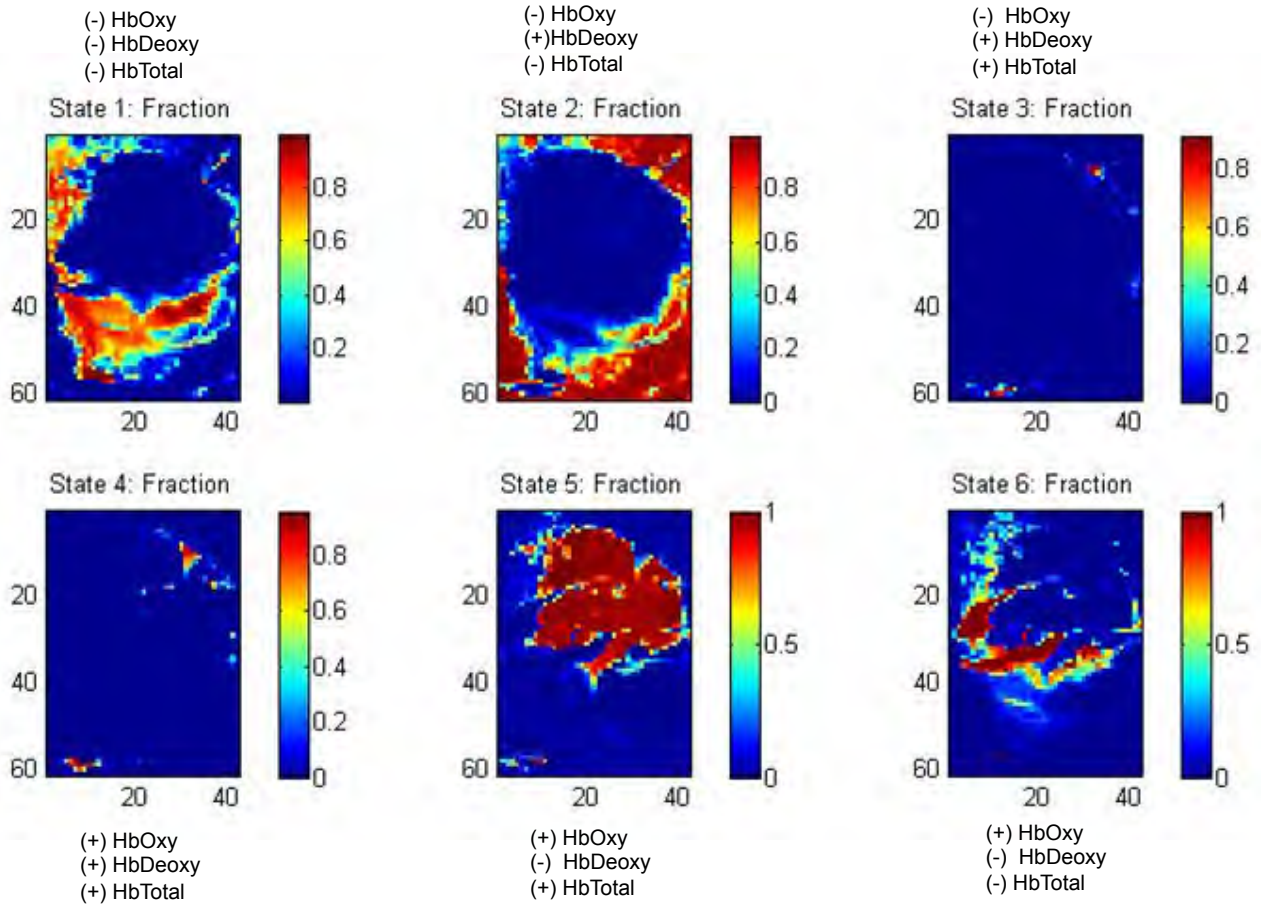
Hb state response to seizure

CCD Image





Hb state map at time frame 501



Temporal state fraction during an acute seizure (time fames: 300-700)

