Da neuroimagem às interfaces cérebro-computador

[Workshop]

Alexandre Sayal
Bruno Direito
Carolina Travassos
João Pereira
Teresa Sousa

XVI ENEEB, March 6

CIBIT
Coimbra Institute for Biomedical Imaging and Translational Research

1290
Instituto de Ciências Nucleares Aplicadas à Saúde
Universidade de Coimbra

Outline

- Introduction
  - CIBIT and Team
- Neuroimaging
  - Basic concepts and Applications
    - History and evolution
    - Modalities
  - Brain-Computer Interfaces:
    - Neurofeedback and Classification
- Hands-on Session
  - fNIRS: Experimental setup and data acquisition, processing and analysis
  - Neurofeedback
  - Classification

Introduction

Team

Alexandre Sayal

Bruno Direito

Carolina Travassos

João Pereira

Teresa Sousa

CIBIT

Coimbra Institute for Biomedical Imaging and Translational Research

Multimodal biomedical imaging and translational research

Cognitive, Translational and Clinical Neuroscience

Imaging modalities:

pre-clinical and clinical MR,

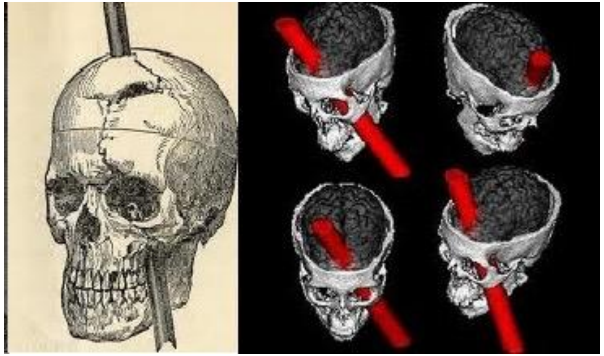
EEG, TMS, tDCS,

fNIRS, PET, OCT.

Neuroimaging

Basic concepts and Applications

Neurology and neurosciences before neuroimaging - *Phrenology* and *localizationism*



Phineas Gage

Link between brain trauma, prefrontal brain damage and personality change.

Thiebaut De Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., et al. (2015). Cereb. Cortex 25, 4812–4827. doi:10.1093/cercor/bhv173.

Neurology and neurosciences before neuroimaging - *Phrenology* and *localizationism*

Louis Victor Leborgne ("tan tan")

First non-fluent aphasic patient (reported by Paul Broca, 1861) - post-mortem validation of injury in the inferior frontal gyrus

---

Mohammed, N., Narayan, V., Patra, D. P., and Nanda, A. (2018). Louis Victor Leborgne ("Tan"). *World Neurosurg.* 114, 121–125. doi:10.1016/j.wneu.2018.02.021.

Neurology and neurosciences before neuroimaging - *Phrenology* and *localizationism*

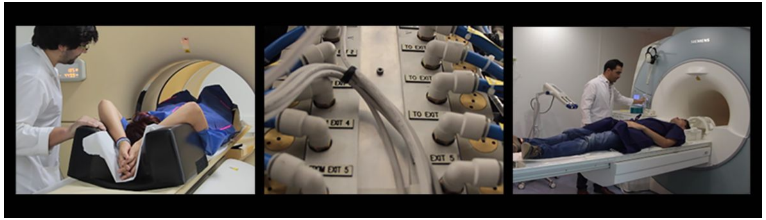
H.M. (Henry Molaison)

Epilepsy history, surgical removal of medial temporal lobe - anterograde amnesia.

Thiebaut De Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., et al. (2015). Cereb. Cortex 25, 4812–4827. doi:10.1093/cercor/bhv173.

How neuroimaging is changing our perception of how the brain works

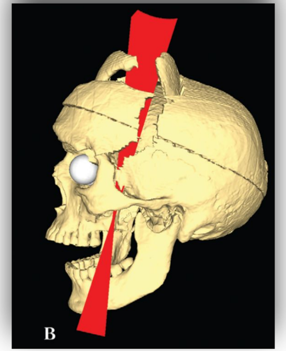
- Developments in neuroimaging
  - Information about areas previously unavailable to other imaging techniques
    - "Direct" access to brain function
    - Identification of neural correlates/functional networks

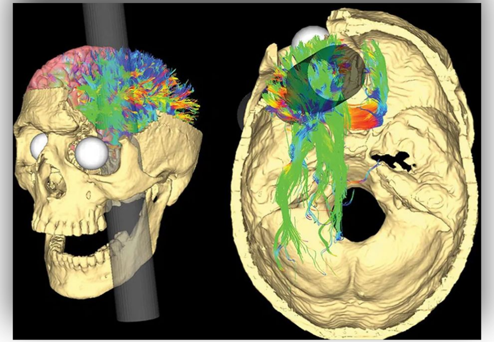


Imaging equipment at CIBIT

How neuroimaging is changing our perception of how the brain works

- (Re)visit history
  - Closer look at injuries suffered by Phineas
    - Importance of each site, but also the connections *"to"* and *"from"*

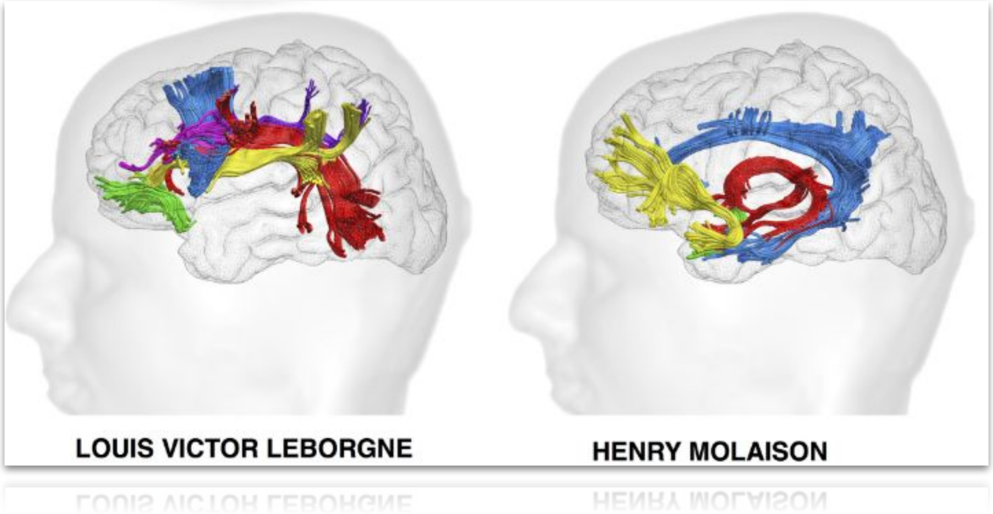




van Horn, J. D., et al.(2012). Mapping connectivity damage in the case of phineas gage. PLoS ONE, 7(5). https://doi.org/10.1371/journal.pone.0037454

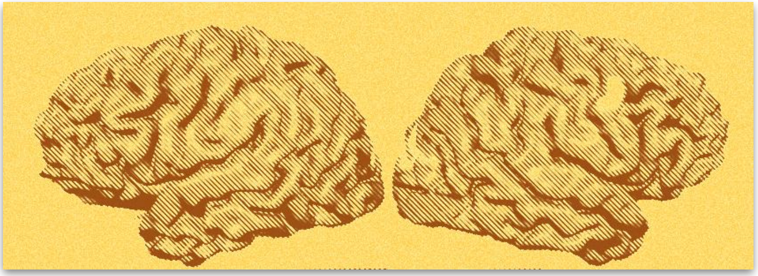
How neuroimaging is changing our perception of how the brain works

- (Re)visit history
  - Reconstruct the damages in the brain of "Tan" and H.M.



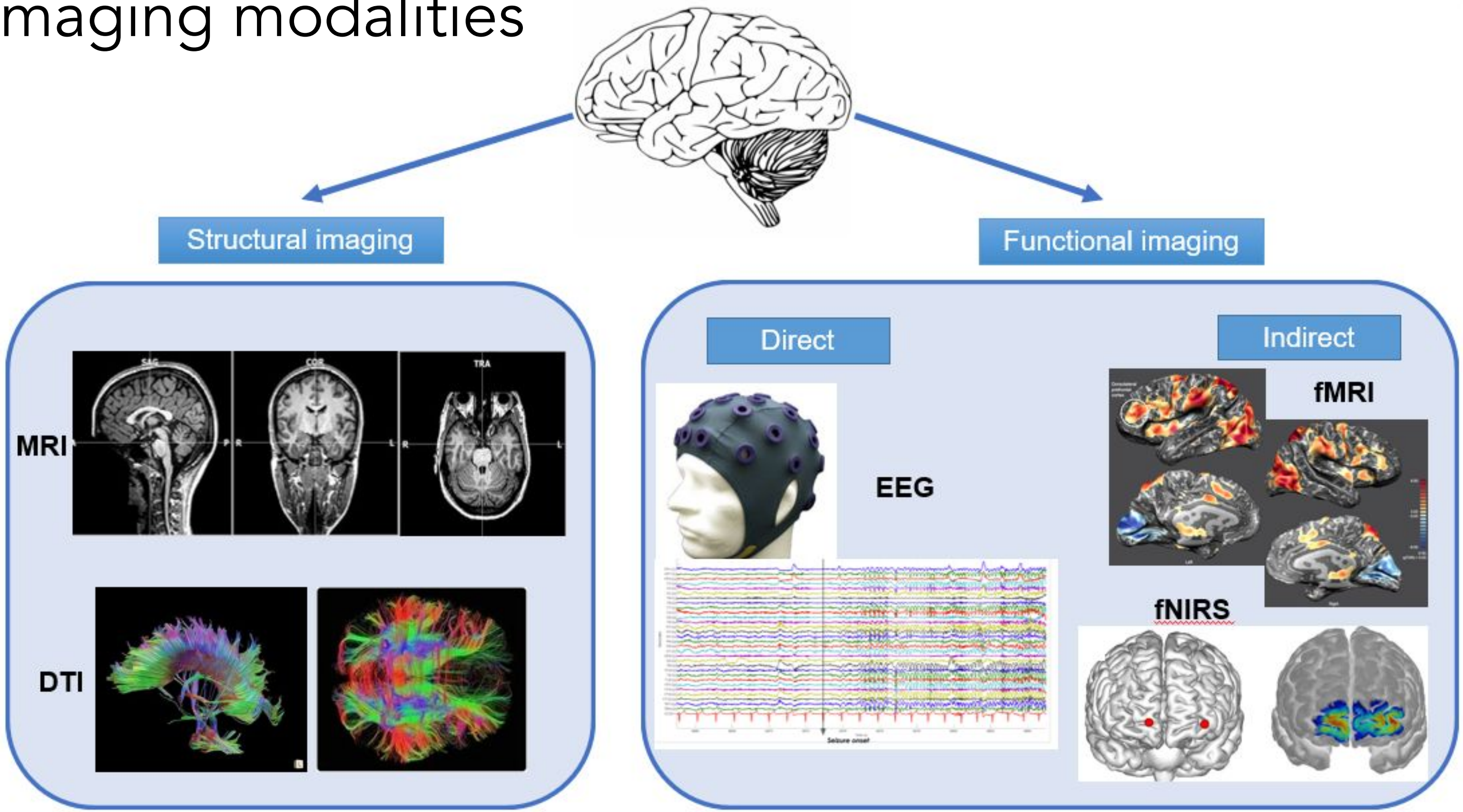
Thiebaut De Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., et al. (2015). Cereb. Cortex 25, 4812–4827. doi:10.1093/cercor/bhv173.

