Multimodal integration of fMRI, EEG, and NIRS

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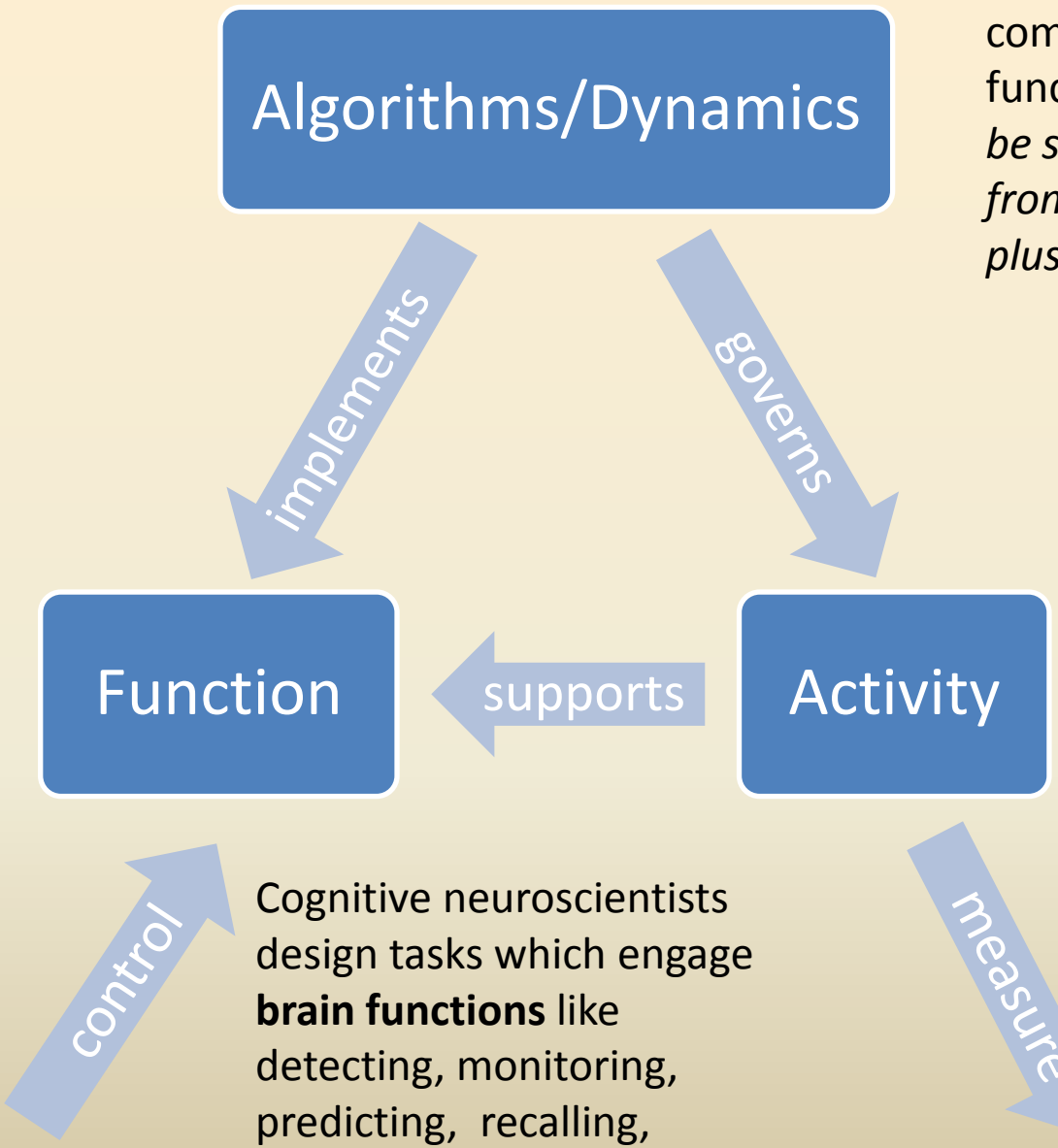
Overview

1. Neuromodalities and multimodal integration
2. fMRI-EEG
3. fMRI-NIRS
4. EEG-NIRS
5. Prospects for fMRI-EEG-NIRS
6. Analysis software environments

How do mental faculties and functions emerge from activities of the brain?

- [Brodmann, 1909] “Mental faculties” (such as memory, will, imagination, and spatial perception) “are notions used to designate extraordinarily involved complexes of mental functions. One cannot think of their taking place in any other way than through an infinitely complex and involved interaction and cooperation of numerous elementary activities…distributed more or less widely over the cortical surface.”



Brain dynamics physically govern brain activity, while **brain algorithms** computationally implement brain functions. *Algorithms/dynamics must be studied indirectly, i.e., inferred from experimental data plus theory plus modeling*.

Conjecture: Brain algorithms are dynamic, and brain dynamics are algorithmic. I.e., physics and computation are deeply united in the brain at all organizational levels.

Cognitive neuroscientists design tasks which engage **brain functions** like detecting, monitoring, predicting, recalling, deciding, controlling, etc.

Neuroimaging and neurophysiological measures reflect **brain activity**, e.g., hemodynamic (~energy) or neuroelectric (~information)

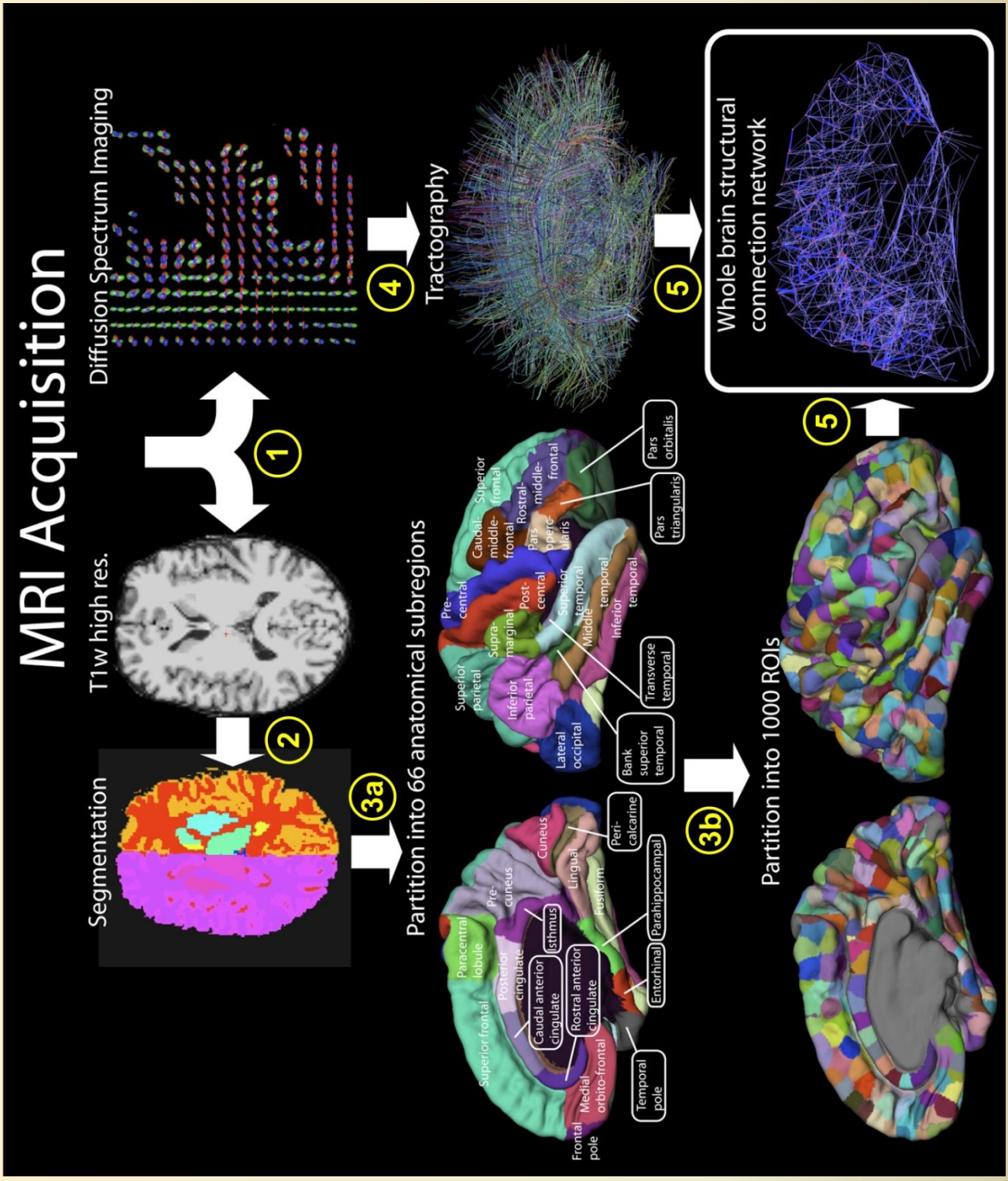
This kind of scientific inference is challenging. It generally requires:

- Theory-driven experimental design
  - Task to elicit the functions of interest
  - Data suitable for modeling
- Human participants engaged in the task
- Refined sensing instruments
  - Adequate coverage for brain regions of interest
  - Multiple modalities to converge on signals of interest
- Computational environment for integrated data analysis and modeling

Primary neuromodalities

- Magnetic Resonance Imaging (MRI)
  - **Structural MRI (sMRI)**
  - **Diffusion MRI (dMRI)**
  - Functional MRI (fMRI)
  - Magnetic Resonance Spectroscopy (MRS)
- Positron Emission Tomography (PET)
- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- Near-Infrared Spectroscopy (NIRS)

Hagmann, P., Cammoun, L., Gigandet, X., Meuli, R., Honey, C.J., Wedeen, V.J., Sporns, O., Friston, K.J. (2008). Mapping the Structural Core of Human Cerebral Cortex. PLoS Biology, 6(7), e159. DOI: 10.1371/journal.pbio.0060159

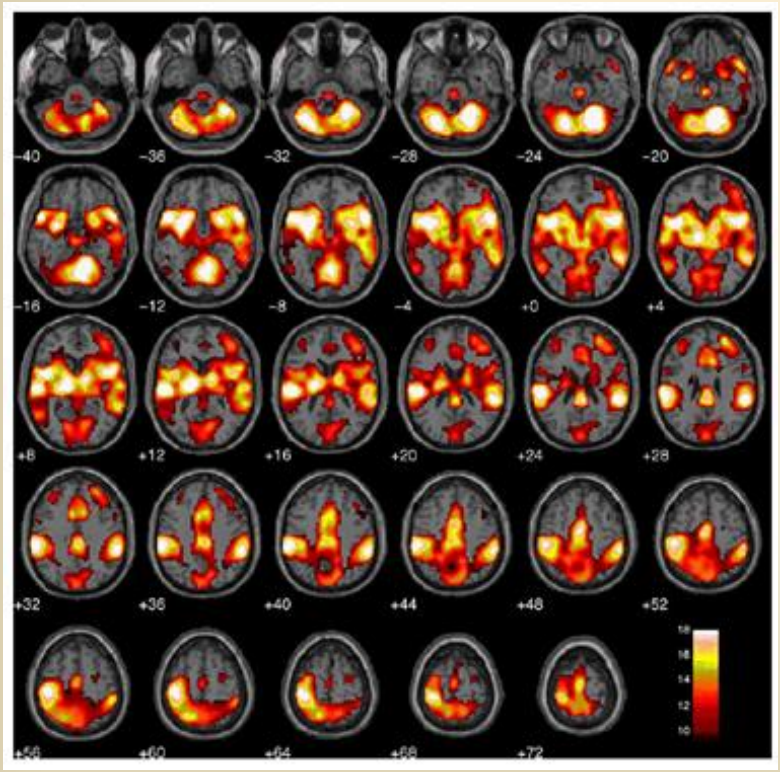


Primary neuromodalities

- Magnetic Resonance Imaging (MRI)
  - Structural MRI (sMRI) & Diffusion MRI (dMRI)
  - **Functional MRI (fMRI)**
    - **BOLD = Blood Oxygen Level Dependent**
    - **ASL = Arterial Spin Labeling**
  - Magnetic Resonance Spectroscopy (MRS)
- Positron Emission Tomography (PET)
- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- Near-Infrared Spectroscopy (NIRS)

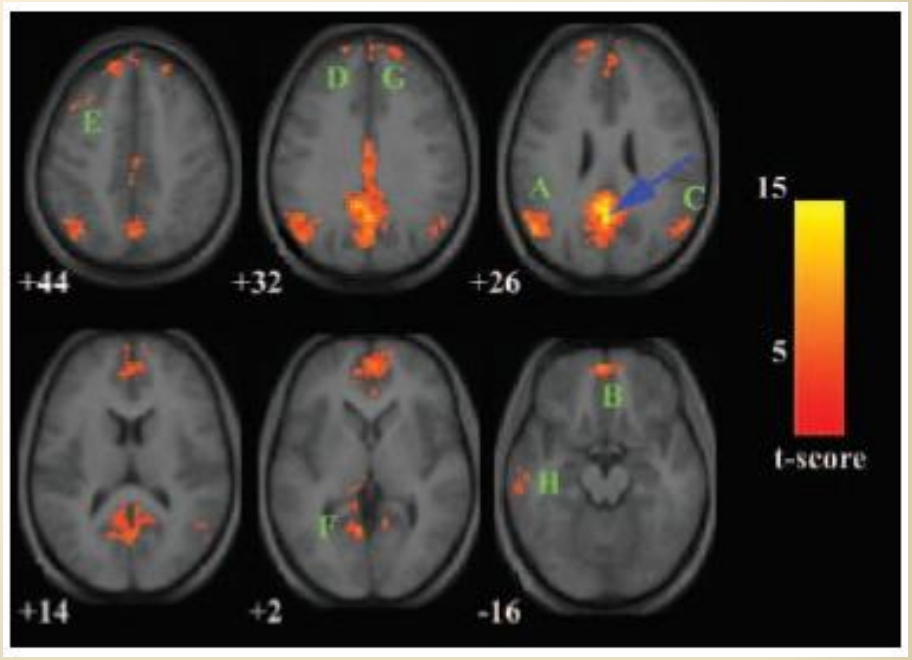
BOLD signal mapping

Statistical contrast



Kiehl et al., 2005

Resting correlation



Grecius et al., 2003

Computational tools: sMRI-fMRI

- Matlab (open source)
  - SPM
- C/C++ (open source)
  - FSL
  - AFNI
  - FreeSurfer
- Python (open source)
  - NiPy
- C/C++ (commercial)
  - BrainVoyager

