fNIRS原理簡介&實驗設計

教育訓練工作坊

http://www.ym.edu.tw/~cflu/CFLu_course_fnirsWorkshop.html

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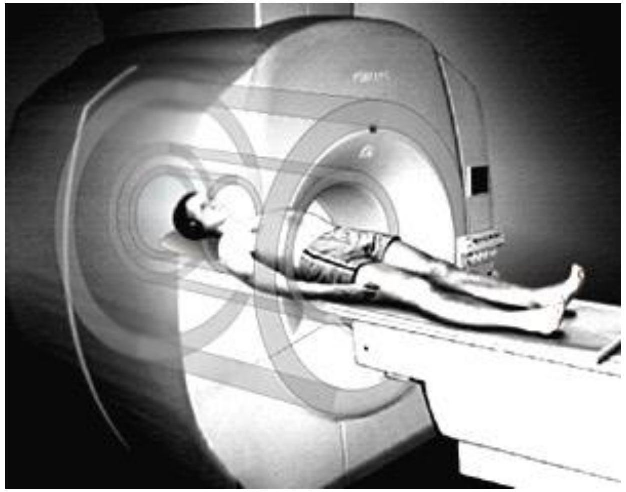
講習內容安排

- **9:00~10:20 fNIRS原理簡介&實驗設計**
- 10:30~12:00 NIRSport2硬體介紹&操作
- 12:00~13:30 用餐與休息
- 13:30 ~14:50 Homer 3訊號處理
- 15:10~16:00 基礎統計分析&GLM

fNIRS原理簡介

Basic Principles of fNIRS

Monitoring Brain Activity

EEG/MEG	fMRI	fNIRS
		

EEG/MEG

- **High temporal resolution**
- **Neural activity**
- Superficial cortex
- **Semi-open/close environment**
- **Low cost**
- Physiological noise
- Electronic noise

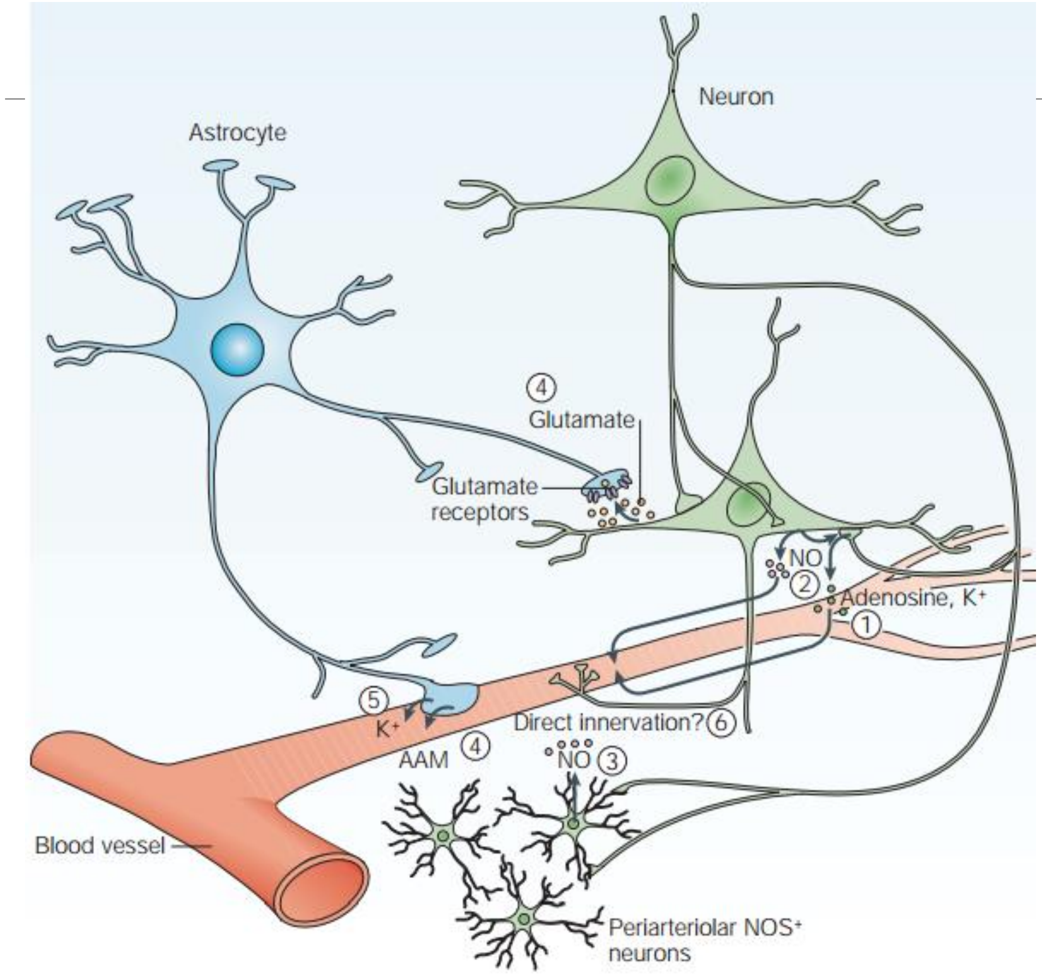
fMRI

- Low temporal resolution
- BOLD signal
- **Superficial & deep cortex**
- Close environment
- High cost
- **High spatial resolution**
- **High tissue contrast**
- Magnetic and posture limitation