Neuroimaging and the study of dysfunctions

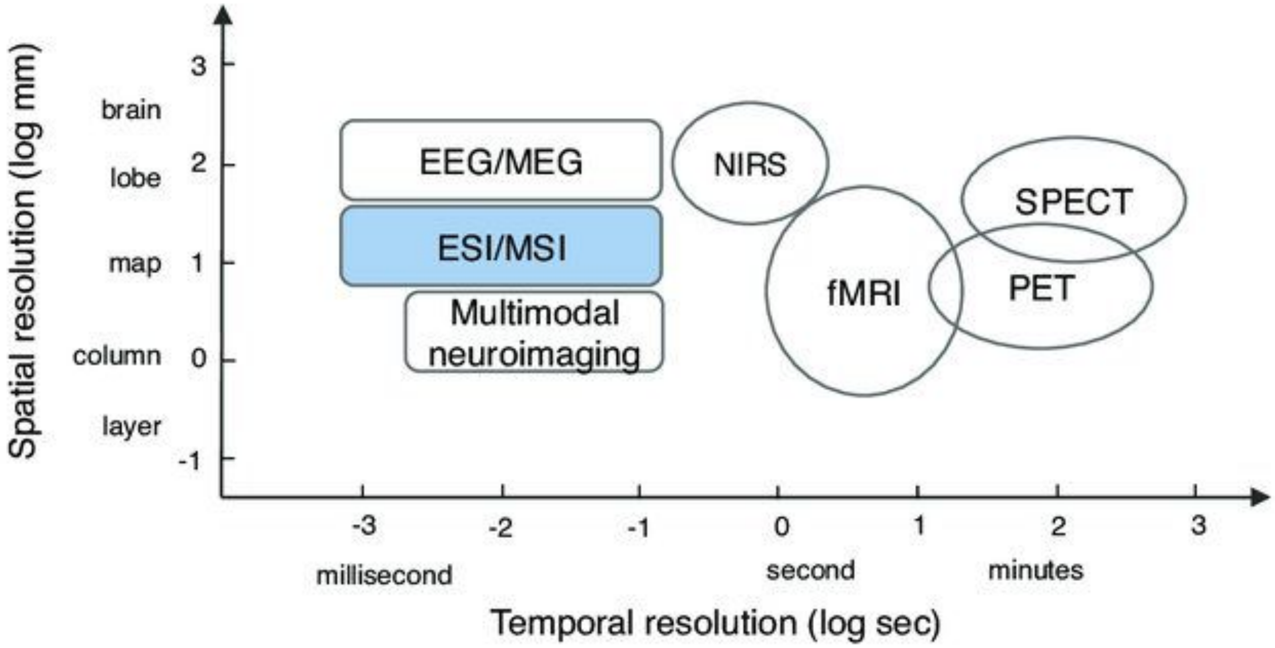


- Understanding the dysfunctions
  - Comparison between control and clinical groups
  - Access to the mechanisms involved
- Creation/development of interventional tools/applications
  - Direct/personalised intervention on the dysfunctional mechanisms

Neuroimaging modalities



Functional Neuroimaging Modalities



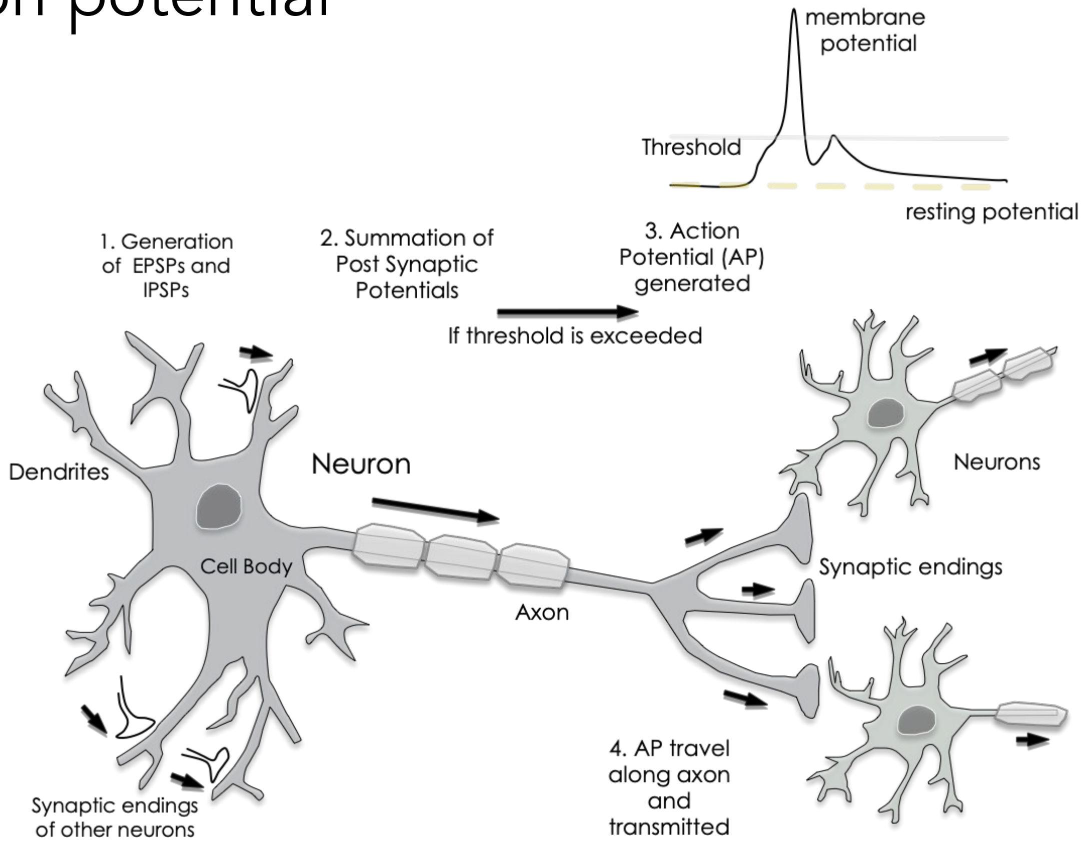
George Strobbe (2015). Advanced forward models for EEG source imaging (PhD Thesis)

The neural basis of functional neuroimaging

1 - Action potential

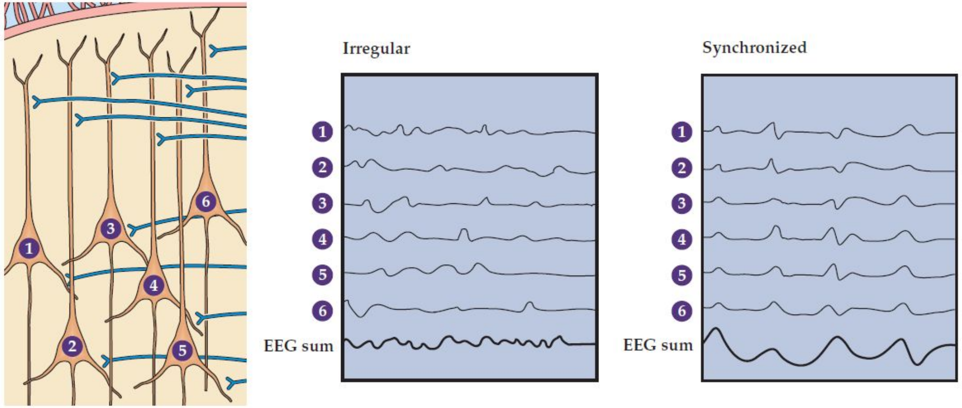
2 - Neurovascular coupling

1 - Action potential



Electroencephalogram (EEG)

Figure: EEG cap with electrodes.



Irregular neuronal activity leads to high frequency and low amplitude EEG.

Synchronized activity leads to low frequency and high amplitude EEG.

Purves, D. et al., 2004. Neuroscience 3rd Ed., Sinauer Associates, Inc.

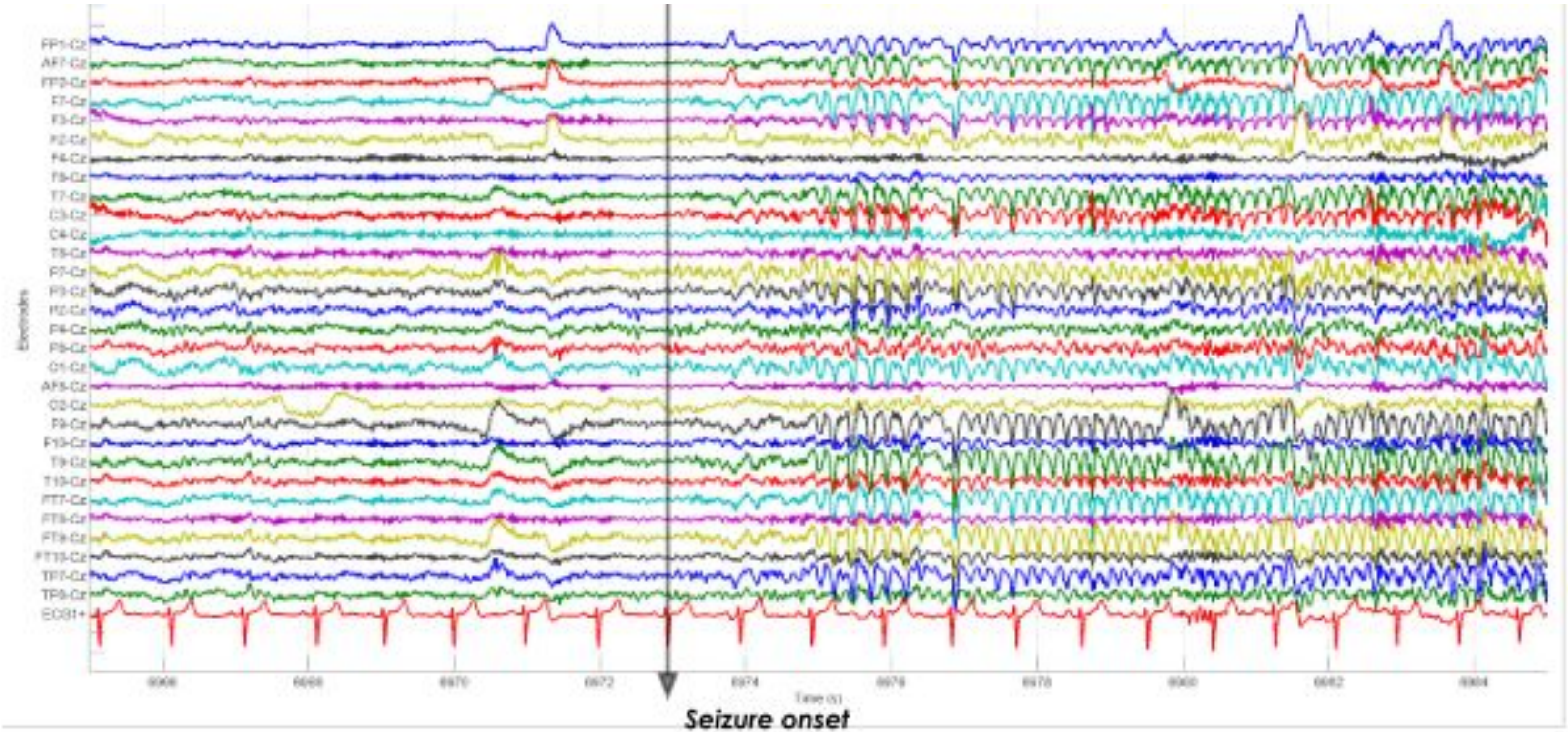
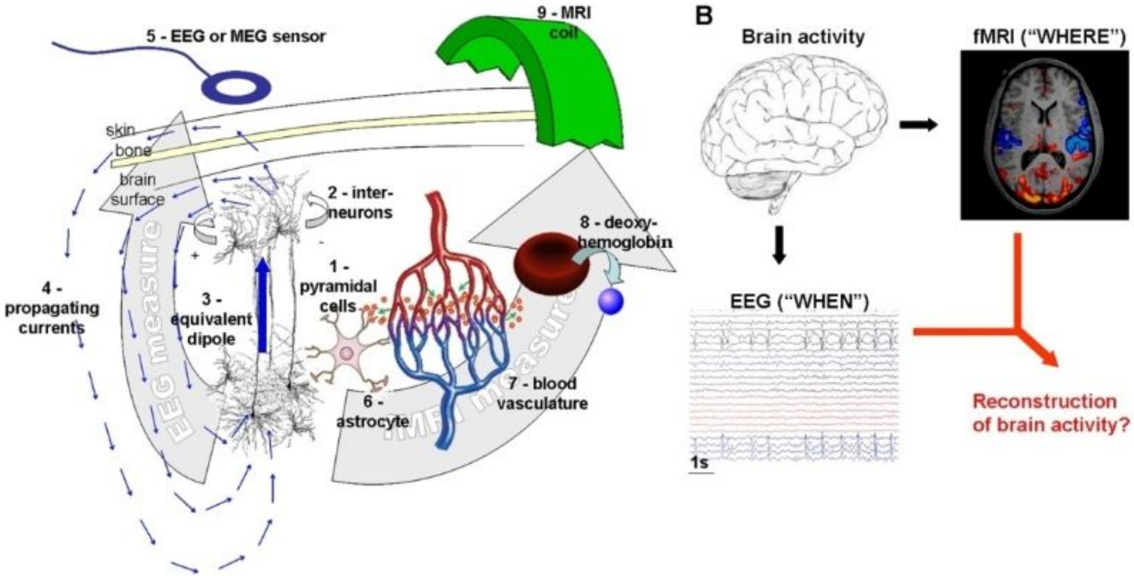


Figure: EEG rhythms corresponding to the channels of an EEG recording before and during a seizure.