Data Driven Metrics

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

Cap Setup

NIRS-BBCI*

Instrument Setup

Brain Comp. Interface

Task Definition

Connectivity-

DCM, GC

NIRStim

NAVI*
Tomography

Event Recording

Stat. Para. Mapping

Data Editing

Hb State Computation

nirsLAB*
Topography

*http://www.nitrc.org/projects/fnirs_downstate

Cap Setup

Brain Products
EASYCAP™

EGI

g.tec

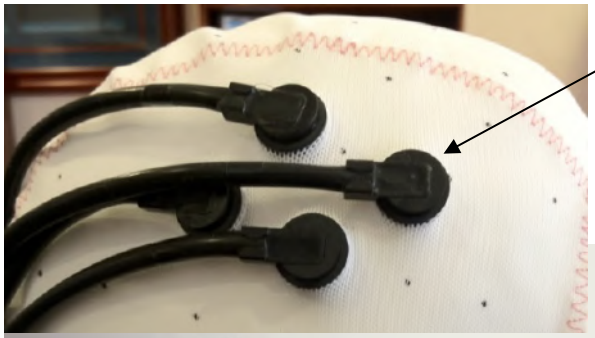
Advanced Neuro Technologies

BrainProducts ActiCap™

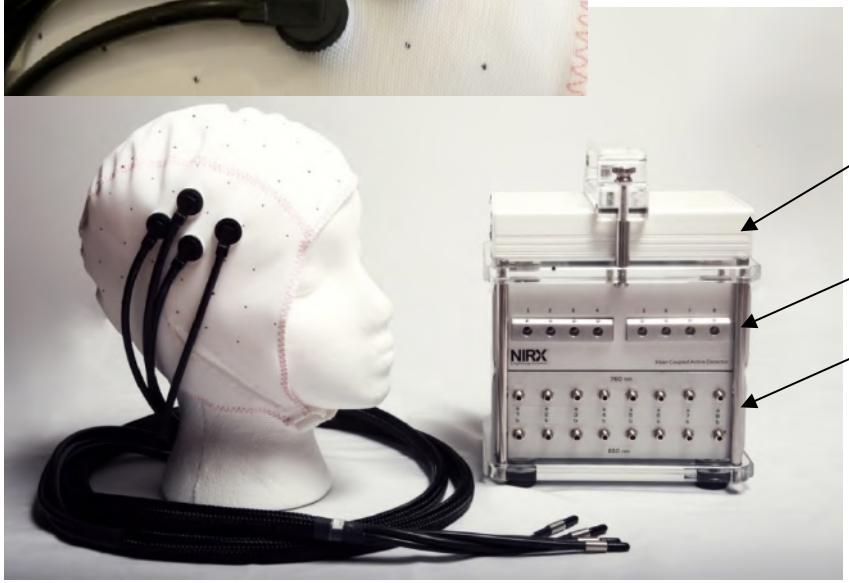
Dedicated neoprene headbands

Probes for infants/newborns

OPTICAL COUPLING SOLUTION



6 mm profile

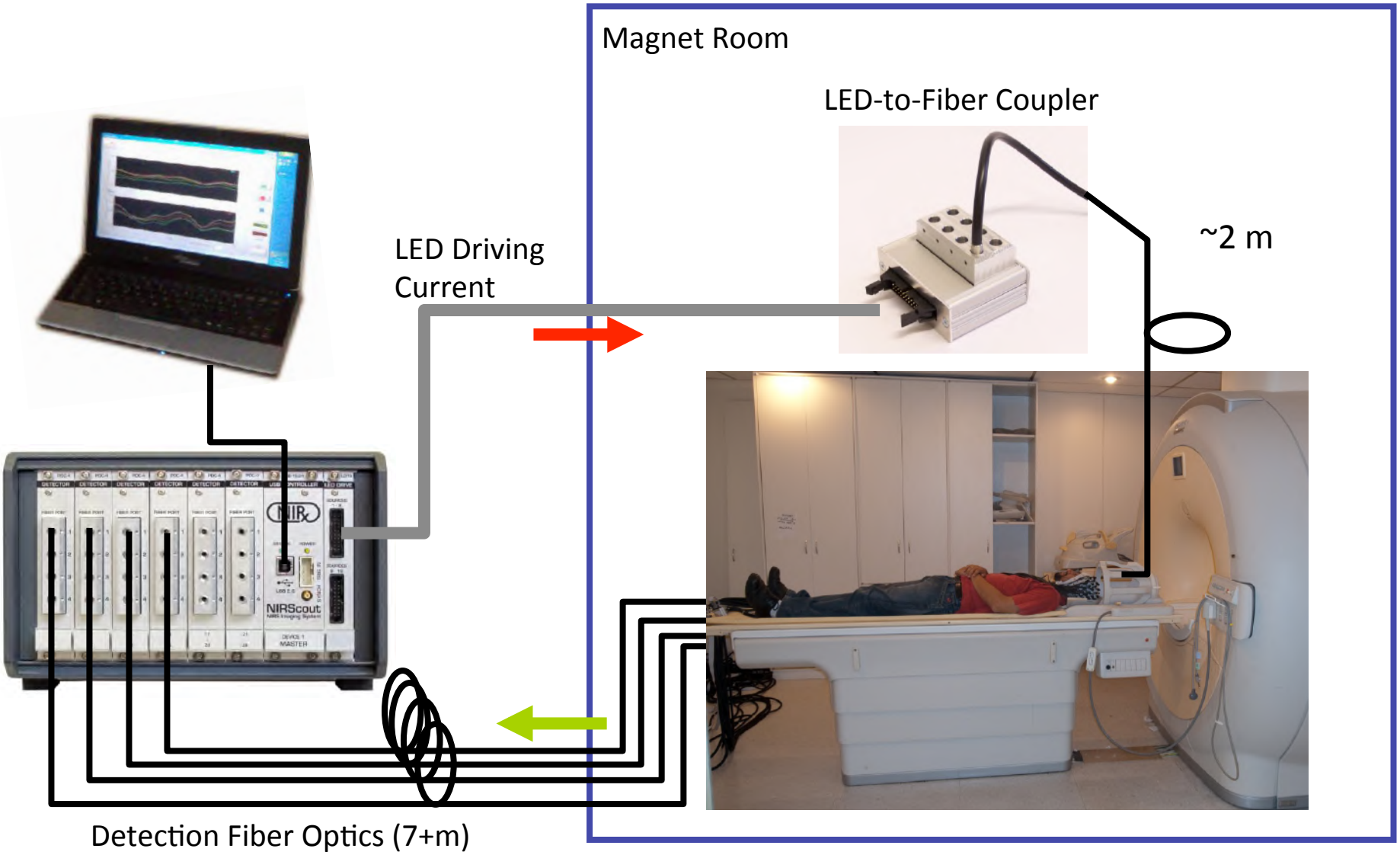


External Detector Unit

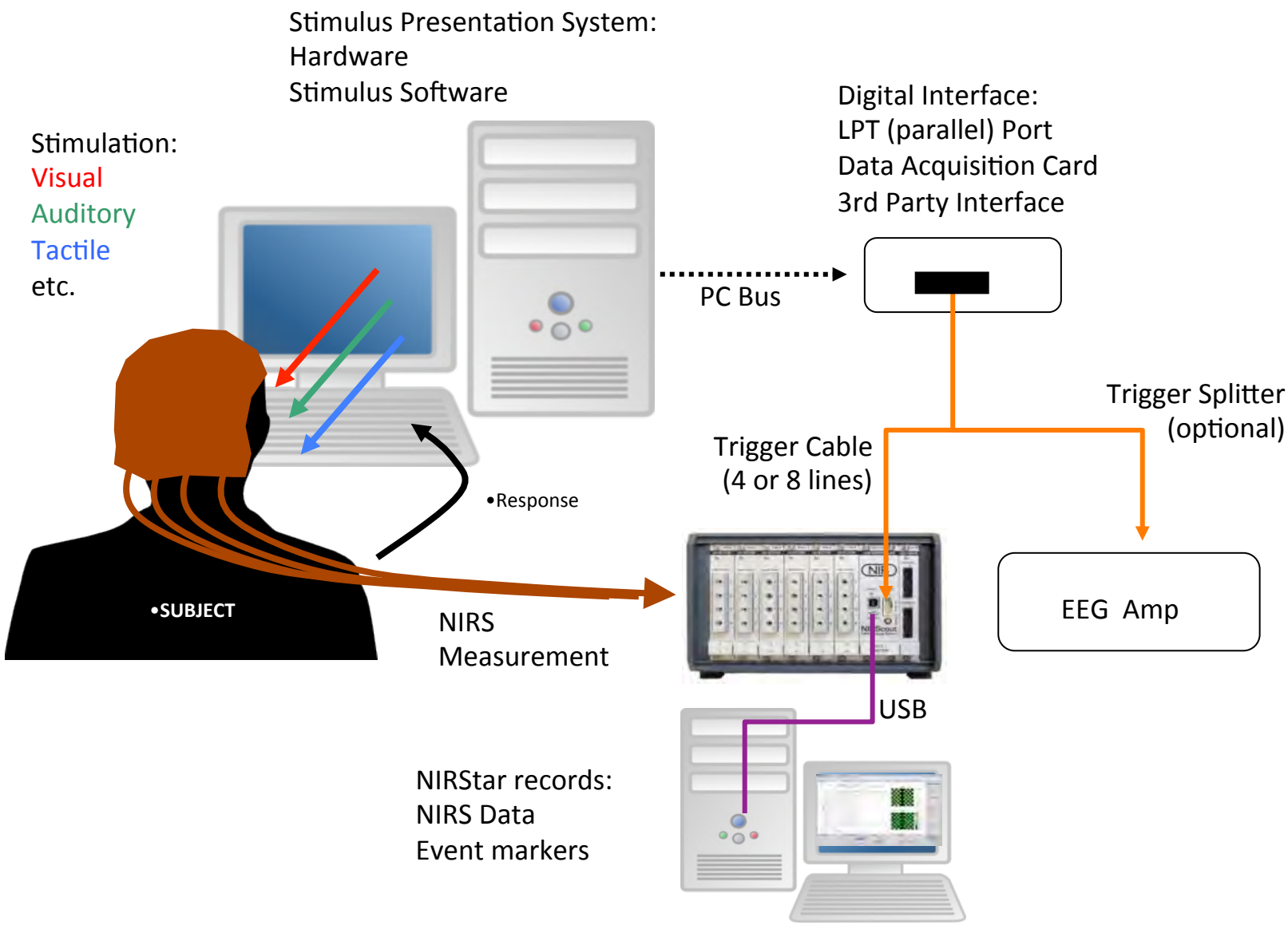
External Source Unit

TMS/fMRI Fiber Solution

fNIRS/fMRI – Concurrent Measurements



NIRS-EEG Experimental Setup



Sensor Registration

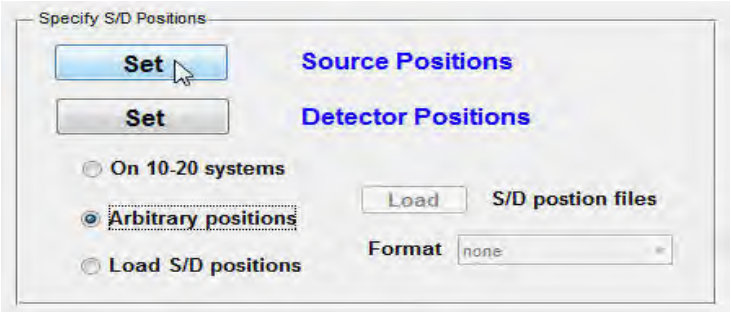


Figure 7-12. Specification of arbitrary probe locations.

2-D Montage

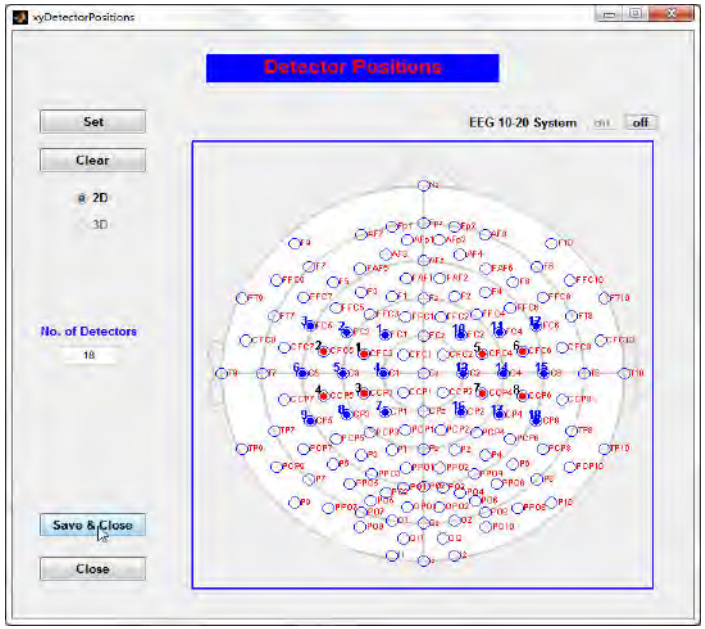
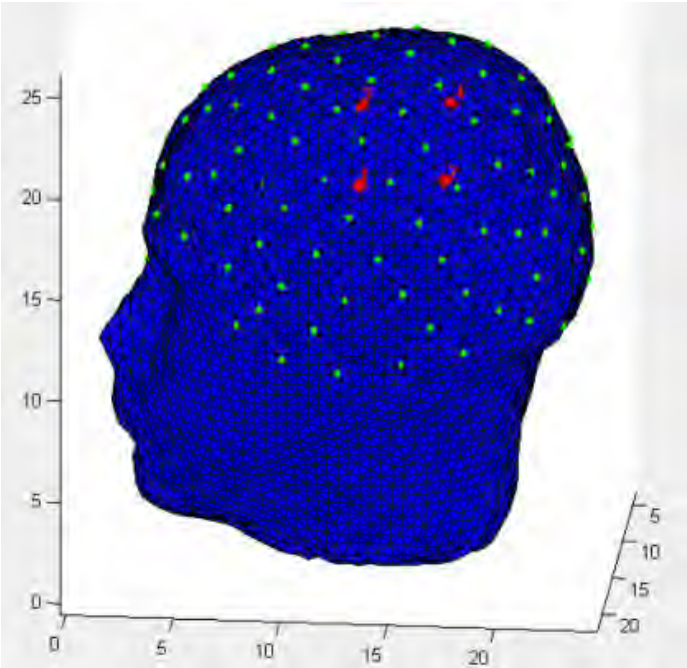


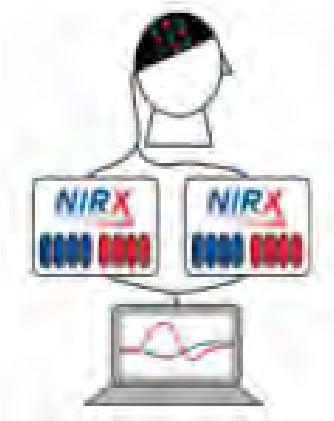
Figure 7-10. Graphical specification of detector locations.