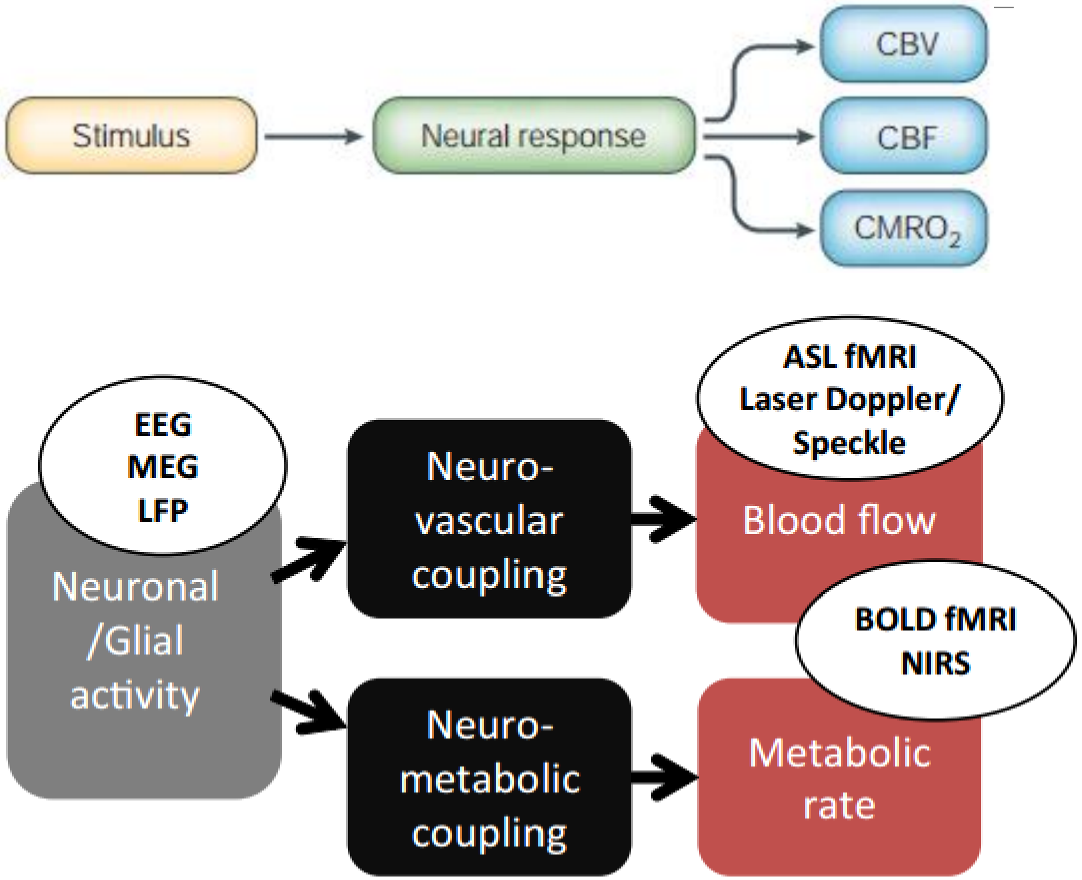
fNIRS

- **High temporal resolution**
- Hemoglobin oxygenation
- Superficial cortex
- **Open environment**
- **Low cost**
- **Wearable system**

