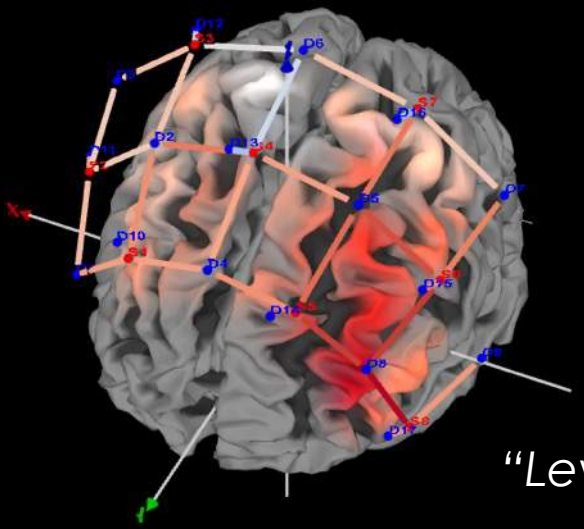
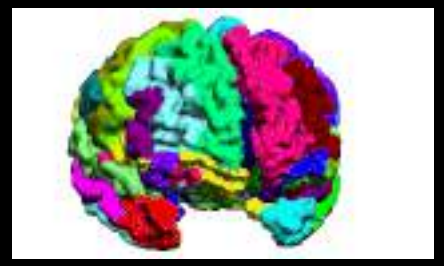
UNVEILING THE BRAIN THROUGH FUNCTIONAL NEAR-INFRARED SPECTROSCOPY



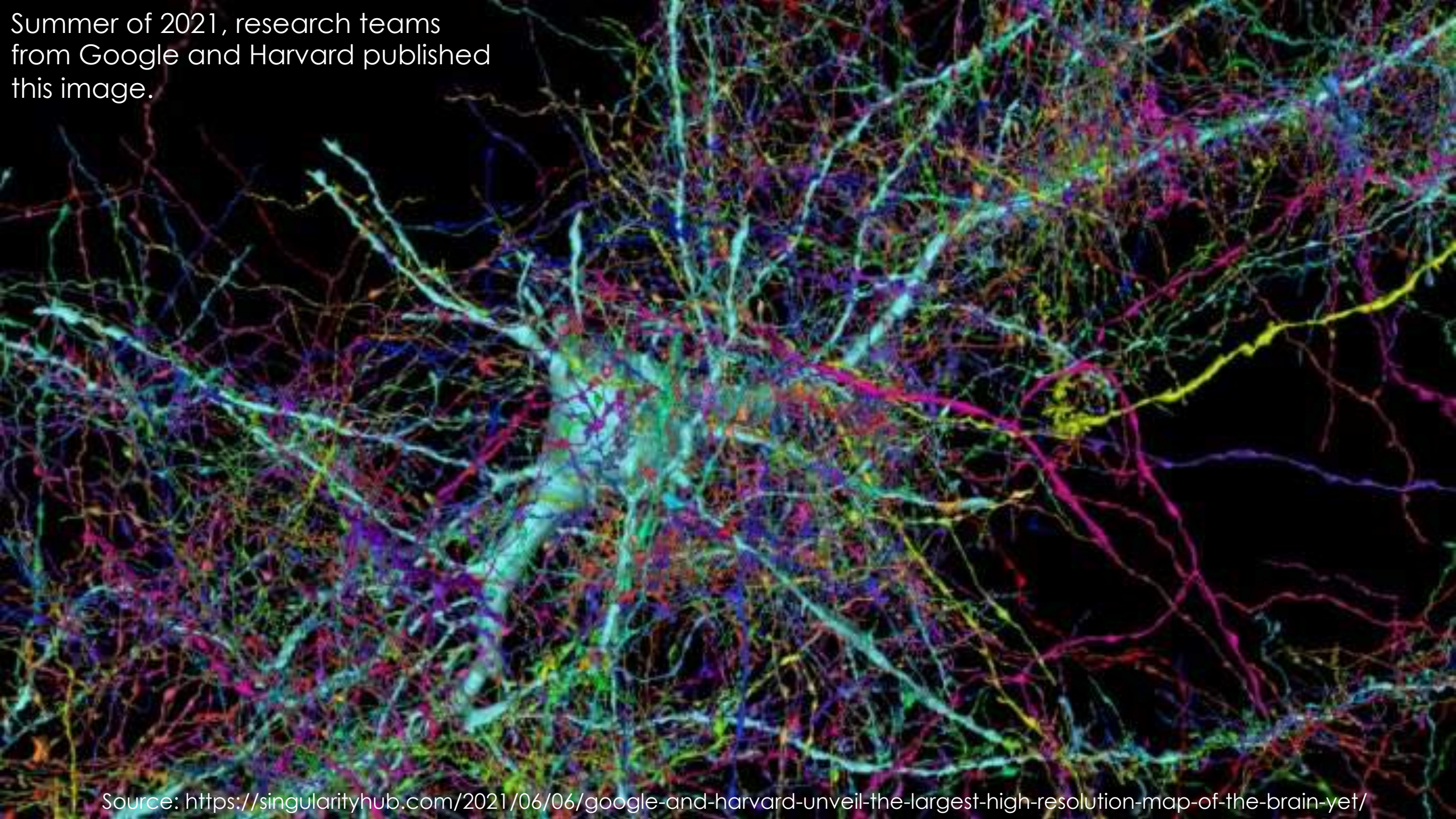
2023-24 Methodology Applications Series
"Leveraging Cutting-Edge Technologies to Advance Research and Methods."

- Neuroimaging for Language, Literacy, and Learning (NL3) Lab
- Yingying Wang, Ph.D.
- May 3, 2024

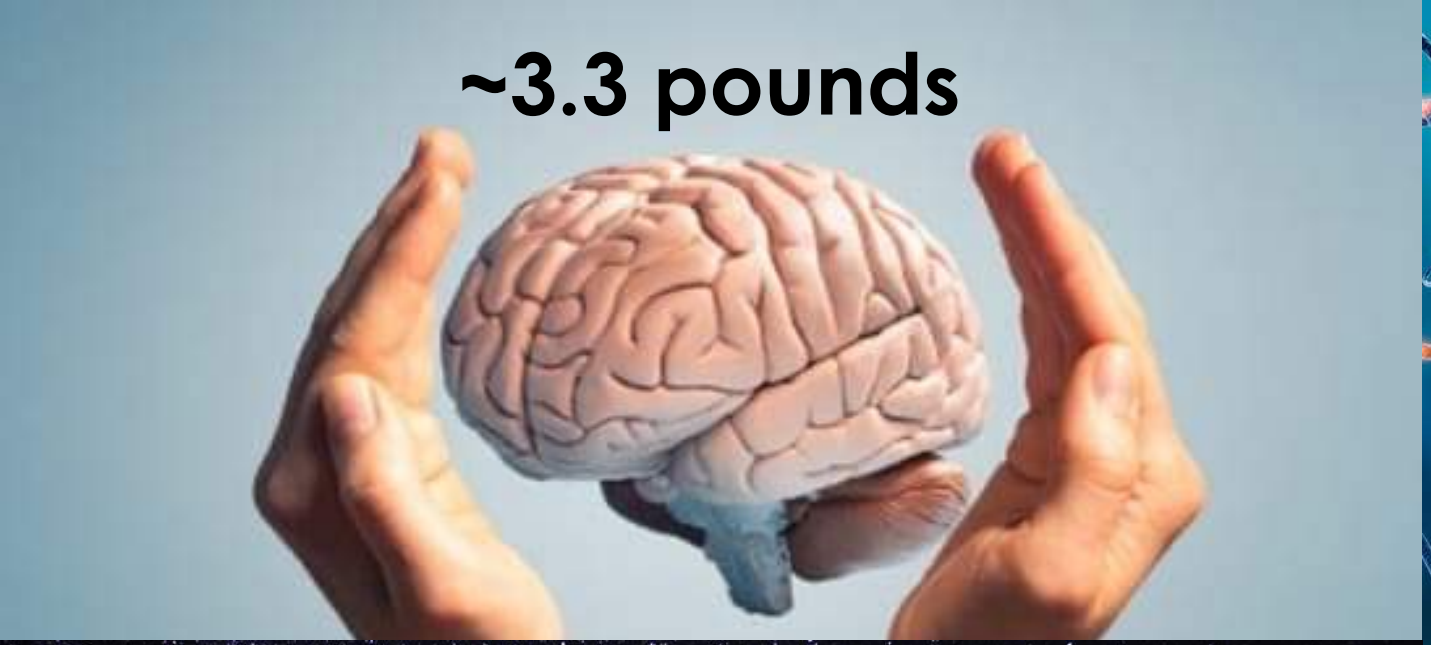
http://nl3.unl.edu



Summer of 2021, research teams from Google and Harvard published this image.

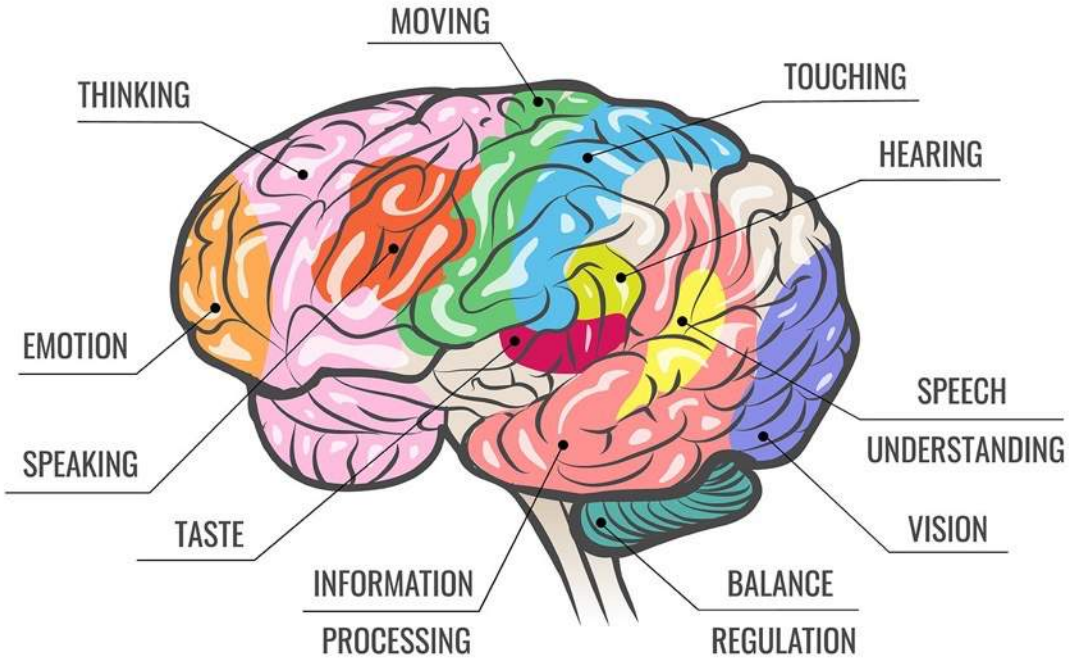


Source: https://singularityhub.com/2021/06/06/google-and-harvard-unveil-the-largest-high-resolution-map-of-the-brain-yet/


~3.3 pounds


86 billions
neurons


Milky Way


MOVING
THINKING
TOUCHING
HEARING
EMOTION
SPEECH
UNDERSTANDING
SPEAKING
TASTE
VISION
INFORMATION
PROCESSING
BALANCE
REGULATION

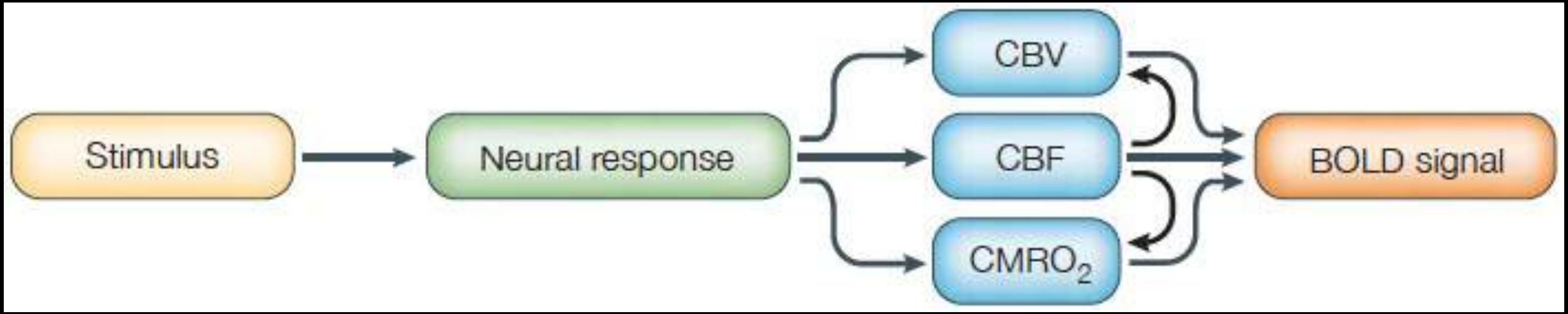
OUTLINES

- What is fNIRS?
- What can we do with fNIRS?
- How shall we start fNIRS research?

WHAT IS FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (FNIRS)?

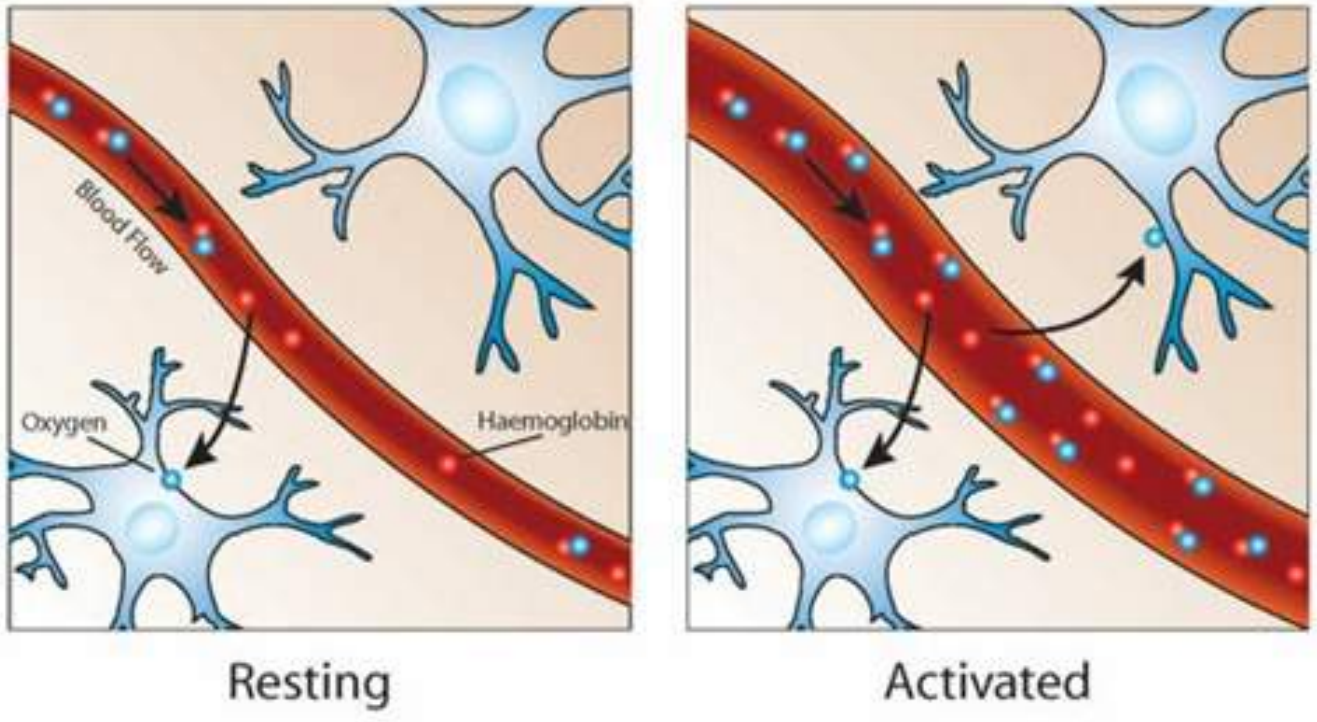
NEUROVASCULAR COUPLING

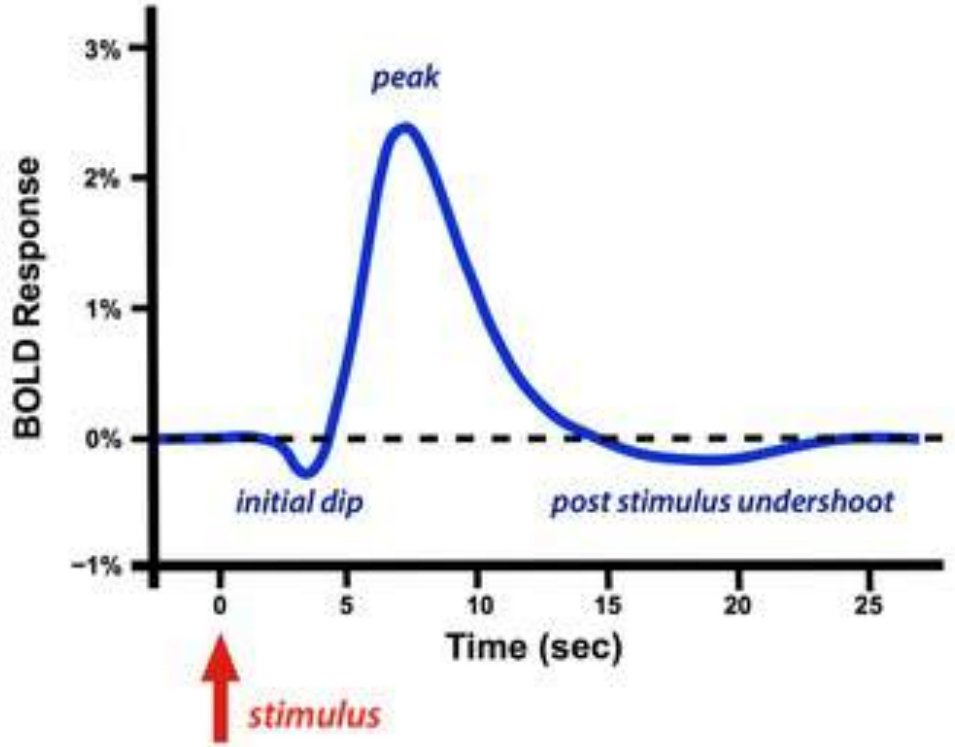
Source: D'Esposito 2003, DOI: 10.1038/nrn1246