3-D Montage



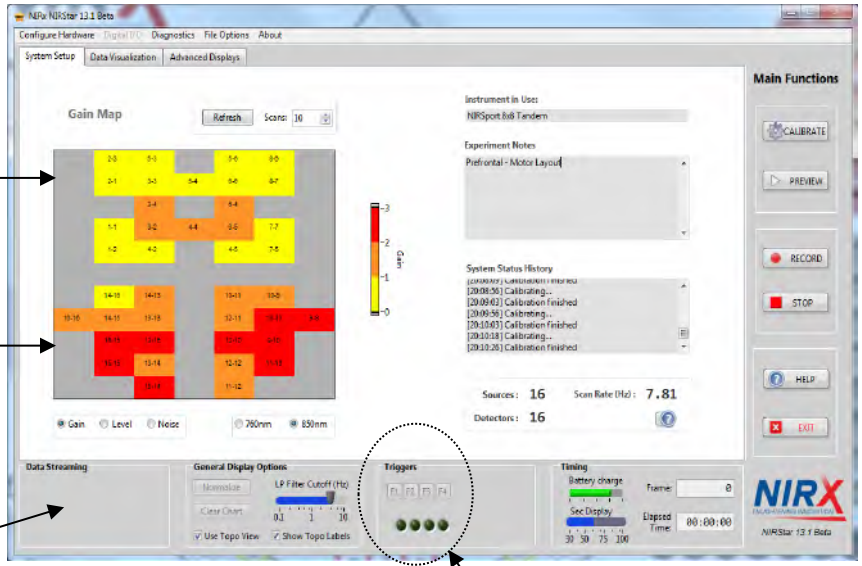
Instrument Setup

Tandem



Instrument 1

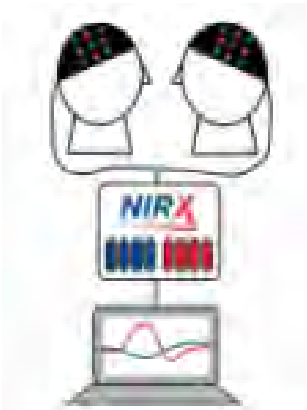
Instrument 2



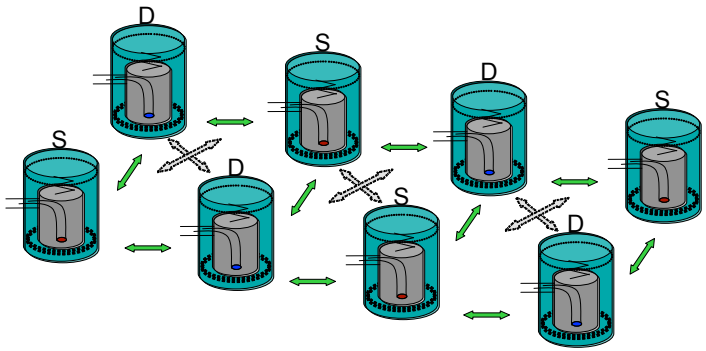
SDK

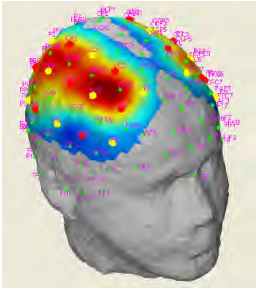
Triggers -NIRStim

Hyperscan



S-D Layout/Registration





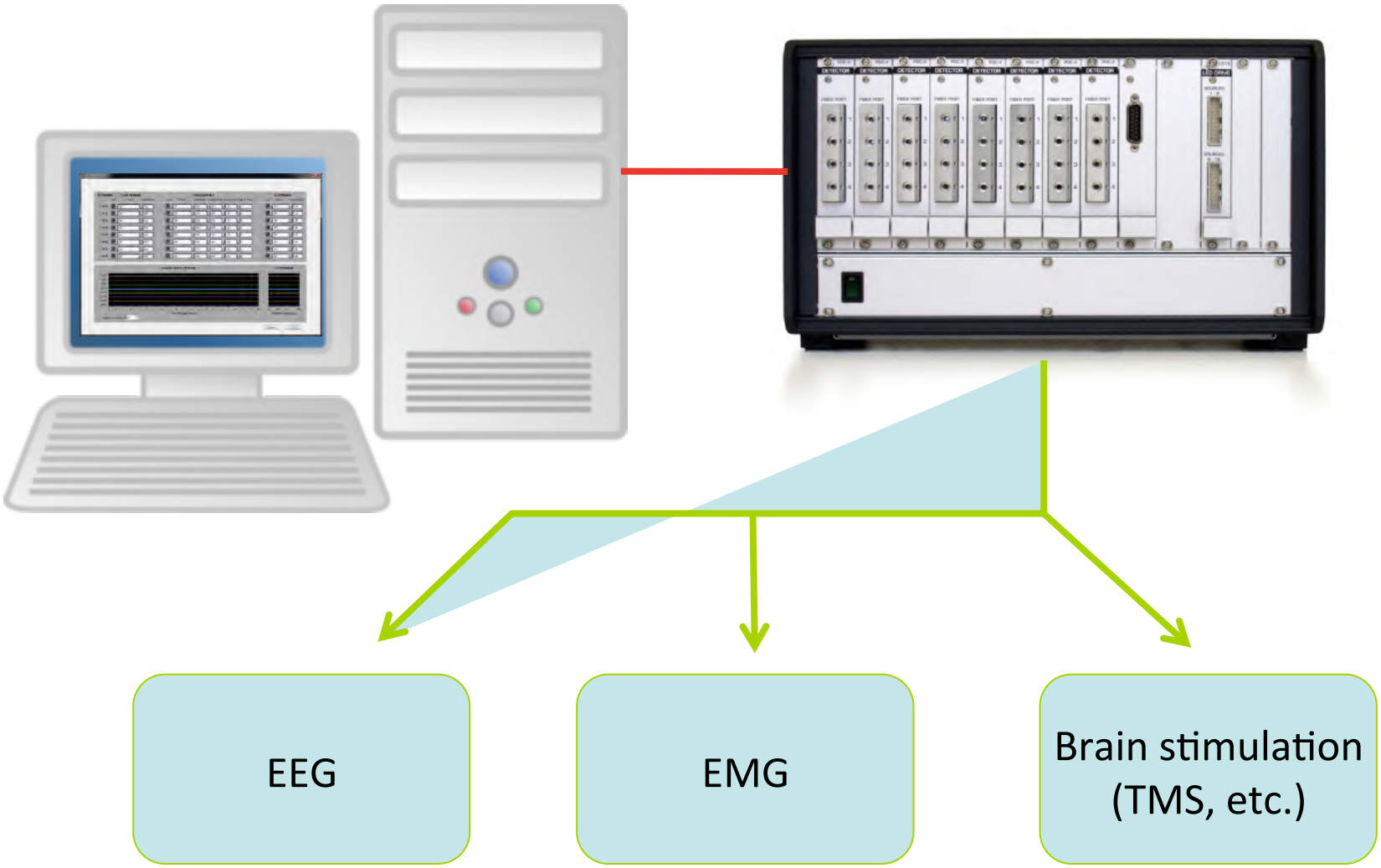
Tandem mode

- 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

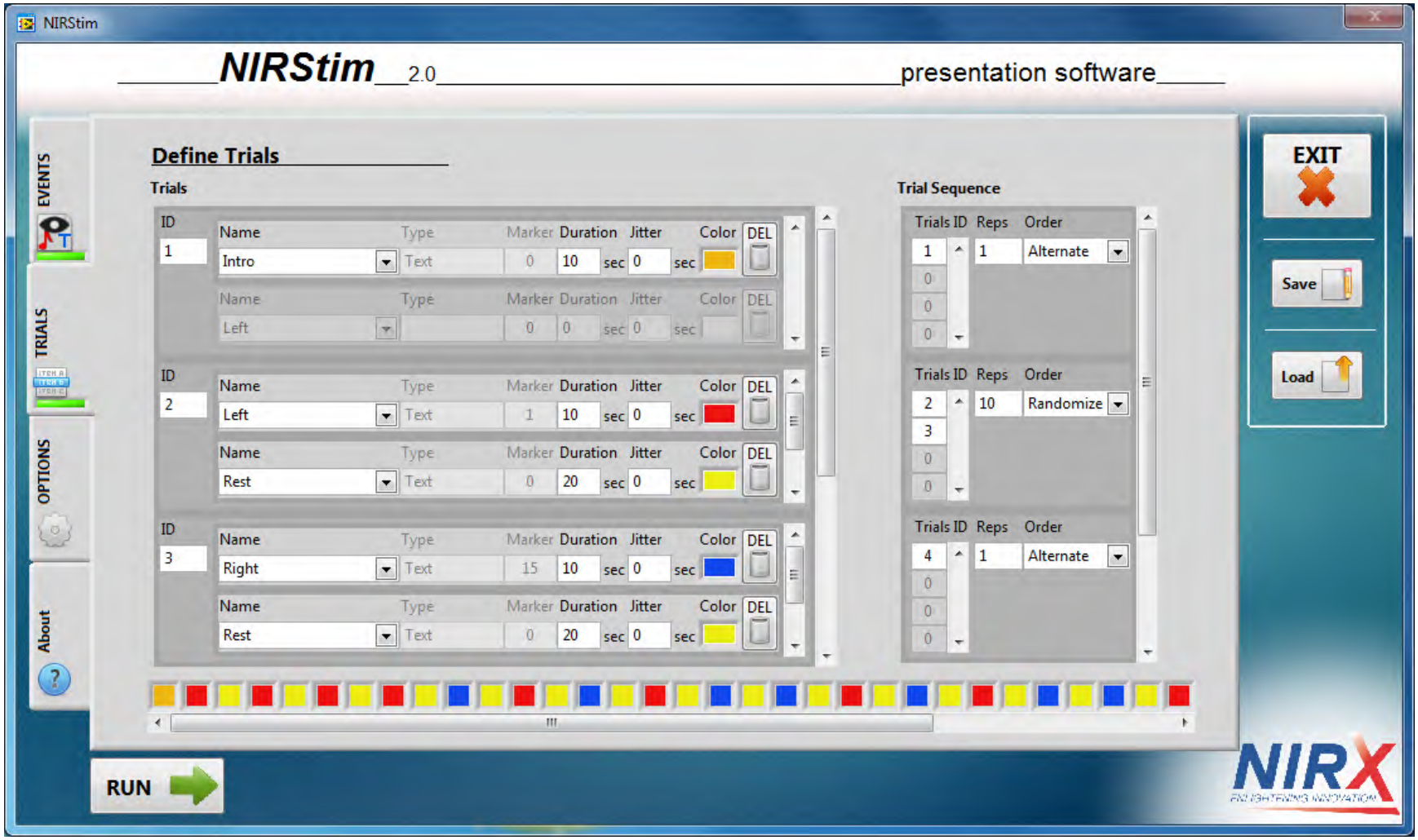


Direct, programmable digital (TTL) control of other systems

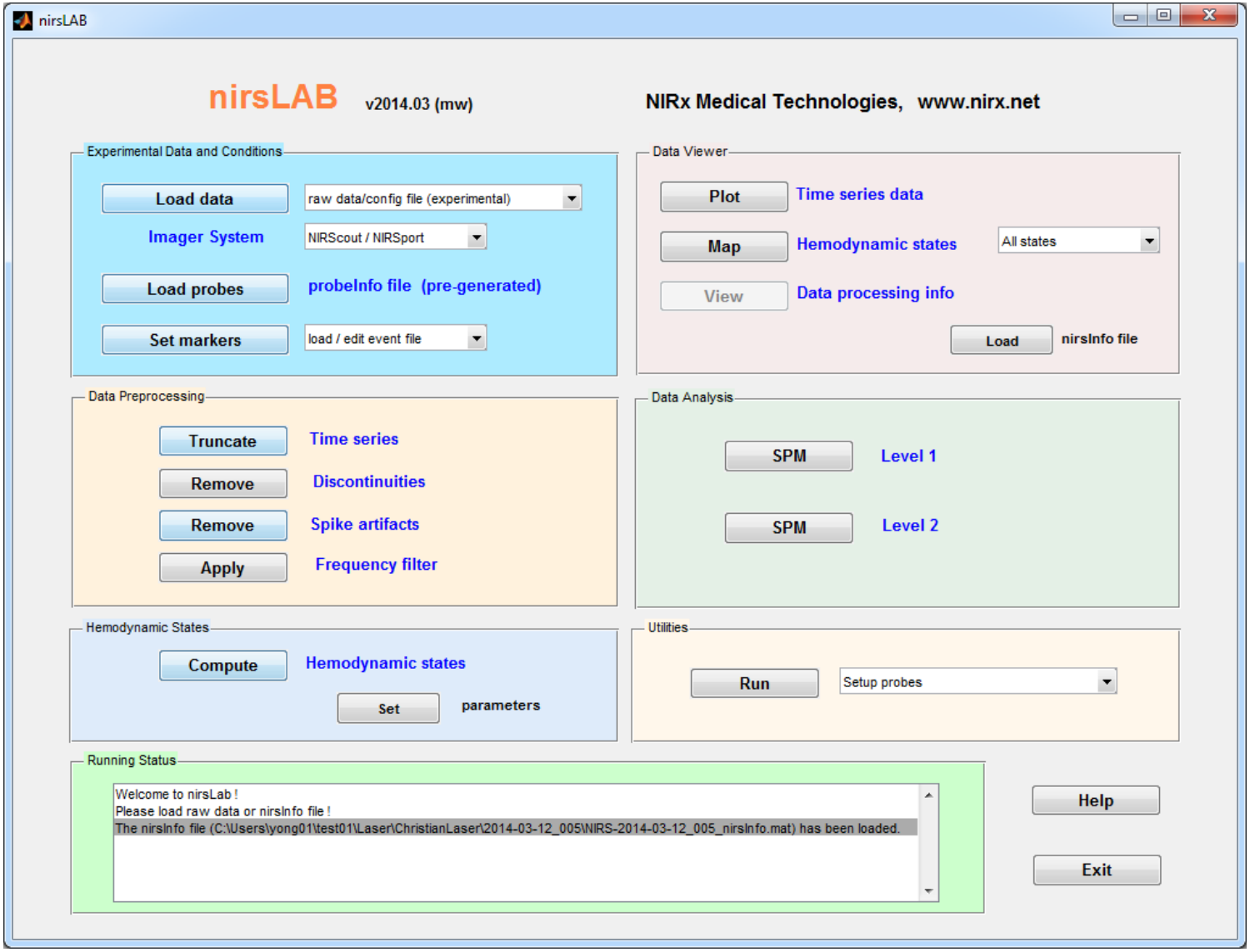
NIRS Instrumentation Highlights

- 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, …)