Neurovascular Coupling

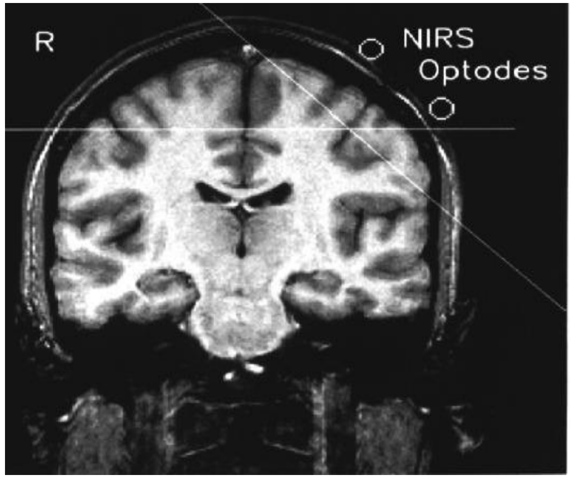


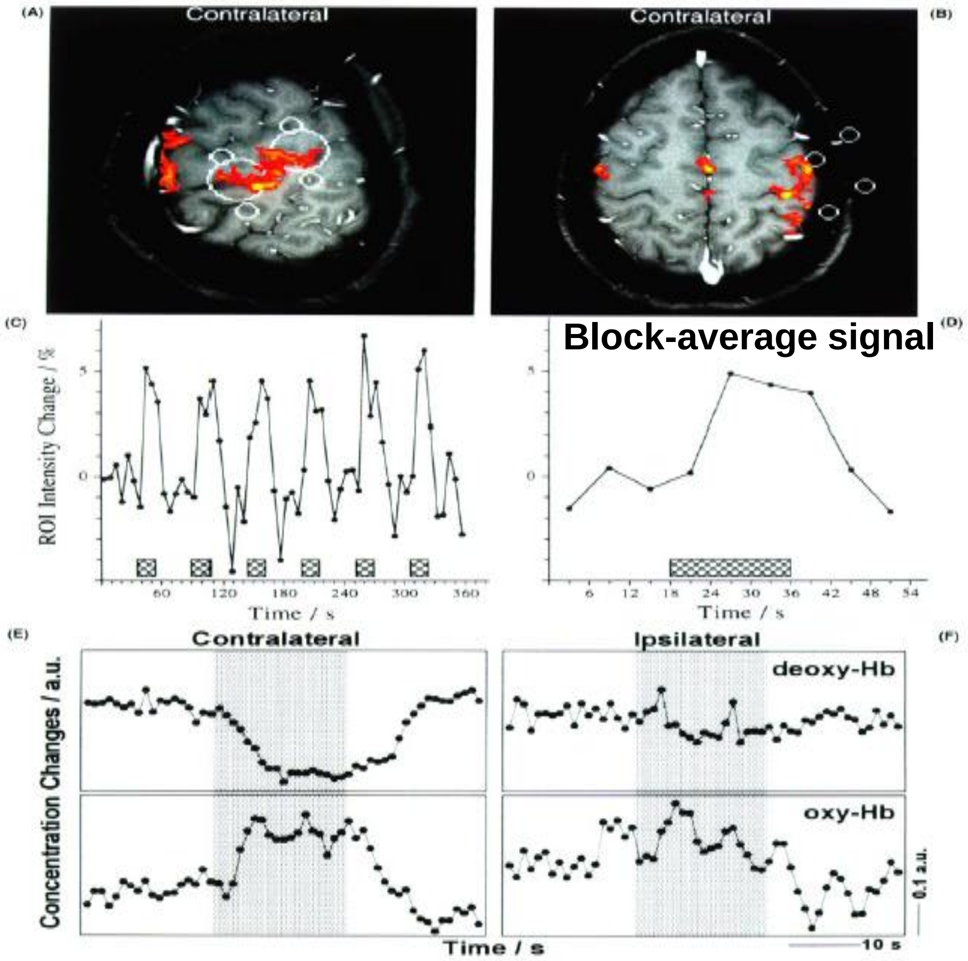
D'Esposito et al, Nature Reviews Neuroscience, 2003.



Huneau et al, Frontiers in Neuroscience, 2015.

fNIRS vs. fMRI (finger taping)





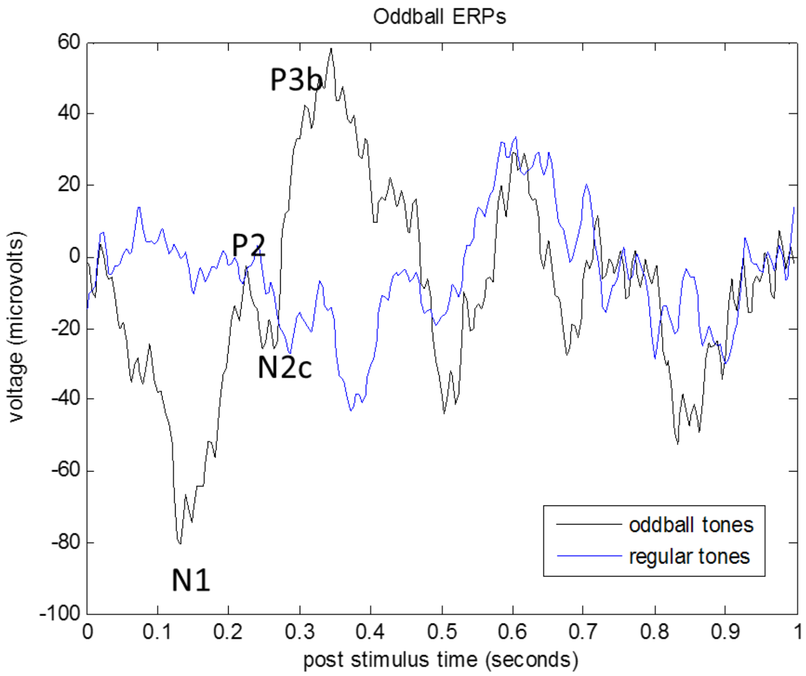
JCBFM. 1996, 16:817-826.