Primary neuromodalities

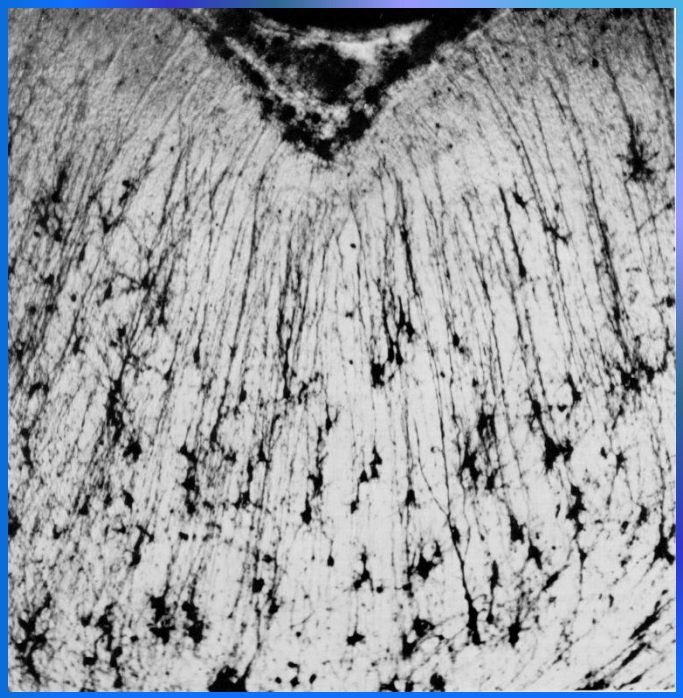
- Magnetic Resonance Imaging (MRI)
  - Structural MRI (sMRI) & Diffusion MRI (dMRI)
  - Functional MRI (fMRI): BOLD, ASL
  - Magnetic Resonance Spectroscopy (MRS)
- Positron Emission Tomography (PET)
- **Electroencephalography (EEG)**
  - **Event-related (ERP, ERBP/ERSP, ERCoh,…)**
- Magnetoencephalography (MEG)
- Near-Infrared Spectroscopy (NIRS)

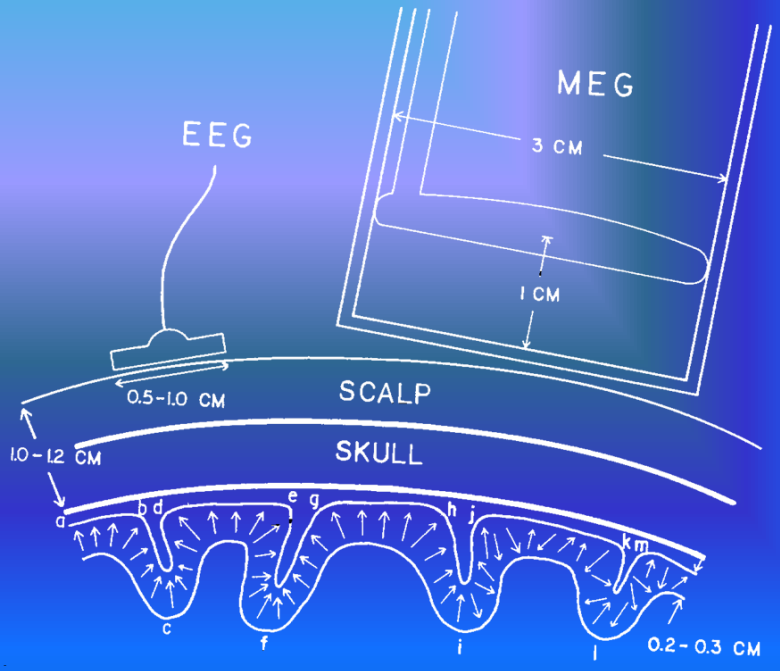

Shugo Suwazono circa 1998
Tom Nakada’s lab at Niigata U

Source space of current dipoles

Equivalent current dipole element =

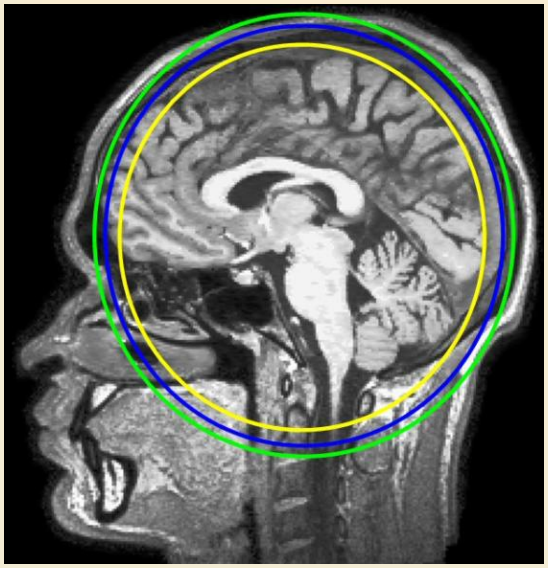
Source/sink of intrinsic (neural) current



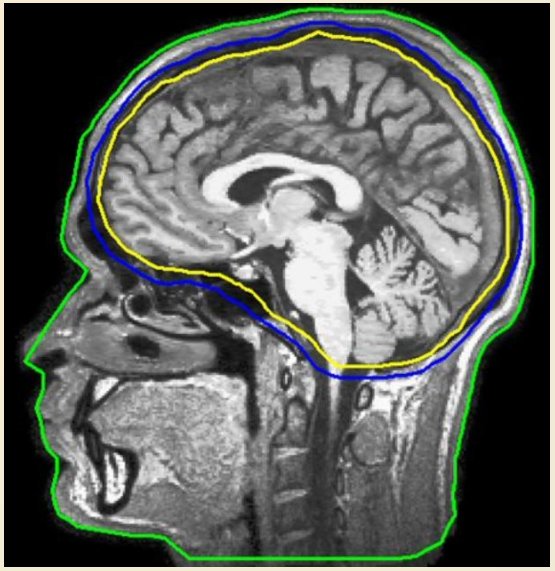


To be measurable at the surface, patch must be 0.5 cm^2 - 5 cm^2

Volume conductor models



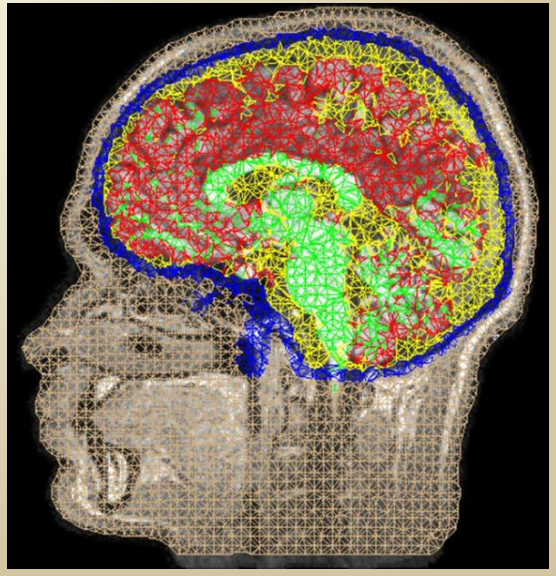
Spherical (analytic)

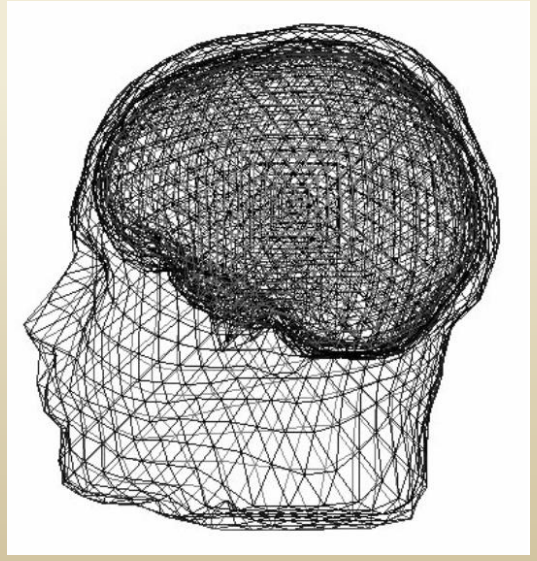


Boundary Element Method

RE Greenblatt, “Source estimation in clinical magnetoencephalography”