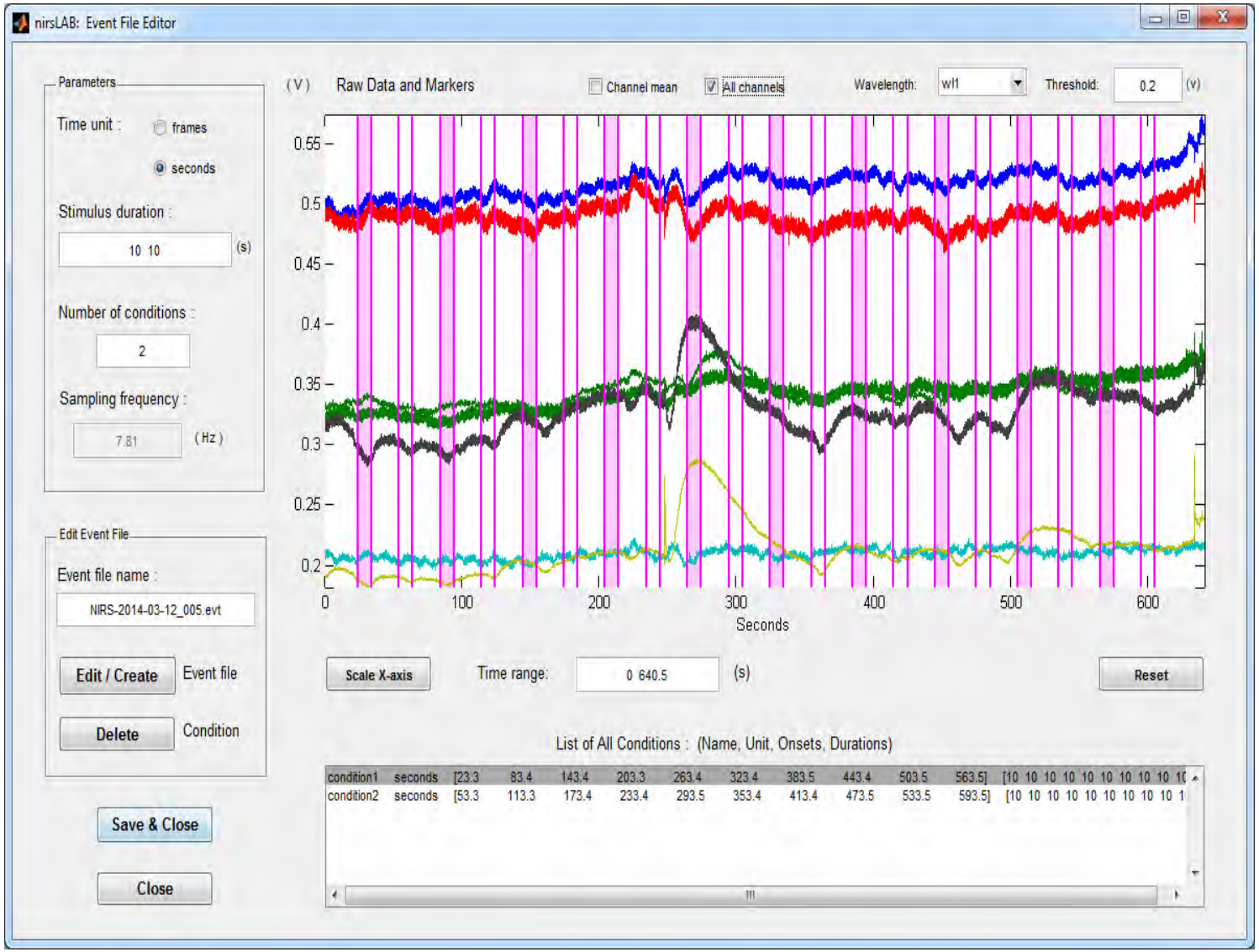
Task Definition: NIRStim



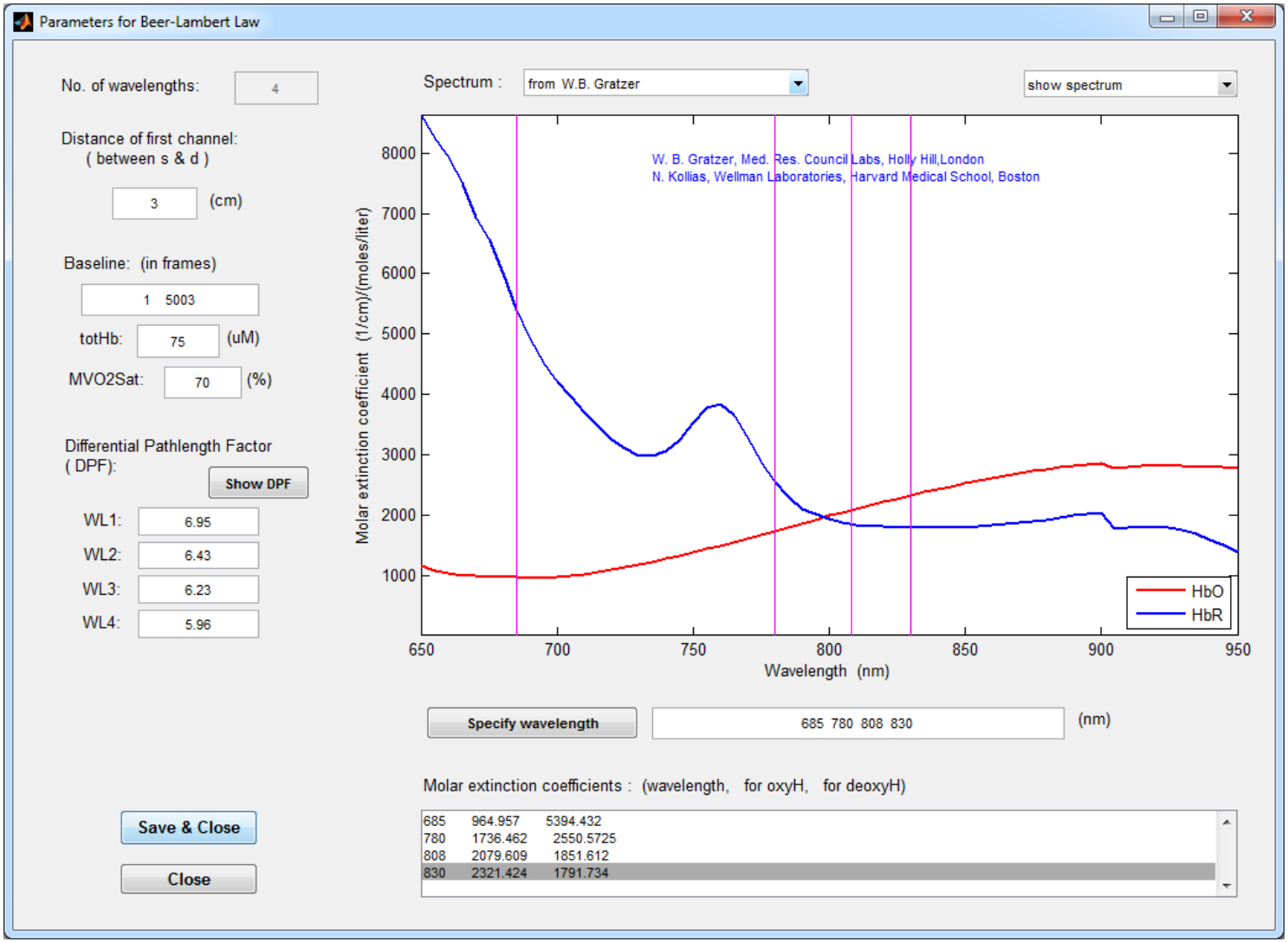
nirsLAB


nirsLAB
nirsLAB v2014.03 (mw)
NIRx Medical Technologies, www.nirx.net
Experimental Data and Conditions
Load data
raw data/config file (experimental)
Imager System
NIRScout / NIRSport
Load probes
probeInfo file (pre-generated)
Set markers
load / edit event file
Data Viewer
Plot
Time series data
Map
Hemodynamic states
All states
View
Data processing info
Load
nirsInfo file
Data Preprocessing
Truncate
Time series
Remove
Discontinuities
Remove
Spike artifacts
Apply
Frequency filter
Data Analysis
SPM
Level 1
SPM
Level 2
Hemodynamic States
Compute
Hemodynamic states
Set
parameters
Utilities
Run
Setup probes
Running Status
Welcome to nirsLab !
Please load raw data or nirsInfo file !
The nirsInfo file (C:\Users\yong01\test01\Laser\ChristianLaser\2014-03-12_005\NIRS-2014-03-12_005_nirsInfo.mat) has been loaded.
Help
Exit