- **Decreases in deoxy-Hb, which reduce the microscopic susceptibility effects, yield fMRI BOLD signal increases.**

fNIRS vs. EEG (oddball task)

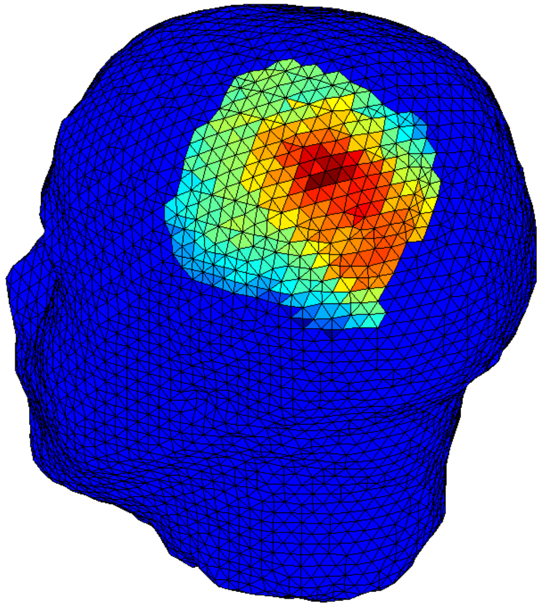
fNIRS + Mindo

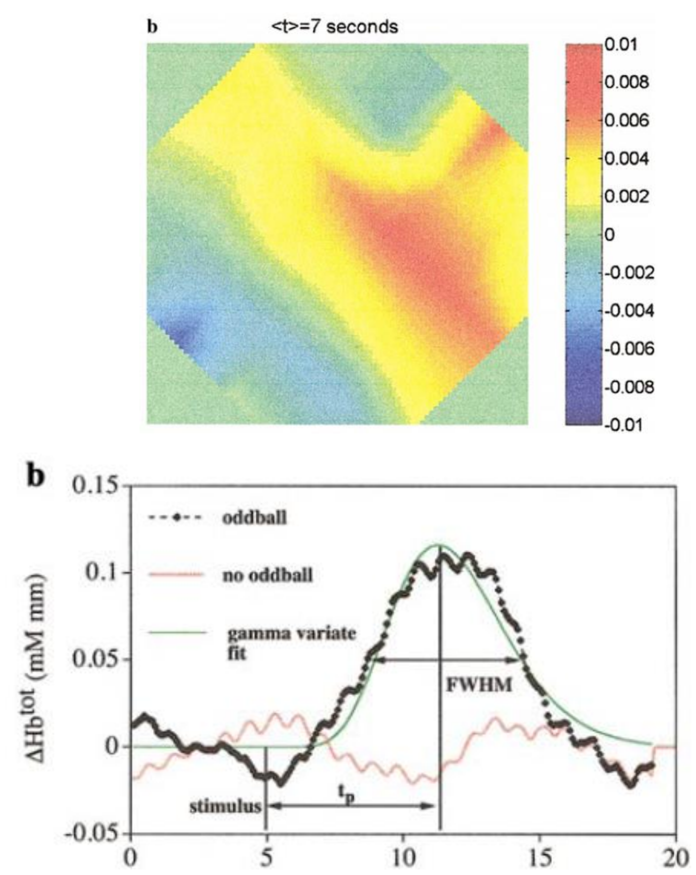
EEG at Pz



fNIRS

4.2s after stimuli





Kennan et al. NeuroImage 2002: 16, 587-592.