2 - Neurovascular coupling and BOLD signal

Local neural activity ⟷ Changes in cerebral blood flow (CBF)



Huneau et al., (2015). Front Neuroscience, 9: 467; Deneux, T. (2011), EEG-fMRI Fusion: Adaptations of the Kalman Filter for Solving a High-Dimensional Spatio-Temporal Inverse Problem In Adaptive Filtering, edited by Lino Garcia Morales. InTech.

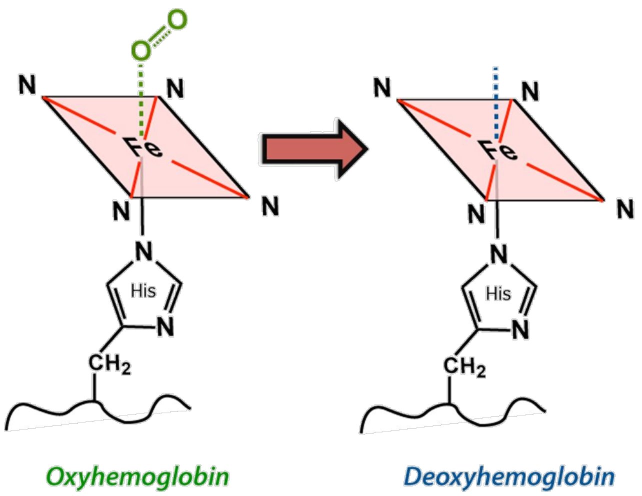


Figure: Deoxyhemoglobin is paramagnetic due to 4 unpaired electrons at each iron center

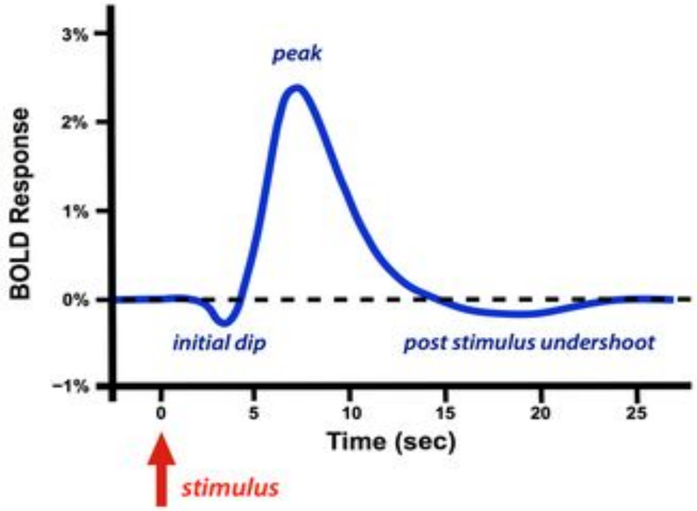


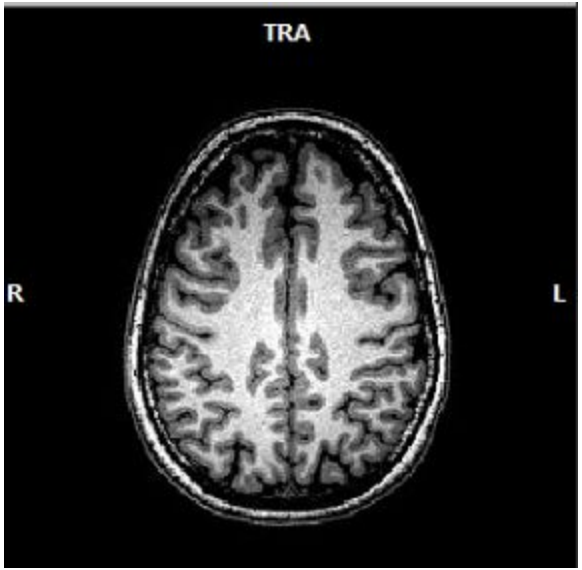
Figure: Typical blood oxygenation level dependent (BOLD) hemodynamic response function (HRF).

Neurovascular coupling + Magnetic properties of hemoglobin → BOLD signal

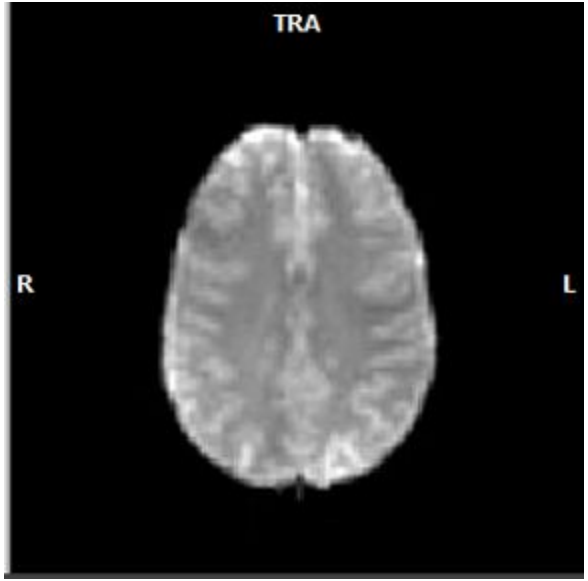
Huneau et al., (2015). Front Neuroscience, 9: 467; http://mriquestions.com/bold-contrast.html .

Functional magnetic Resonance Imaging (fMRI)

Figure: [Siemens Trio MRI machine](#).



Anatomic image



Functional image

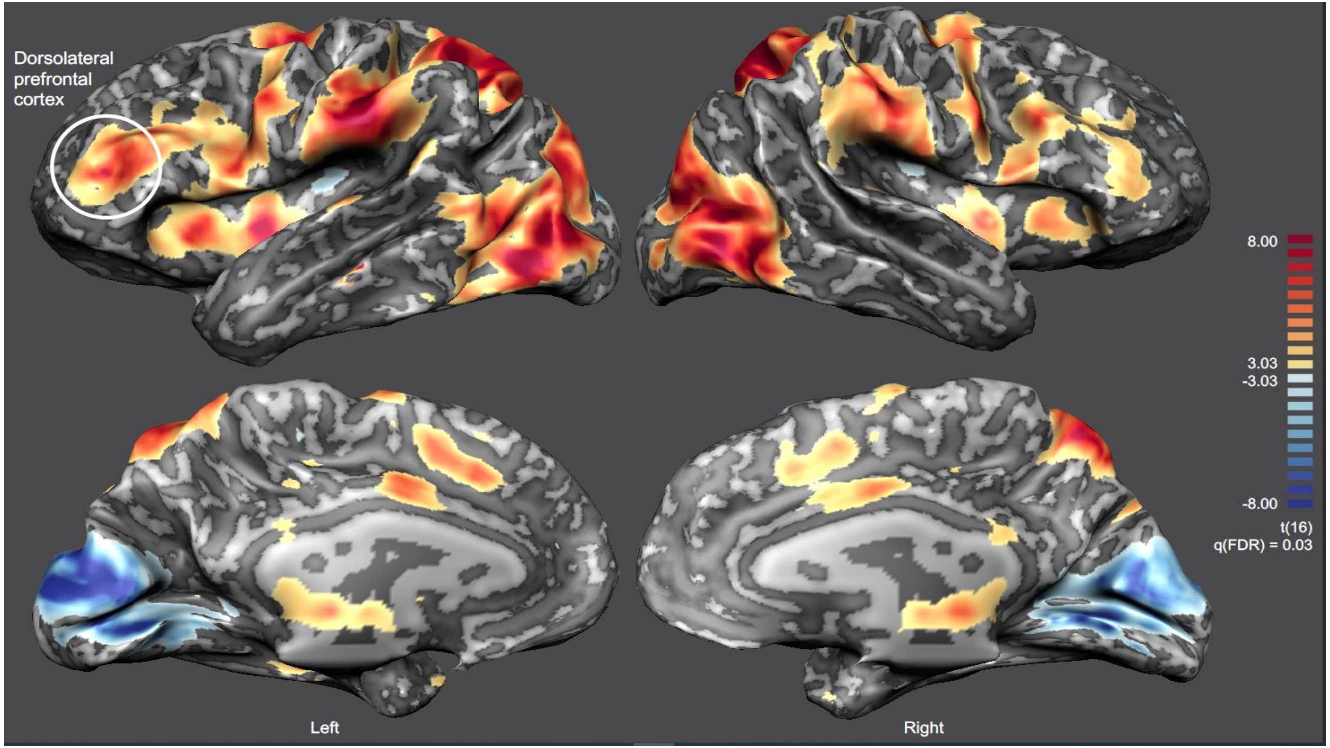
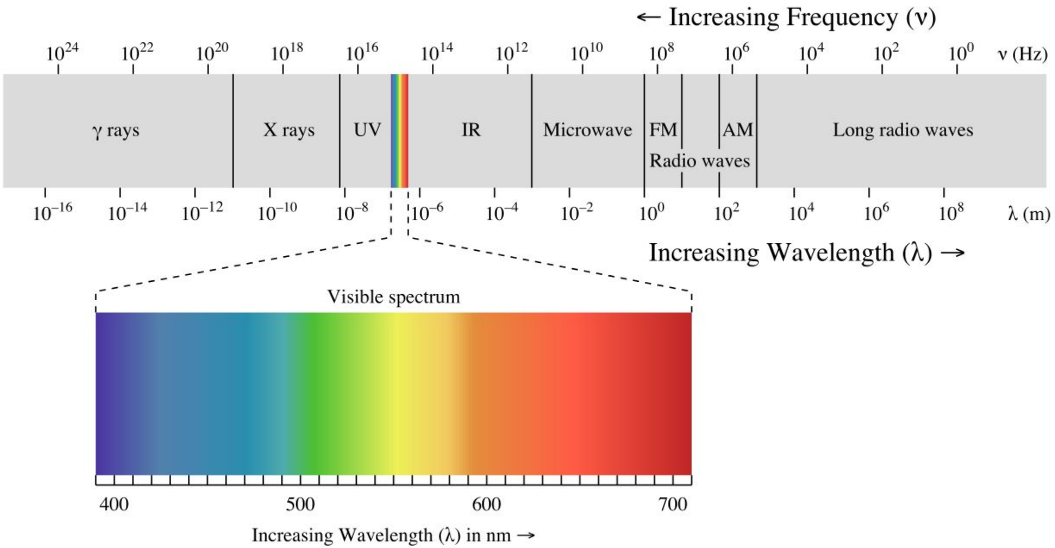


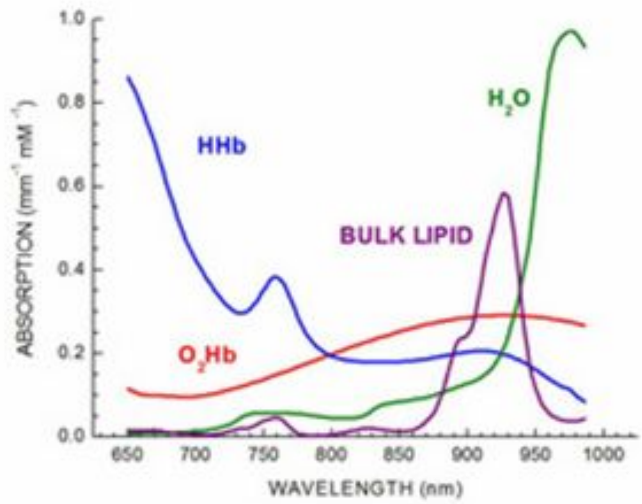
Figure: Inflated cortex representation of the statistical map corresponding to the contrast Pain Images > Neutral Images of the localizer run. The neurofeedback target (left DLPFC) is highlighted (Travassos et al., 2020, Frontiers in Neurology)

Functional near-infrared spectroscopy (fNIRS)



Shown is a simple demonstration that red light is penetrating in tissue. Wavelengths in the near infrared region are even more penetrating.