Event Markers



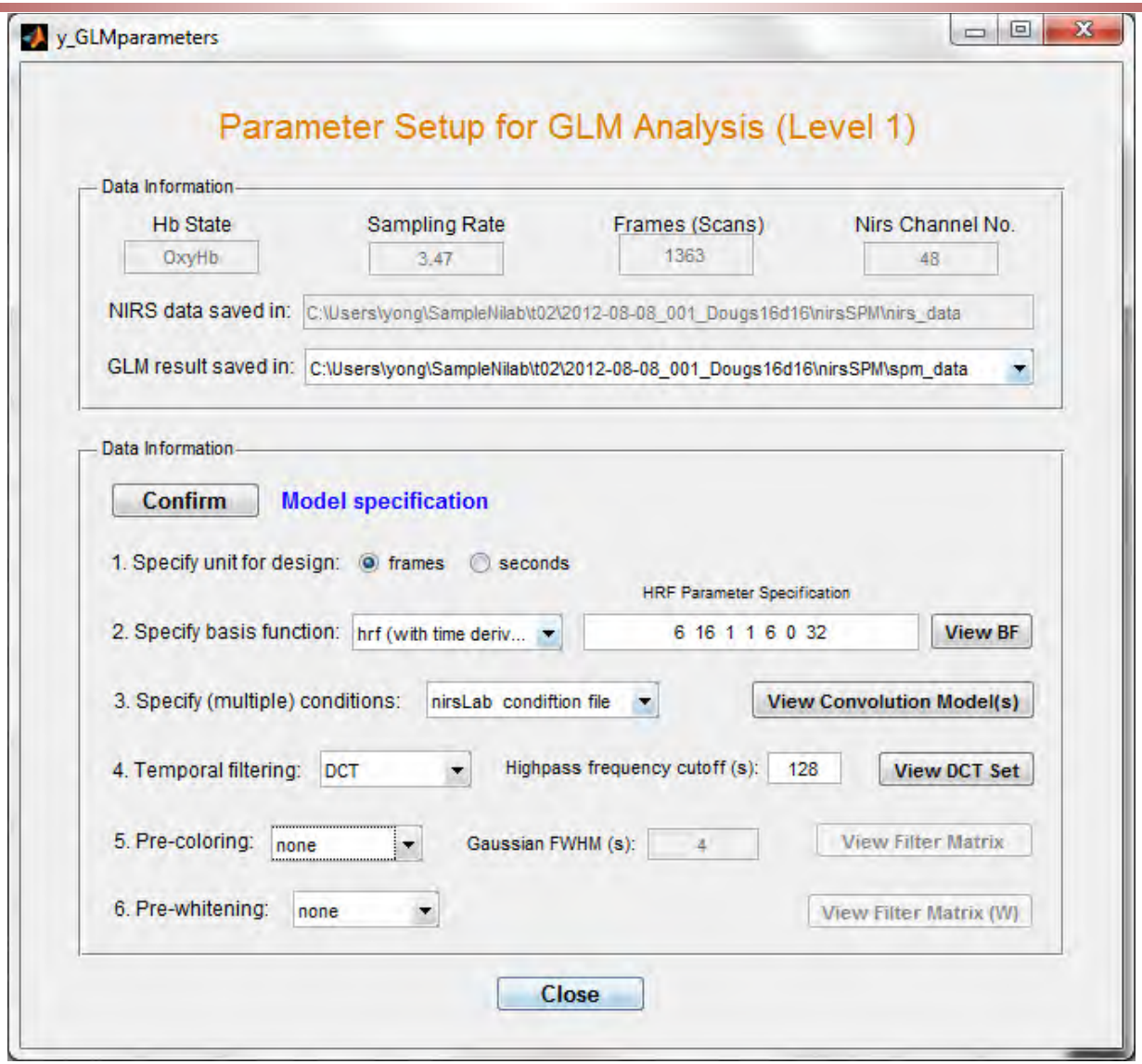
Beer-Lambert Analysis



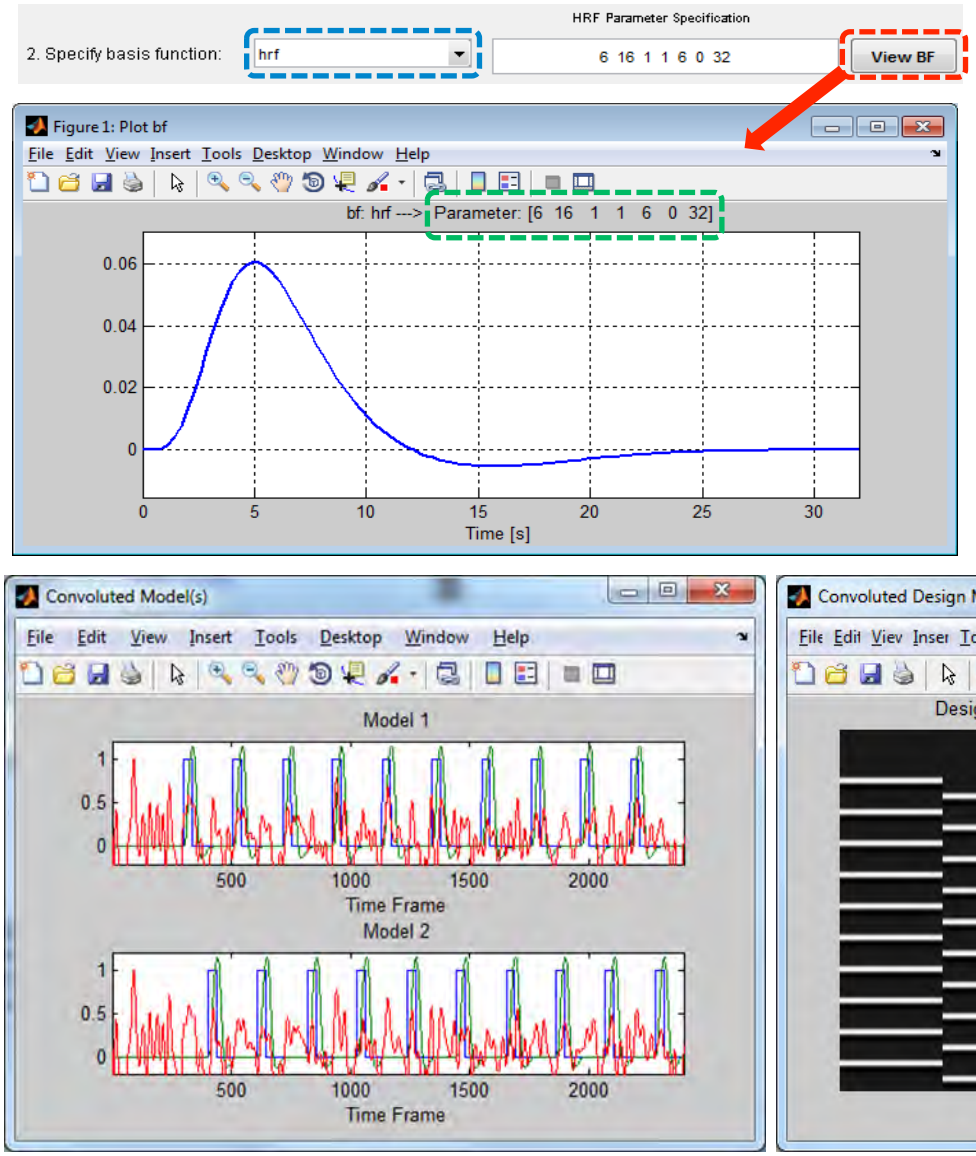
$I/Io = \exp{-(lec)}$

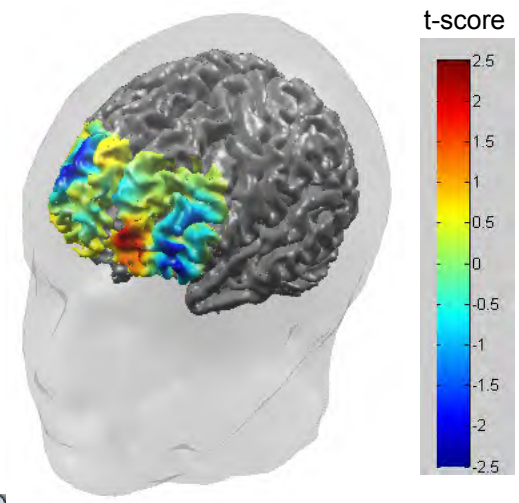
l = pathlength
e = ext. coeff.
c = conc.