- **CBV**: cerebral blood volume
- **CBF**: cerebral blood flow
- **$CMRO_2$**: cerebral metabolic rate of oxygen --- cerebral blood oxygen consumption
- **BOLD**: blood-oxygen-level-dependent (BOLD) signal/response

HEMODYNAMIC RESPONSE FUNCTION (HRF)

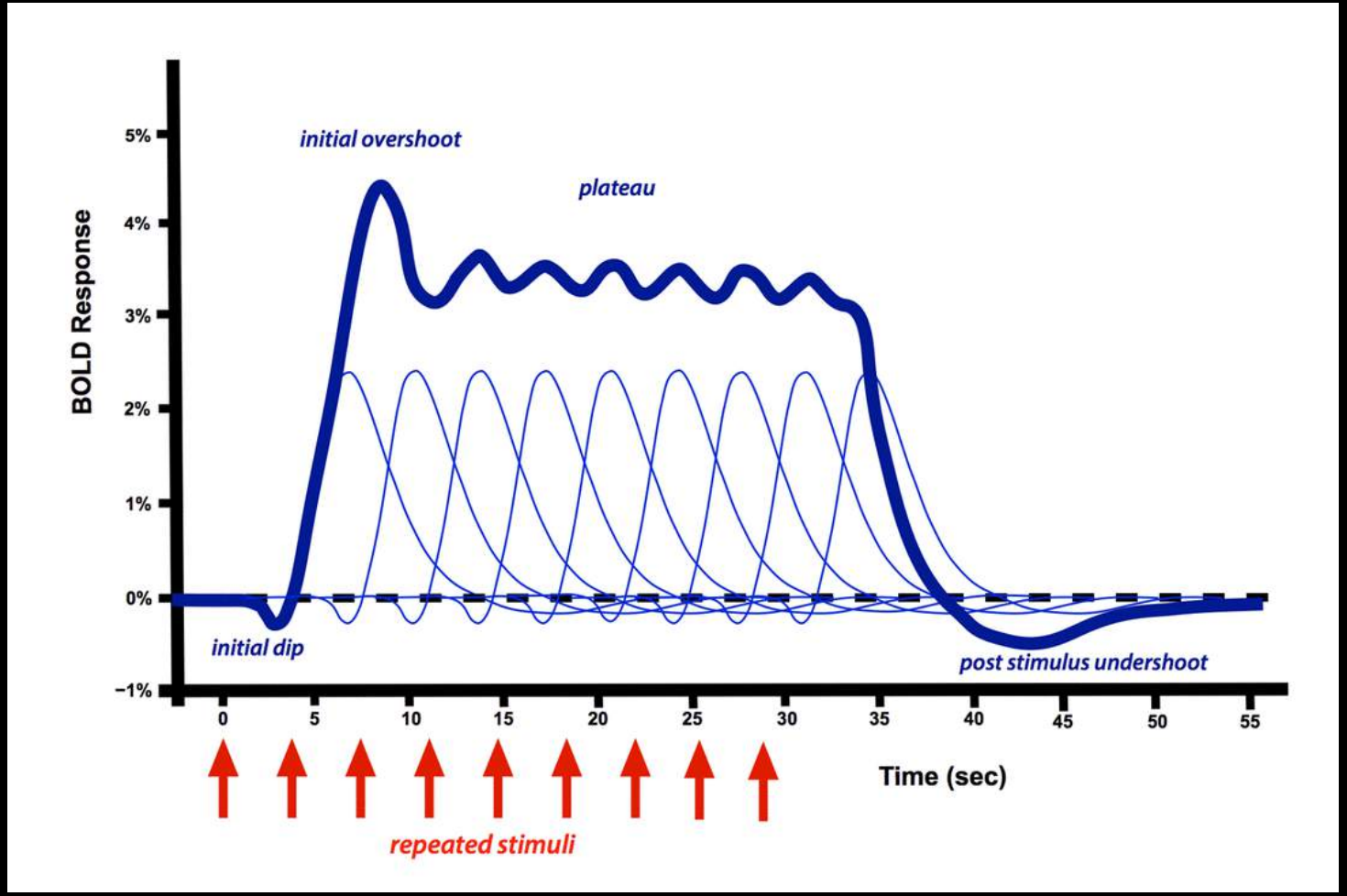




From Oxford Sparks

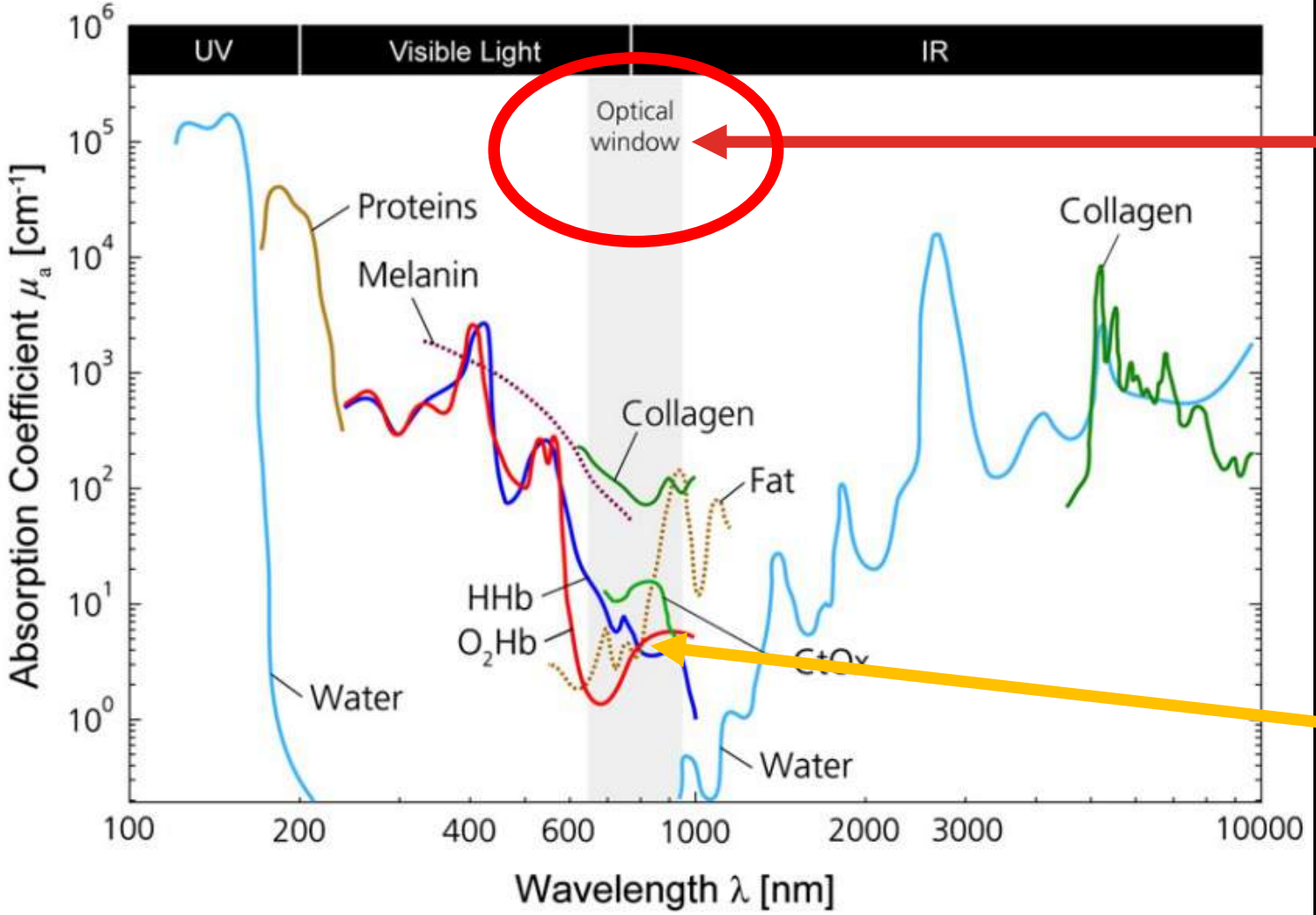
Source: https://mriquestions.com/does-boldbrain-activity.html

REPEATED STIMULI



Source: https://mriquestions.com/does-boldbrain-activity.html

HOW DOES FNIRS WORK?

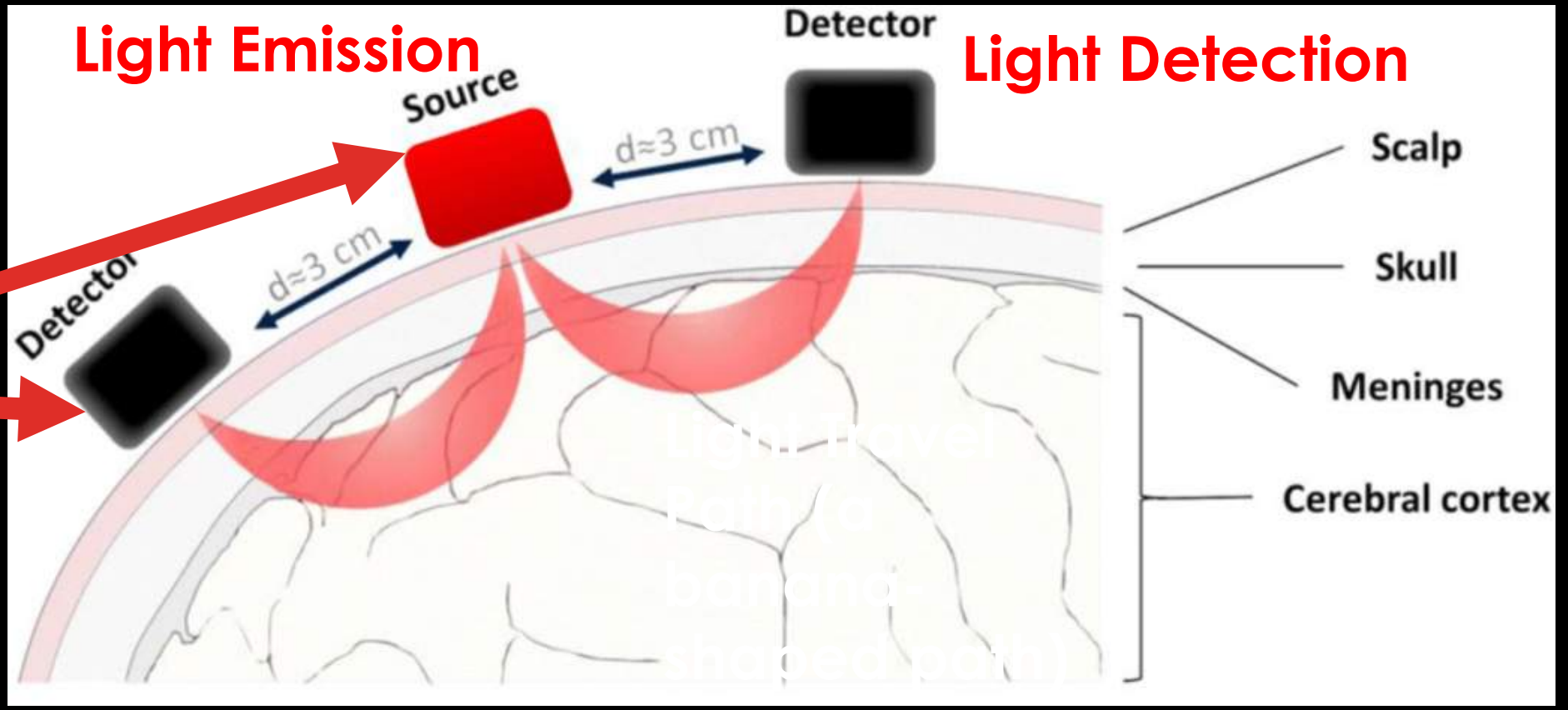


~650–950 nm

Absorption spectra (natural logarithm base) for different chromophores present in human tissue.

~800 nm

HOW DOES FNIRS WORK?



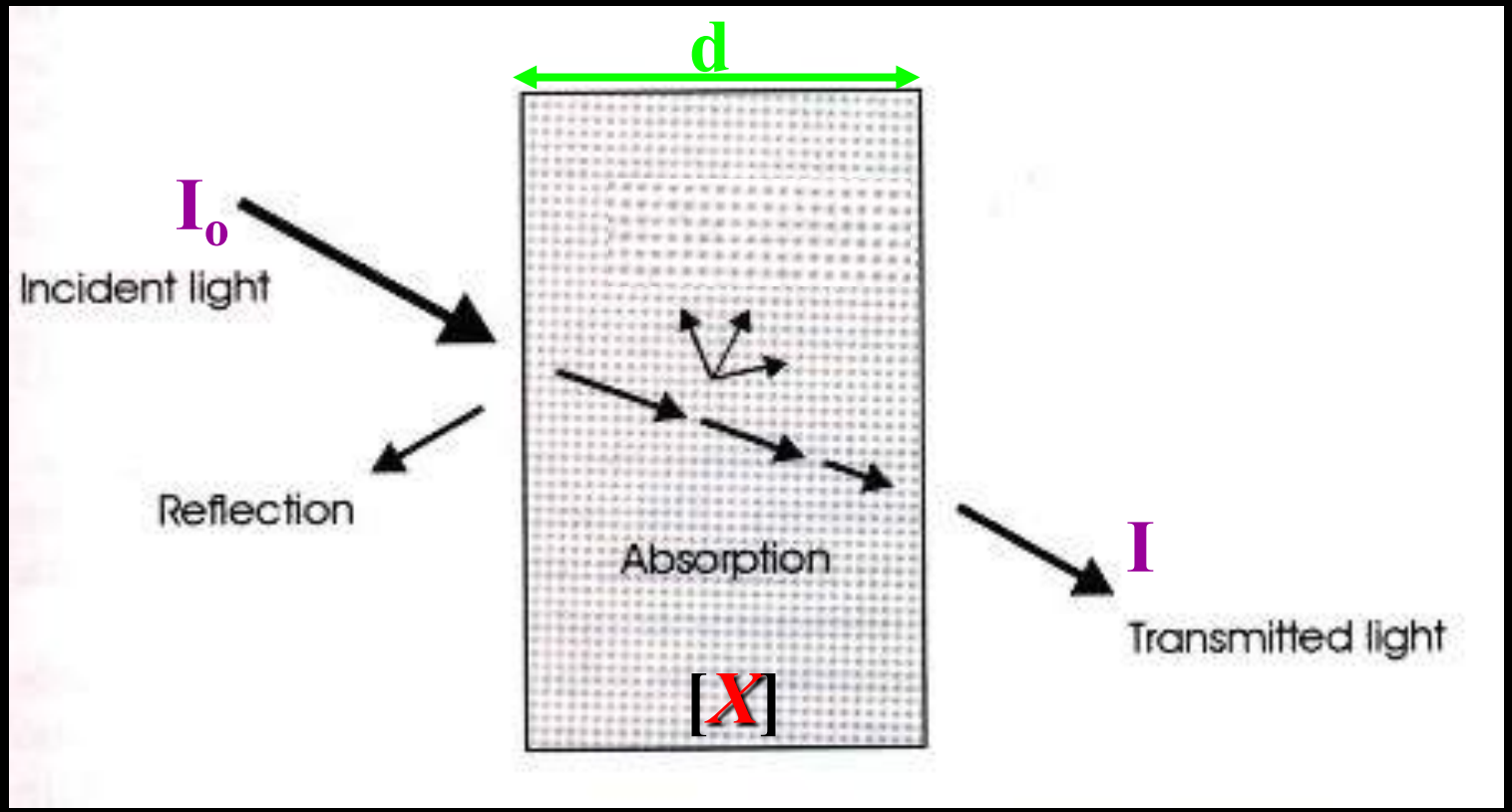
Source: https://link.springer.com/article/10.1007/s11357-019-00122-x#Fig1