Brain hemodynamics



Oxy- and deoxy-hemoglobin are the dominant tissue absorbers within the near infrared range.

fNIRS Hemodynamics

Neural activation

↓

Metabolic demand

↓

Increased blood flow

↓

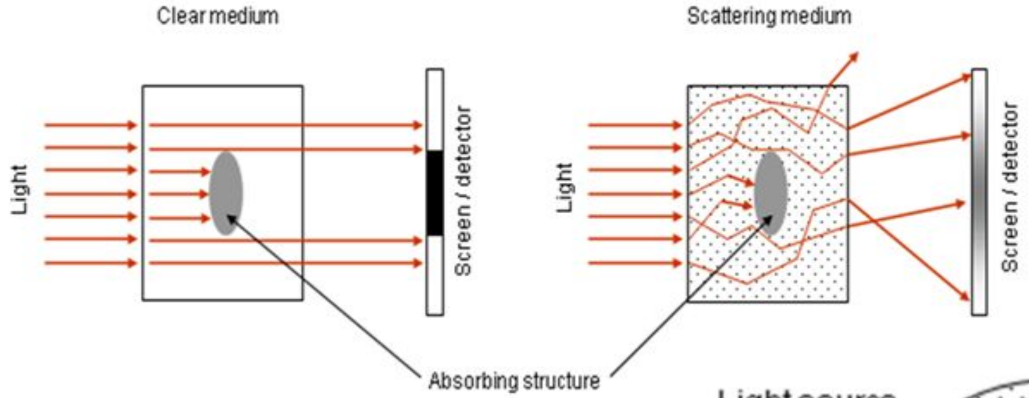
Increase in oxy-hemoglobin

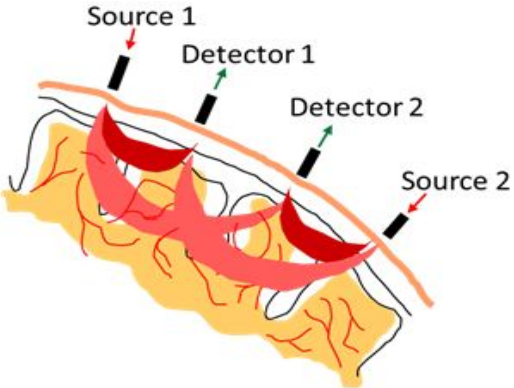
&

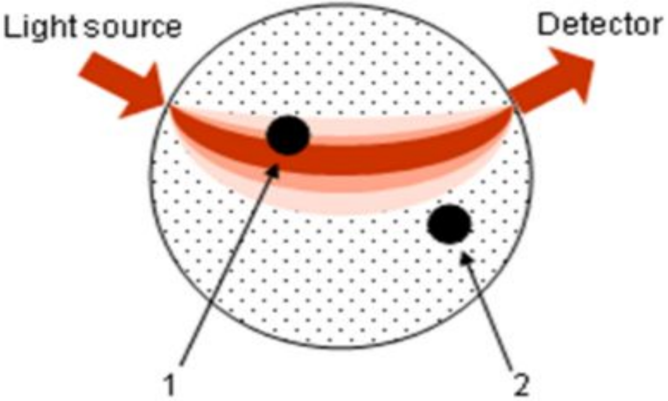
Wash-out of deoxy-hemoglobin

Kohl, Matthias, et al. "Physical model for the spectroscopic analysis of cortical intrinsic optical signals." Physics in Medicine & Biology (2000). 45.12

Principles of NIRS







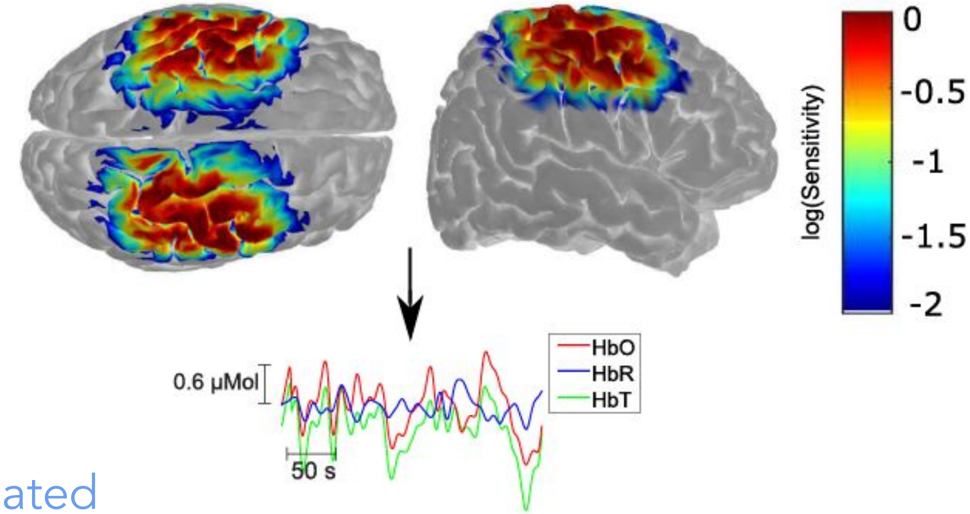
Source: Nirx Medical Technologies.

From wavelength to brain function

Table 1 Parameters to calculate concentration changes using MBLL.

	DPF^{λ}	$\varepsilon_{HbO_2}\left(\frac{l}{cm\,mmol}\right)$	$\varepsilon\left(Hb, \frac{l}{cm\,mmol}\right)$
$\lambda_1 = 760$ nm	6.40	1.4865865	3.843707
$\lambda_2 = 850$ nm	5.75	2.526391	1.798643

DPF - differential path length
ε - molar extinction coefficient



Modified Beer Lambert's Law

Oxygenated blood signal

Deoxygenated blood signal

Forero, Edwin J., et al."Use of near-infrared spectroscopy to probe occlusion severity in patients diagnosed with carotid atherosclerotic disease." Medical Research Archives (2017) 5.6.

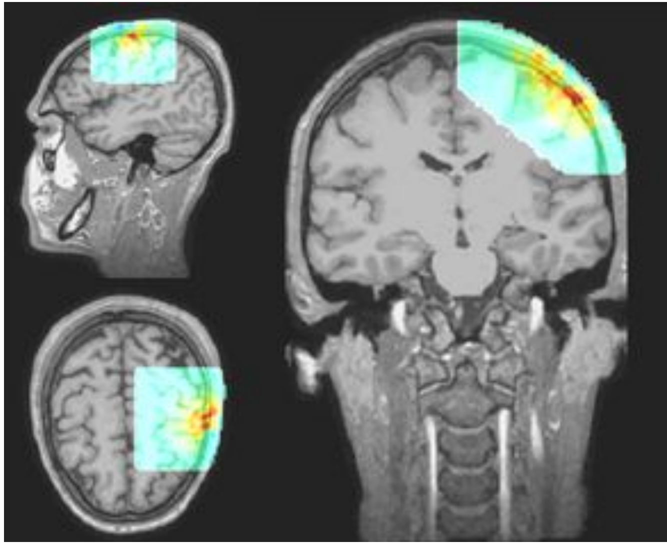
fNIRS as a neuroimaging modality

Advantages

- Safe and non-invasive
- Small, relatively inexpensive technology
- Good temporal resolution
- Correction of noise

Downsides

- Only cortical measures: no whole brain analysis
- Spatial resolution



Ferrari, Marco, and Valentina Quaresima. "A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application." Neuroimage 63.2 (2012): 921-935.

What can we get with fNIRS

Review

A Mini-Review on Functional Near-Infrared Spectroscopy (fNIRS): Where Do We Stand, and Where Should We Go?

Valentina Quaresima * and Marco Ferrari

Department of Life, Health and Environmental Sciences, University of L'Aquila, 67100 L'Aquila, Italy
* Correspondence: valentina.quaresima@univaq.it

Received: 3 July 2019; Accepted: 31 July 2019; Published: 1 August 2019

check for updates

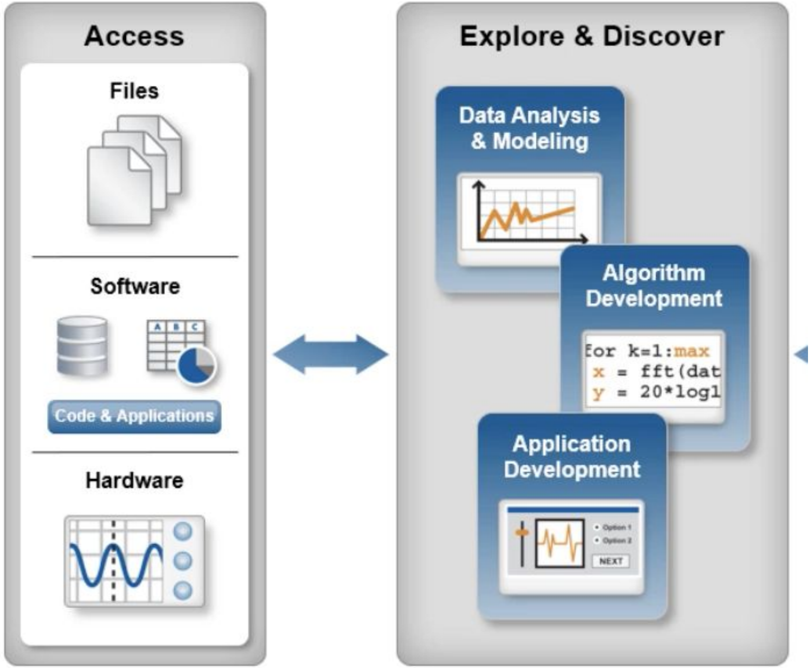
Medicine	Attention deficit disorder	2018	11	C	Mauri [78]
	Auditory cortex plasticity after cochlear implant	2018	7	A	Basura [79]
	Autism spectrum disorder	2019 2019	15 30	C C	Liu [80] Zhang [81]
	Cognitive aging	2017	34	A	Agbangla [82]
	Developmental age attention deficit/hyperactivity disorder	2019	13	C	Grazioli [83]
	Eating disorders	2015	11	A	Val-Laillet [50]
	Epilepsy	2016	23	A	Peng [84]
	Gait disorders	2017	12	A	Gramigna [85]
	Mild cognitive impairment	2017	8	A	Beishon [86]
	Neurofeedback training	2018	127	A	Ehlis [87]
	Pain assessment in infants	2017	9	C	Benoit [88]
	Parkinson's disease and walking balance tasks	2018	5	A	Stuart [77]
	Prolonged disorder of consciousness	2018	7	A	Rupawala [89]
	Psychiatry	2014	168	A	Ehlis [90]
	Robot-assisted gait training	2019	2	A	Berger [91]
	Schizophrenic disorders	2017	17	A	Kumar [92]
	Stroke therapy/recovery/rehabilitation	2019	66	A	Yang [93]

A: Adults; C: Children; EEG: Electroencephalography; N: Number of reviewed articles; Ref: Reference number.

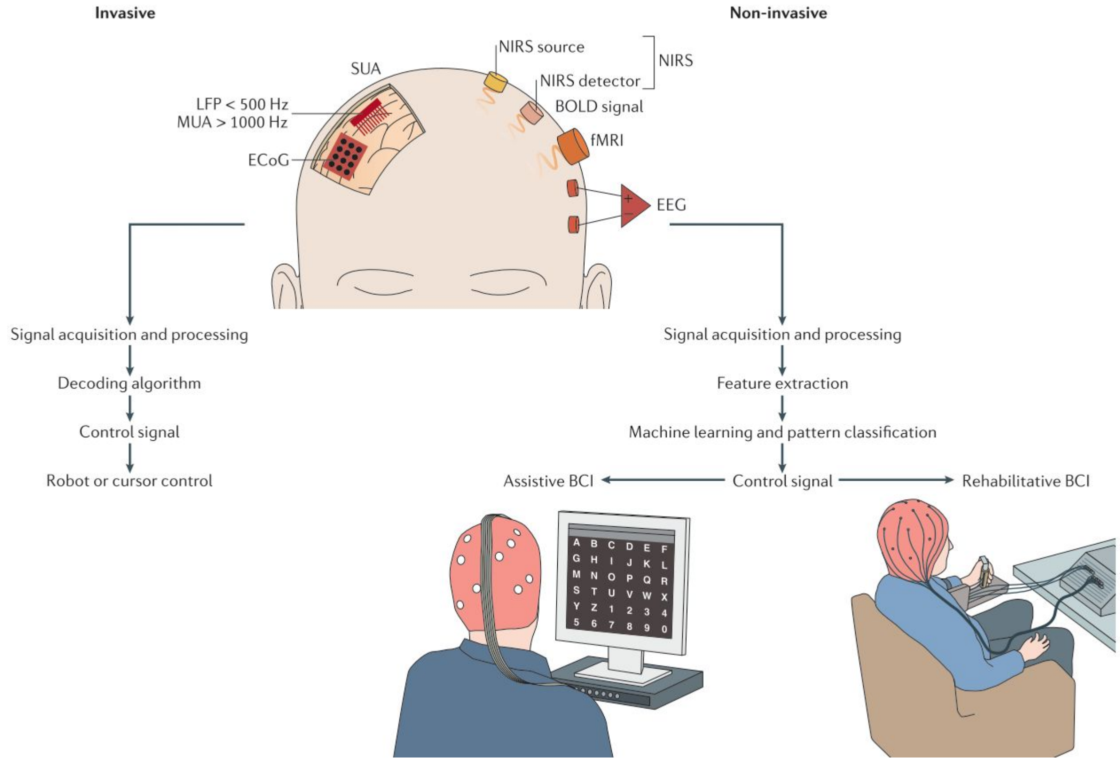
What can we get with fNIRS

Source: Nirx Medical Technologies.