GLM-Based SPM Analysis



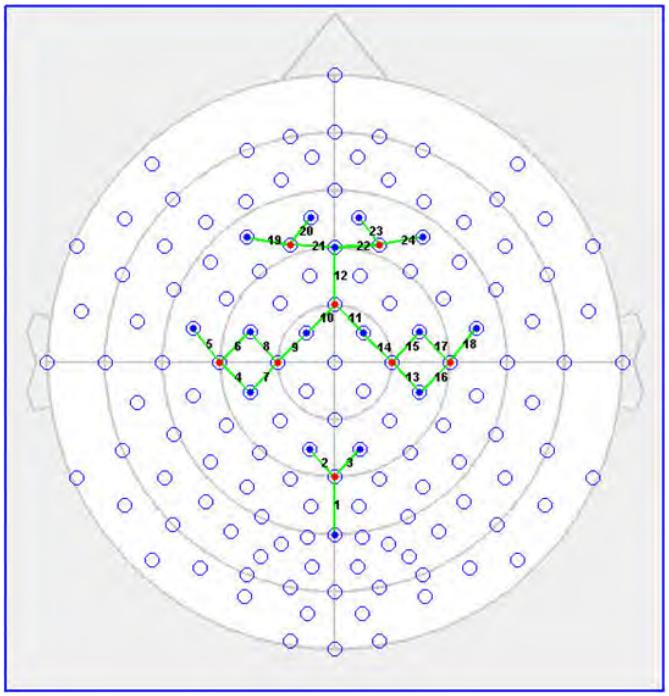
SPM Analysis



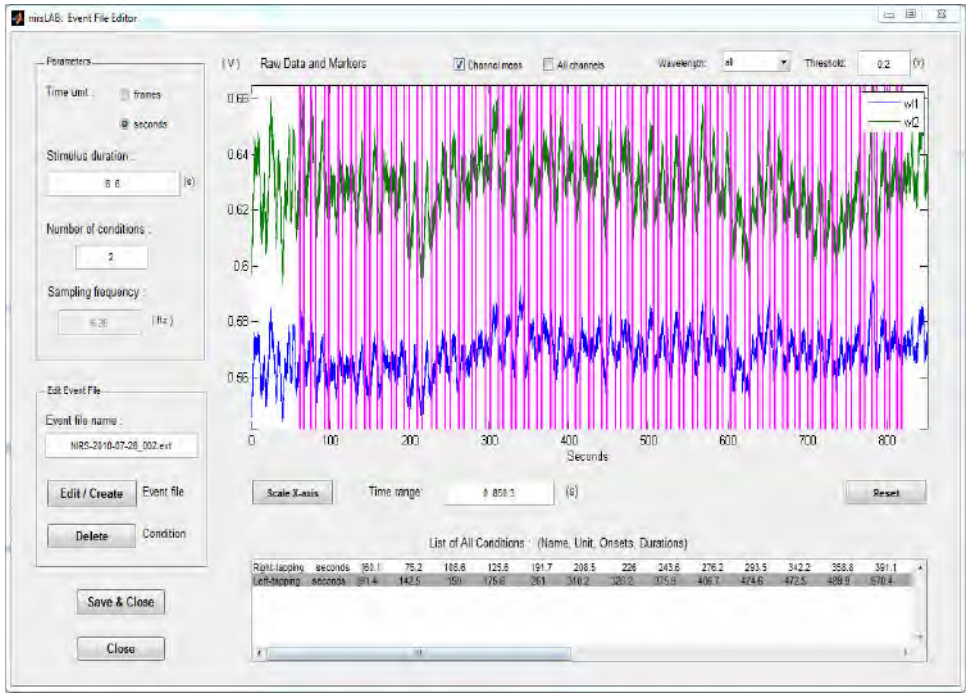


nirsBCI: BBCI toolbox + nirsLAB

Experiment: Left and right finger tapping



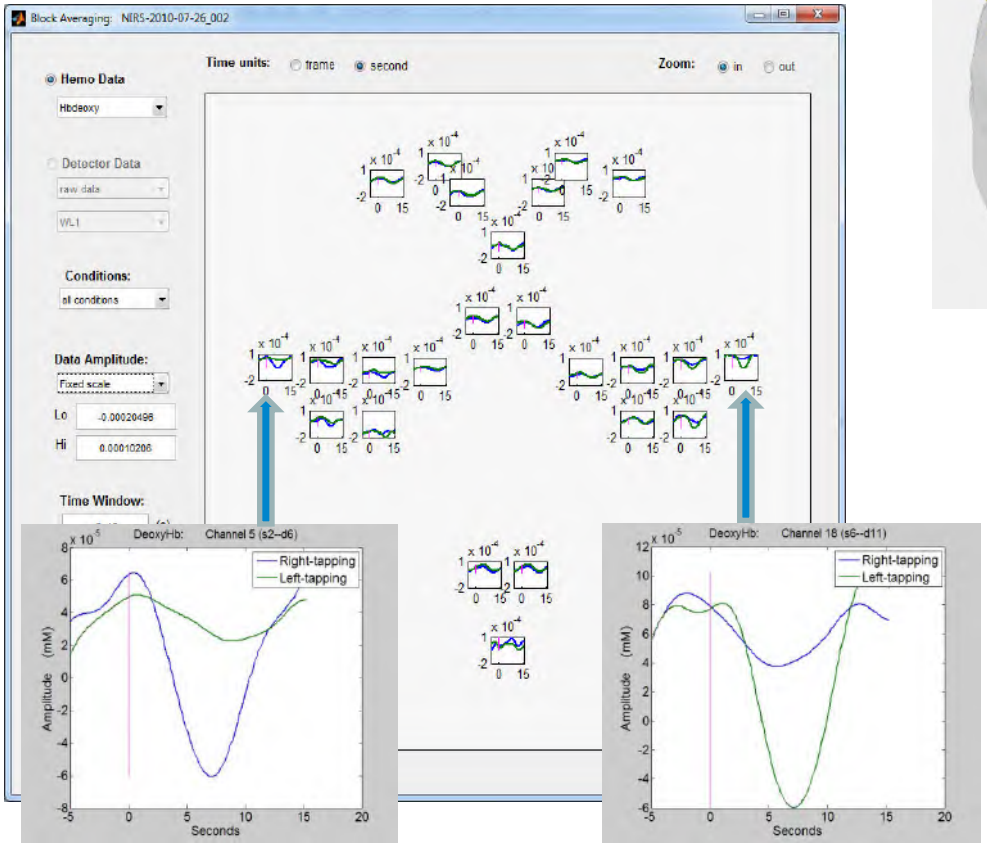
Source (red) and detector (blue) layout



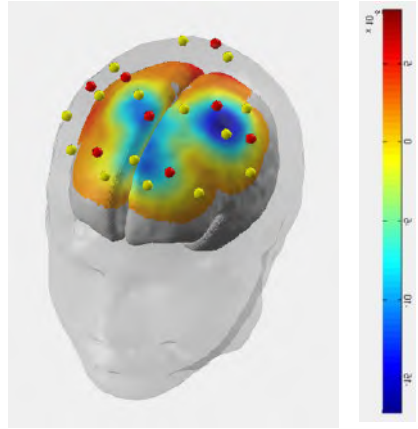
Event (left and right finger tapping) markers

Finger tapping response: Training vector

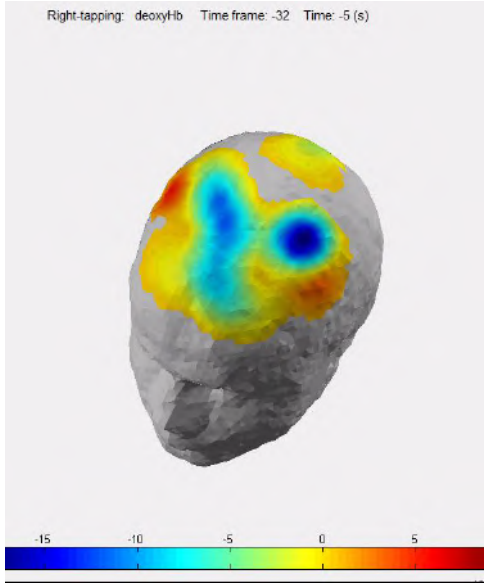
nirs Signals: oxyHb and deoxyHb



DeoxyHb changes during finger tapping (block-averaged)



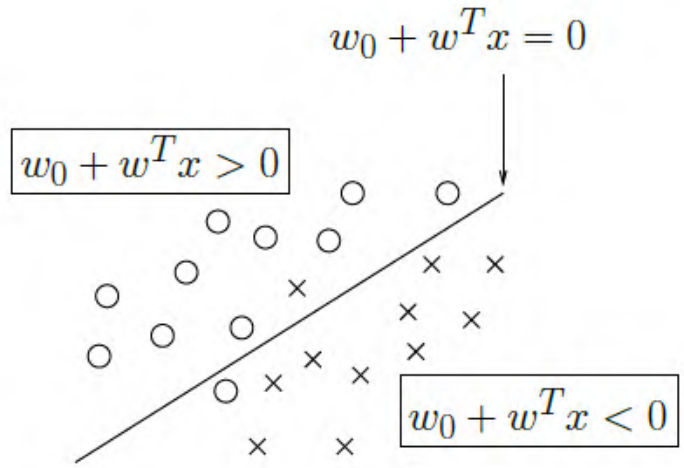
Brain (left) and head (below) surface mapping (block-averaged deoxyHb)



BBCI toolbox

BBCI toolbox: (publicly available under **http://www.bbci.de/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)

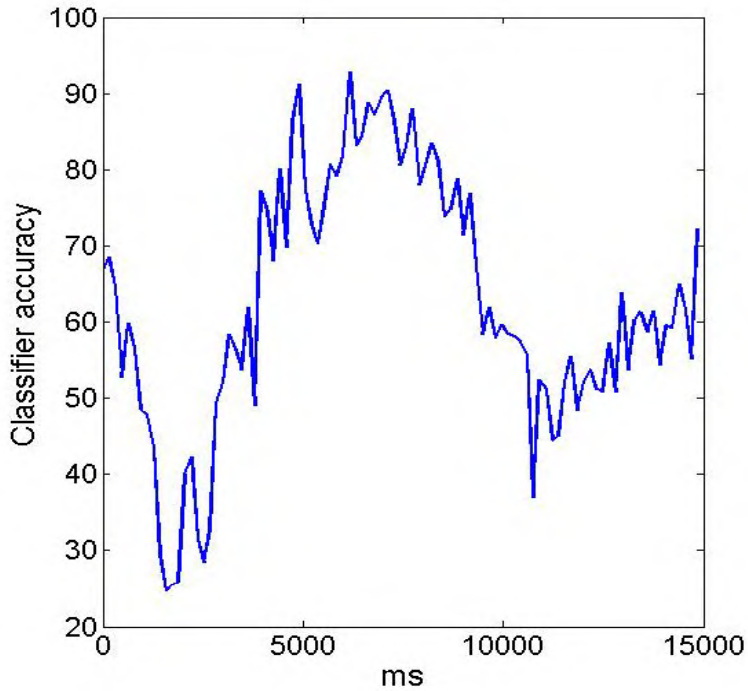


A hyperplane which separates two classes: the "circles" and the "crosses"

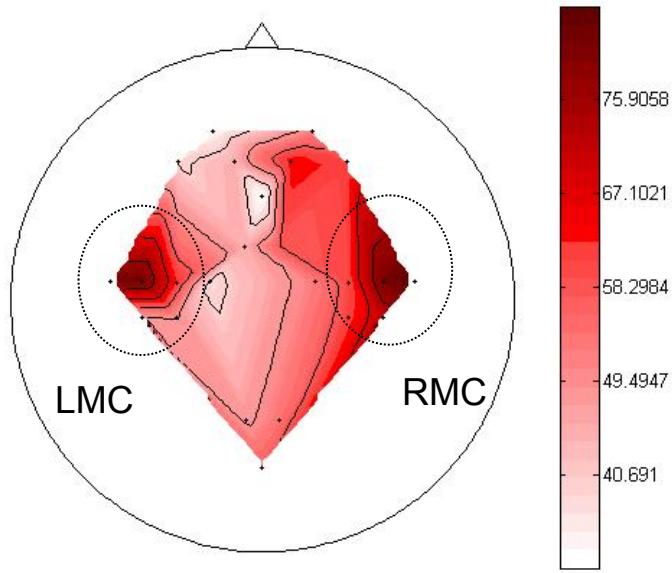
*Blankertz B, Tangermann M, Vidaurre C, Fazli S, Sannelli C, Haufe S, Maeder C, Ramsey LE, Sturm I, Curio G, **Mueller KR**, The Berlin Brain-Computer Interface: Non-Medical Uses of BCI Technology, Open Access Front Neuroscience, 4:198, 2010