BEER-LAMBERT LAW

Transmittance, $T = I/I_o$
Absorbance, $A = -\log(I/I_o)$

Beer-Lambert Law:
$A = \varepsilon [X] d$

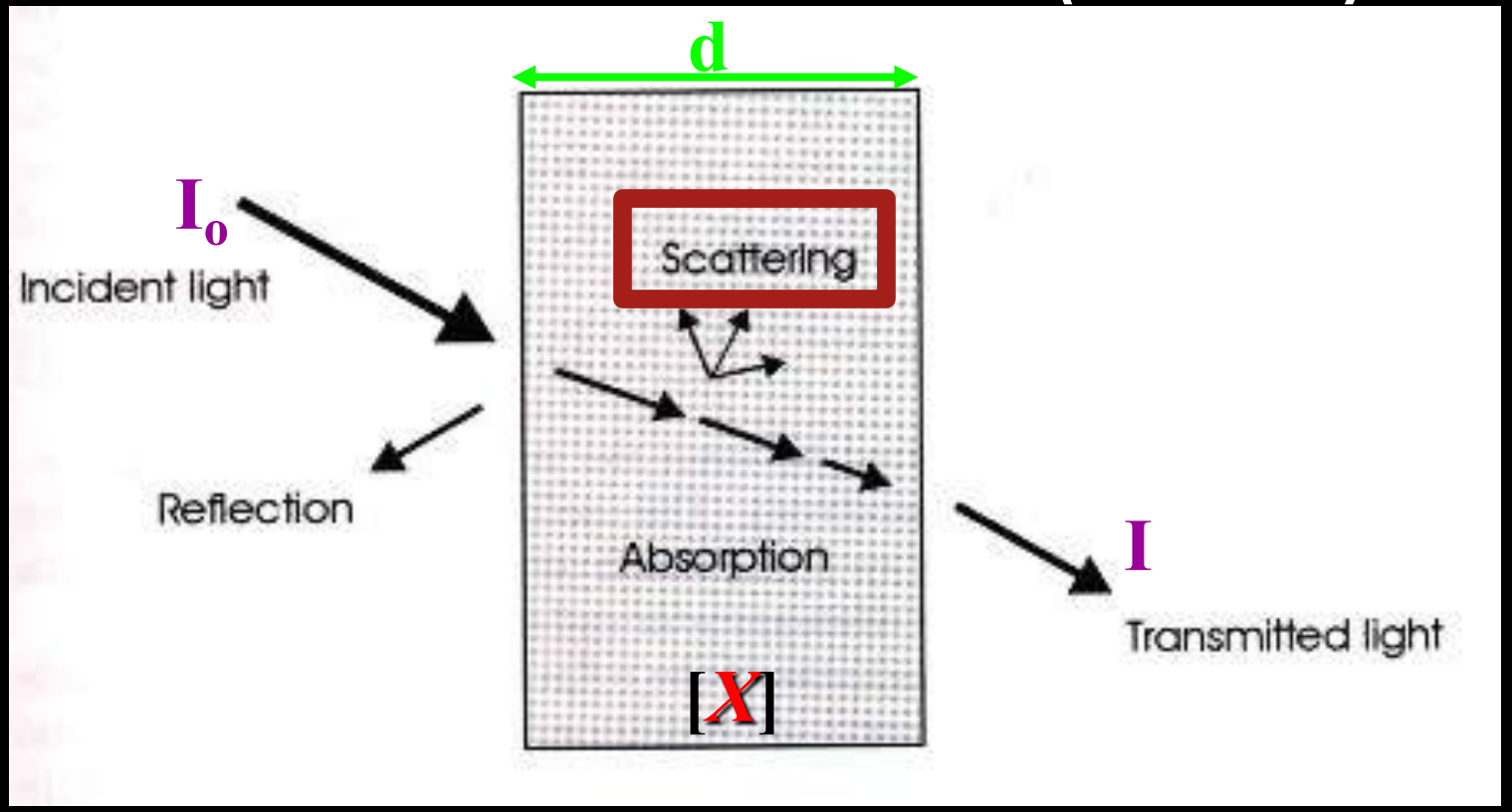
where:
d = distance between I_0 and I
ε = absorptivity (M^{-1} cm^{-1})
[*X*] = concentration of absorber (M)



MODIFIED BEER-LAMBERT LAW (MBLL)

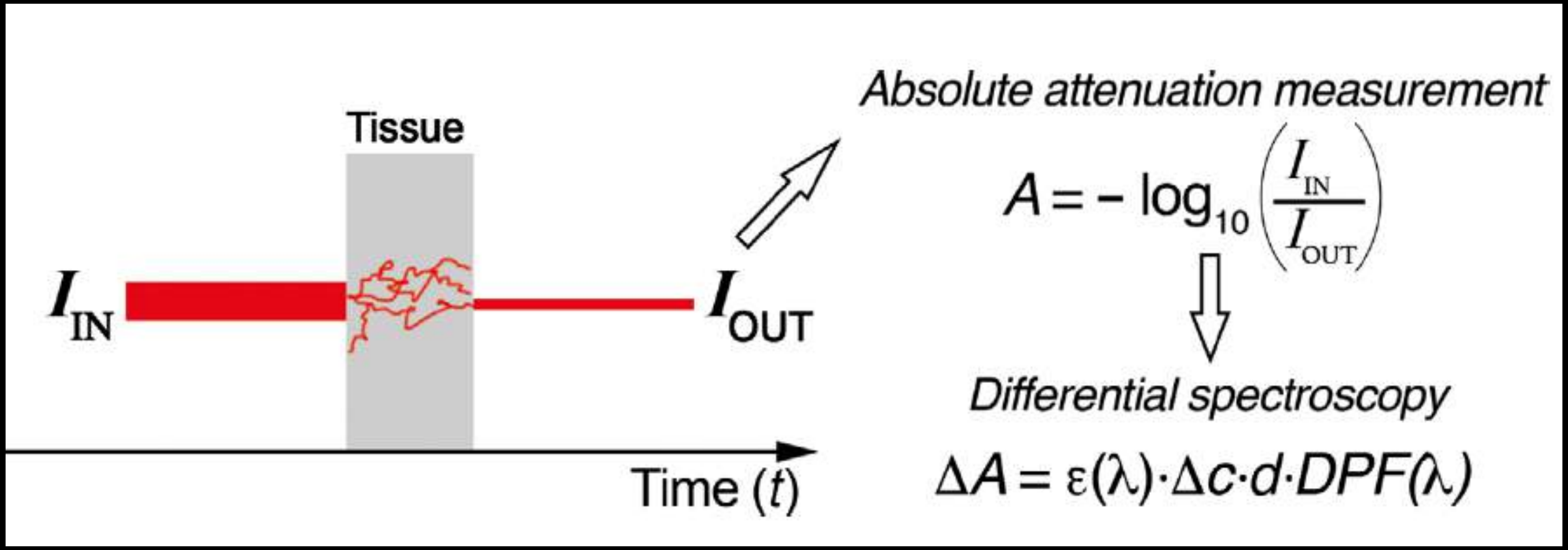
Transmittance, $T = I/I_o$
Absorbance, $A = -\log(I/I_o)$

Modified Beer-Lambert Law:
$A = \varepsilon\,[X]\,d \times DPF + G$



where:
d = distance between I_o and I
ε = absorptivity (M^{-1} cm^{-1})
[X] = concentration of absorber (M)
DPF **= differential pathlength factor**
G = Scattering loss factor (generally unknown)

DIFFERENTIAL SPECTROSCOPY



Source: Pinti, P., Tachtsidis, I., Hamilton, A., Hirsch, J., Aichelburg, C., Gilbert, S., & Burgess, P. W. (2020). The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience. *Annals of the New York Academy of Sciences*, *1464*(1), 5-29.

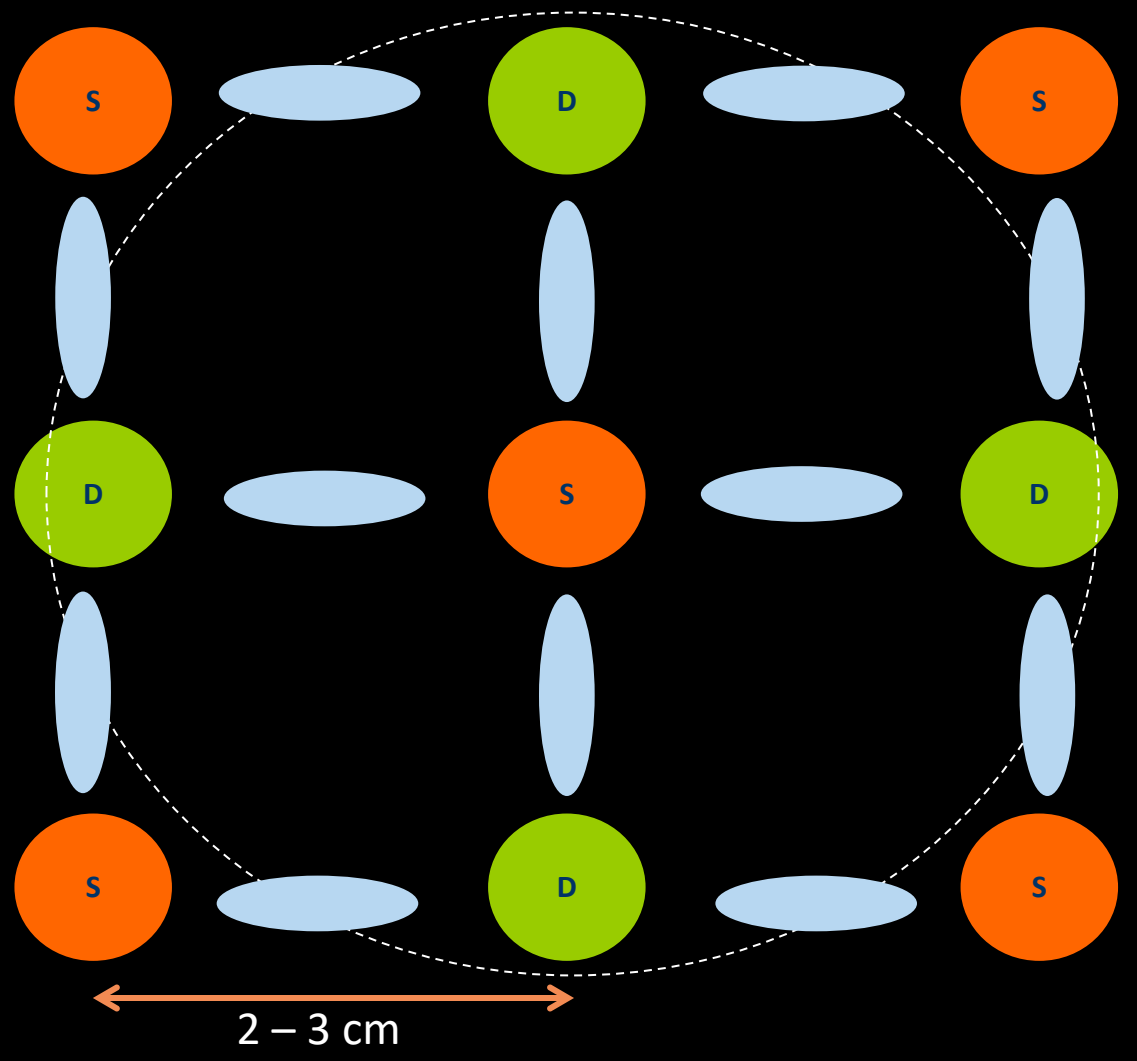
TOPOGRAPHY

'Nearest-neighbor' measurements are done with spacing of 2-3 cm between sources and detectors.

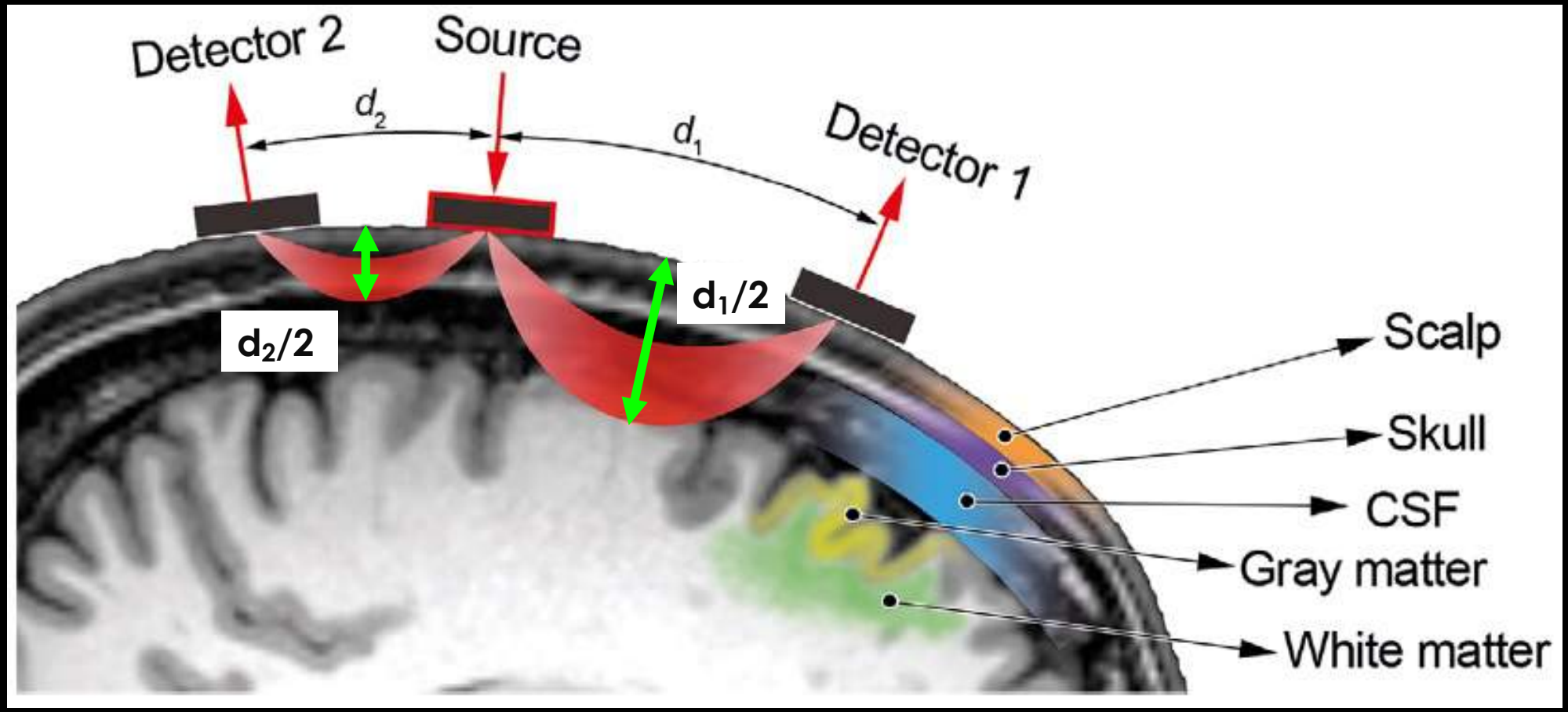
S = light source

D = light detector

= data channel



PENETRATION



Source: Fig 1. from Pinti, P., Tachtsidis, I., Hamilton, A., Hirsch, J., Aichelburg, C., Gilbert, S., & Burgess, P. W. (2020). The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience. *Annals of the New York Academy of Sciences*, *1464*(1), 5-29.

TRUE OR FALSE QUESTION

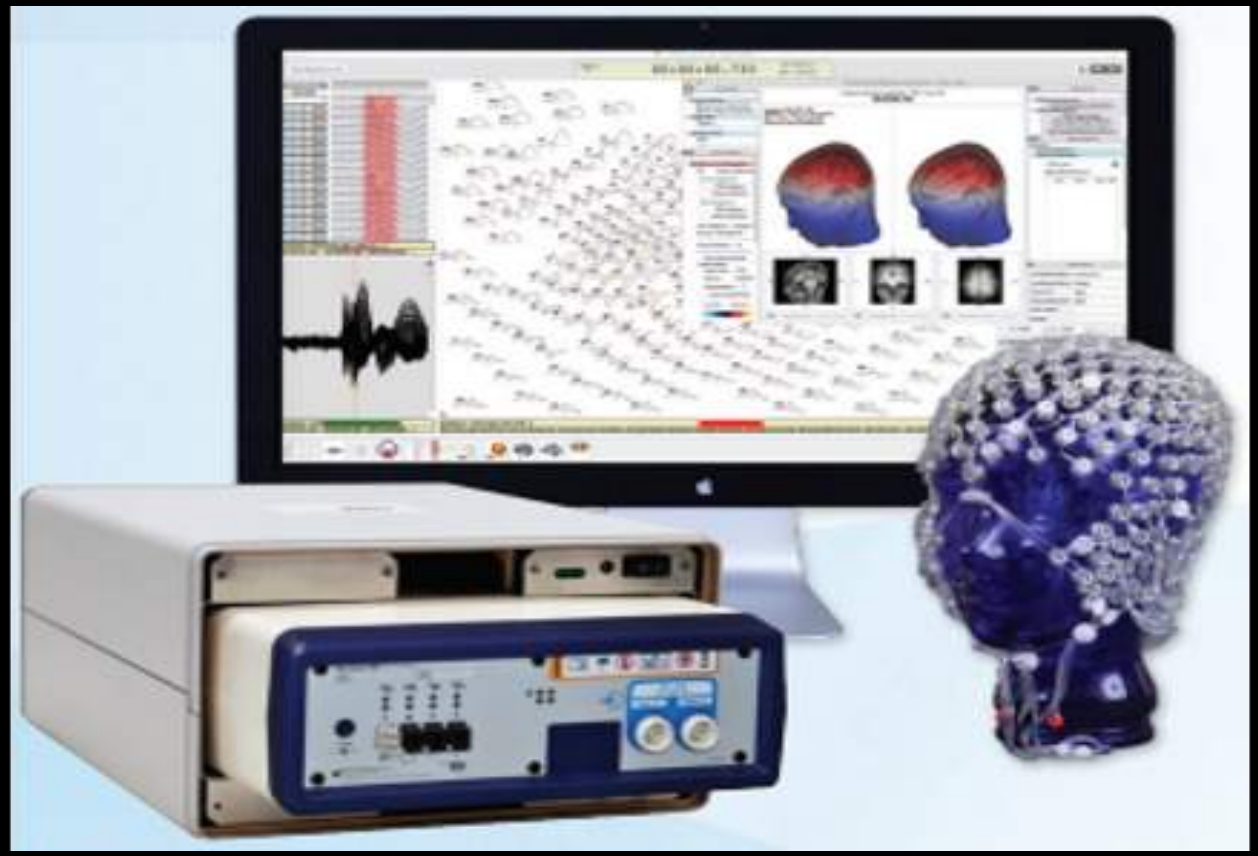
- FNIRS measure the absolute concentration of oxygenated hemoglobin in the blood flow.