Brain Computer Interfaces
Main components of the setup



Brain-Computer Interfaces (BCI)



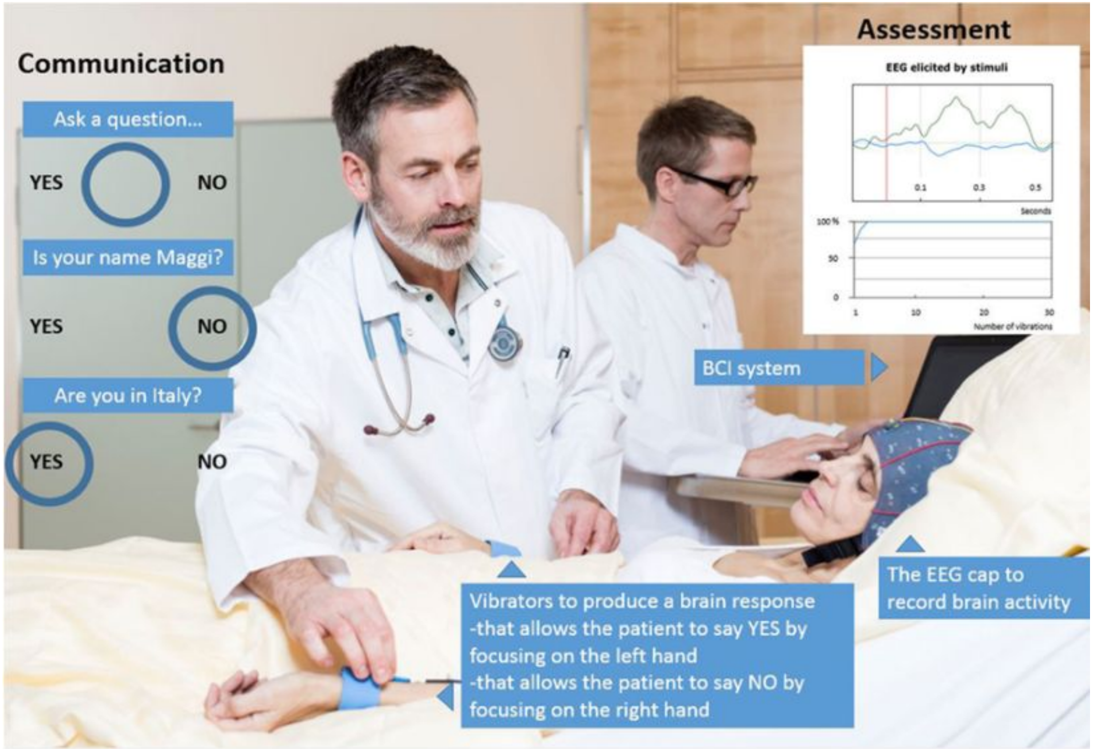
Chaudhary, U., Birbaumer, N., Ramos-Murguialday, A. Nature Reviews Neurology 2016, 12: 513-525.

BCI applications: communication

BCI speller

Pires, G., Nunes, U., Castelo-Branco, M. Clinical Neurophysiology 2012, 123(6):1168-1181.

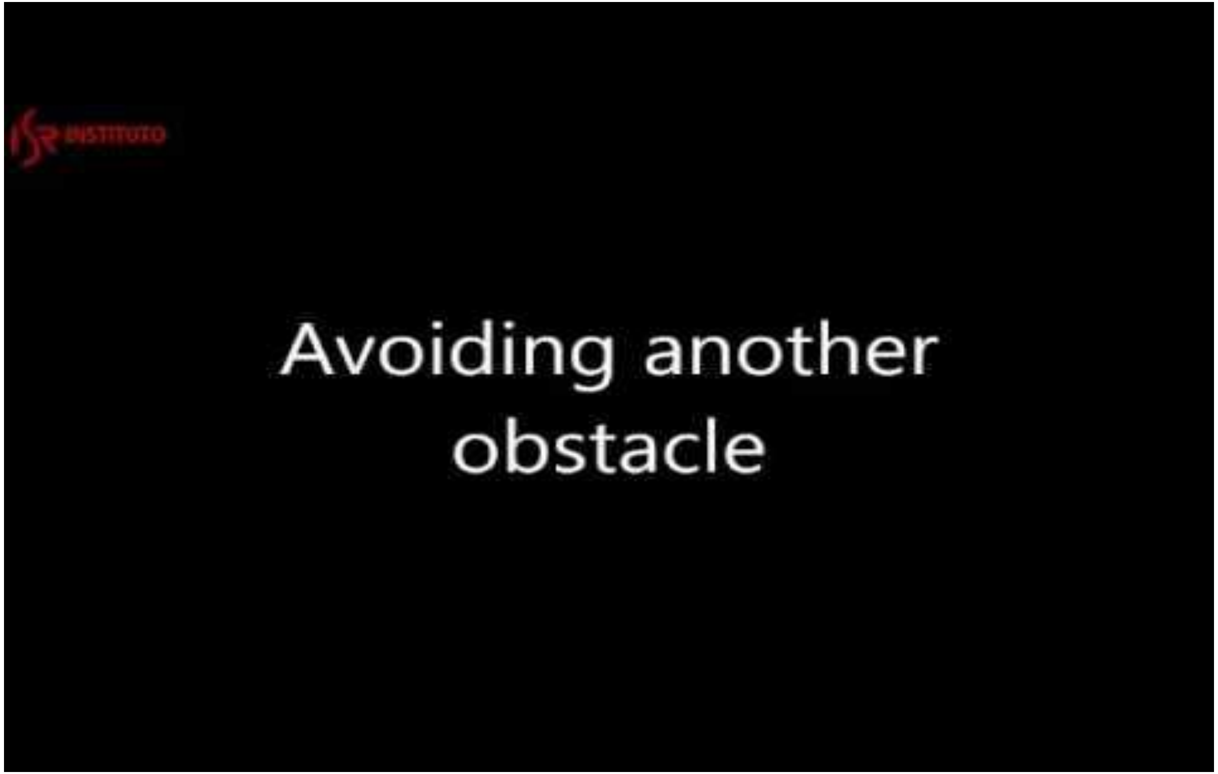
BCI applications: communication



How Can Completely Locked-in Persons Communicate With a Brain–Computer Interface?

Guger, C. et al. Front. Young Minds 2018, 6:24.

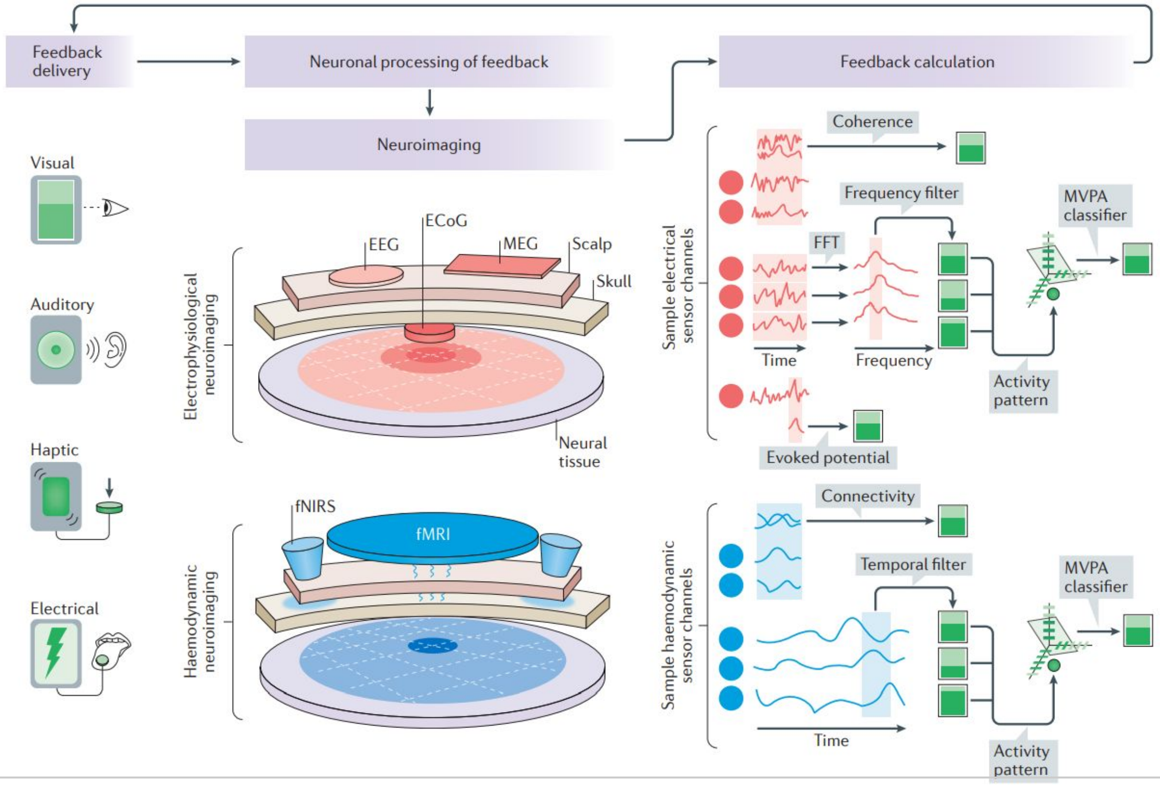
BCI applications: devices control



Brain-actuated wheelchair

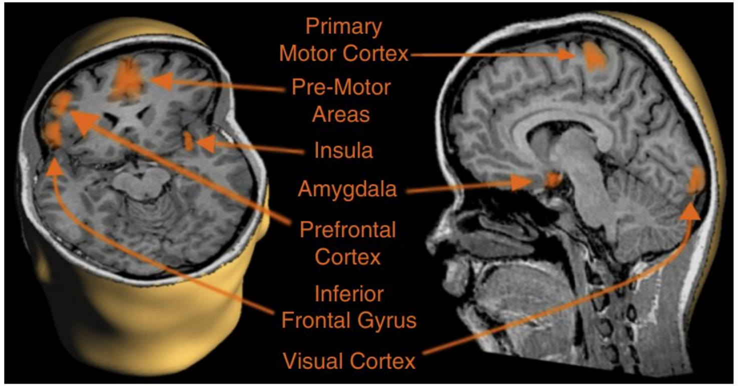
Pires, G., Nunes, U., Castelo-Branco, M. Clinical Neurophysiology 2012, 123(6):1168-1181.
Cruz, A., Pires, G., Lopes, A., Carona, C., Nunes, U. IEEE Transactions on Human-Machine Systems 2021.

BCI applications: Neurofeedback (NF)



Sitaram, R., et al. Nature Reviews Neuroscience 2016, 18: 86-100.

State-of-the-art and current challenges



Current Opinion in Behavioral Sciences

Table 1
Overview of studies using real-time neurofeedback in patients suffering from various neurological and psychiatric disorders. Control subjects generally received no feedback or no real feedback ("sham-feedback").