Finite Element Method





Physical approximations +
Geometry +
Conductivity parameters +
Solver

Tissue Conductivity (S/m)

Tissue	*Lowest*	*Highest*	*Baseline*
White matter	**0.08**	**1.18**	**0.2**
Gray matter	**0.16**	**0.48**	**0.33**
CSF	**1.0**	**1.79**	**1.79**
Skull	**0.004**	**0.07**	**0.0132**
Fat	**0.02**	**0.07**	**0.045**
Muscle	**0.043**	**0.67**	**0.35**
Eye	**0.5**	**0.5**	**0.5**
Skin	**0.35**	**0.35**	**0.35**

The Problematic Inverse Problem

- *Non-unique*
  - There may be ‘silent’ sources
    - Spatial cancellation: ‘closed field’ arrangement
    - Temporal cancellation: random phase source signals
- *Ill-posed*
  - There may be more unknowns (sources) than knowns (measured signals)
- *Ill-conditioned*
  - The exact solution may be *unstable*
    - in the presence of noise (i.e., real data)
    - with slightly different signals (e.g., nearby time slices)
    - with different initial conditions (typically, when dipole fitting)

Four classical kinds of dual pseudoinverses

	Discrete *Source Space* (*sources < channels*)	***Distributed*** *Source Space* (sources > channels)
Global ***Model*** Most likely model of all the data	*Type I* Multiple dipole modeling (overdetermined)	*Type II* Minimum norm family (underdetermined)
Local ***Filter*** Best tuned filter for a region of interest	*Type III* LCMV beamformers (underdetermined)	*Type IV* Optimally localized average (overdetermined)

Spatial filters are designed using models, but their outputs are filtered data, not models of data.

Computational tools: sMRI-EMEG

- Matlab (open source)
  - BrainStorm
  - EEGLAB
  - FieldTrip
  - SPM
- C/C++ (commercial)
  - ASA
  - BESA
  - Curry
  - EMSE

Primary neuromodalities

- Magnetic Resonance Imaging (MRI)
  - Structural MRI (sMRI) & Diffusion MRI (dMRI)
  - Functional MRI (fMRI): BOLD, ASL
  - Magnetic Resonance Spectroscopy (MRS)
- Positron Emission Tomography (PET)
- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- **Near-Infrared Spectroscopy (NIRS)**
  - **Diffuse Optical Tomography (DOT)**
  - **Fast Optical Signal (FOS)**

Computational tools: sMRI-NIRS

- NIRFAST/NIRViz (general purpose)
  - FEM mesh generation from MRI; NIR-DOT solutions; overlay on MRI/CT
- NAVI-EMSE integration (specialized for brain)
  - FEM mesh generation from MRI (EMSE); NIR-DOT solutions (NAVI); overlay on MRI (NAVI) and interpolated display on cortical surface (EMSE)
  - Ready for EEG-NIRS integration
  - Yong Xu, Harry Graber, David Nichols, Alex Ossadtchi

Historical trends in multimodal integration

- Structure-Structure
  - sMRI-CT
- Function-Structure
  - fMRI-sMRI
- Function-Structure // Function-Structure
  - fMRI-sMRI // MEG-sMRI
- (Function-Function)-Structure
  - (fMRI-EEG)-sMRI
  - Utilize information contained in joint data

fMRI-EEG

- The lure: *Compensate for primary weaknesses?*
  - BOLD fMRI signal is indirect and sluggish
  - EEG inverse solutions are ambiguous
- Study *neurovascular coupling* itself
- EEG artifacts in MRI environments:
  - Ballistocardiogram
  - RF pulse
  - Gradient switching
- Ullsperger and Debener: *Simultaneous EEG and fMRI: Recording, Analysis, and Application*. Oxford, 2010.

fMRI-EEG analysis approaches

- *Model-driven fusion* (e.g., Valdes-Sosa)
  - Detailed biophysical modeling
  - Solve jointly for neuronal activity
- *Data-driven fusion* (e.g., Calhoun)
  - Joint or parallel ICA
  - No underlying model
- *Convolution models* of BOLD HRF with *generic spatial filters* for EEG source estimators
  - GLM with EEG band power as a regressor

fMRI-NIRS

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Magnetic Resonance Imaging 24 (2006) 495–505

MAGNETIC RESONANCE IMAGING

Illuminating the BOLD signal: combined fMRI–fNIRS studies

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Abstract

Functional magnetic resonance imaging (fMRI) is currently combined with electrophysiological methods to identify the relationship between neuronal activity and the blood oxygenation level-dependent (BOLD) signal. Several processes like neuronal activity, synaptic activity, vascular dilation, blood volume and oxygenation changes underlie both response modalities, that is, the electrophysiological signal and the vascular response. However, accessing single process relationships is absolutely mandatory when aiming at a deeper understanding of neurovascular coupling and necessitates studies on the individual building blocks of the vascular response. Combined fMRI and functional near-infrared spectroscopy studies have been performed to validate the correlation of the BOLD signal to the hemodynamic changes in the brain. Here we review the current status of the integration of both technologies and judge these studies in the light of recent findings on neurovascular coupling.

Keywords: Hemodynamic response function (HRF); fMRI; fNIRS; BOLD

BOLD signal change related to arterial blood flow change and [HbR] change

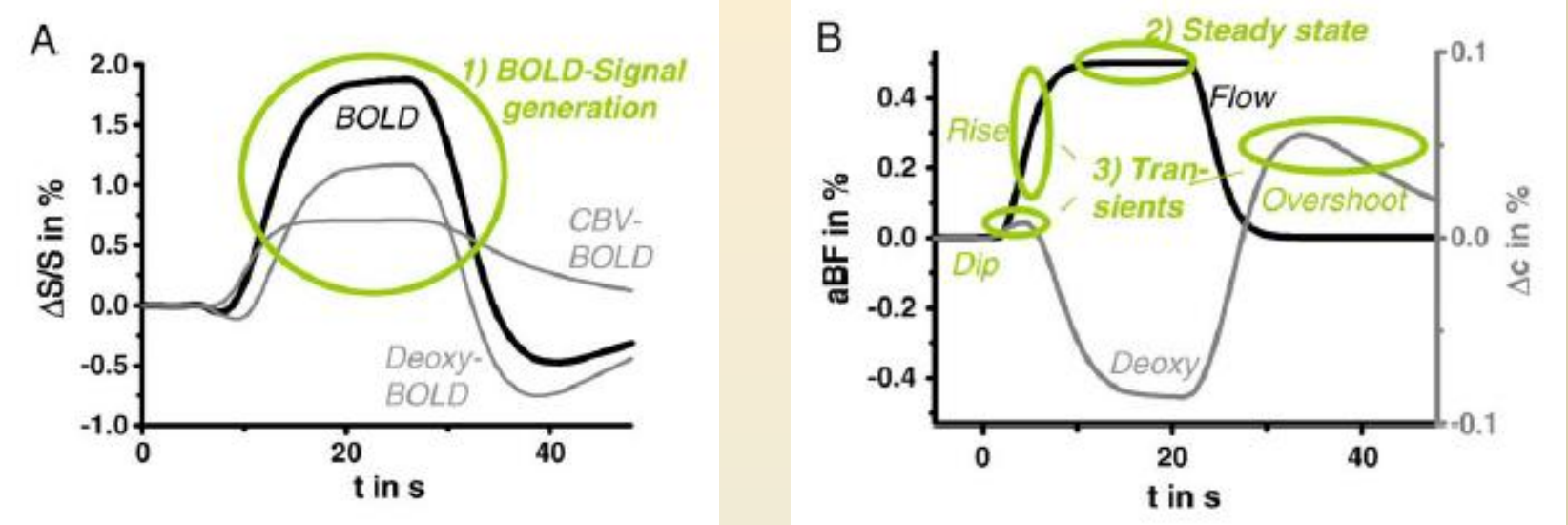

Fig. 1. (A) The typical BOLD-signal change observed after functional stimulation. (B) The changes of [deoxy-Hb] (gray) show transients, which are also observed in the BOLD response. The plots were generated from a model of the hemodynamic response described in the text.