TRUE OR FALSE QUESTION

- The penetration distance is 15 mm for source-detector distance of 30 mm. ✅

ADVANTAGES: FMRI VS. FNIRS

ADVANTAGES: EEG VS. FNIRS



SUMMARY OF ADVANTAGES: FNIRS

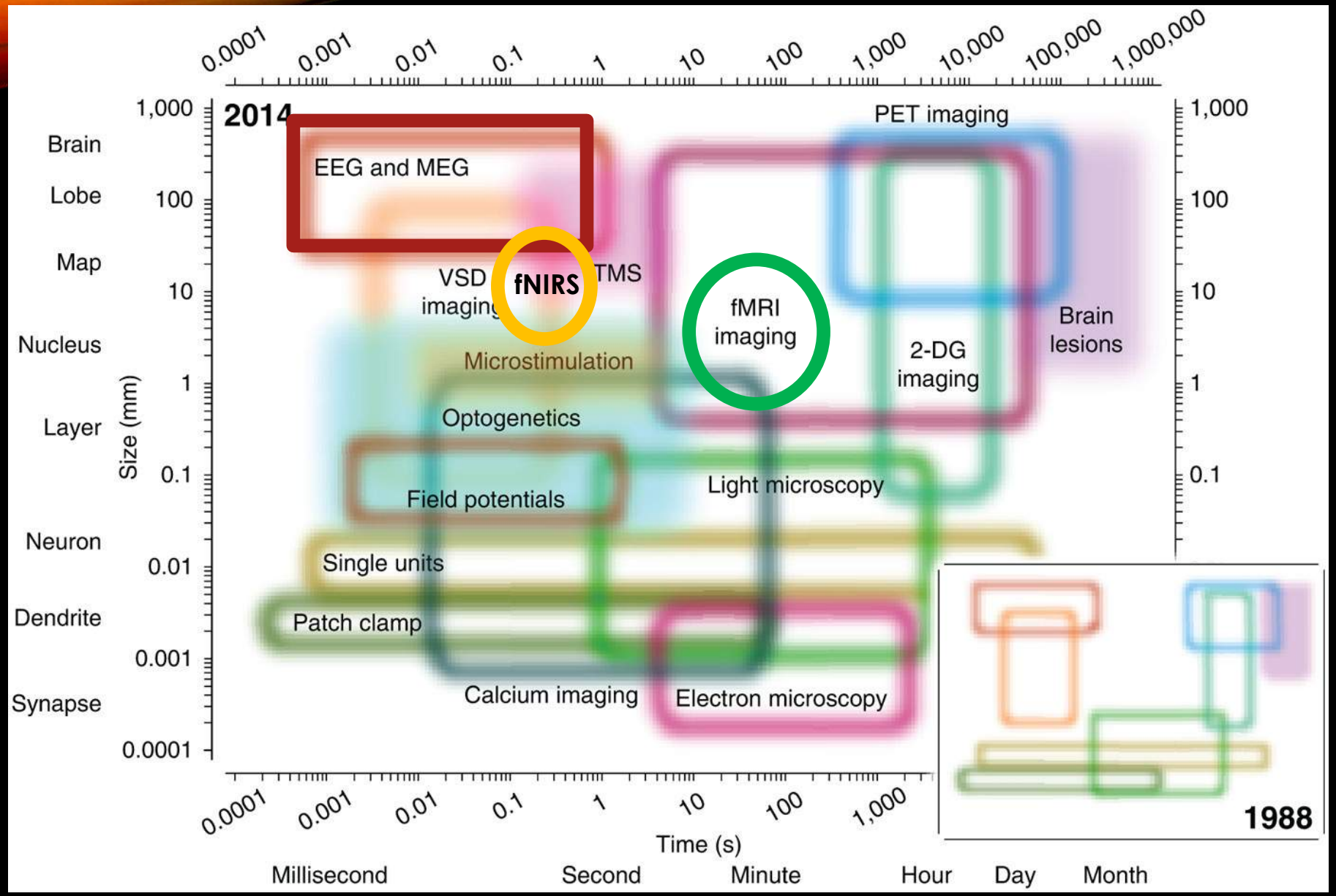
- Compact, low-cost sensing hardware
- Noninvasive, continuous measures
- Highly configurable and scalable platforms
- Information-rich sensing data

- BOLD-like response *without* the magnet
- Source localization >> EEG
- Minimal sensitivity to movement artifacts

LIMITATIONS OF FNIRS

- Cannot measure hemodynamic responses involving “deep” brain regions (e.g., basal ganglia, amygdala).
- Relatively lower spatial resolution (1-1.5 cm): Precise identification of brain areas is improved, but not perfected, with 3D MRI.

NEUROIMAGING METHODS COMPARISONS



Adapted from Sejnowski, 2014

NIRSCOUTX SYSTEM @ UNL

- 16 sources and 20 detectors
- Can be configured up o 64 sources and 32 detectors
- 8-bit trigger input and output
- LED sources

	Laser	LED
Measurement depth	+	-
Portability	-	+
Price	-	+
Wavelength	+	-
Safety	+	+

TRUE OR FALSE QUESTIONS

- FNIRS has higher temporal resolution than fMRI. ✅
- EEG has higher spatial resolution than fNIRS and fMRI. ❌
- If you are interested in neuronal response in amygdala, you can use fNIRS. ❌
- Both fNIRS and fMRI are based on the mechanisms of neurovascular coupling. ✅
- LED-based fNIRS system can measure deeper response than Laser-based fNIRS system. ❌

OUTLINES

- What is fNIRS?
- What can we do with fNIRS?
- How shall we start fNIRS research?

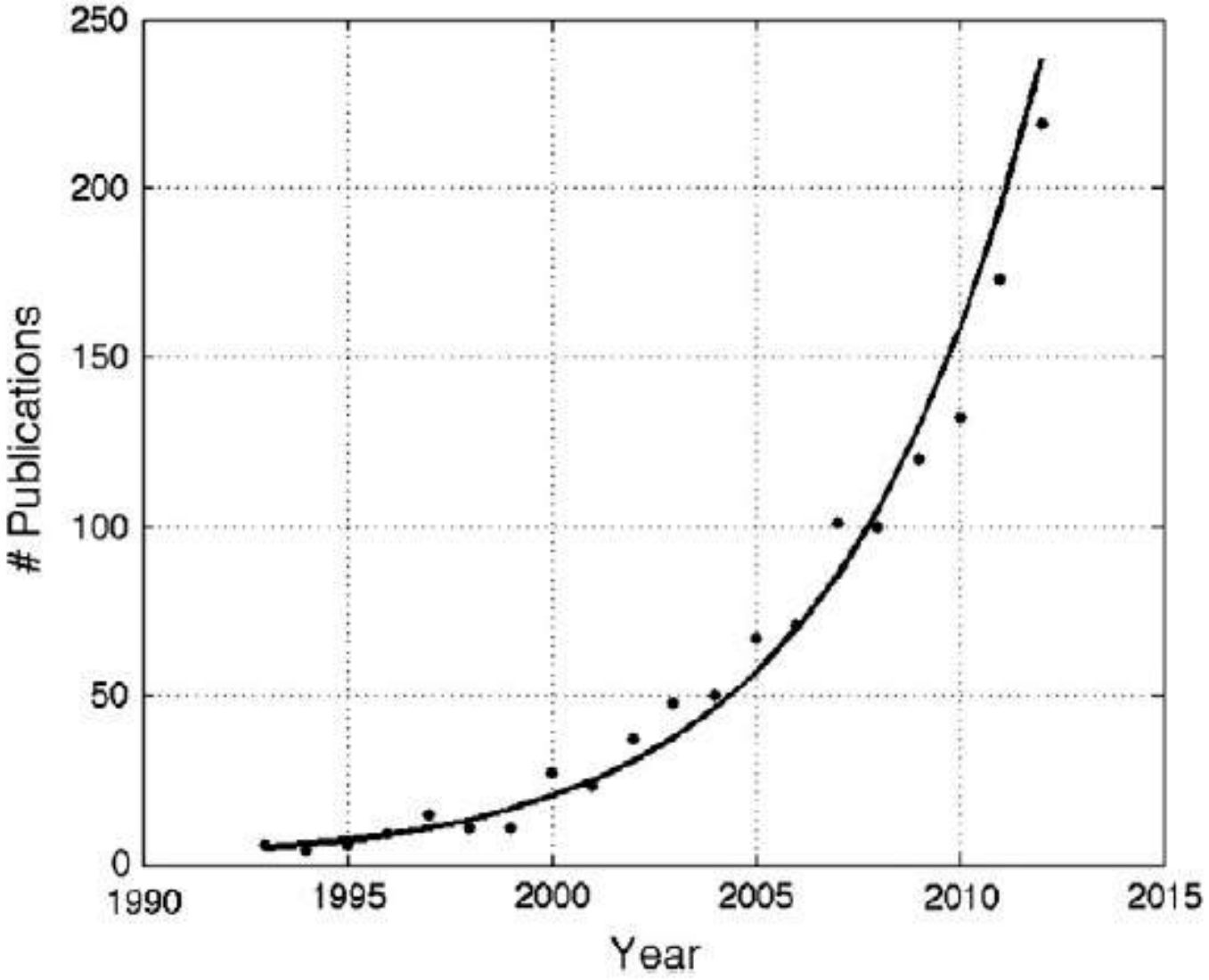


Fig. 1. Number of fNIRS publications per year.

Boas 2014

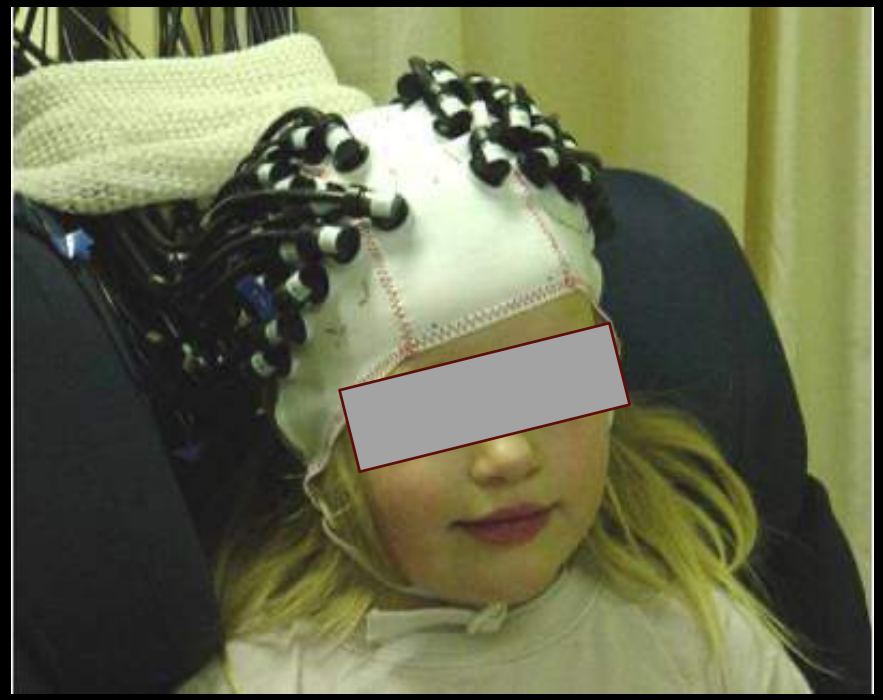
fNIRS research is rapidly growing; the number of publications has doubled every 3.5 years over the past 20 years, passing 200 per year in 2012 (Fig. 1).

This growth reflects the increasing number of scientists and clinicians beginning to utilize fNIRS for a broad range of applications.

APPLICATIONS OF FNIRS

Neurology	Psychiatry	Psychology & Education	General Research
Alzheimer's	Anxiety Disorders	Attention	BCI
Dementia	Behavioral Disorders	Body Representation	Multi-Modal Fusion
Depression	Childhood Disorders	Comprehension	Neuroeconomics
Epilepsy	Eating Disorders	Developmental Disorders	Neuroergonomics
Intra-operative monitoring	Personality Disorders	Emotion	Pain
Parkinson's	Substance Abuse	Language/Linguistics	Sleep
Rehabilitation	Schizophrenia	Learning	Sports Sciences
Stroke recovery		Memory	

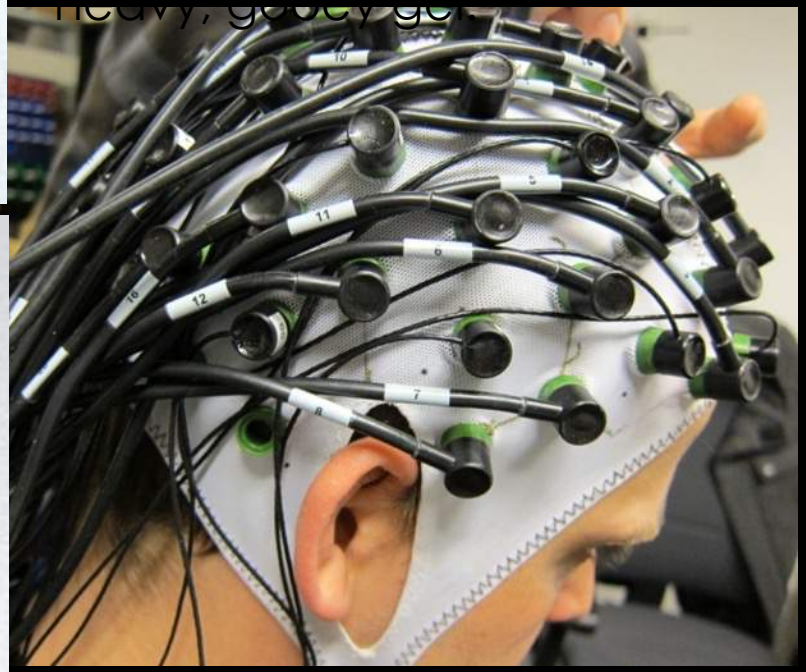
Subjects: Infants & Adults



Standard NIRScaps can be worn for several hours with minimal discomfort. Long-term monitoring caps are available upon request, with specialized components to increase comfort and reduce

flat probes is ideal for subjects with sensitive skin or heads.

NIRx NIRScaps are comfortable and conforming. Most end-users find it more comfortable than EEG, as it does not involve the use of any scalp abrasion, or heavy, gooey gel.

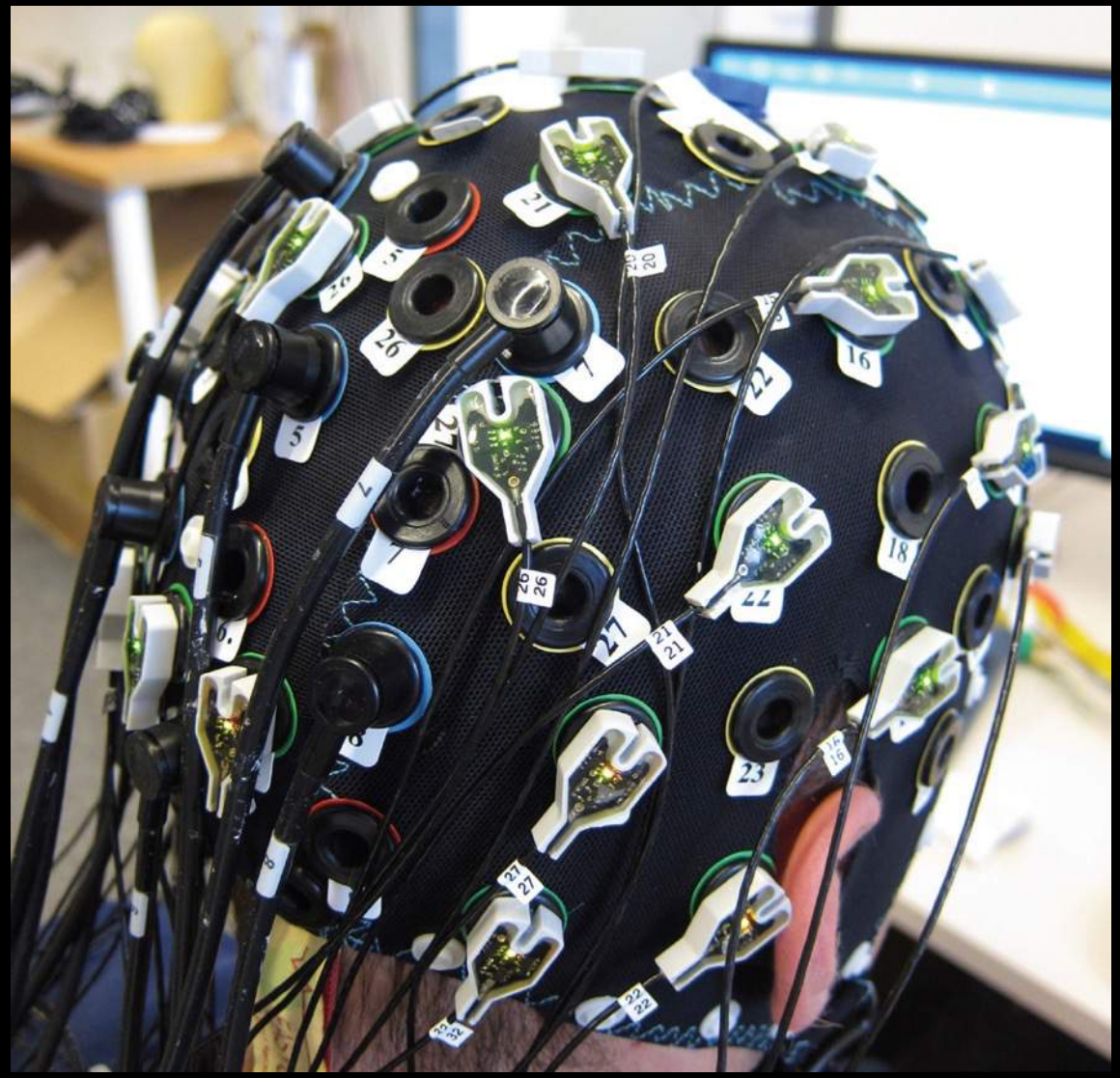


HYPERSCANNING = MULTI-SUBJECT MEASUREMENTS

Multi-subject concurrent measurements have become increasingly popular lately.