Study	Disorder	N subjects/control group	Brain regions
deCharms et al. (2005)	Chronic pain	12/36[a]	ACC
Ruiz et al. (2013)	Schizophrenia	9/0	Insular cortex
Haller et al. (2010)	Chronic tinnitus	6/0	Auditory cortex
Subramanian et al. (2011)	Parkinson's disease	5/5	Supplementary motor complex
Linden et al. (2012)	Major depression	8/8	Brain regions involved in positive emotions (VLPFC R/L, insular cortex R/L, DLPFC R/L, medial temporal lobe R/L, OFC)
Sitaram et al. (2012)	Chronic stroke	2/4[b]	Ventral premotor cortex L
Li et al. (2012)	Nicotine addiction	10/0	ACC, mPFC

Abbreviations: ACC anterior cingulate cortex, VLPFC ventrolateral prefrontal cortex, DLPFC dorsolateral prefrontal cortex, mPFC medial prefrontal cortex, OFC orbitofrontal cortex, R right, L left.

[a] Healthy subjects as control participants, furthermore other groups receiving different forms of feedback and training (4 patients, 24 healthy subjects).

[b] Healthy subjects as control group.

Scharnowski, F., Weiskopf, N. Current Opinion in Behavioral Sciences 2015, 4:122–127.
Sulzer, J., et al. Neuroimage 2013, 76: 386-399.

State-of-the-art and current challenges

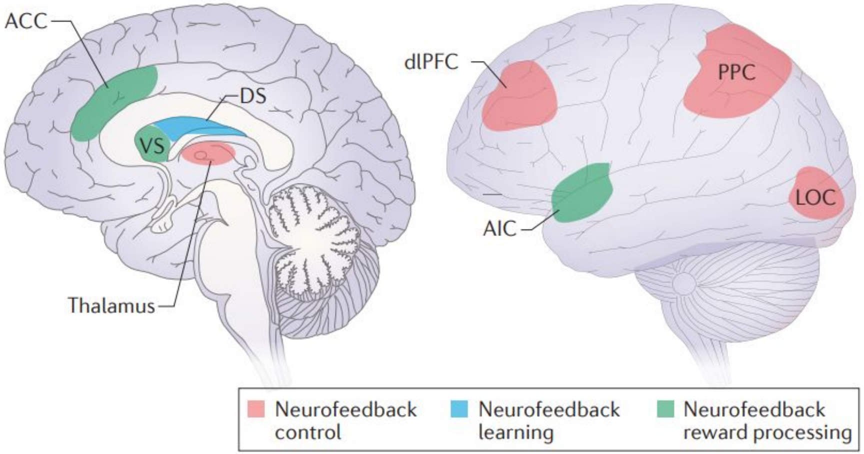


Table 1
Overview of studies using real-time neurofeedback in patients suffering from various neurological and psychiatric disorders. Control subjects generally received no feedback or no real feedback ("sham-feedback").

Study	Disorder	N subjects/control group	Brain regions
deCharms et al. (2005)	Chronic pain	12/36[a]	ACC
Ruiz et al. (2013)	Schizophrenia	9/0	Insular cortex
Haller et al. (2010)	Chronic tinnitus	6/0	Auditory cortex
Subramanian et al. (2011)	Parkinson's disease	5/5	Supplementary motor complex
Linden et al. (2012)	Major depression	8/8	Brain regions involved in positive emotions (VLPFC R/L, insular cortex R/L, DLPFC R/L, medial temporal lobe R/L, OFC)
Sitaram et al. (2012)	Chronic stroke	2/4[b]	Ventral premotor cortex L
Li et al. (2012)	Nicotine addiction	10/0	ACC, mPFC

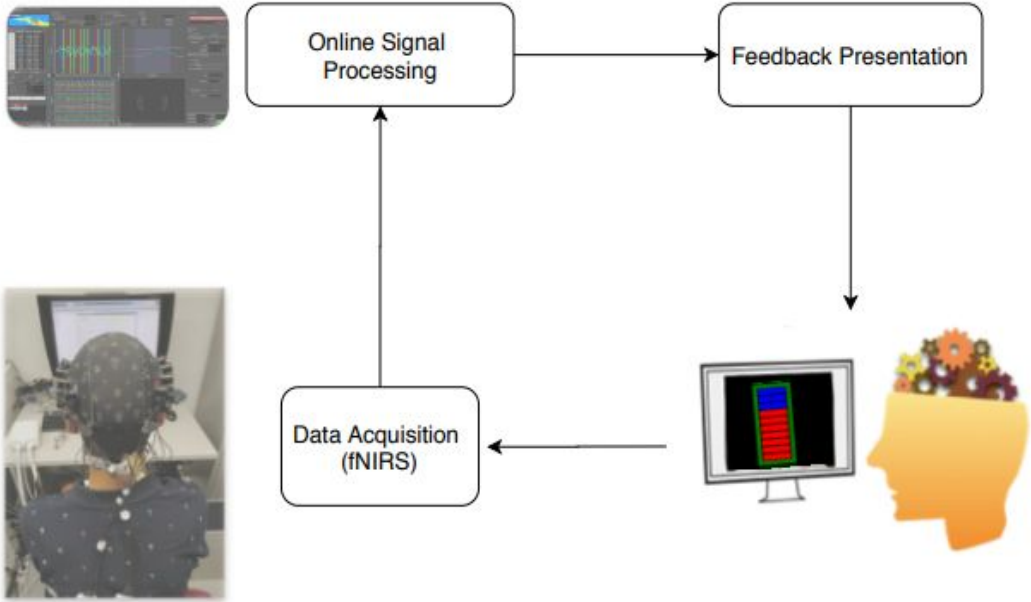
Abbreviations: ACC anterior cingulate cortex, VLPFC ventrolateral prefrontal cortex, DLPFC dorsolateral prefrontal cortex, mPFC medial prefrontal cortex, OFC orbitofrontal cortex, R right, L left.

[a] Healthy subjects as control participants, furthermore other groups receiving different forms of feedback and training (4 patients, 24 healthy subjects).

[b] Healthy subjects as control group.

Sitaram, R., et al. Nature Reviews Neuroscience 2016, 18: 86-100.
Sulzer, J., et al. Neuroimage 2013, 76: 386-399.

Neurofeedback training (example)

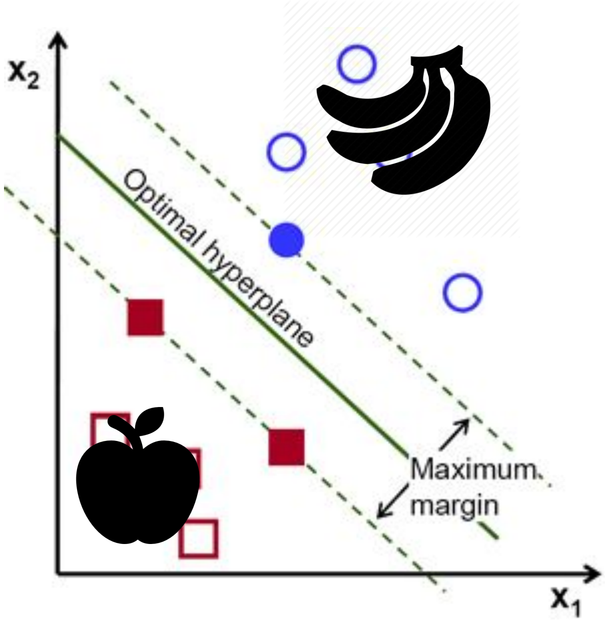


Classification

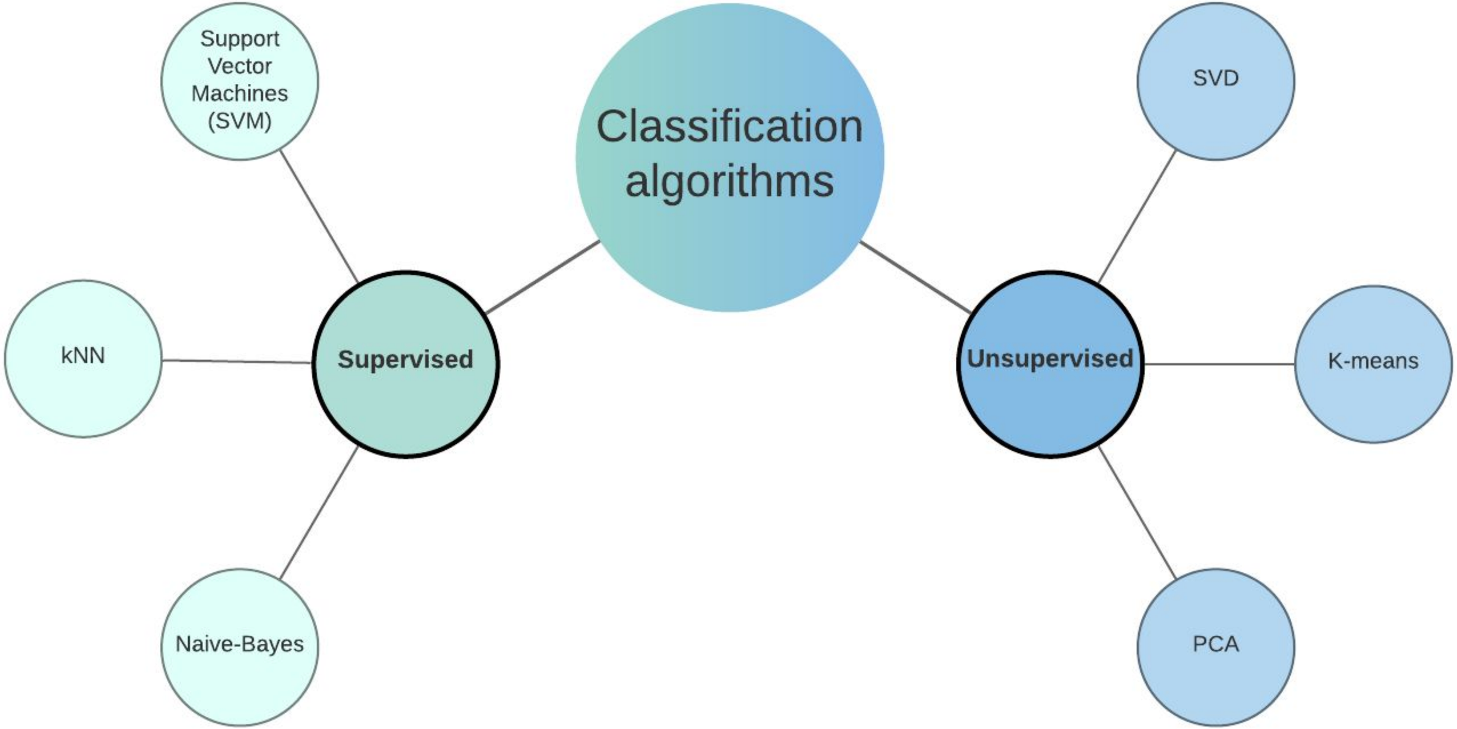
The goal: automatically distinguish points between categories based on a set of characteristics

OR

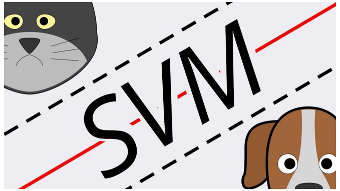
Find an hyperplane in a N-dimensional space, where N is the number of features, that distinctly classifies the data points in groups.



Many classification algorithms...



Classification step by step



Train/Test

The first step is to split our dataset into 'train' and 'test' datasets.

The 'train' dataset will be used to optimize the classification algorithm.

The 'test' dataset is used to assess the classifier's performance.

Feature selection

Some features of the dataset may be better than others - more 'discriminant'.

A number of methods allow us to choose the best features for our classification problem.

Train the classifier

Use the 'train' data to optimize the classifier model.

Test the classifier

Using the 'test' data, i.e., data points that the classifier does not know, we are able to assess the performance of the classifier.

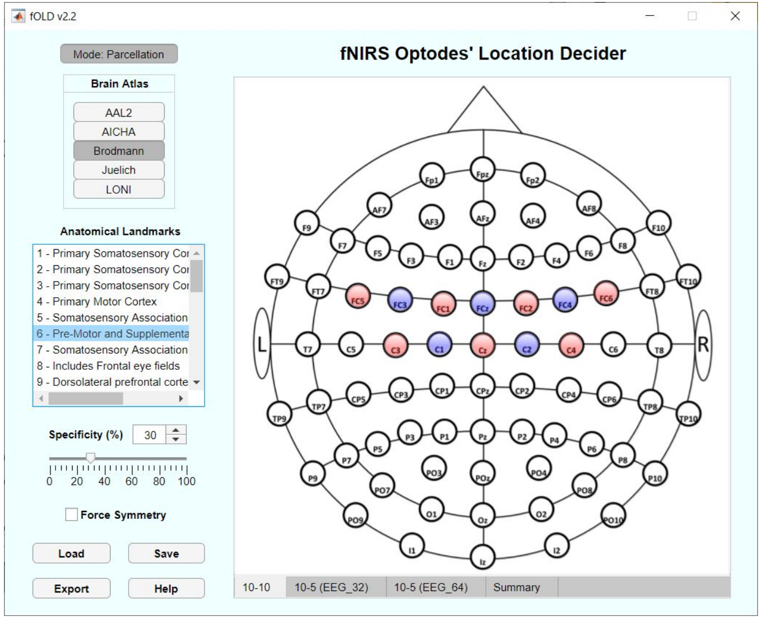
Usual metrics include accuracy, sensitivity, and sensibility.