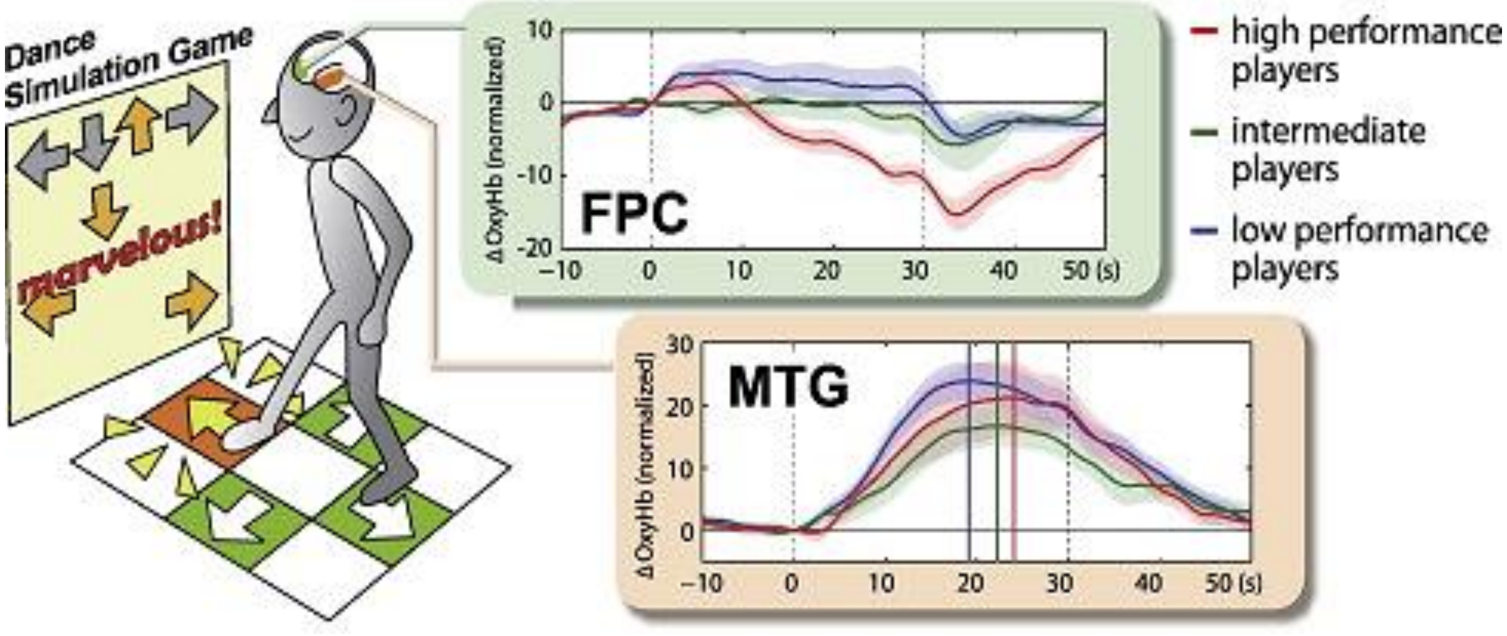
1000 Hz tone

2000 Hz oddball

Open Environment

Frontopolar cortex (FPC): top-down regulatory mechanisms of motor behavior;
Middle temporal gyrus (MTG): bottom-up integration of visual and auditory cues.

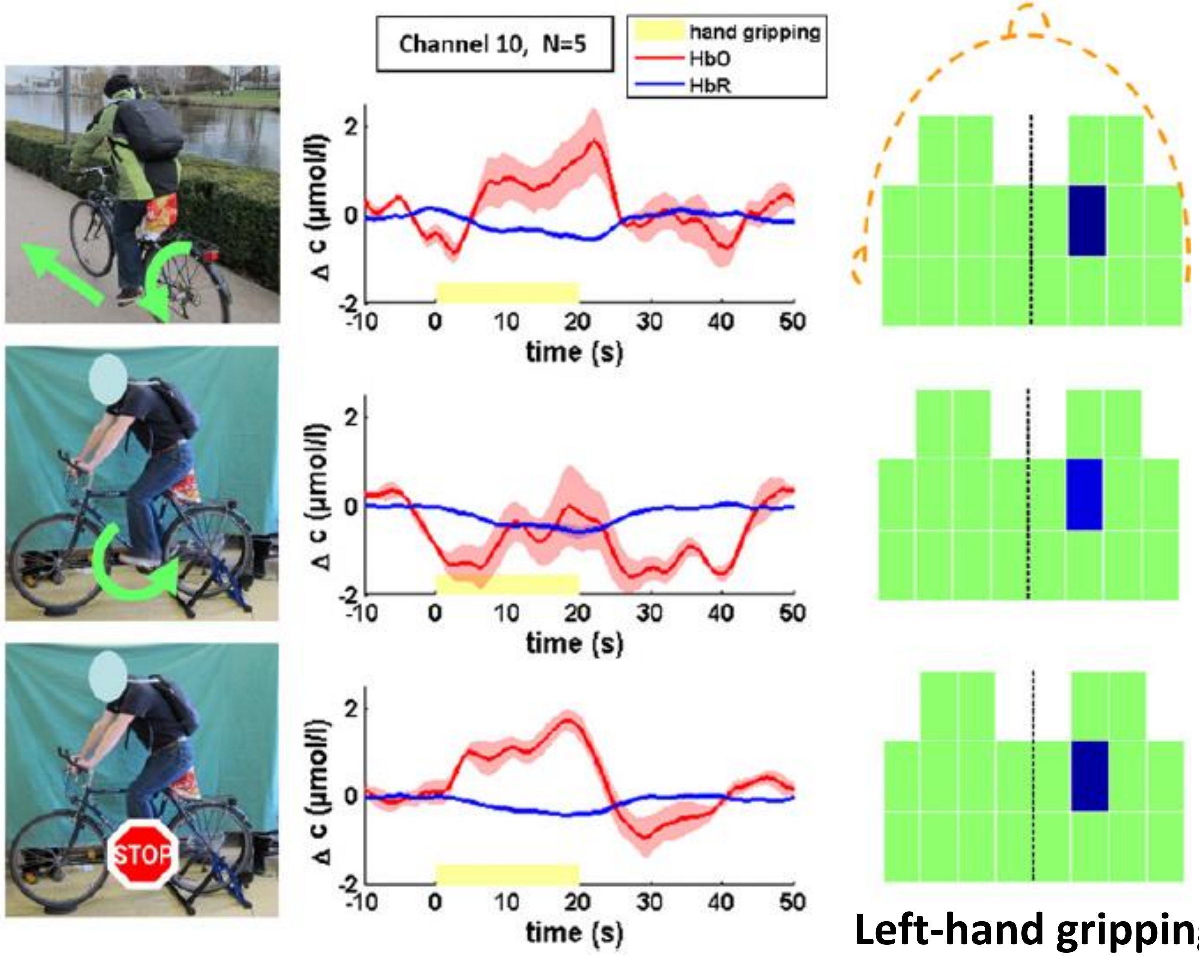
J. Adam Noah, Journal of Visualized Experiments, 2015.