Peer group, parent-child, and other relationships are effectively quantifiable with the use of our hyperscanning setups.

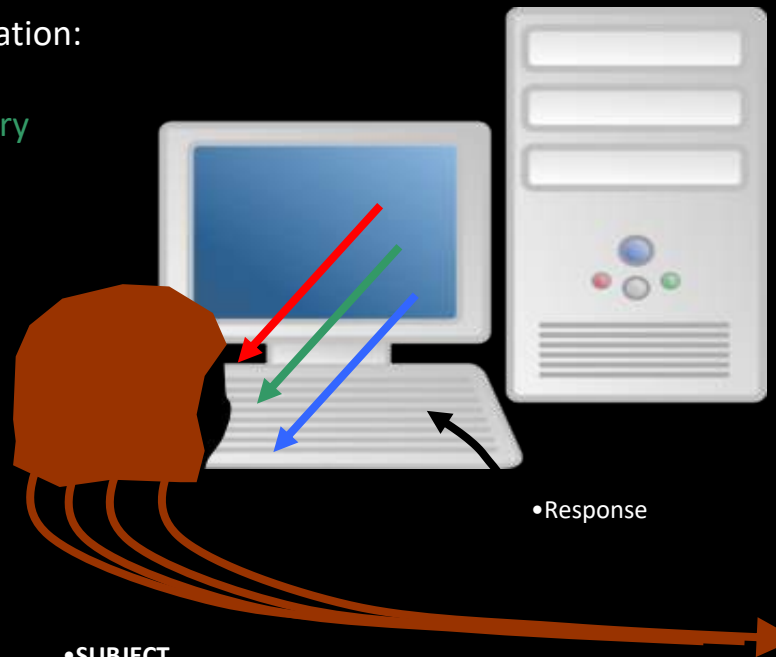
NIRS/EEG – Concurrent Measurements



NIRx's integrated EEG/NIRS solutions are numerous. Here we see integration with the NIRScoutX system and an active electrode EEG setup.

Synchronization of NIRS & EEG

Stimulation:
Visual
Auditory
Tactile
etc.



NIRS
Measurement

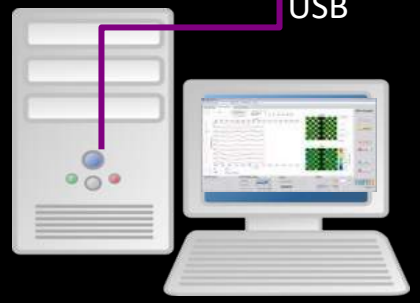
Digital Interface:
LPT (parallel) Port
Data Acquisition Card
3rd Party Interface

PC Bus

Trigger Cable
(4 or 8 lines)

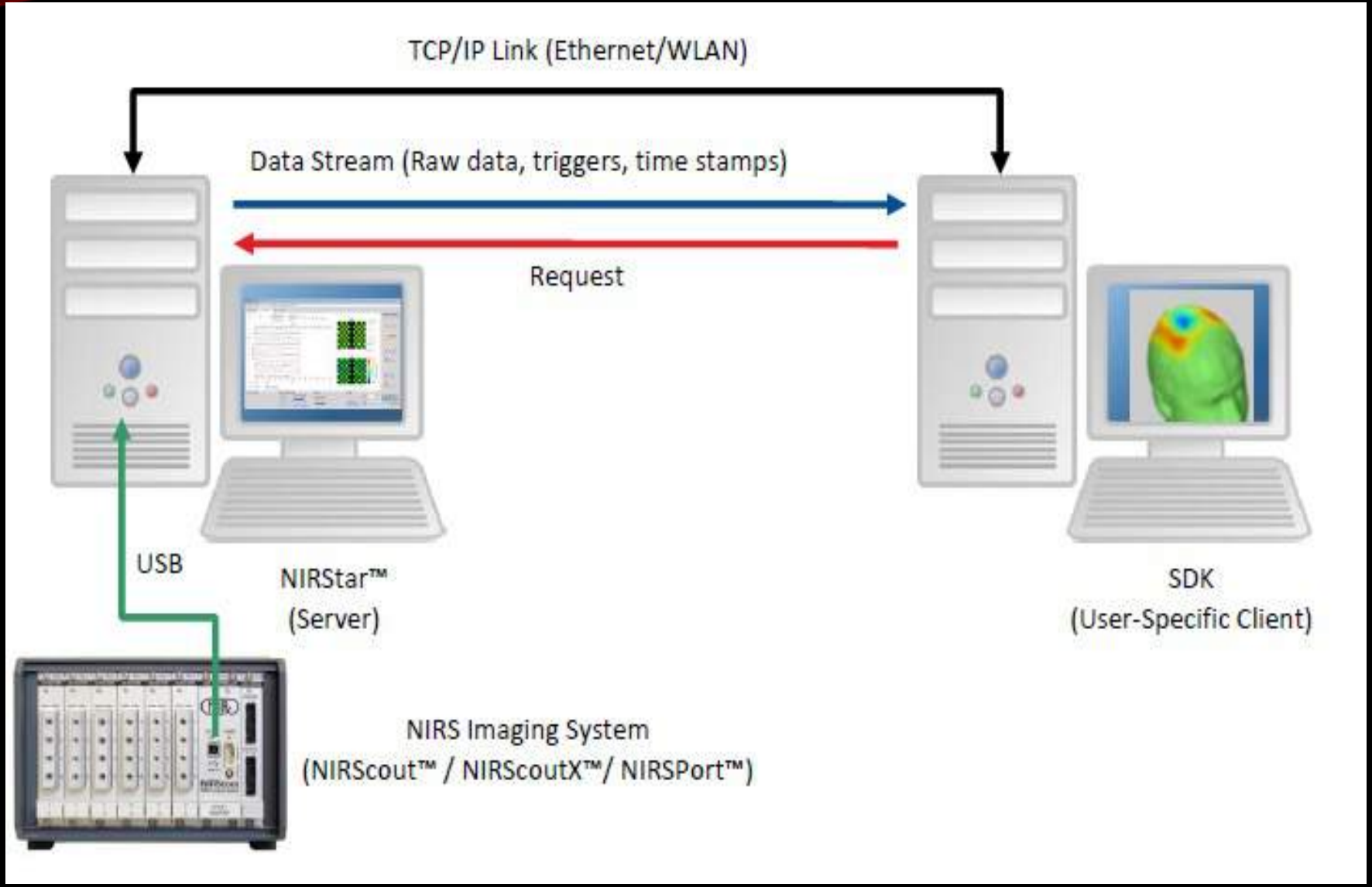
Trigger Splitter
(optional)

USB

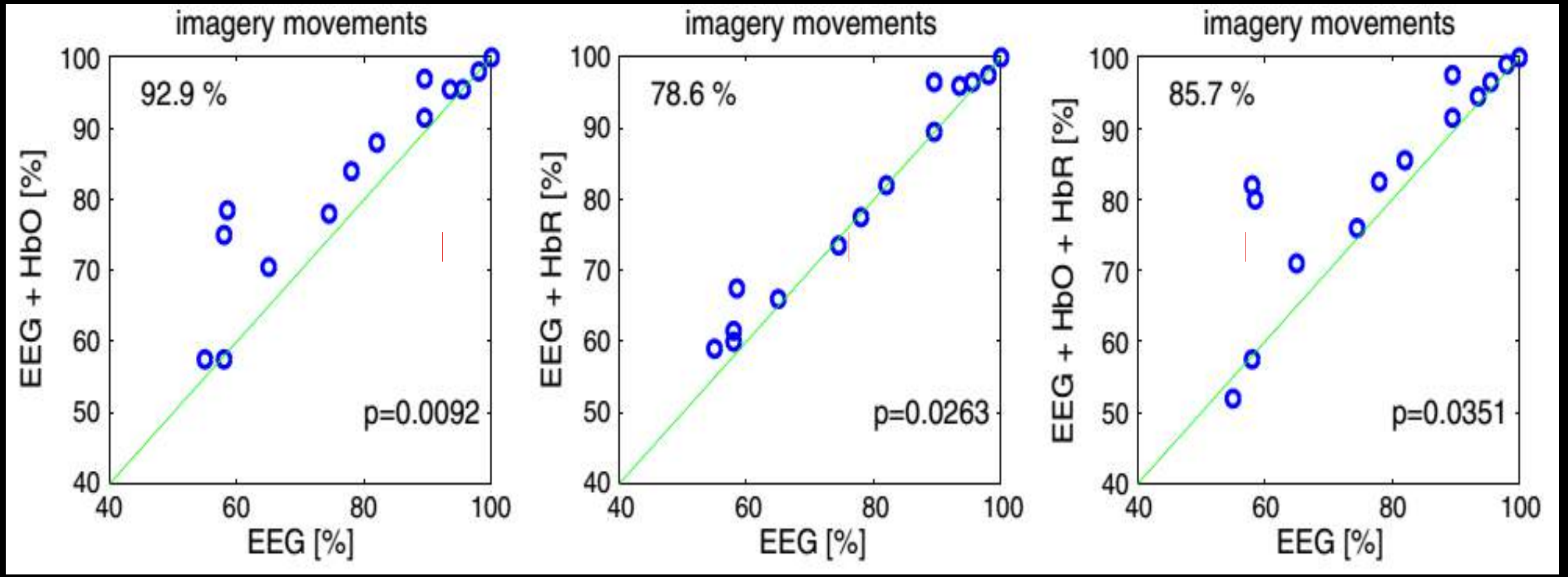


NIRStar records:
NIRS Data
Event markers

Brain-Computer Interface with NIRS Streaming



BCI PERFORMANCE IMPROVEMENT: EEG + HBO

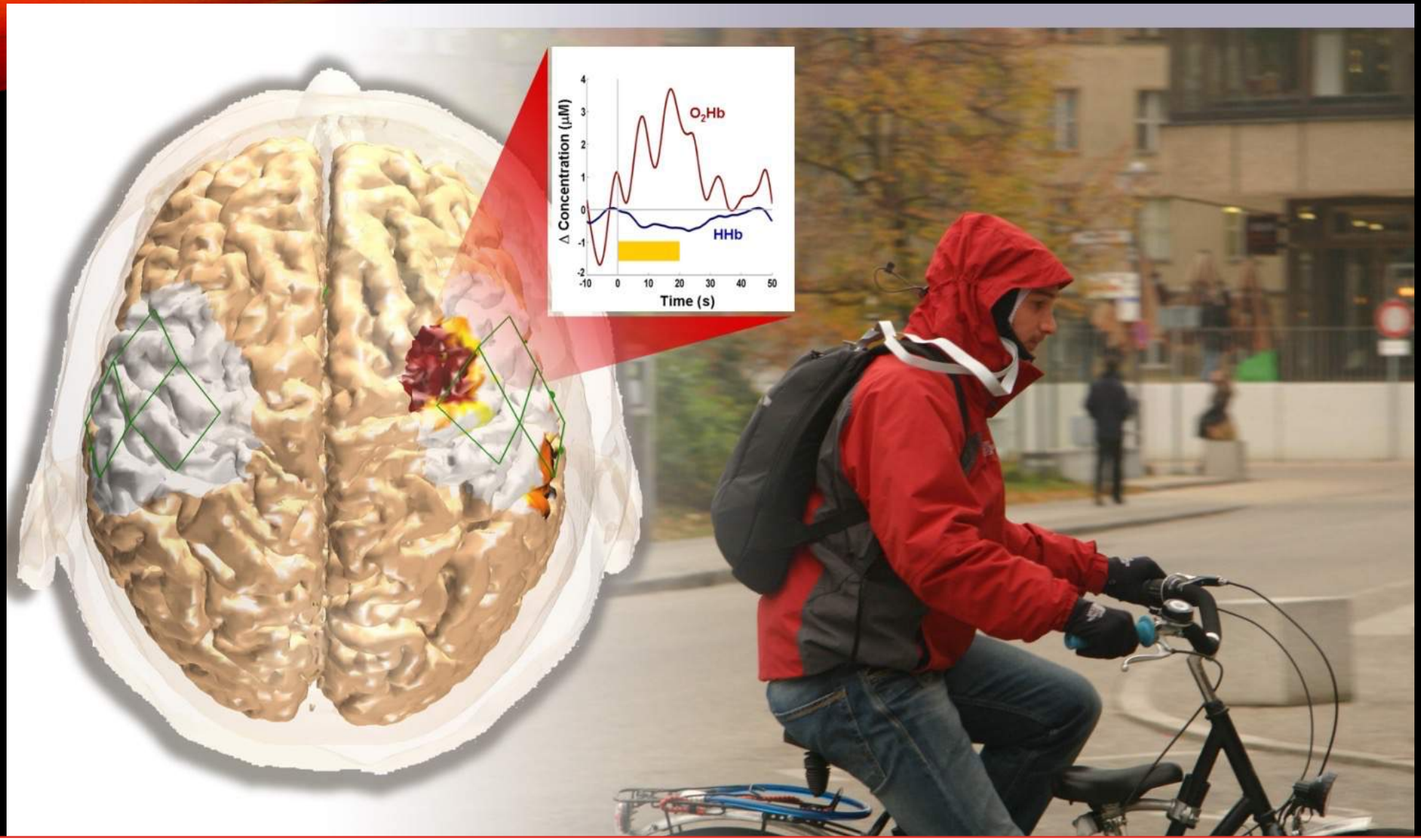


Fazli et al, Neuroimg. 2011

Portable fNIRS laboratories

The NIRSport is lightweight and compact. It is easily setup in any environment, allowing researchers to meet subjects anywhere!

Wearable NIRS Study while biking



(Piper et al. Neuroimage 2013): The study exhibited the viability of the portable solution. The subject rode a bicycle while wearing a 16-probe NIRS system.

WIGGINS 2016 -- RELIABILITY

Research Paper

Speech-evoked activation in adult temporal cortex measured using functional near-infrared spectroscopy (fNIRS): Are the measurements reliable?

Ian M. Wiggins [a, b, c, *], Carly A. Anderson [a, b], Pádraig T. Kitterick [a, b], Douglas E.H. Hartley [a, b, c, d]

[a] National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, 113 The Ropewalk, Nottingham, NG1 5DU, United Kingdom
[b] Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, NG7 2UH, United Kingdom
[c] Medical Research Council (MRC) Institute of Hearing Research, University of Nottingham, University Park, Nottingham, NG7 2RD, United Kingdom
[d] Nottingham University Hospitals NHS Trust, Derby Road, Nottingham, NG7 2UH, United Kingdom

WIGGINS 2016 -- RELIABILITY

- The reliability of auditory-evoked activation measured using fNIRS is largely unknown.
- Investigated the test-retest reliability of speech-evoked fNIRS responses in normally-hearing adults.
- Seventeen participants underwent fNIRS imaging in two sessions separated by three months.