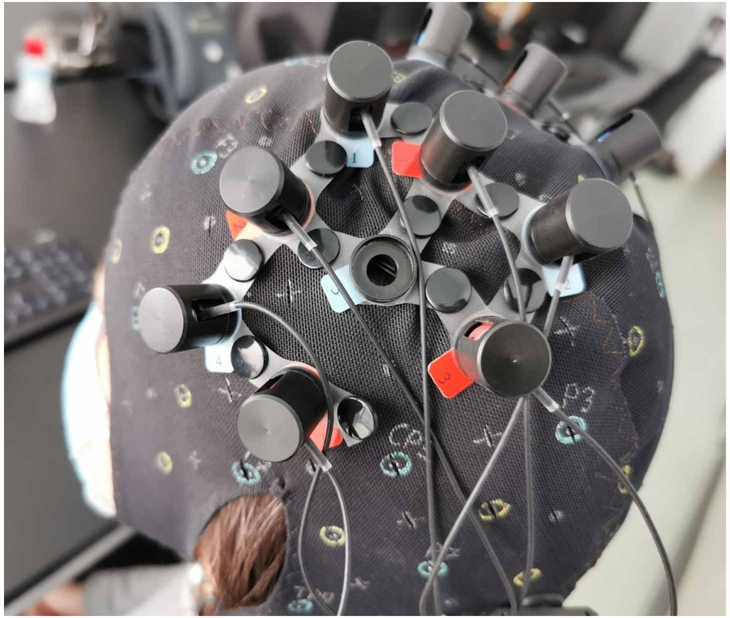
Q&A

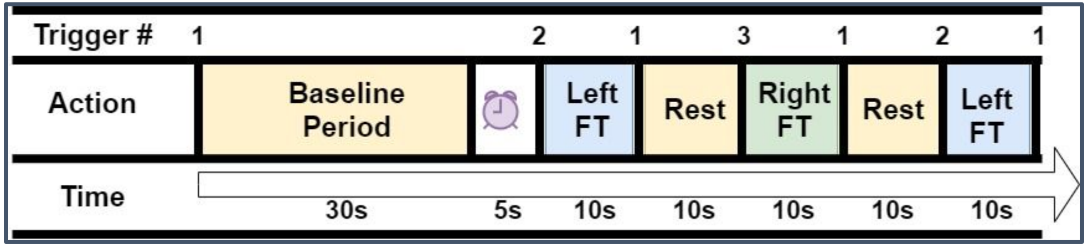
Hands-on

- fNIRS, NF and Classification -

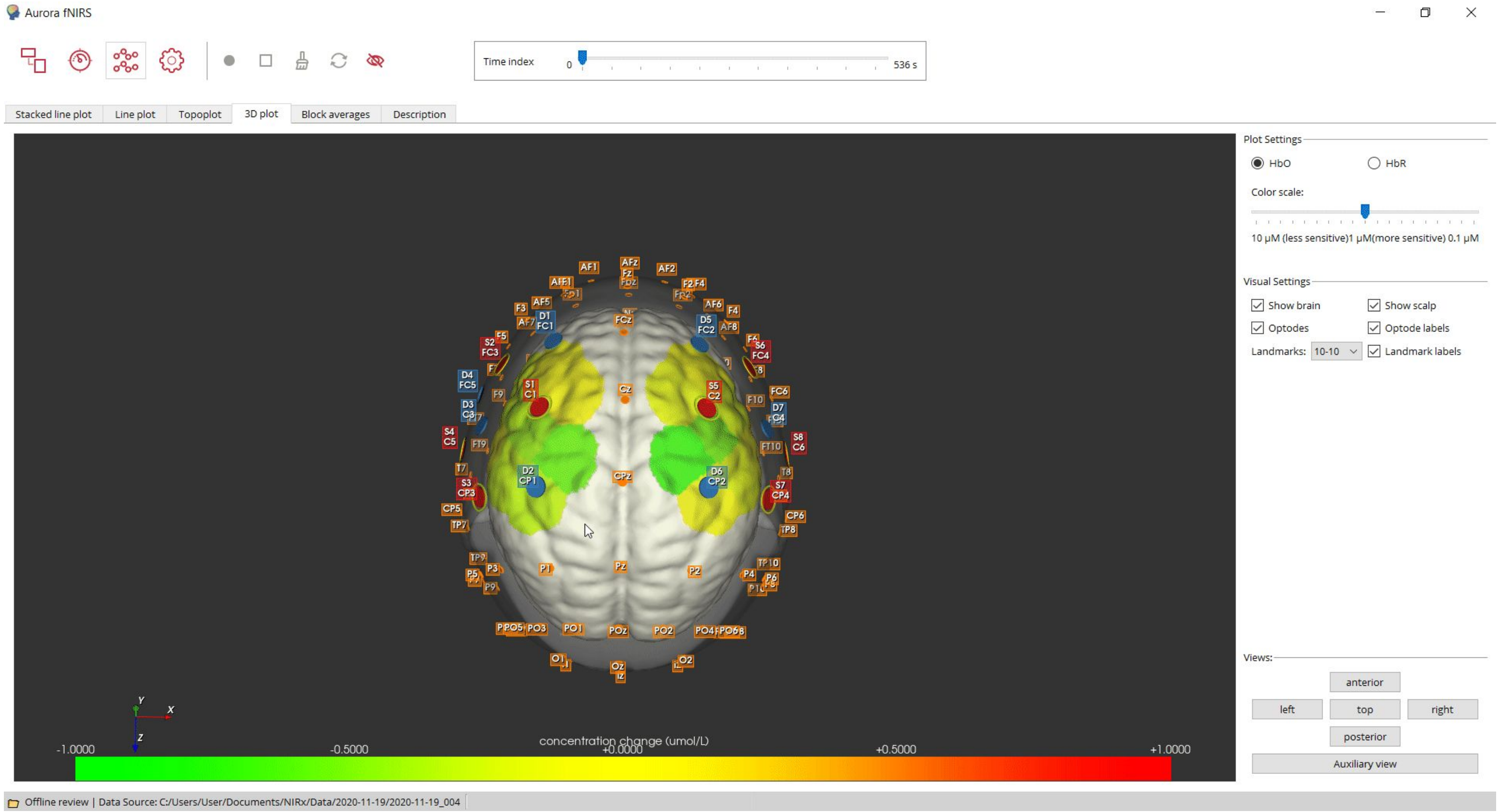
Experimental setup



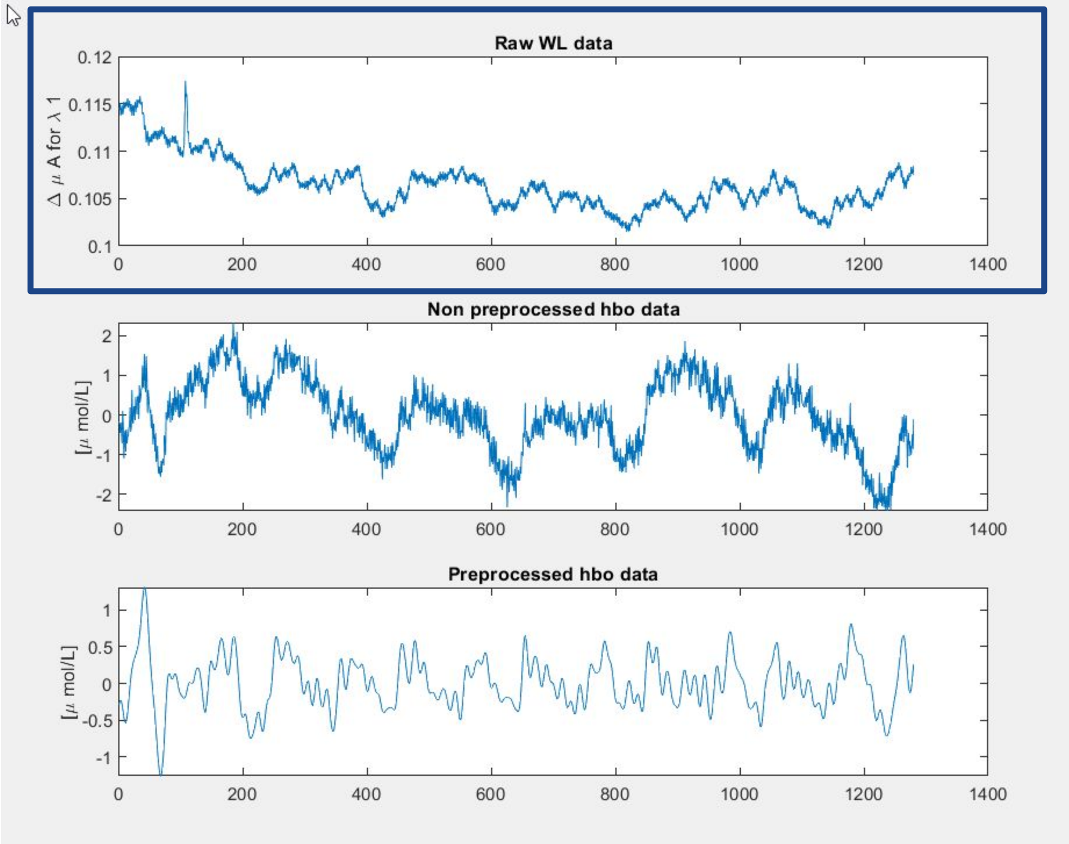




fNIRS Data acquisition

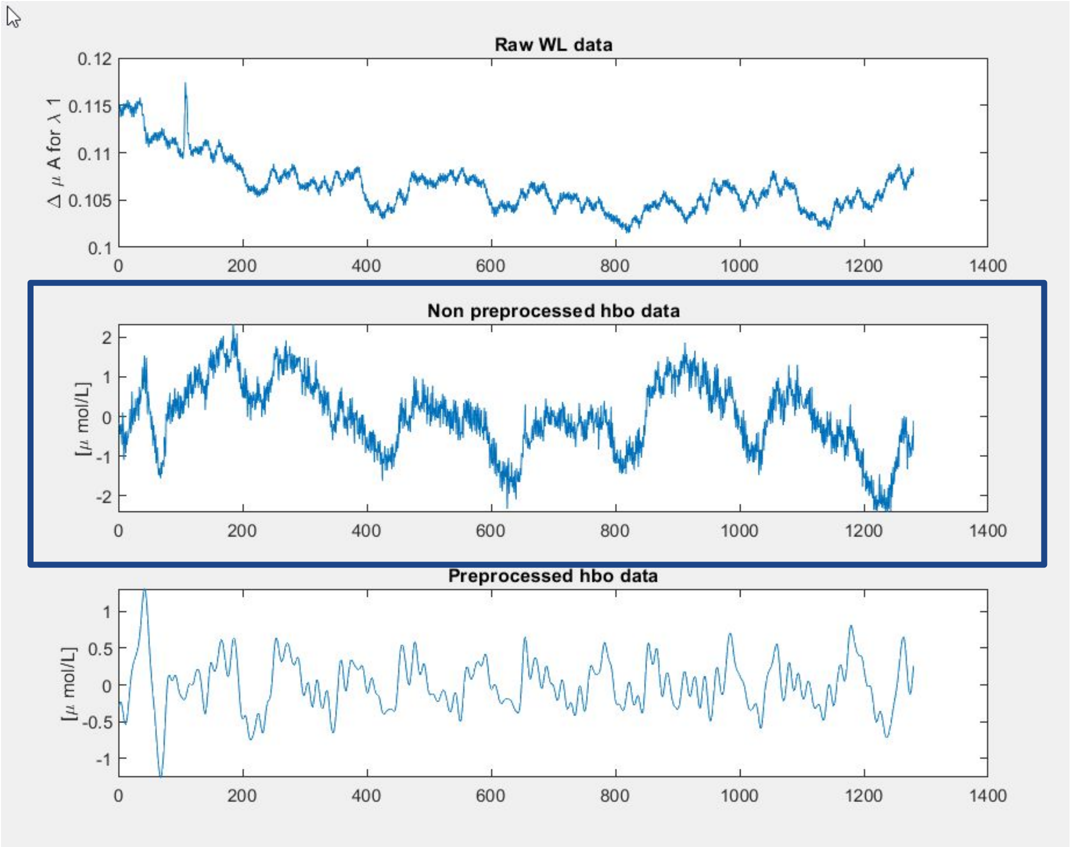


fNIRS Data Preprocessing



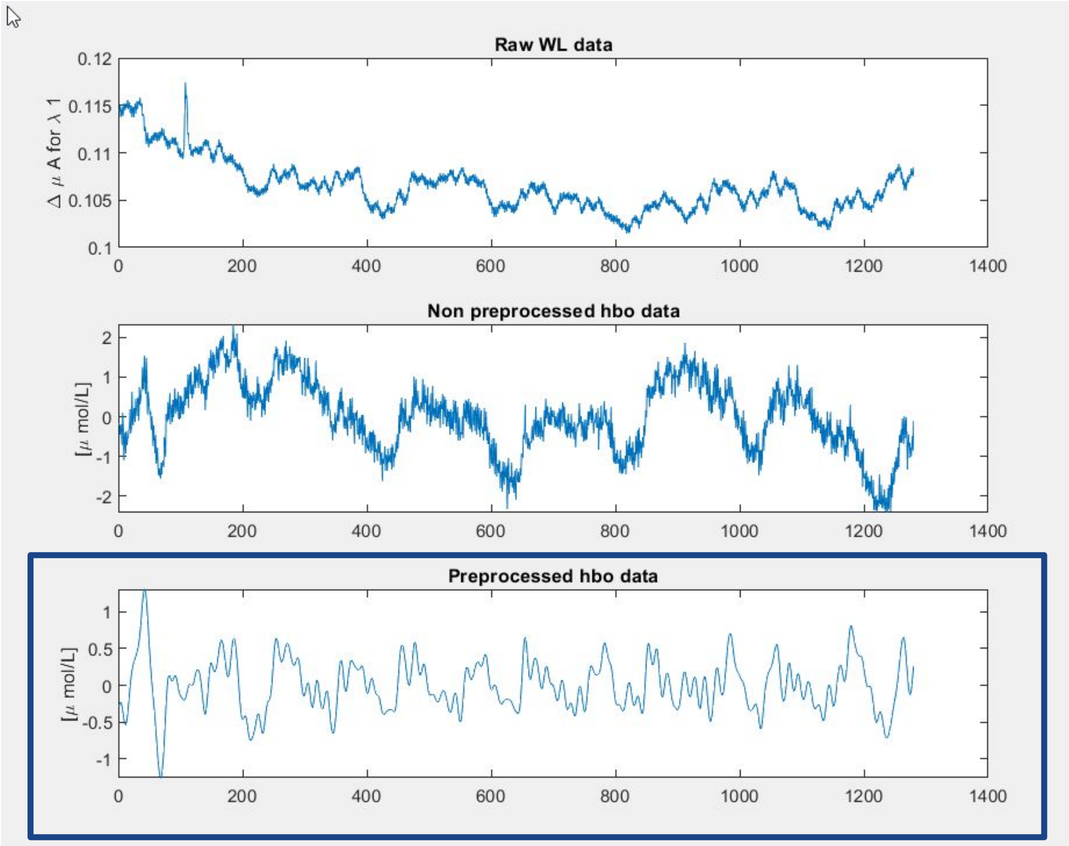

```
%% Load fNIRS data
% Define path for data folder
rootDir = 'C:\Users\User\Documents\GitHub\ENEEB\data\TappingLeftRight';
RawWL = nirs.io.loadDirectory(fullfile(rootDir), {'subjects', 'runs'});

job = nirs.modules.RenameStims();
job.listOfChanges = {
    'channel_1', 'Baseline';
    'channel_2', 'Left';
    'channel_3', 'Right'
    };
RawWL = job.run( RawWL );
job = nirs.modules.Resample( );
job.Fs= 4;
RawWL =job.run(RawWL);

figure;
subplot(3,1,1)
plot (RawWL(:,6))
ylabel('\Delta \mu A for \lambda 1')
title('Raw WL data')
```

fNIRS Data Preprocessing



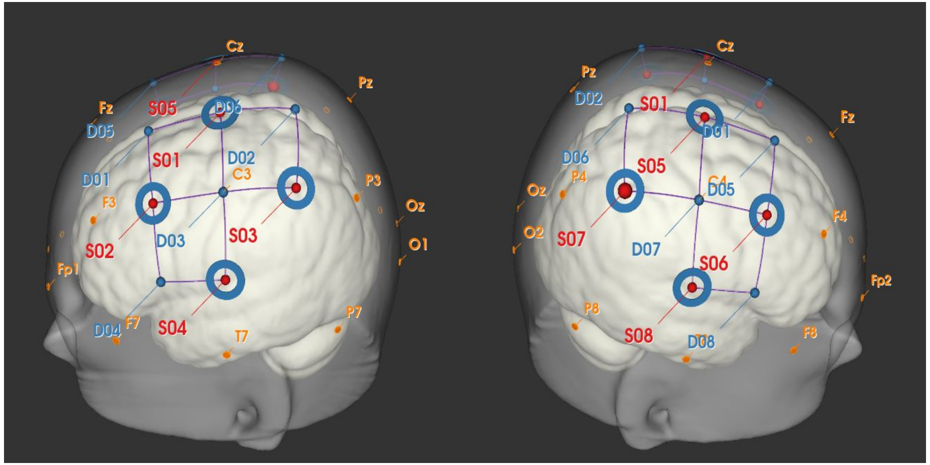

```
%% Transform WL signal to HbO and HbR Signal
job = nirs.modules.OpticalDensity( );
job = nirs.modules.BeerLambertLaw(job);
HbData = job.run(RawWL);

subplot(3,1,2)
h1 = plot (HbData(:,6));
set (h1, 'YData', get(h1, 'YData')*0.1)
ylabel('[\mu mol/L]')
title('Non-preprocessed hbo data')
```

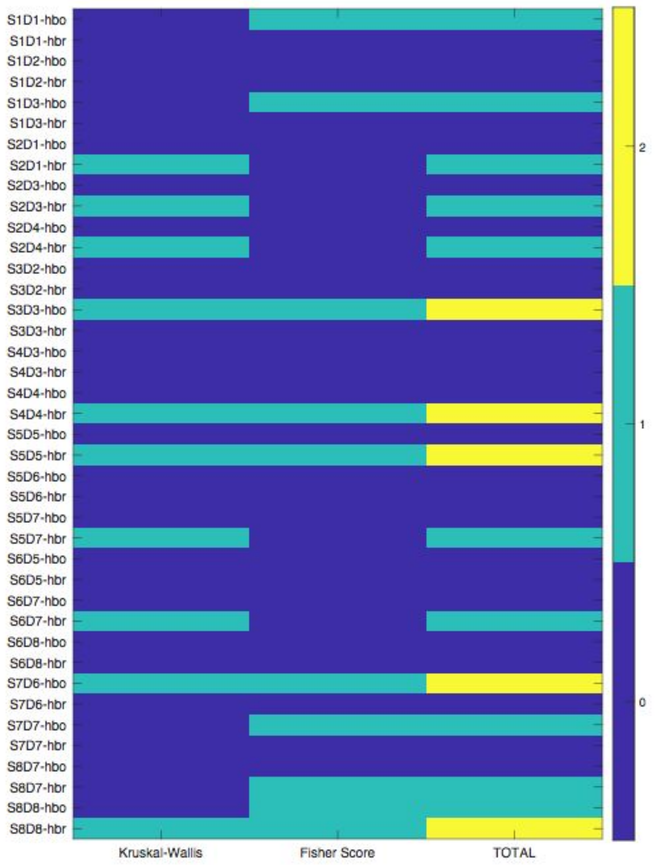
fNIRS Data Preprocessing