Steinbrink et al., MRI 24 (2006) p 497

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Quantification of $CMRO_2$ without hypercapnia using simultaneous near-infrared spectroscopy and fMRI measurements

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Abstract

Estimation of the cerebral metabolic rate of oxygen ($CMRO_2$) and cerebral blood flow (CBF) is important to investigate the neurovascular coupling and physiological components in blood oxygenation level-dependent (BOLD) signals quantitatively. Although there are methods that can determine $CMRO_2$ changes using functional MRI (fMRI) or near-infrared spectroscopy (NIRS), current approaches require a separate hypercapnia calibration process and have the potential to incur bias in many assumed model parameters. In this paper, a novel method to estimate $CMRO_2$ without hypercapnia is described using simultaneous measurements of NIRS and fMRI. Specifically, an optimization framework is proposed that minimizes the differences between the two forms of the relative $CMRO_2$–CBF coupling ratio from BOLD and NIRS biophysical models, from which hypercapnia calibration and model parameters are readily estimated. Based on the new methods, we found that group average CBF, $CMRO_2$, cerebral blood volume (CBV), and BOLD changes within activation of the primary motor cortex during a finger tapping task increased by $39.5 \pm 21.4\%$, $18.4 \pm 8.7\%$, $12.9 \pm 6.7\%$, and $0.5 \pm 0.2\%$, respectively. The group average estimated flow-metabolism coupling ratio was 2.38 ± 0.65 and the hypercapnia parameter was $7.7 \pm 1.7\%$. These values are within the range of values reported from other literatures. Furthermore, the activation maps from CBF and $CMRO_2$ were well localized on the primary motor cortex, which is the main target region of the finger tapping task.

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Somatosensory activation of two fingers can be discriminated with ultrahigh-density diffuse optical tomography

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Multimodal imaging

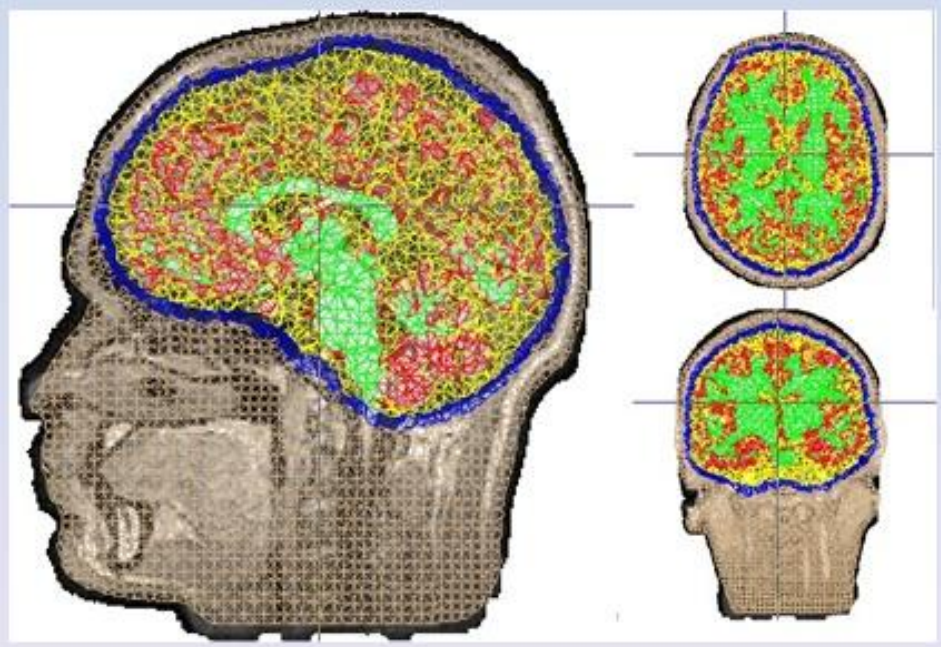
ABSTRACT

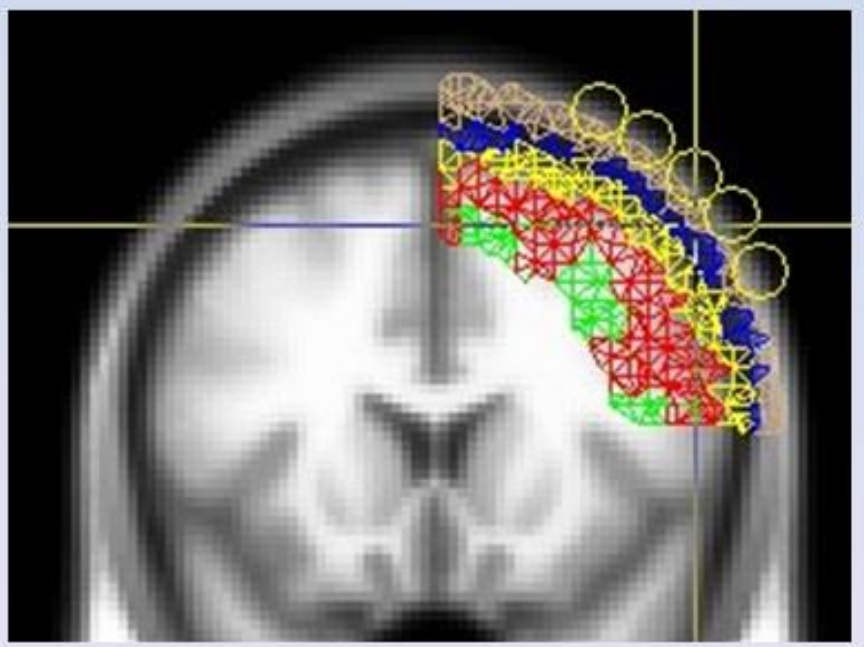
Topographic non-invasive near infrared spectroscopy (NIRS) has become a well-established tool for functional brain imaging. Applying up to 100 optodes over the head of a subject, allows achieving a spatial resolution in the centimeter range. This resolution is poor compared to other functional imaging tools.
However, recently it was shown that diffuse optical tomography (DOT) as an extension of NIRS based on high-density (HD) probe arrays and supplemented by an advanced image reconstruction procedure allows describing activation patterns with a spatial resolution in the millimeter range. Building on these findings, we hypothesize that HD-DOT may render very focal activations accessible which would be missed by the traditionally used sparse arrays.
We examined activation patterns in the primary somatosensory cortex, since its somatotopic organization is very fine-grained. We performed a vibrotactile stimulation study of the first and fifth finger in eight human subjects, using a 900-channel continuous-wave DOT imaging system for achieving a higher resolution than conventional topographic NIRS. To compare the results to a well-established high-resolution imaging technique, the same paradigm was investigated in the same subjects by means of functional magnetic resonance imaging (fMRI).
In this work, we tested the advantage of ultrahigh-density probe arrays and show that highly focal activations would be missed by classical next-nearest neighbor NIRS approach, but also by DOT, when using a sparse probe array. Distinct activation patterns for both fingers correlated well with the expected neuroanatomy in five of eight subjects. Additionally we show that activation for different fingers is projected to different tissue depths in the DOT image. Comparison to the fMRI data yielded similar activation foci in seven out of ten finger representations in these five subjects when comparing the lateral localization of DOT and fMRI results.