NeuroImage 85 (2014) 461–470.

Open Environment

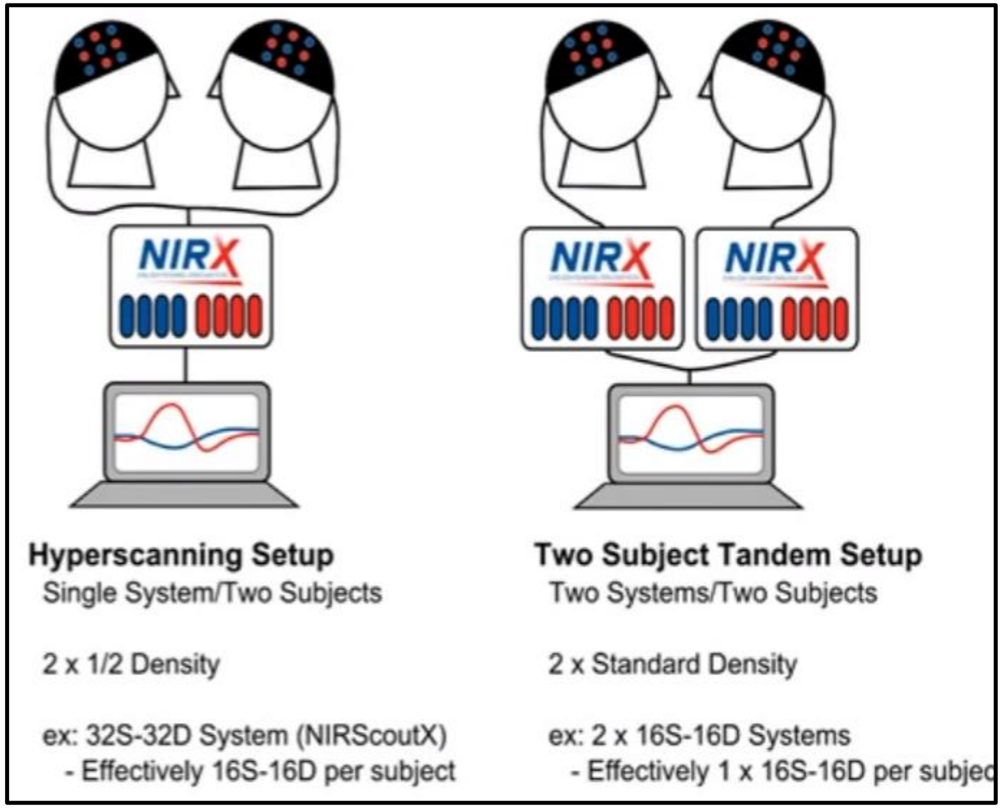
NeuroImage 85 (2014) 64–71



Left-hand gripping

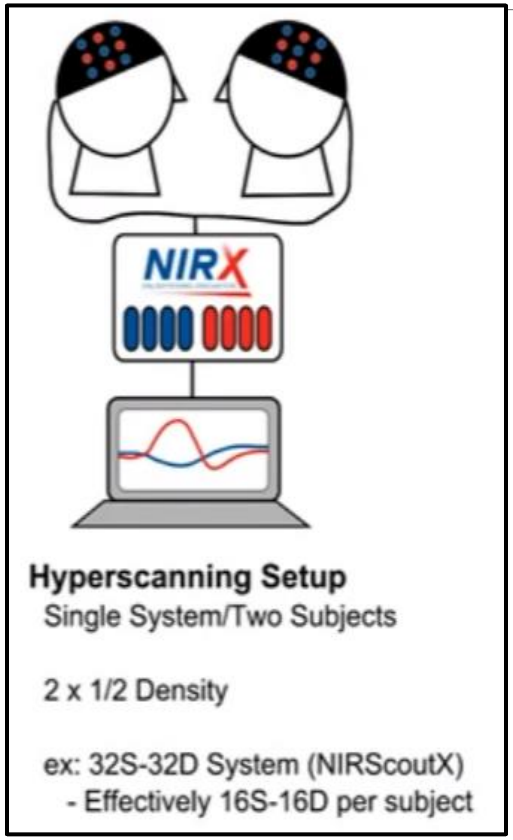
Interaction/Competition

Social cognition is fundamentally different when we interact with others rather than merely observing them.