https://doi.org/10.1016/j.heares.2016.07.007

WIGGINS 2016 -- RELIABILITY

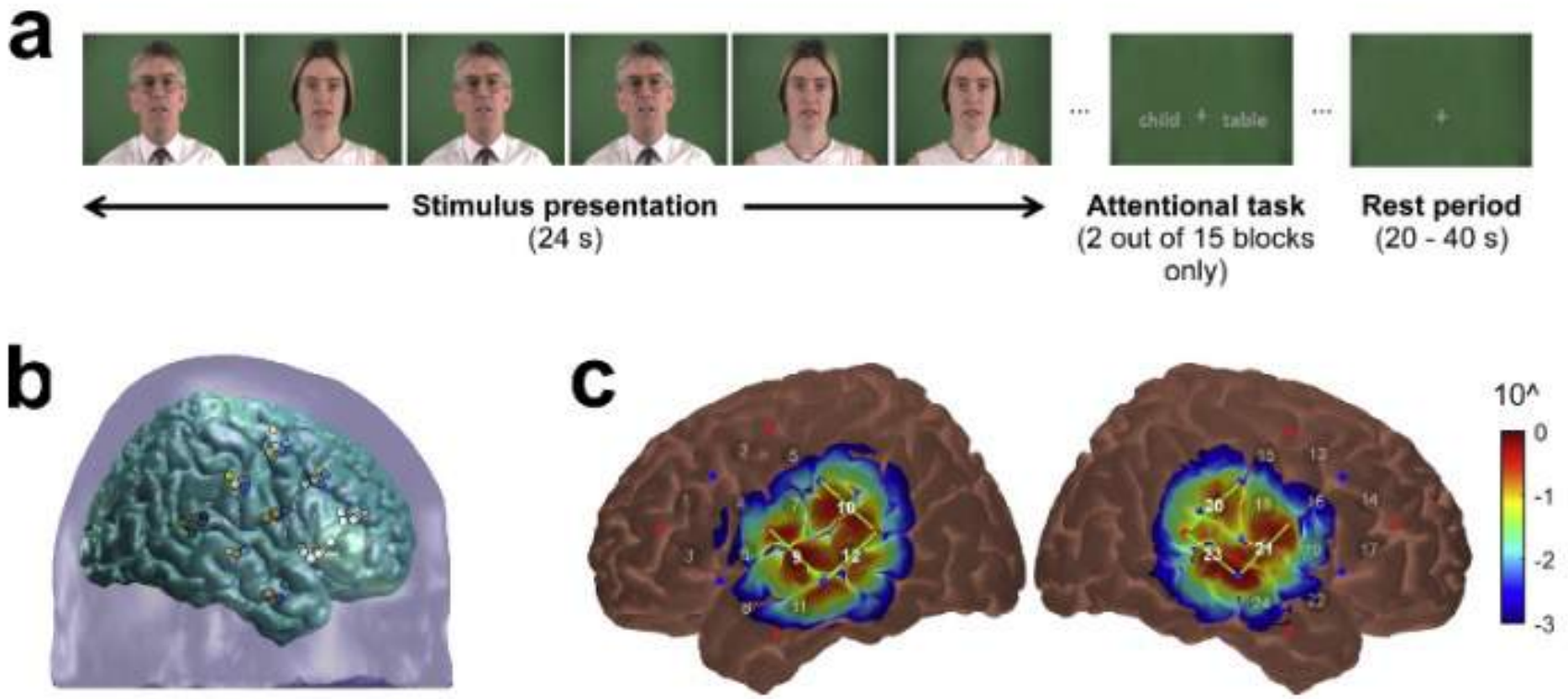
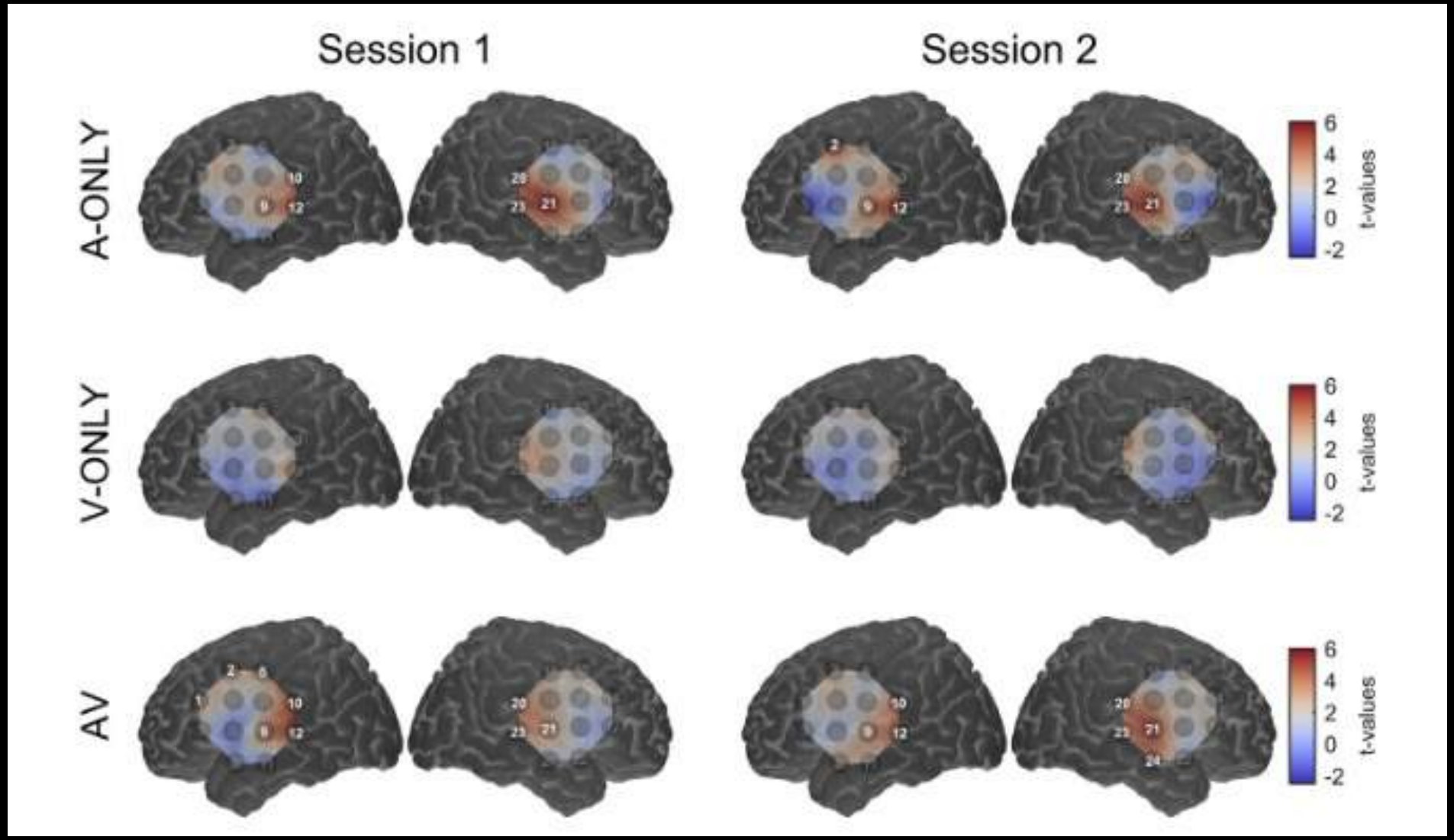
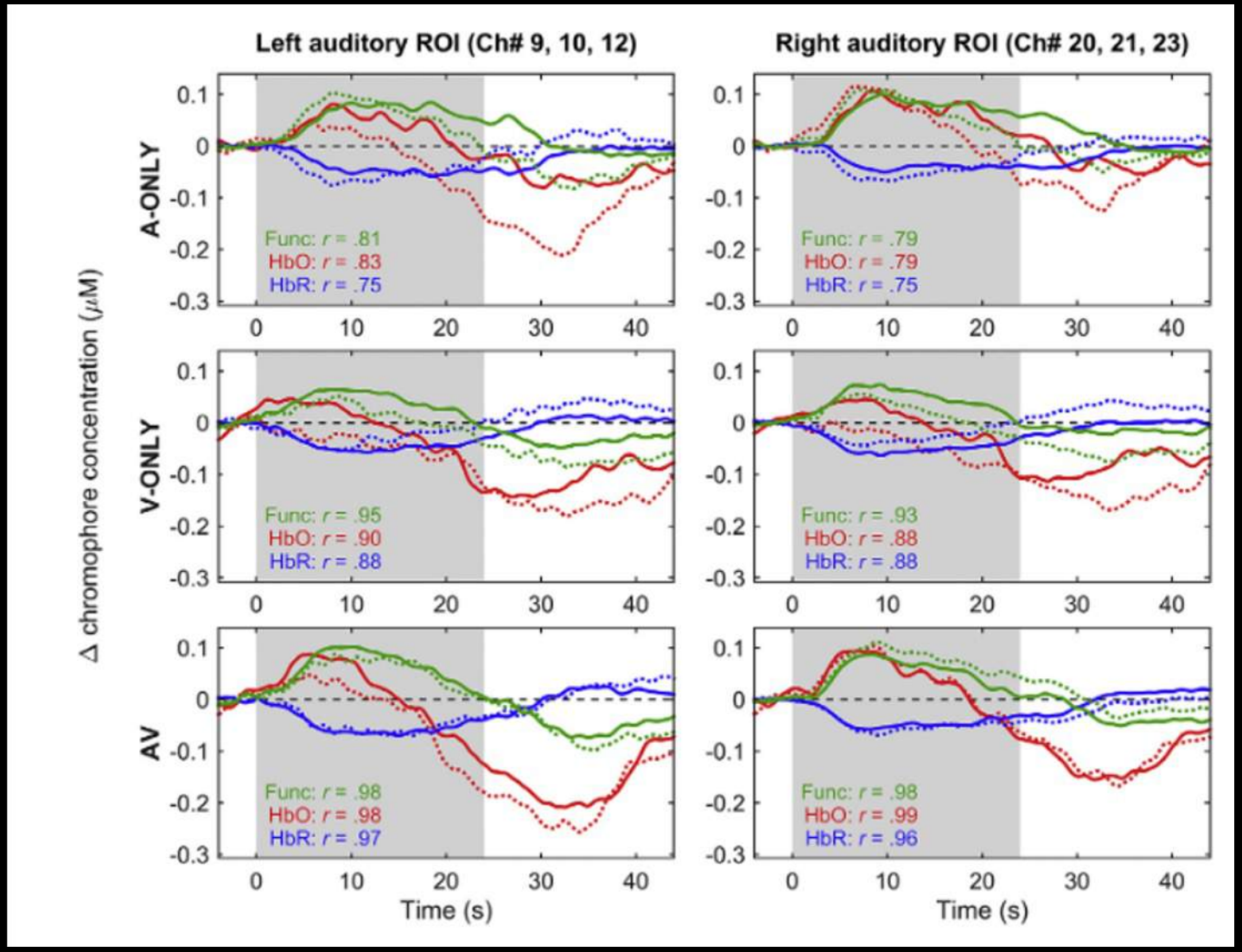


Fig. 1. (a) Schematic representation of one cycle of the block-design stimulus presentation paradigm; (b) Variability in optode positioning across six volunteers after registration to a standard atlas brain. Optode positions for each volunteer are represented by different coloured dots. Variability was similar in the left hemisphere (data not shown); (c) Aggregate sensitivity profiles for the predefined auditory regions-of-interest, which comprised the three highlighted measurement channels in each hemisphere. The colour scale depicts relative sensitivity logarithmically from 0.001 to 1.

WIGGINS 2016 -- RELIABILITY



WIGGINS 2016 -- RELIABILITY

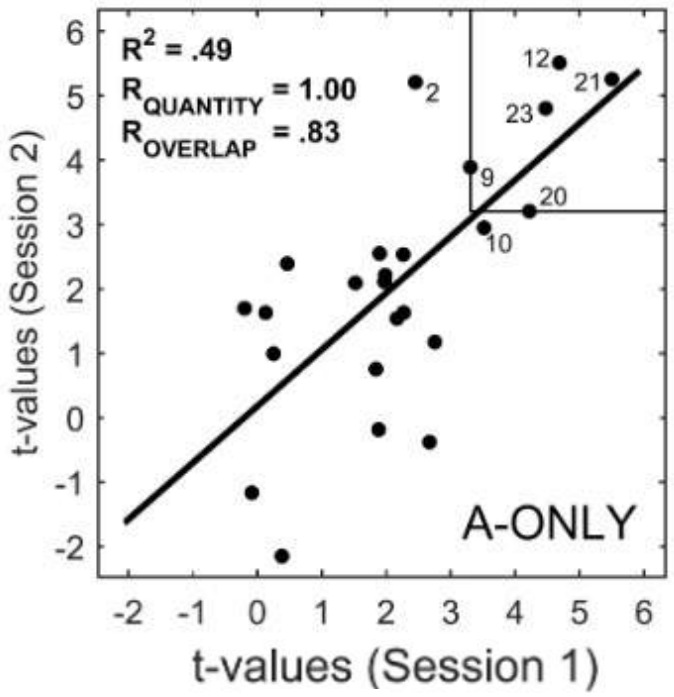


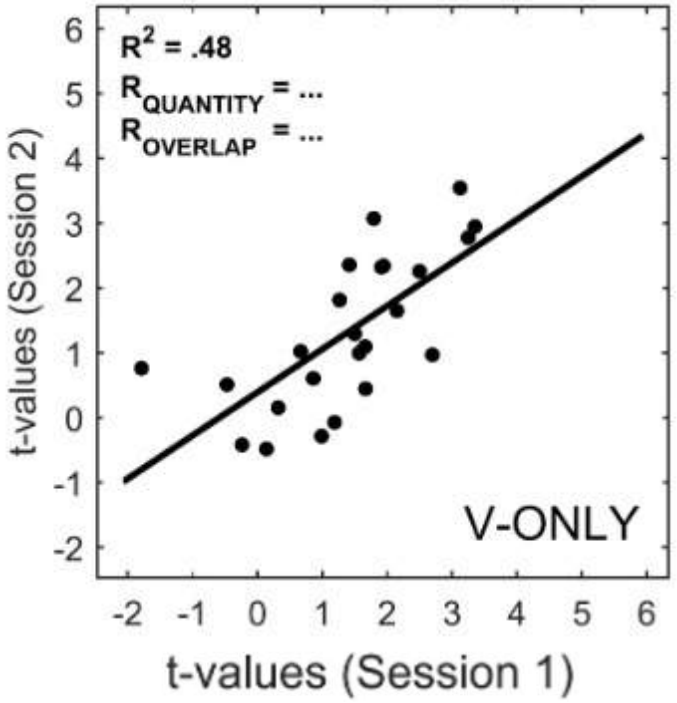
Grand-average time courses within the predefined ROIs for session 1 (solid lines) and session 2 (dotted lines).

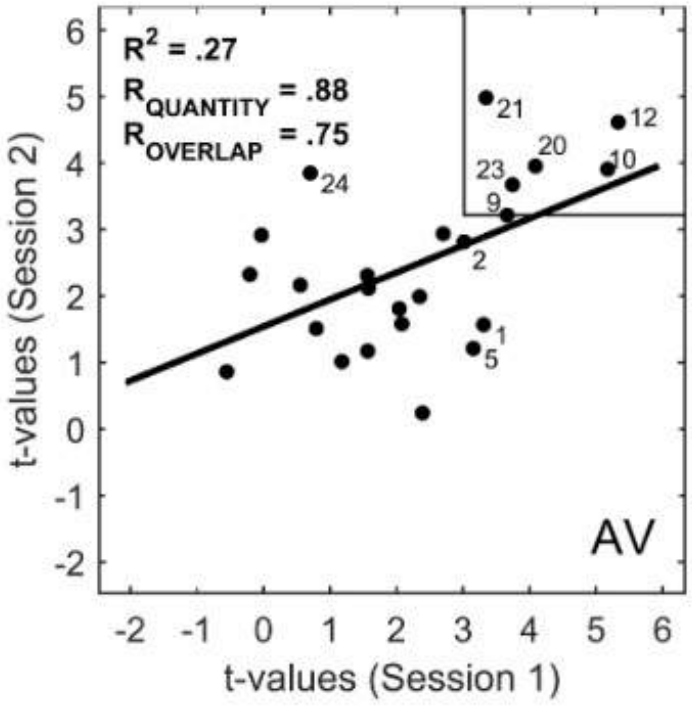
Results for each stimulation condition are shown in a separate row.

The shaded grey areas indicate the stimulation period.

WIGGINS 2016 -- RELIABILITY







OUTLINES

- What is fNIRS?
- What can we do with fNIRS?
- How shall we start fNIRS research?

Montage Design

- Design your montage.

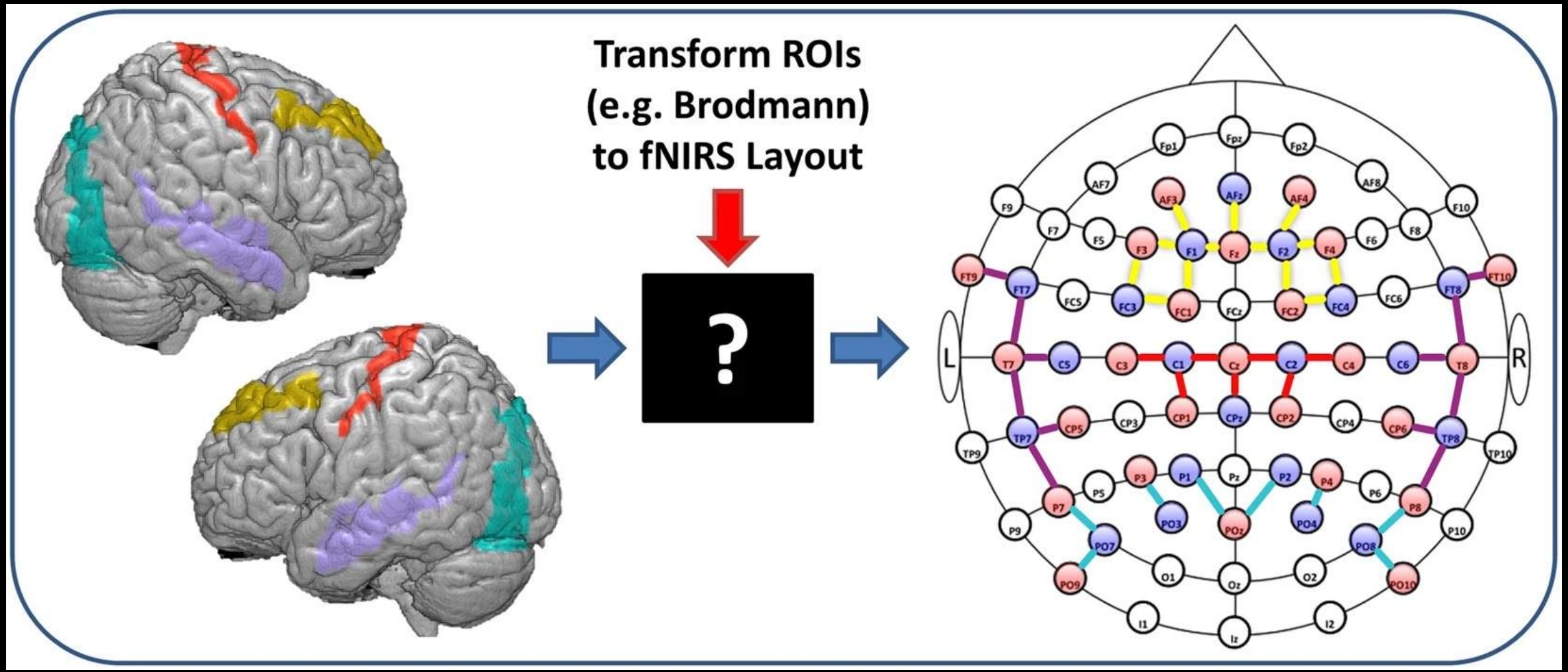
Study Design

- Design your task (s).