EEG-NIRS

- EEG and NIRS measurements depend on different physical properties (conductivities vs. absorption and scattering coefficients) of the same head tissues, such as scalp, skull, CBF, gray matter, and white matter.
- Forward models are needed to estimate neuroelectric sources (EEG) or cerebral hemodynamic states (NIRS) in a common anatomical space using suitable inverse methods.

Whole head FEM mesh suitable for an EEG head modeling, and submesh under optodes suitable for NIR-DOT





Enhanced performance by a Hybrid NIRS-EEG Brain Computer Interface

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[c]*Berlin NeuroImaging Center, University Hospital Charité, Berlin, Germany*
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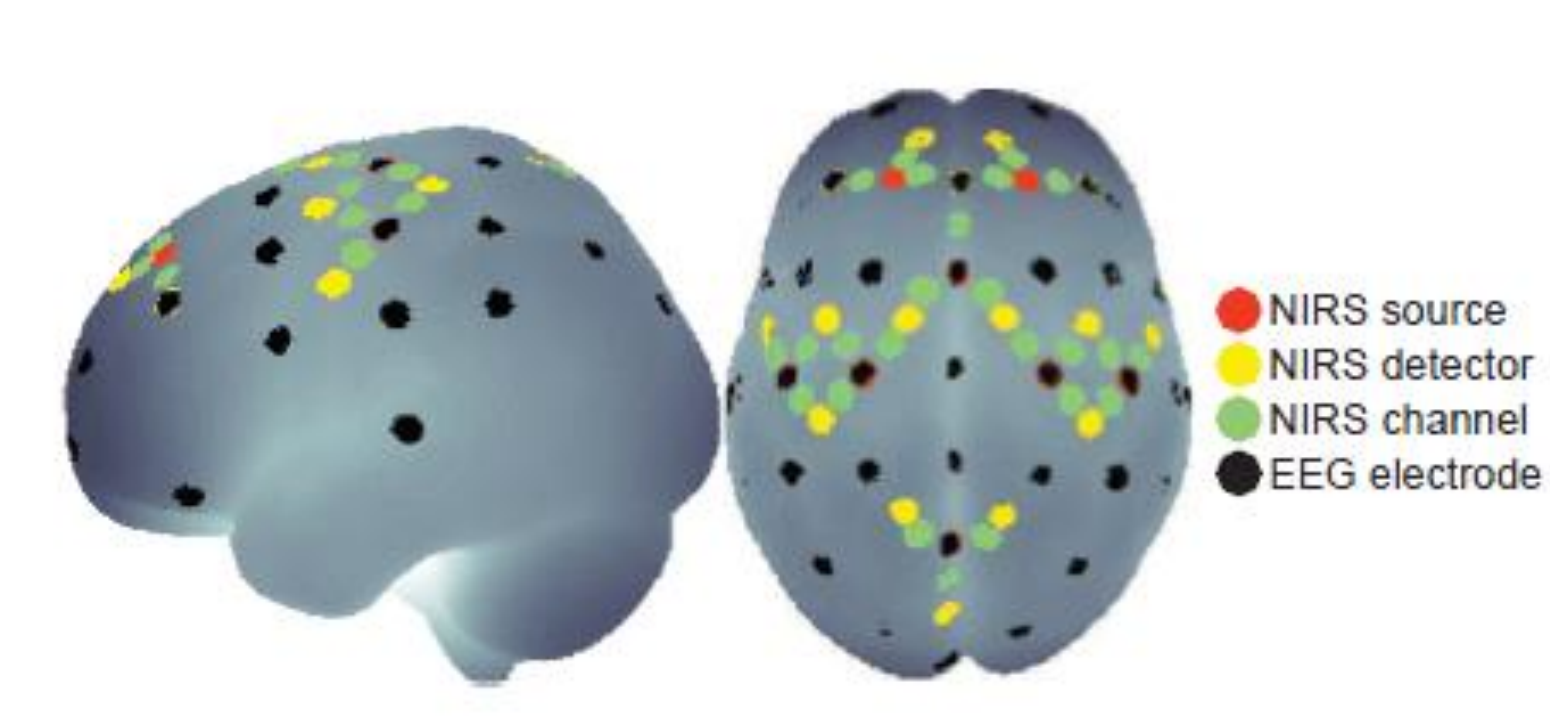
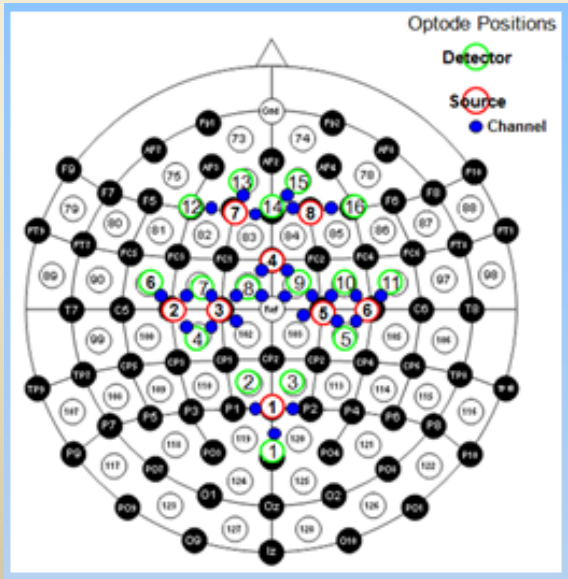
Abstract

Noninvasive Brain Computer Interfaces (BCI) have been promoted to be used for neuroprosthetics. However, reports on applications with electroencephalography (EEG) show a demand for a better accuracy and stability. Here we investigate whether near-infrared spectroscopy (NIRS) can be used to enhance the EEG approach. In our study both methods were applied simultaneously in a real-time Sensory Motor Rhythm (SMR)-based BCI paradigm, involving executed movements as well as motor imagery. We tested how the classification of NIRS data can complement ongoing real-time EEG classification. Our results show that simultaneous measurements of NIRS and EEG can significantly improve the classification accuracy of motor imagery in over 90% of considered subjects and increases performance by 5% on average ($p < 0.01$). However, the long time delay of the hemodynamic response may hinder an overall increase of bit-rates. Furthermore we find that EEG and NIRS complement each other in terms of information content and are thus a viable multimodal imaging technique, suitable for BCI.