NIRx Medical Technologies, http://nirx.net/nirscout/

Interaction/Competition



NIRx Medical Technologies

http://nirx.net/nirscout/

fNIRS Instruments

< portable/movable >

ISS instrument

NIRx NIRScount

Hitachi ETG-4000

DYNOT system

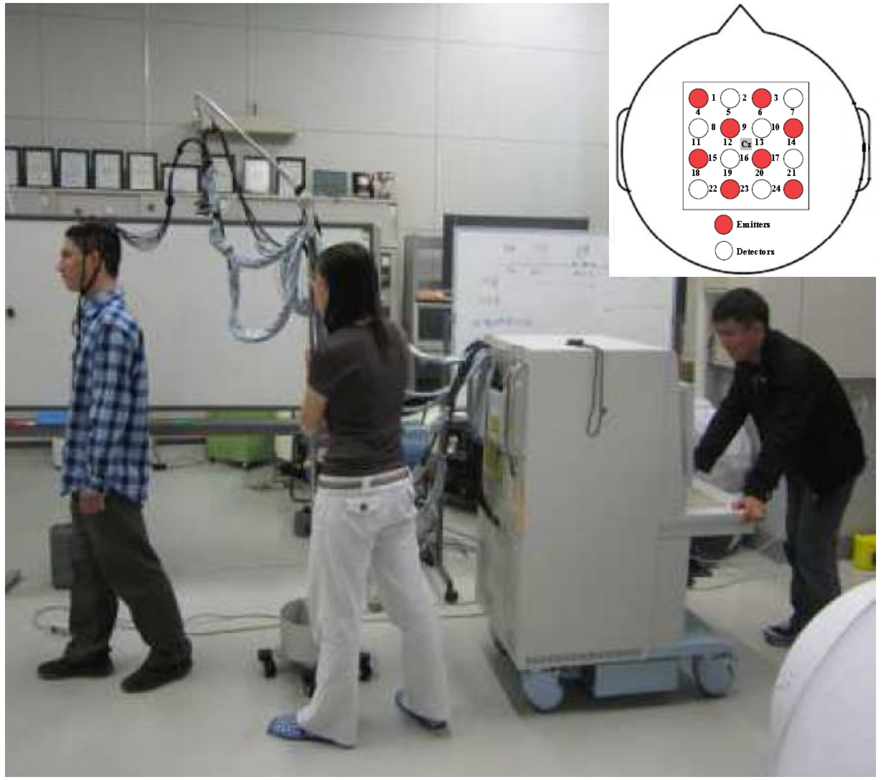
< wearable >

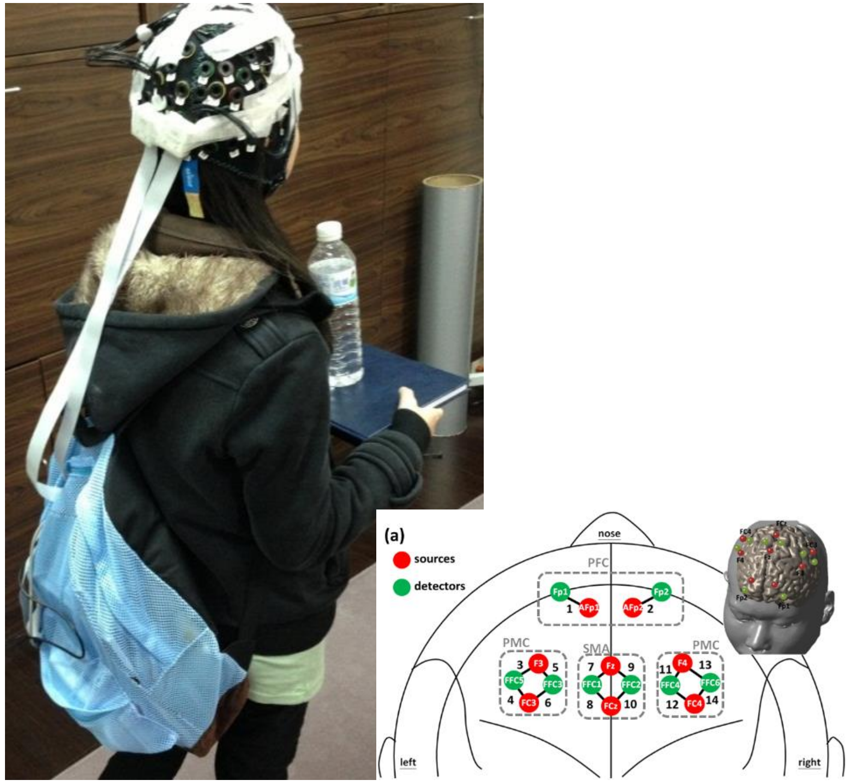
NIRx NIRSport 8x8

NIRx NIRSport2 16x16

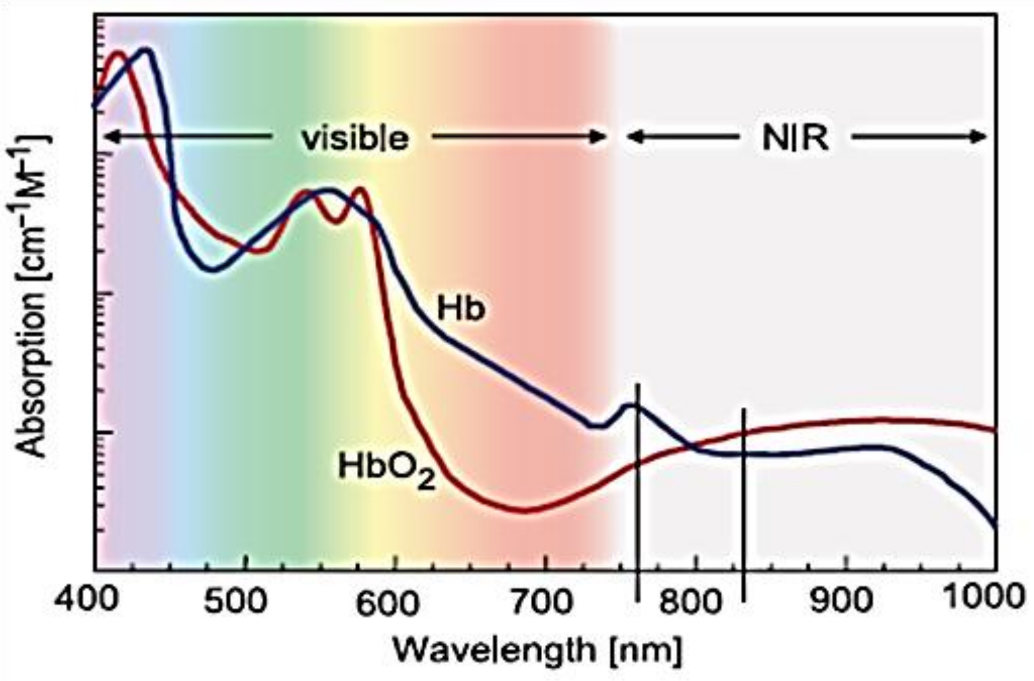