Test Runs

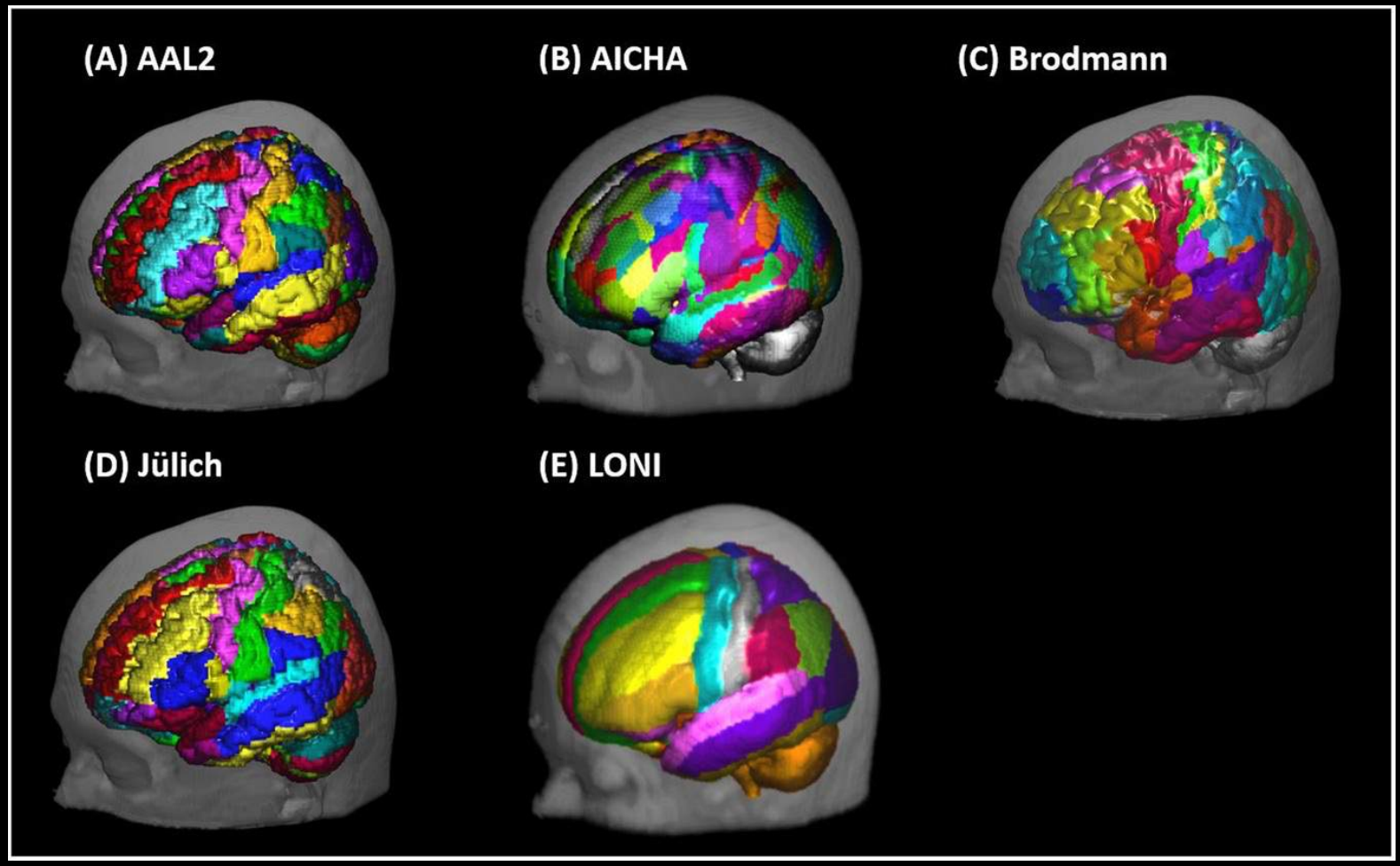
- Measure what you are intended to measure.

MONTAGE DESIGN

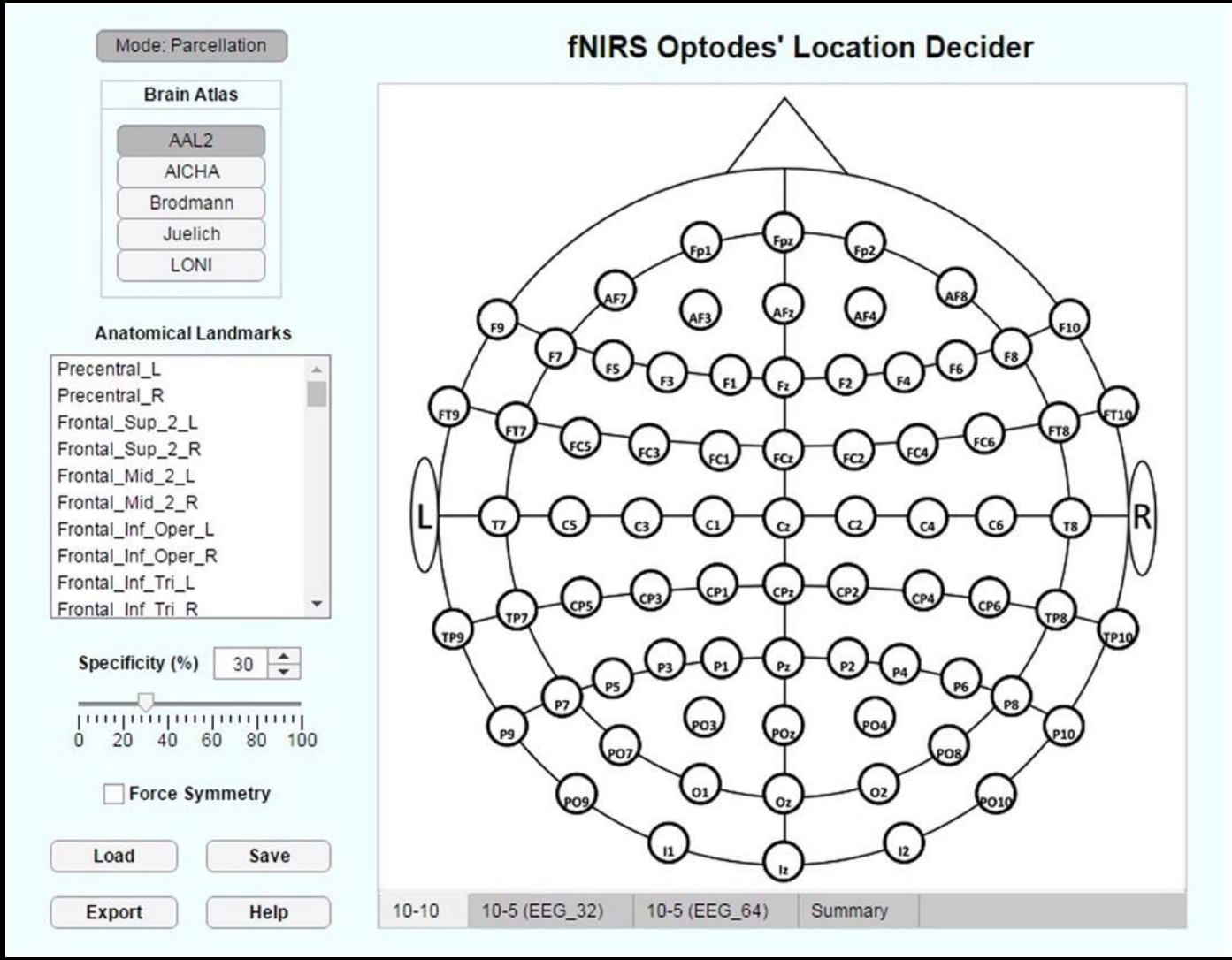


MONTAGE DESIGN

- fNIRS Optodes ' Location Decider fOLD: https://github.com/nirx/fOLD-public
- Zimeo Morais *et al, 2018 Neurophotonics*



MONTAGE DESIGN



- Graphical user interface of the fNIRS Optodes' Location Decider (fOLD).
- Depicted is the blank 10–10 layout as displayed upon toolbox initialization.
- Zimeo Morais *et al, 2018 Neurophotonics*

COREGISTRATION

1. Anatomical scans of each subject available. Accurate positions of optodes in 3D space on the head prior to measurement available.
2. No anatomical scans available. Accurate positions of optodes in 3D space available for each participant.
3. No anatomical scans available. Positions of optodes relative to standard 10/20 EEG landmarks available.
4. No anatomical scans available. Optodes have arbitrary positions over the scalp, no reference to standard landmarks

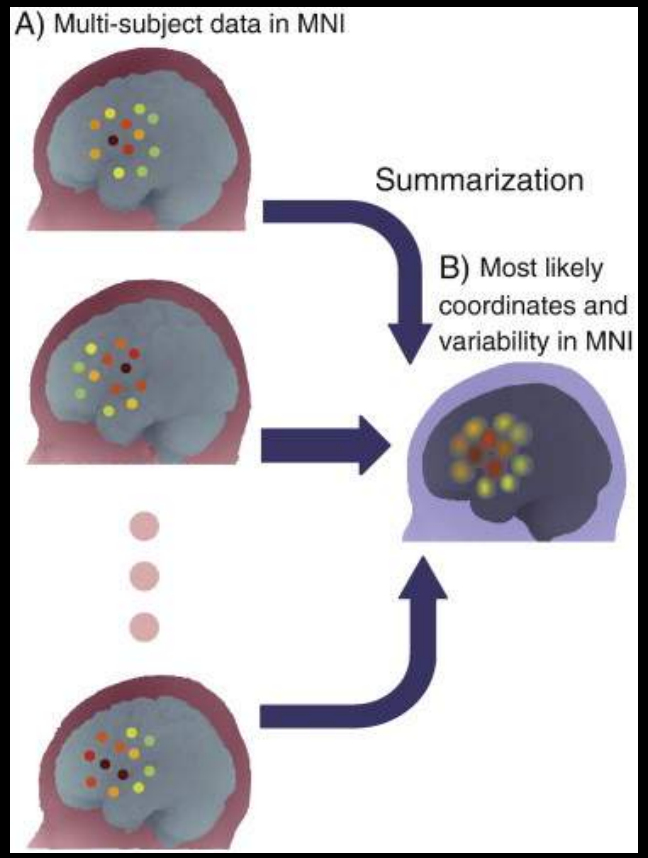
ACCURATE REGISTRATION ON INDIVIDUAL SUBJECT ANATOMY

+

Digitizer, contrast agent in scanner.

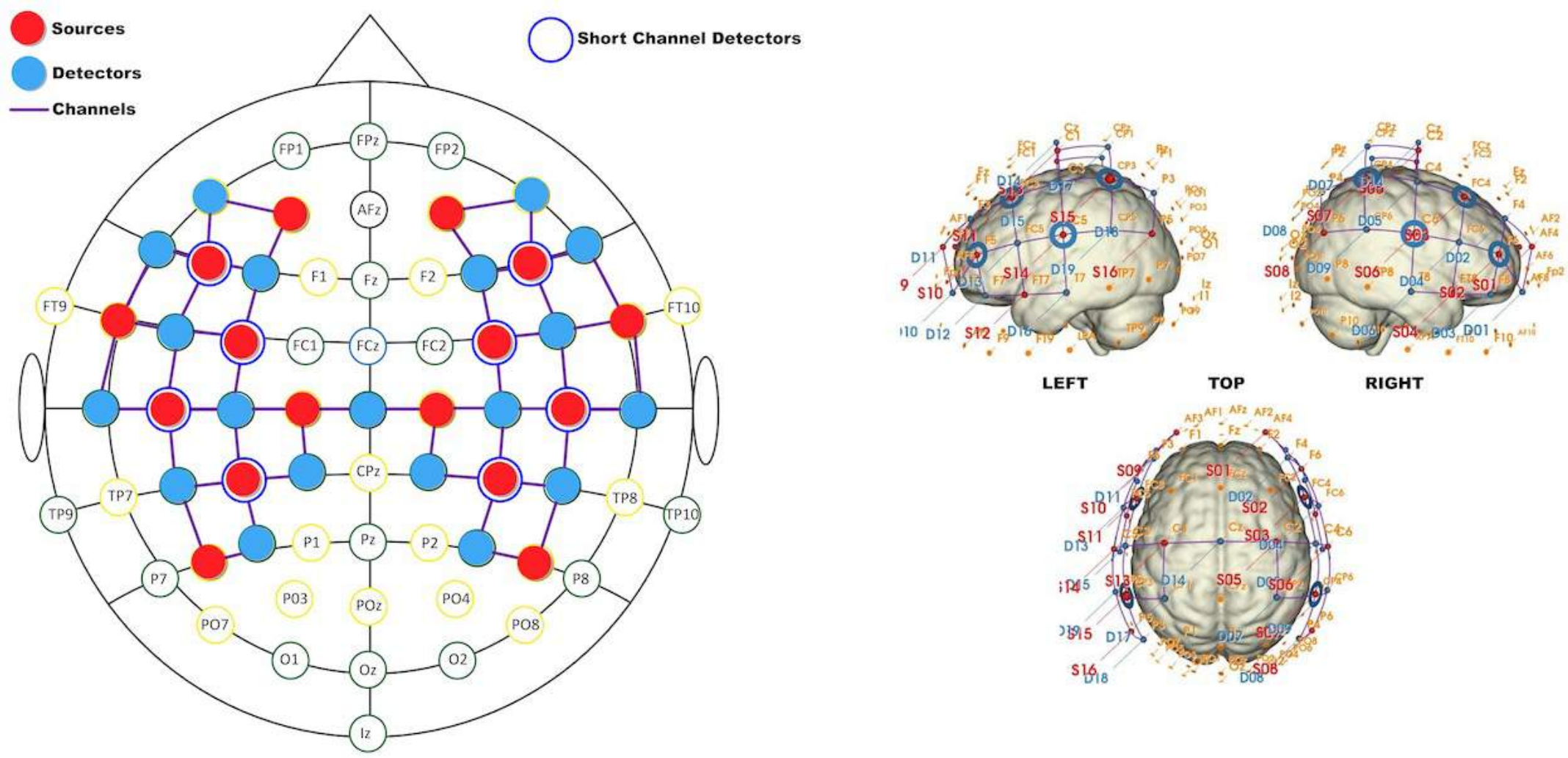
NO ANATOMICAL SCANS AVAILABLE. ACCURATE POSITIONS OF OPTODES IN 3D SPACE AVAILABLE FOR EACH PARTICIPANT

- In this case, there is no need for normalization of individual anatomies. Digitized positions of optodes are projected onto a standard template.
- Cortical structures of interest are then identified as previously.



Tsuzuki, 2014

NO ANATOMICAL SCANS AVAILABLE. POSITIONS OF OPTODES RELATIVE TO STANDARD 10/20 EEG LANDMARKS AVAILABLE



MONTAGE DESIGN

- The Trade Off:
  - Number of channels: Children vs Adult
  - How much time do you have
  - What is your subject's tolerance
- Channel Spacing
  - Infant Children: 1.5-3 cm
  - Adults: 2.5-5 cm
  - Regions of interest: Channel Averaging
  - Subjects Head Size
  - Including these distances in your analysis

Montage Design

- Design your montage.

Study Design

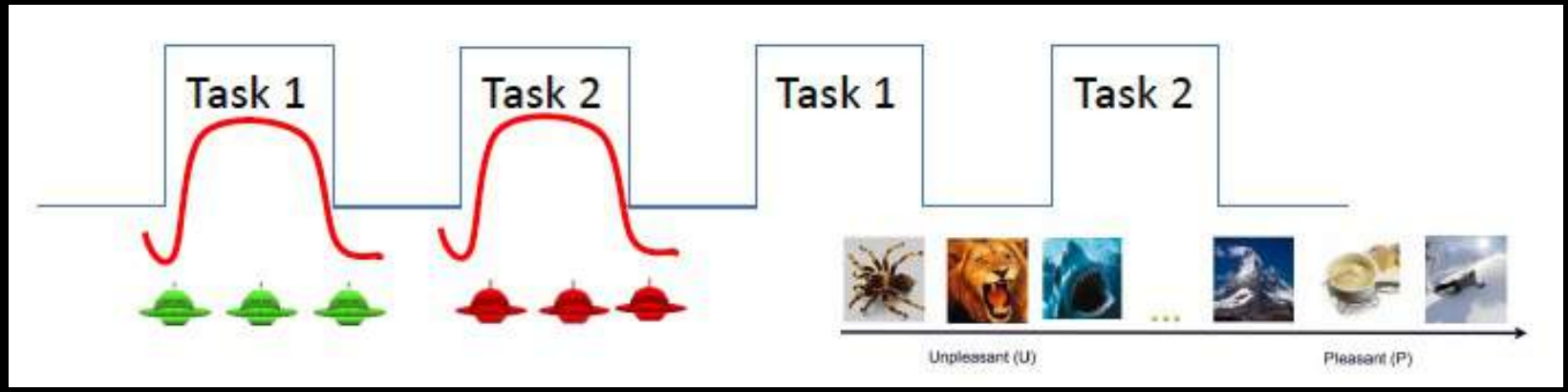
- Design your task (s).