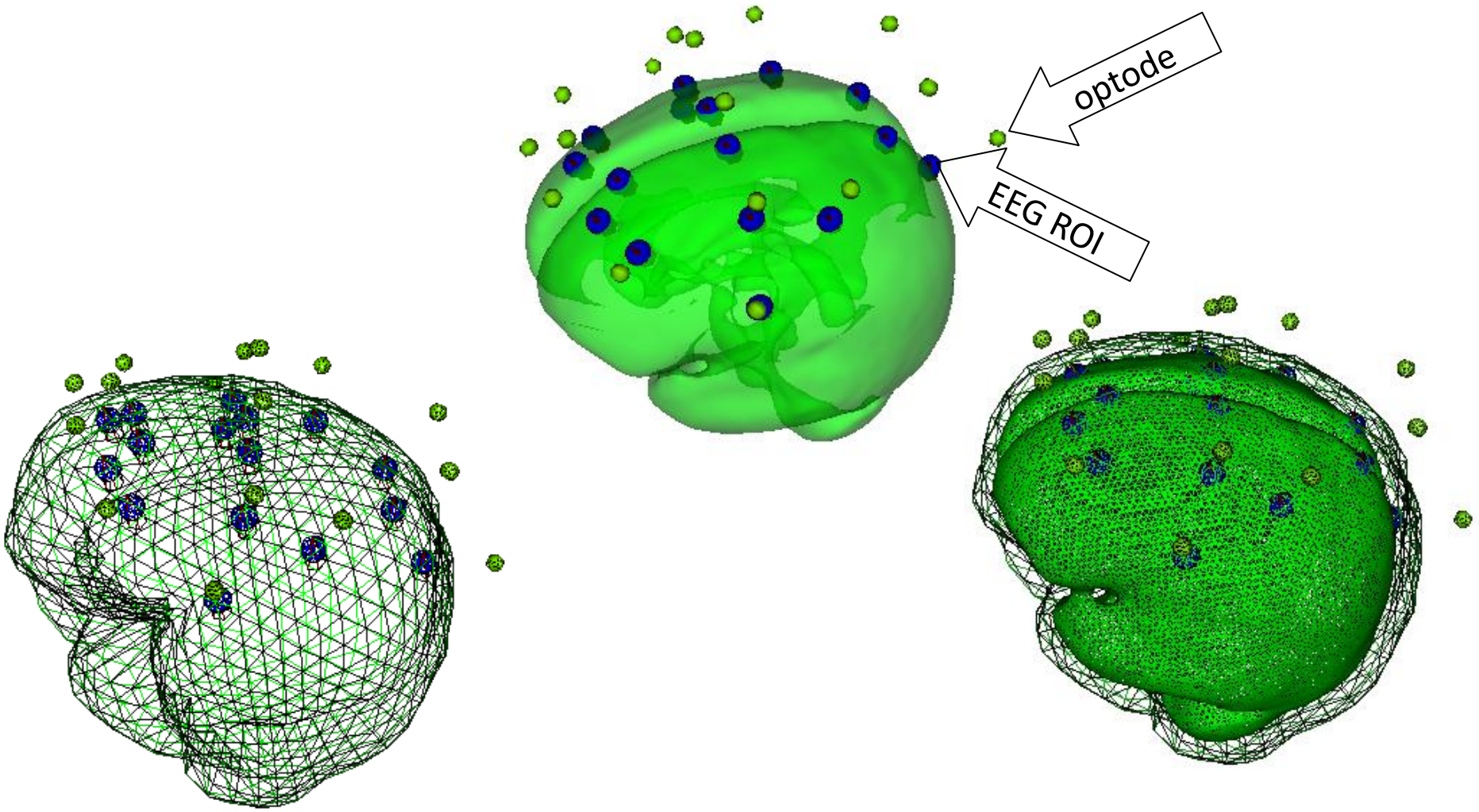


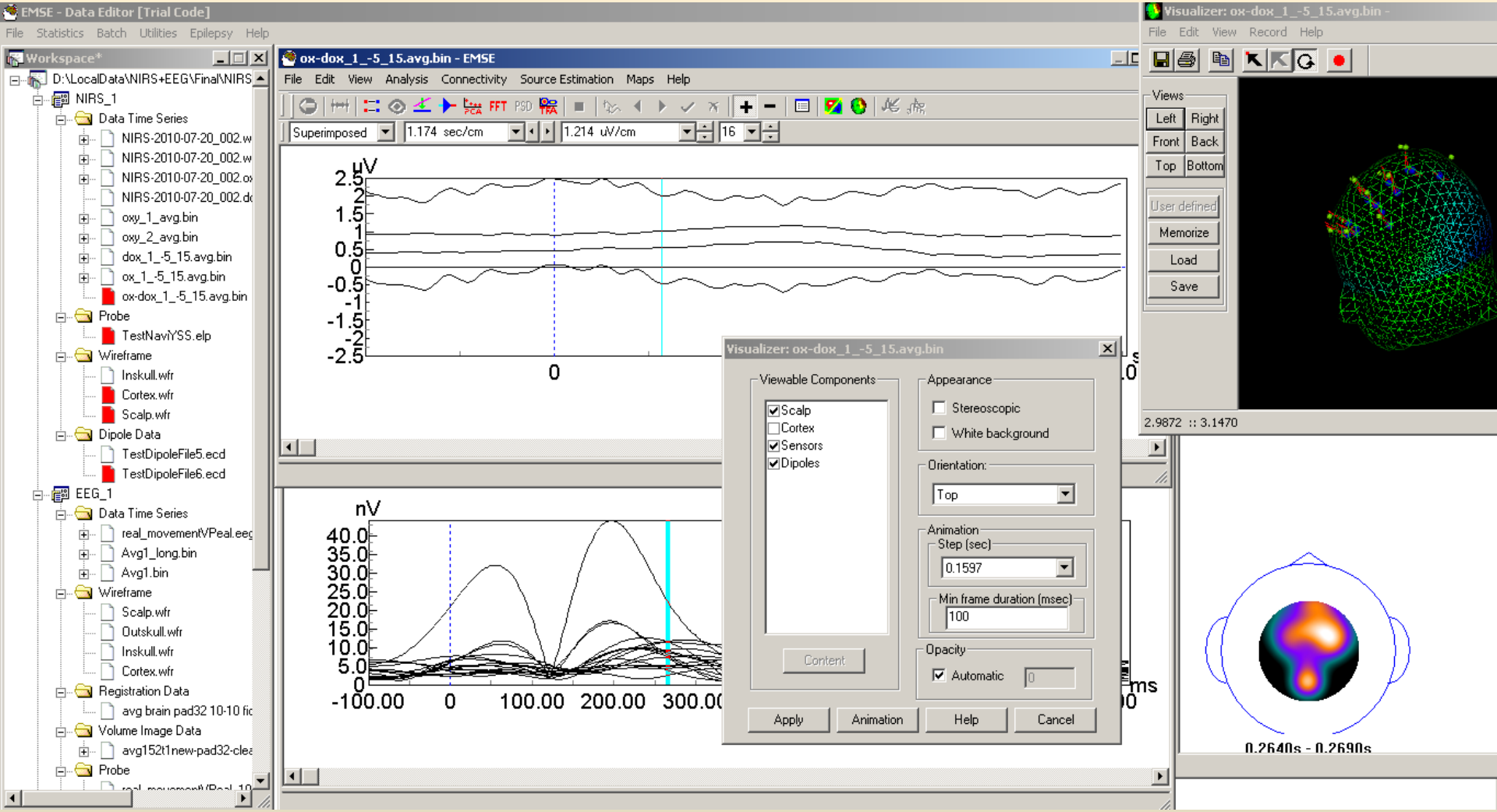


Setup. 8 sources and 16 detectors were used for NIRS acquisition, concurrent with 64-channel EEG acquisition.

Determination of ROIs based on optical sensor positions

- ROIs for beamforming were determined by radially projecting optode locations through the inner skull for 1 cm beneath it.