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

Classifier accuracy is estimated by cross-validation

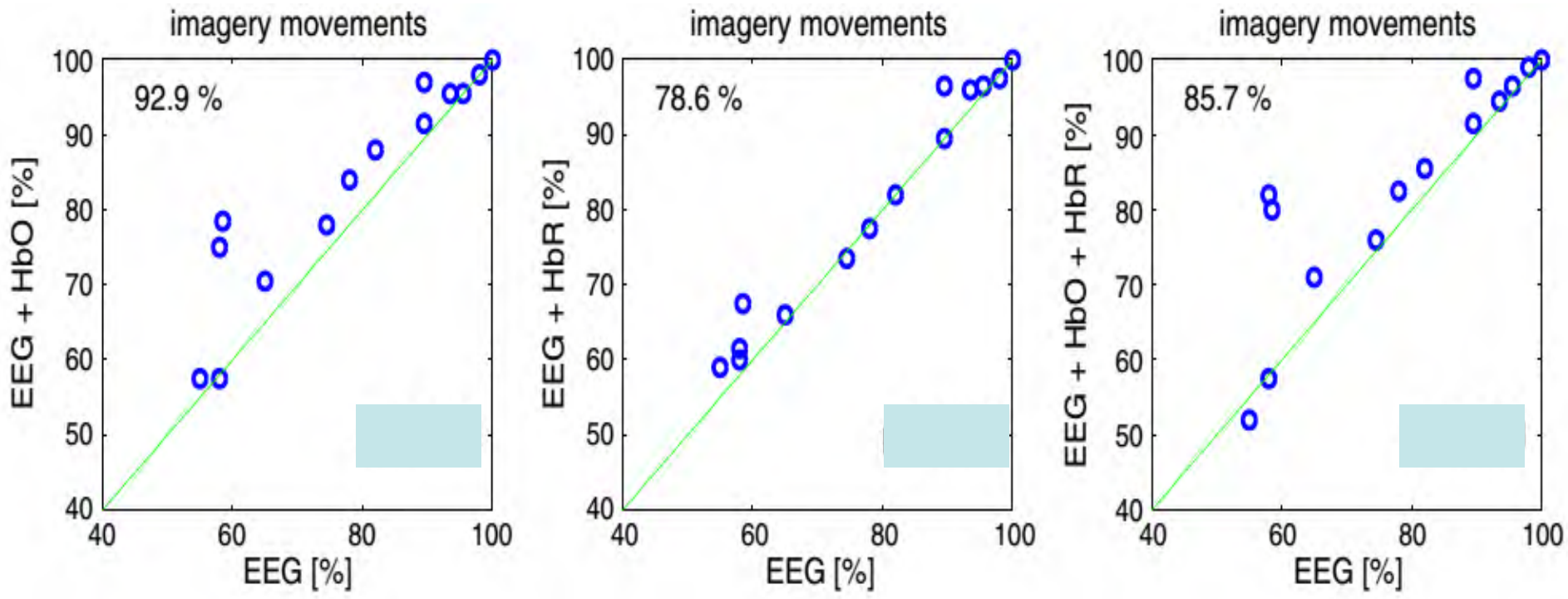


Classifier accuracy based on spatial feature



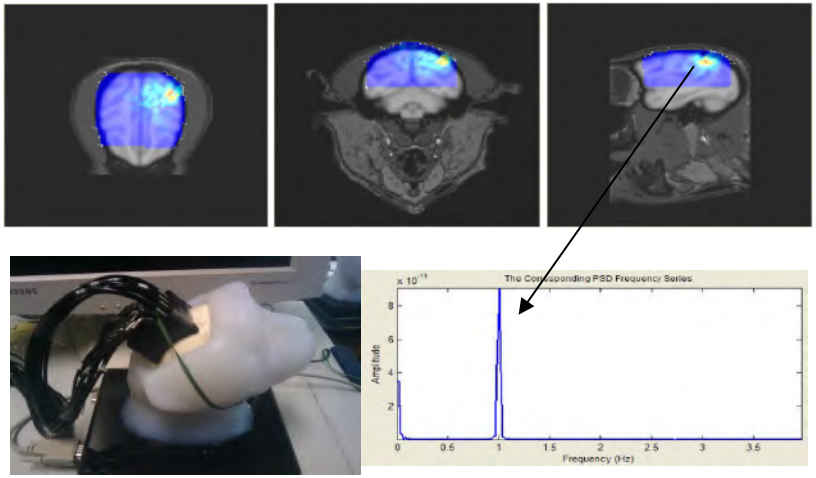
Classifier accuracy based on temporal feature

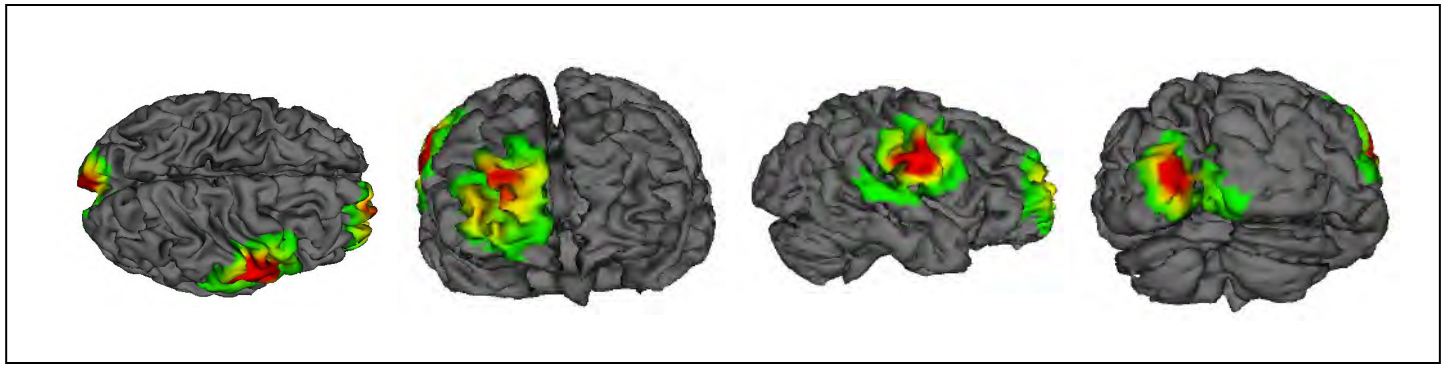
BCI Performance Improvement: EEG+HbO



Fazli et al, Neuroimg. 2011

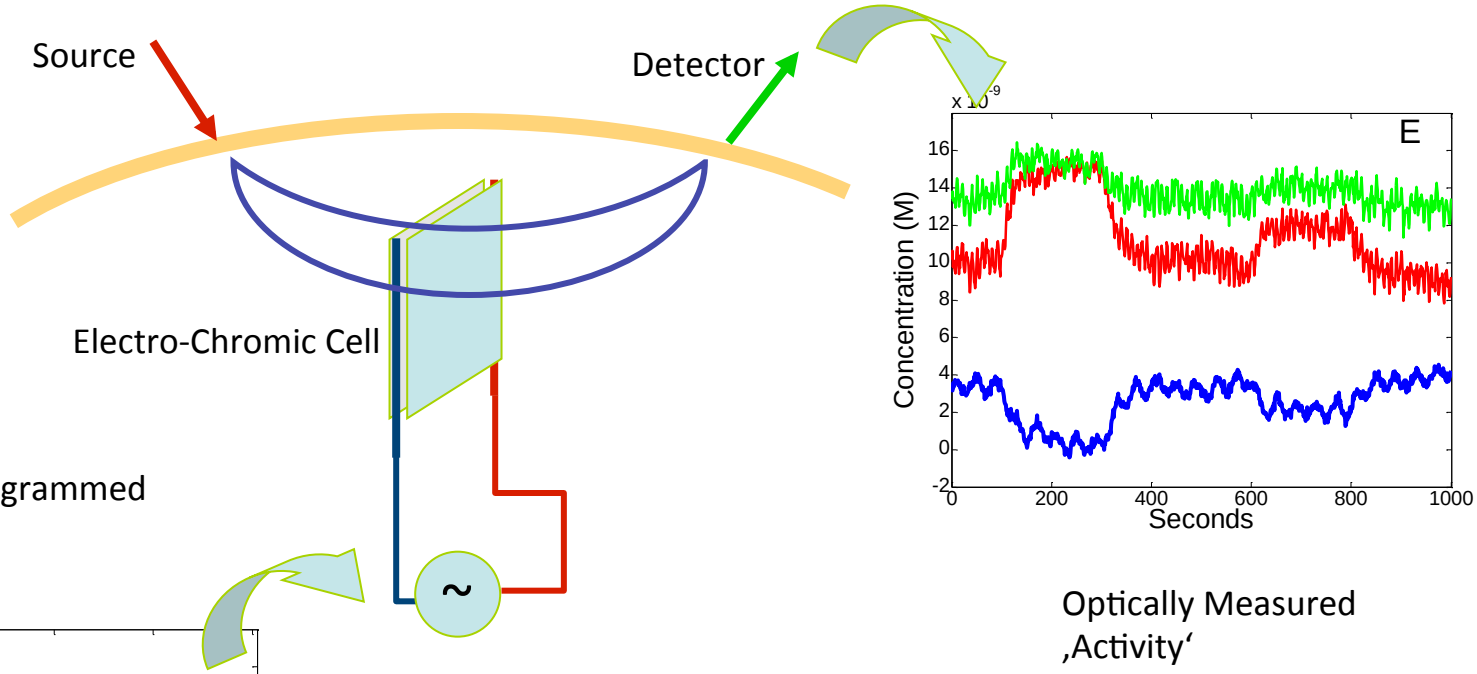
Programmable Phantoms



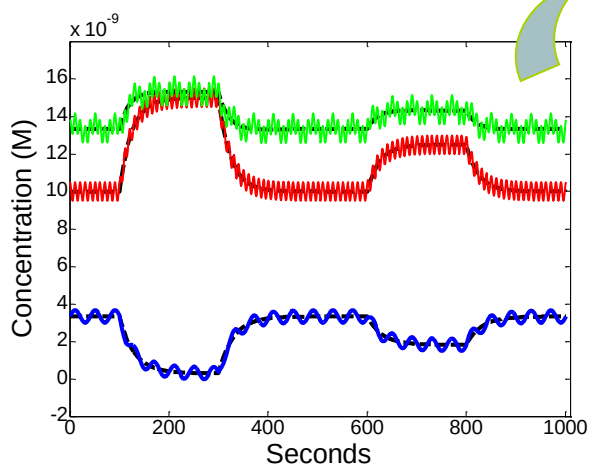


From: R.L. Barbour, et al, *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, Vol. 20, pp. 170-183 (2012).