Test Runs

- Measure what you are intended to measure.

EXPERIMENTAL DESIGN

- What type of task design should be implemented?
- Simple Block Design
  - Improving Signal to Noise Ration (SNR)
  - Like fMRI studies / Repeatable
  - Grouping similar tasks or event
- Not so flexible to the complexity

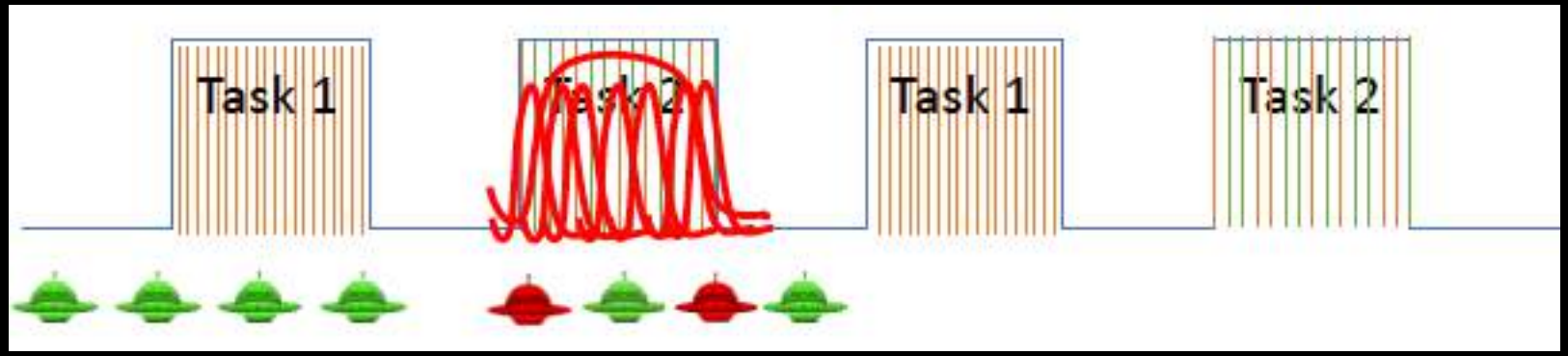


EXPERIMENTAL DESIGN

- Event Related
  - Characterizing the shape of the hemodynamic response
  - You need more trails
  - Timing cost
  - Great if you want to reduce the effect of habituation and expectation
  - Good for behavioral studies, and combining with EEG

EXPERIMENTAL DESIGN

- Mixed Block Design
  - Efficient in detecting the differences in Hemodynamic response amplitude
  - You are generally interested in the size of Hemodynamic response
  - More trials in less time than event related design
    - spacing trials apart to get an estimate for each individual event

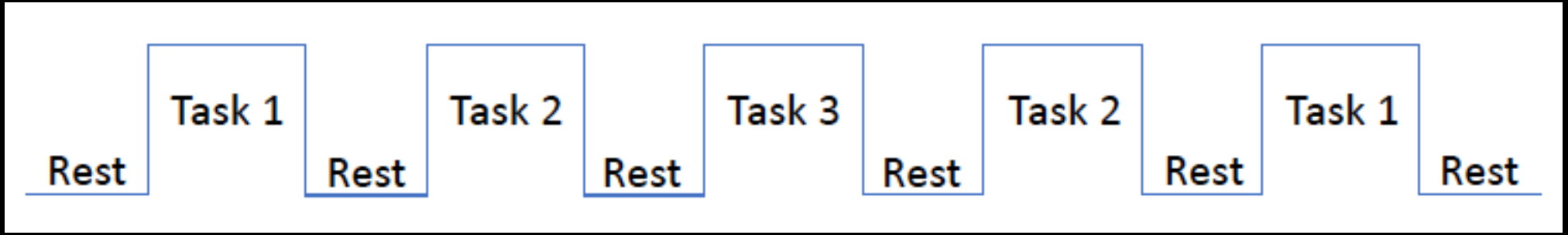


EXPERIMENTAL DESIGN

- Be aware of task length
  - Min ~10 15 seconds per block to capture the hemodynamic response
  - Resting blocks in between to allow the decline
- Randomizing the blocks
- More repetition is better
  - Efficiency of the design can increase with number of blocks
- Collect imaging data for each task in one session
  - Unless you need to compare the data before and after therapy etc.
  - Ensure that your task conditions and environment stay the same.

EXPERIMENTAL DESIGN

- How many rest periods do you need?
  - As much as your task condition.
  - You can sometimes use this rest period to see if you task is working.
  - Better efficiency when the rest timing is equal to average stimulation time of the task related conditions.

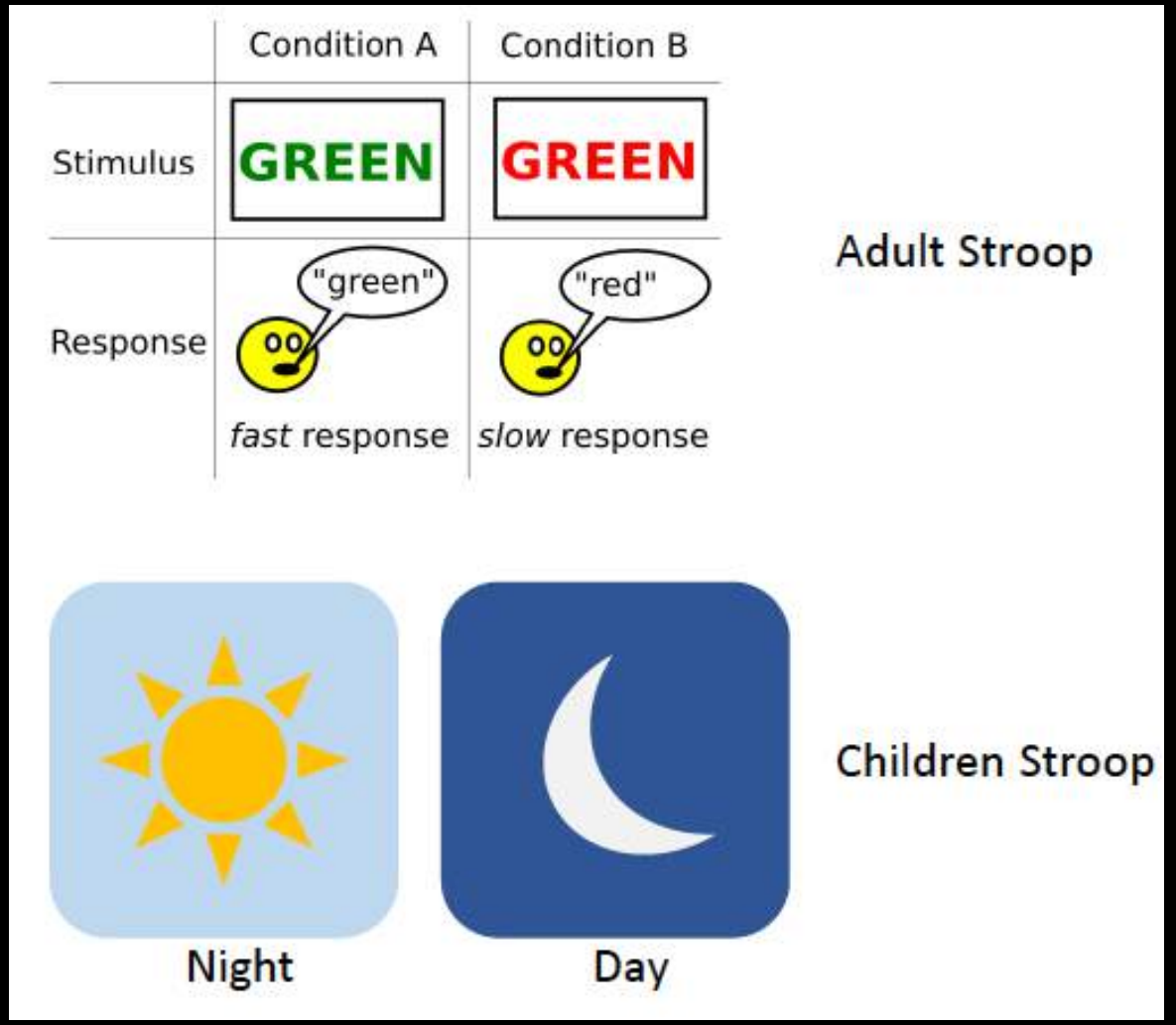


EXPERIMENTAL DESIGN

- Be mindful of your subject population
  - Age correlates with attention span
  - Behavioral phenotypes correlates with both attention and task difficulty
  - Cognitive flexibility can be an issue
  - Changing the task to accommodate the subject population
  - Controlling for subject age, IQ etc. in your analysis

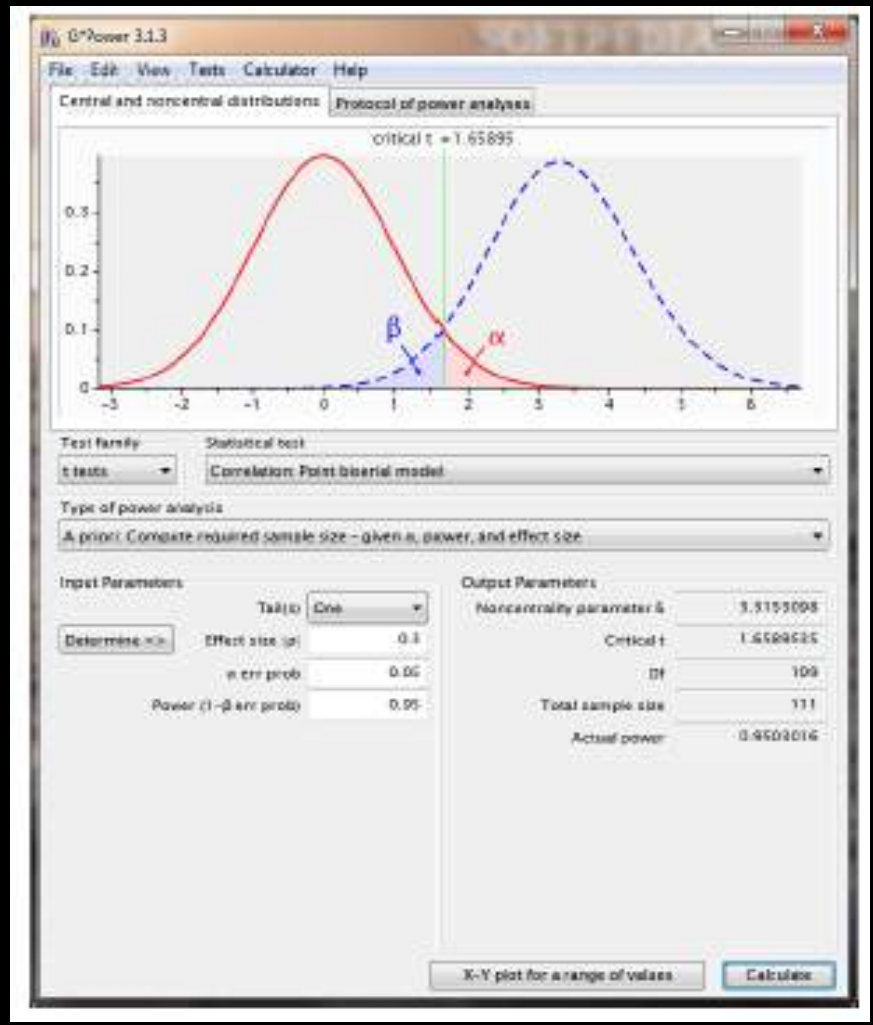
EXPERIMENTAL DESIGN

- Task modification
  - Based on age range
  - Based on neurocognitive profile
  - The type of task depends on your research question, neurocognitive profile and behavioral phenotype



EXPERIMENTAL DESIGN

- Sample Size: Increase the efficiency
  - Study power depends more heavily on number of subjects
- Variability within subject
  - Hair vs no hair
  - Age --> extracerebral tissue
  - Gender --> extracerebral tissue
  - Think about DPF



Montage Design

- Design your montage.

Study Design

- Design your task (s).

Test Runs

- Measure what you are intended to measure.

PILOT DATA COLLECTION

Collect	Analyze	Check
Collect at least pilot data from two participants.	Analyze your pilot data.	Check if your experimental design measures what you expect to measure.

IF YOU WANT TO LEARN MORE NEUROIMAGING TECHNIQUES, YOU CAN TAKE SLPA 856.

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COURSE RECOMMENDATION

- **SLPA 856: Neuroimaging & Language Development – offered every fall semester. Credit: 2-3**

- If you are interested in this course, please email me at yingying.wang@unl.edu

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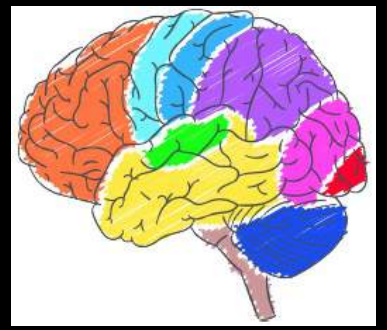

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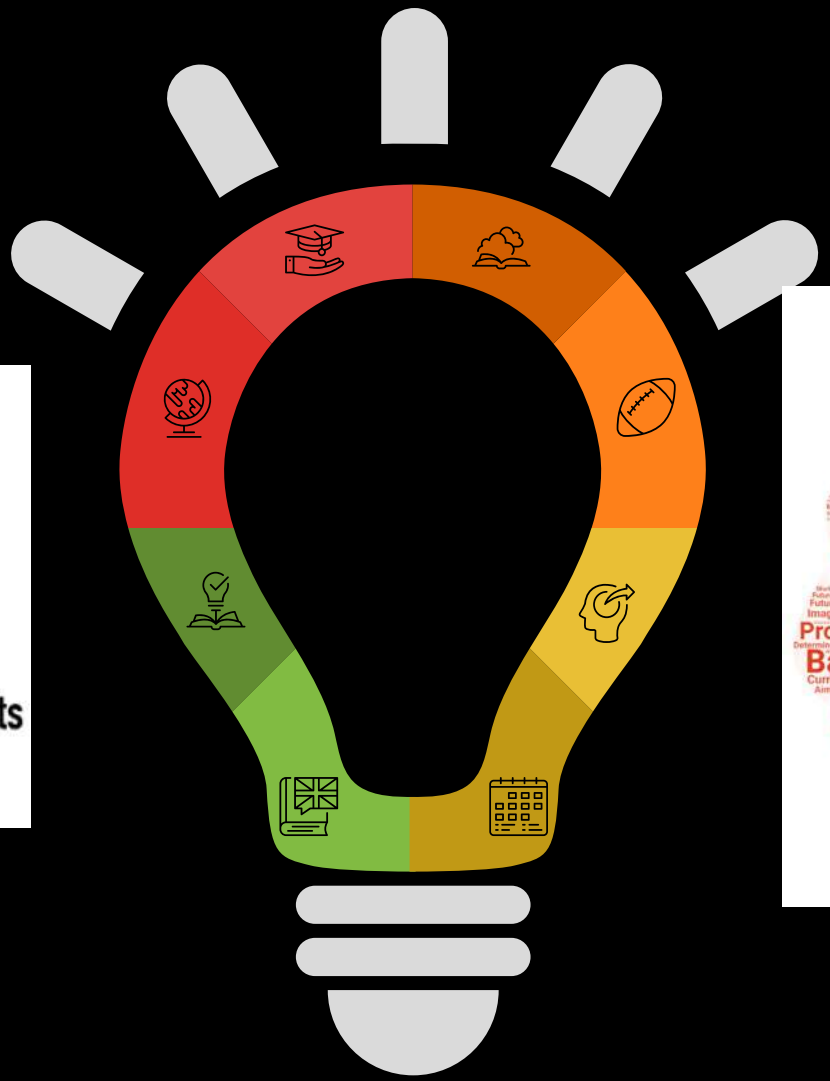

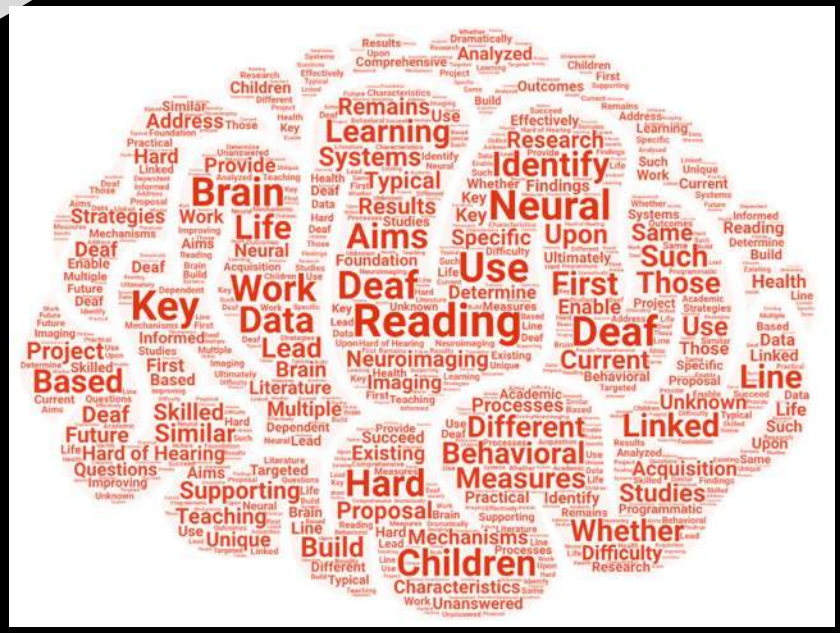
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