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File Statistics Batch Utilities Epilepsy Help
Workspace*
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NIRS_1
Data Time Series
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Viewable Components
Scalp
Cortex
Sensors
Dipoles
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Opacity
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Apply
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Help
Cancel
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Right
Front
Back
Top
Bottom
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0.2640s - 0.2690s

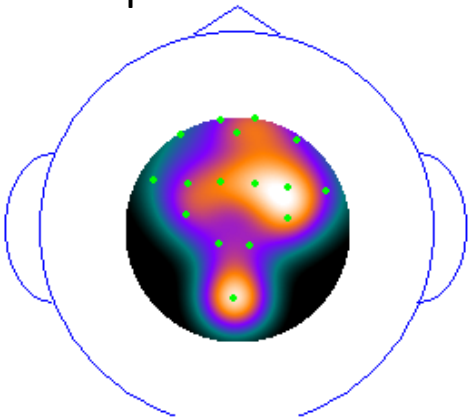
Comparison of EEG and NIRS maps

- Based on the EEG data covariance matirx we calculated beamformer timeseries for the dipolar omni-directional ROIs.

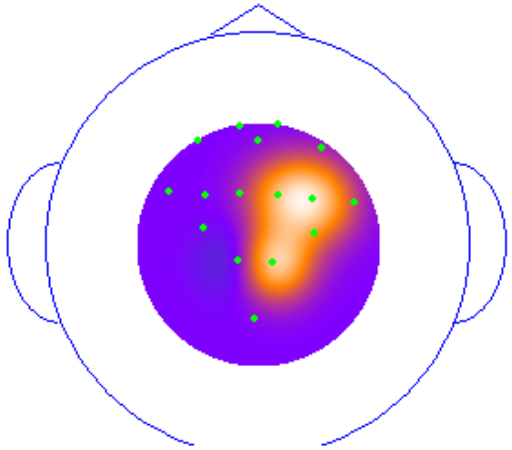
- In order to compare the obtained spatial distribution we visualized it in a similar manner as NIRS data using EMSE topographic display tool

Left hand

EEG based virtual electrodes,
Butterworth IIR 0-5 Hz, order 4,
230 ms post stim



NIRS, oxy-dOxy @ 5.6 s latency



FOS detection via EEG-NIRS

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"Seeing" electroencephalogram through the skull: imaging prefrontal cortex with fast optical signal

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Abstract. Near-infrared spectroscopy is a novel imaging technique potentially sensitive to both brain hemodynamics (slow signal) and neuronal activity (fast optical signal, FOS). The big challenge of measuring FOS noninvasively lies in the presumably low signal-to-noise ratio. Thus, detectability of the FOS has been controversially discussed. We present reliable detection of FOS from 11 individuals concurrently with electroencephalogram (EEG) during a Go-NoGo task. Probes were placed bilaterally over prefrontal cortex. Independent component analysis (ICA) was used for artifact removal. Correlation coefficient in the best correlated FOS–EEG ICA pairs was highly significant ($p < 10^{-8}$), and event-related optical signal (EROS) was found in all subjects. Several EROS components were similar to the event-related potential (ERP) components. The most robust "optical N200" at $t = 225$ ms coincided with the N200 ERP; both signals showed significant difference between targets and nontargets, and their timing correlated with subject's reaction time. Correlation between FOS and EEG even in single trials provides further evidence that at least some FOS components "reflect" electrical brain processes directly. The data provide evidence for the early involvement of prefrontal cortex in rapid object recognition. EROS is highly localized and can provide cost-effective imaging tools for cortical mapping of cognitive processes. [DOI: 10.1117/1.3505007]

Keywords: near-infrared spectroscopy; fast optical signal; event-related signal; electroencephalogram; independent component anaysis; visual object detection.

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Use modality 1 to enhance modality 2

1→2	fMRI	EEG	NIRS
fMRI	ASL→BOLD	• fMRI-constrained source estimation • ROI-tuned spatial filter	Study spatial resolution and depth characteristics of DOT
EEG	Regional HRF to neuroelectric activity	Band_1→Band_2	Enhance and validate FOS detection
NIRS	Study hemodynamic models of the BOLD signal	Slow hemodynamic signal in EEG?	FOS→Hemodynamic

Prospects for fMRI-EEG-NIRS

- Higher-order relationships
  - Improve tests of BOLD signal models by augmenting hemodynamic measures from fMRI-NIRS with estimates of neuronal activity (via EEG or via FOS detection using EEG-NIRS)
  - Cerebral metabolic rate of oxygen estimated with fMRI-NIRS (Tak et al., 2010) may be related to neuroelectric activity via concurrent EEG
- Fruitfulness of studies combining fMRI-EEG and EEG-NIRS in parallel

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Correlates of alpha rhythm in functional magnetic resonance imaging and near infrared spectroscopy

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Abstract

We used simultaneous electroencephalogram-functional magnetic resonance imaging (EEG-fMRI) and EEG-near infrared spectroscopy (NIRS) to investigate whether changes of the posterior EEG alpha rhythm are correlated with changes in local cerebral blood oxygenation. Cross-correlation analysis of slowly fluctuating, spontaneous rhythms in the EEG and the fMRI signal revealed an inverse relationship between alpha activity and the fMRI-blood oxygen level dependent signal in the occipital cortex. The NIRS-EEG measurements demonstrated a positive cross-correlation in occipital cortex between alpha activity and concentration changes of deoxygenated hemoglobin, which peaked at a relative shift of about 8 s. Our data suggest that alpha activity in the occipital cortex is associated with metabolic deactivation. Mapping of spontaneously synchronizing distributed neuronal networks is thus shown to be feasible.

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Clinical Neuroscience

Nonlinear hemodynamic responses in human epilepsy: A multimodal analysis with fNIRS-EEG and fMRI-EEG

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ABSTRACT

Functional magnetic resonance imaging (fMRI) combined with electroencephalography (fMRI-EEG) is a neuroimaging technique based on the blood oxygenation level dependent (BOLD) signal which has been shown to be useful in the study of epilepsy for the localization of the epileptogenic focus. Functional near-infrared spectroscopy (fNIRS) combined with EEG (fNIRS-EEG) is another imaging technique based on the measurement of oxygenated and deoxygenated hemoglobin with complementary clinical potential in epilepsy, for continuous patient monitoring, language lateralization, and focus localization.

In this work fMRI-EEG and fNIRS-EEG are used to quantify nonlinear hemodynamic responses in three cases of human refractory focal epilepsy, by using the Volterra kernel expansion up to second order. Prior to analyzing real data, extensive simulations are carried out to show that nonlinearities are estimable. The Volterra methodology is then applied to multimodal data recorded from 3 epileptic patients selected for their frequent spiking activity. Care is taken to account for variability of hemodynamic responses due to other causes than Volterra nonlinearities. Statistically significant nonlinearities are observed for all patients and all modalities. Good concordance between fNIRS and fMRI is found for both the amplitude of the Volterra responses, and, with limitations, in the localization of the epileptic focus and regions of inverted responses (negative BOLD signals). In one patient, Volterra nonlinearities allowed epileptic focus identification with fMRI, while analyses without nonlinearities failed to see it. In simulations when nonlinearities were included, analysis without Volterra nonlinearities performed poorly. These two observations suggest routinely checking for nonlinearities in functional imaging of patients presenting with frequent spikes.

Computational frameworks suitable for multimodal integration

- Problem Solving Environments (PSEs)
  - *"A PSE is a computer system that provides all the computational facilities needed to solve a target class of problems. These features include advanced solution methods, automatic and semiautomatic selection of solution methods, and ways to easily incorporate novel solution methods. Moreover, PSEs use the language of the target class of problems…" (Gallopoulos et al., 1994)*
  - SCIRun, BioPSE
- Matlab + Toolboxes + applications
- "Pylab": Python + NumPy + SciPy + NiPy
- Hybrid pipelines
  - NiPype (NiPy, AFNI, FSL, SPM, FreeSurfer, …)