Optical Activity



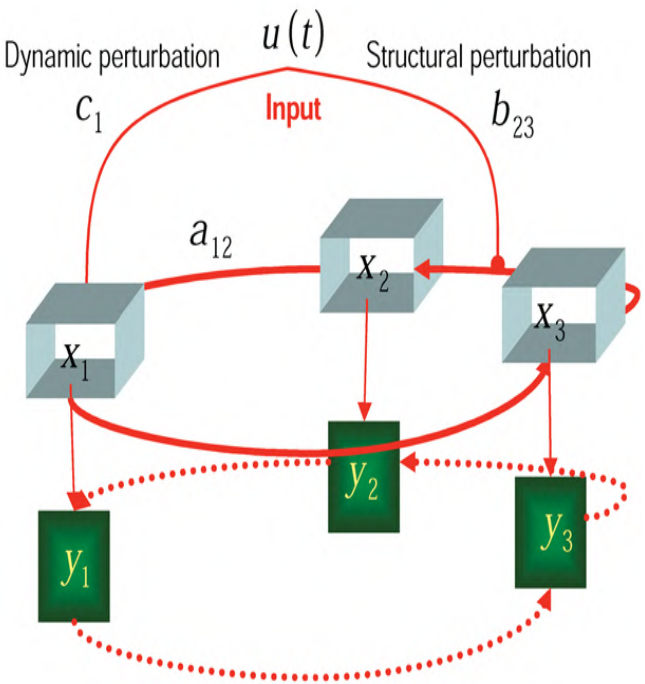
Electrically Programmed
‚Activity‘

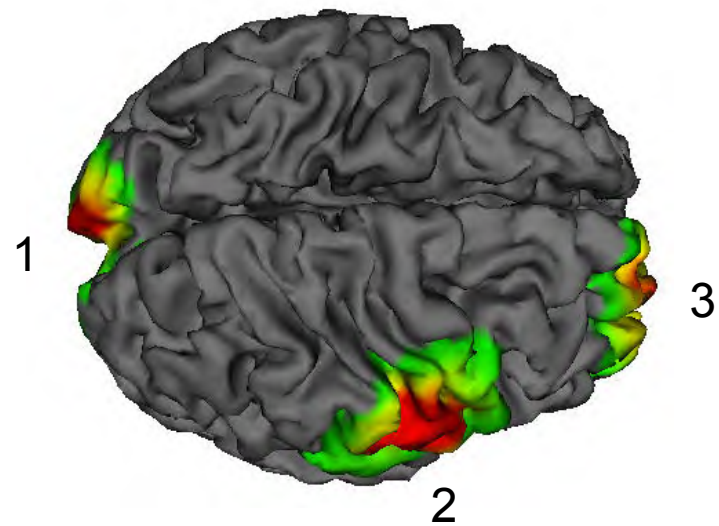


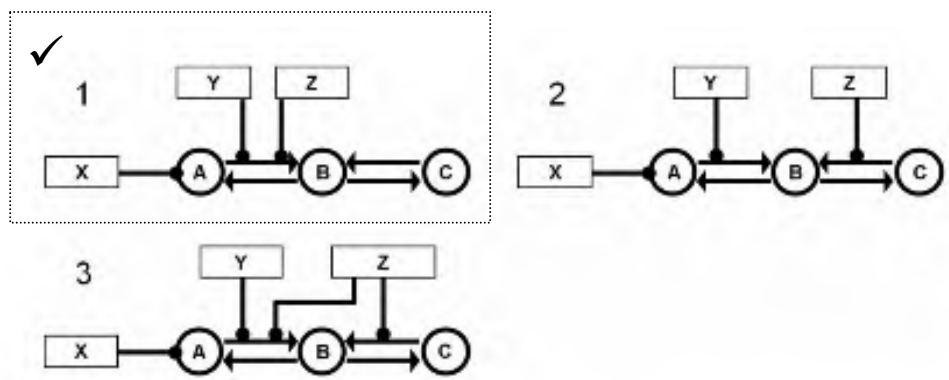
Barbour et al., "A programmable laboratory testbed …, "
IEEE Trans. Neural Sys. and Rehab. Eng., Vol. 20, pp. 170-183 (2012)

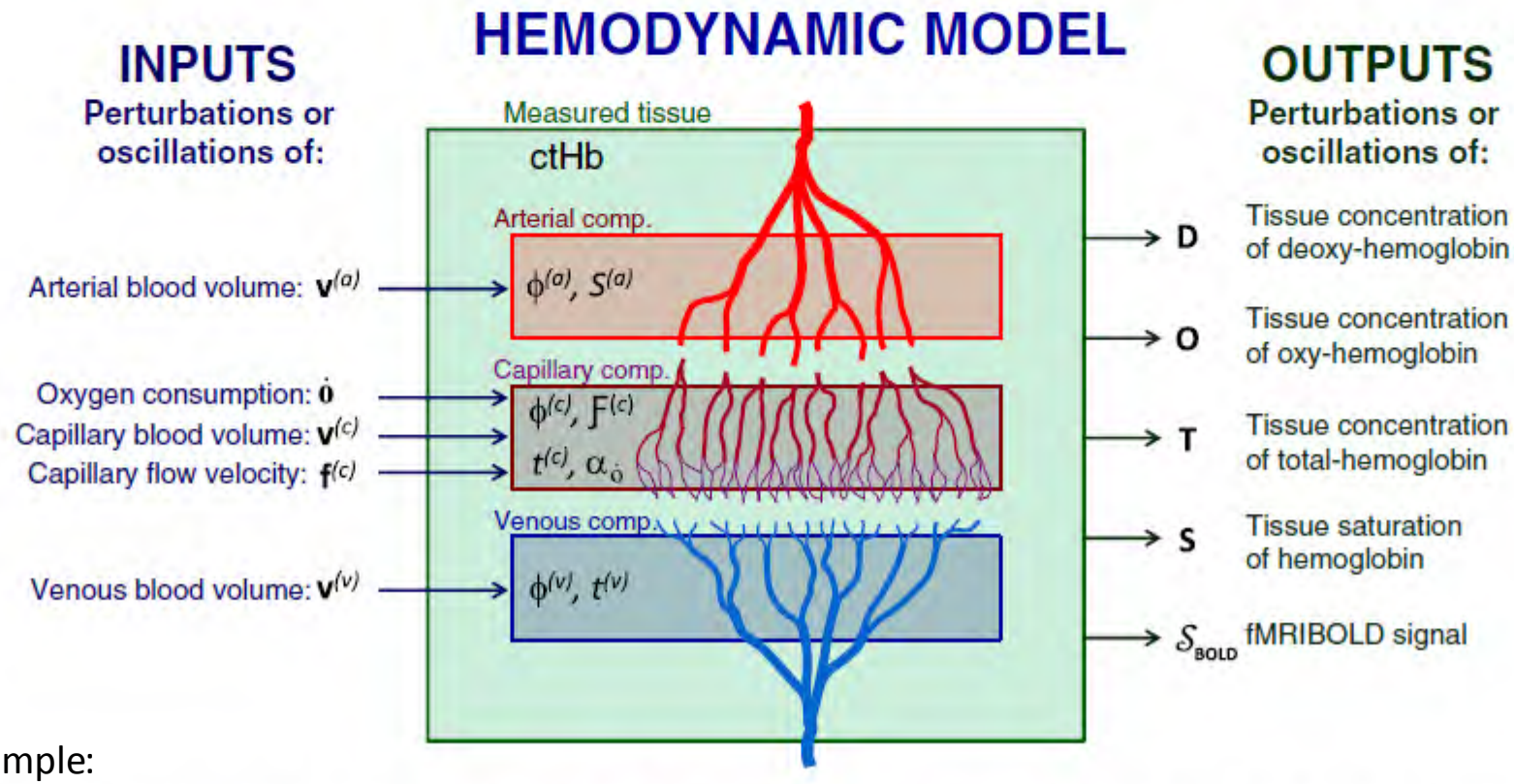
Effective Connectivity

Dynamic Causal Modeling







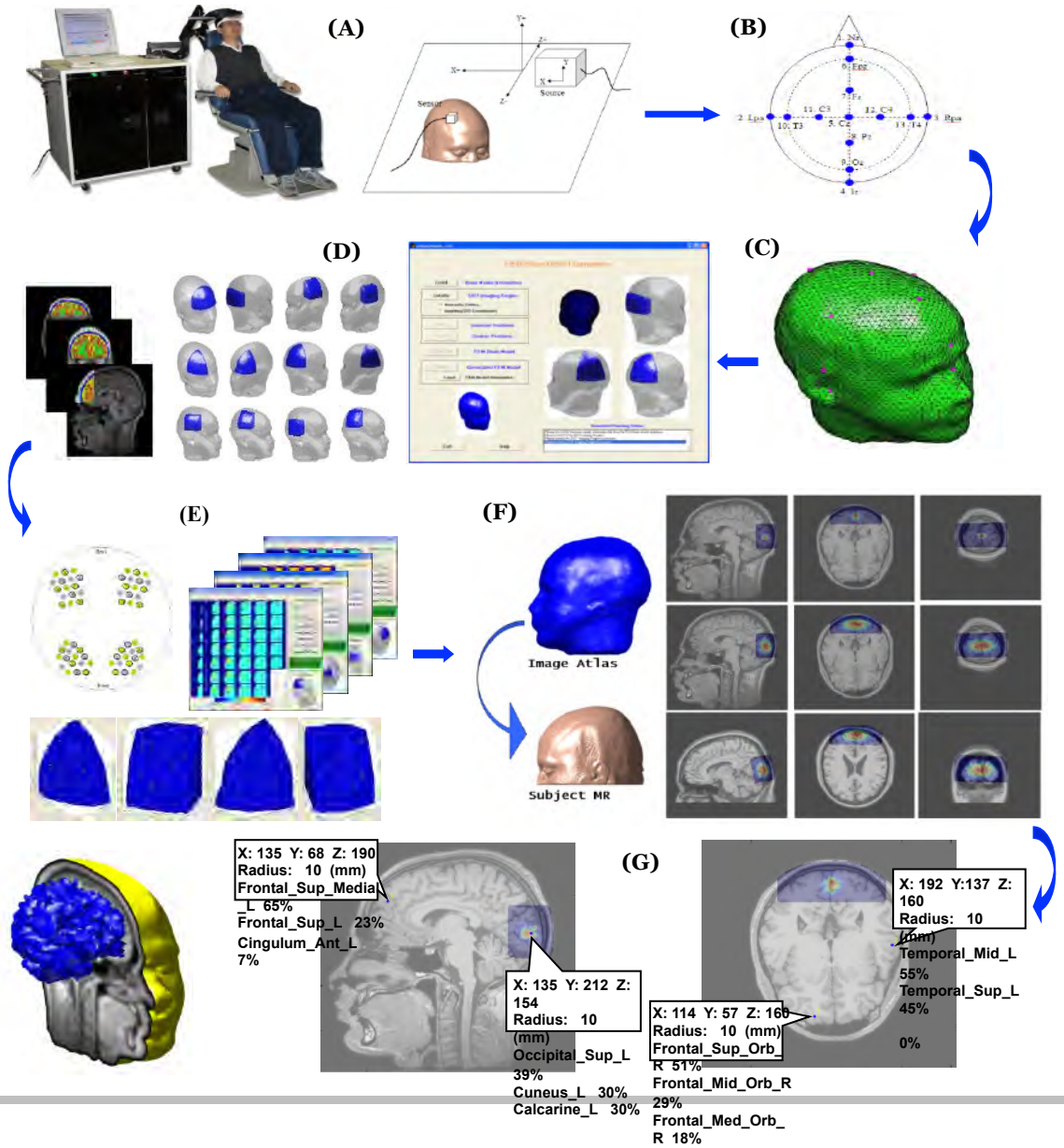


For example:

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

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

Functional Neuroimaging Environment



R.L. Barbour