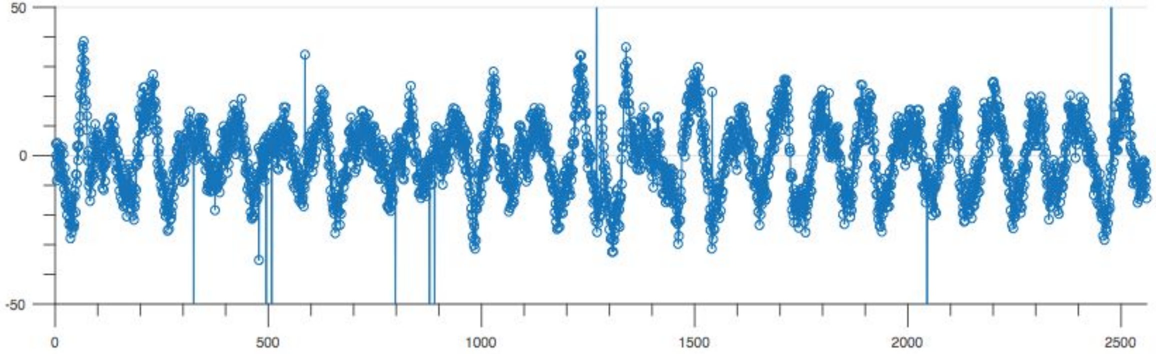

```matlab
%% Data PreProcessing
%BaselineCorrection - Attemps a very conservative motion correction to remove DC-shifts.
%Options:  tune - number of standard deviations to define an outlier
job = nirs.modules.BaselinePCAFilter; % Default tune = 5
hb = job.run(hb);

%'Remove Trend & Motion w/ Wavelets'
job = nirs.modules.WaveletFilter;
hb = job.run(hb);

%Low pass Filter
%y = lowpass(x,fpass,fs) specifies that x has been sampled at a rate of fs hertz.
% fpass is the passband frequency of the filter in hertz.
hbfiltered = hb;

for ii=1: nruns
    HbFIltered.data=lowpass(hb(ii).data, 0.2, 4);
end

subplot(3,1,3)
h2 = plot(ClippedData2(:,6));
set (h2, 'YData', get(h2, 'YData')*0.1)
title('Preprocessed hbo data')
ylabel('[\mu mol/L]')
```

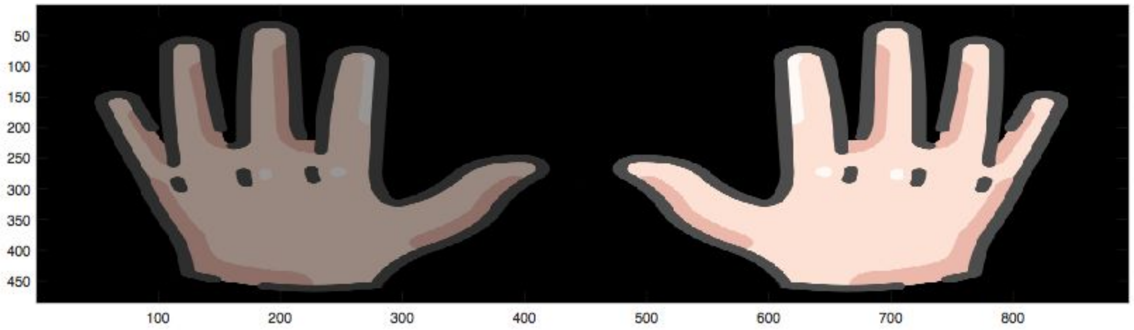
Feature selection





Classification and interface





Neurofeedback (NF)

Q&A

Thank you for your attention!

Alexandre Sayal (@AlexandreSayal, alexandre.campos@uc.pt)
Bruno Direito (@bruno_miguel, bruno.direito@uc.pt)
Carolina Travassos (@ACTravassos, atravassos@uc.pt)
João Pereira (@jafpereira93, jpereira@uc.pt)
Teresa Sousa (@tmssousa, tsousa@uc.pt)

voluntarios.cibit.uc.pt

CIBIT
Coimbra Institute for Biomedical Imaging and Translational Research

1 2 9 0
INSTITUTO DE CIÊNCIAS NUCLEARES APLICADAS À SAÚDE
UNIVERSIDADE D COIMBRA