Hitachi WOT-100

Size, Does it matter?

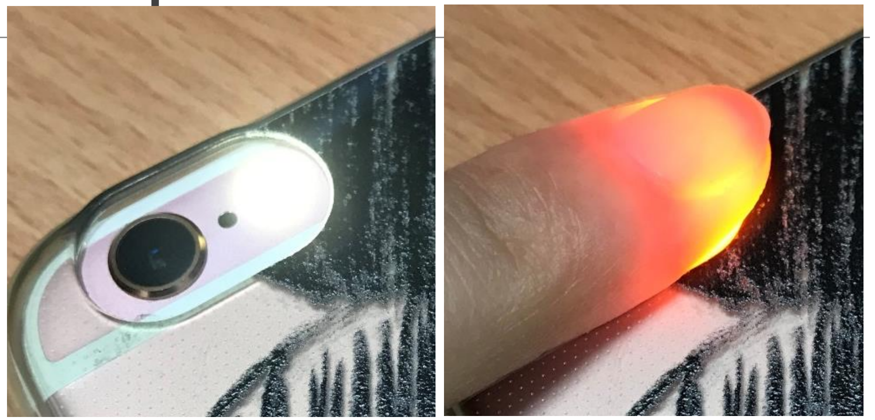




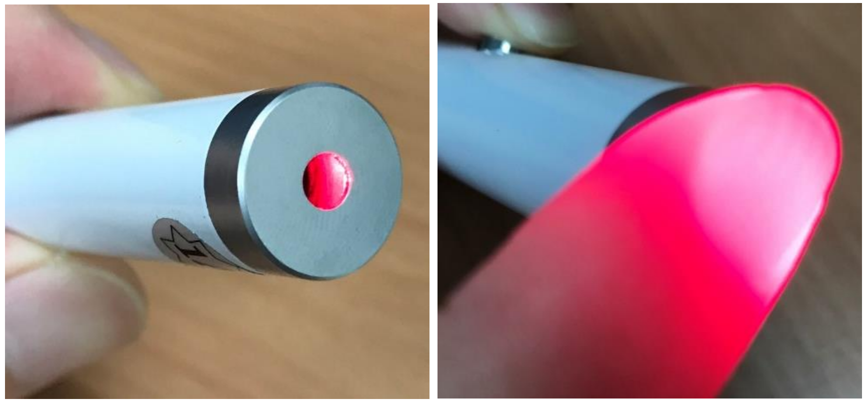
Tissue Migration and Absorption



$$\mu_{780nm} = \varepsilon_{HbO_2}(780nm)\times c_{HbO_2} + \varepsilon_{Hb}(780nm)\times c_{Hb}$$
$$\mu_{820nm} = \varepsilon_{HbO_2}(820nm)\times c_{HbO_2} + \varepsilon_{Hb}(820nm)\times c_{Hb}$$

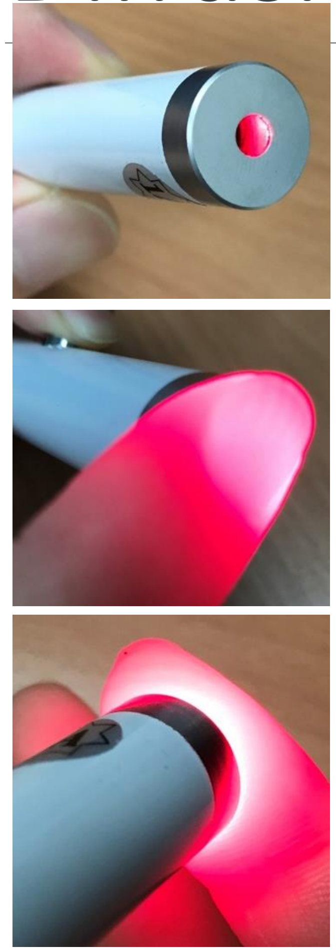


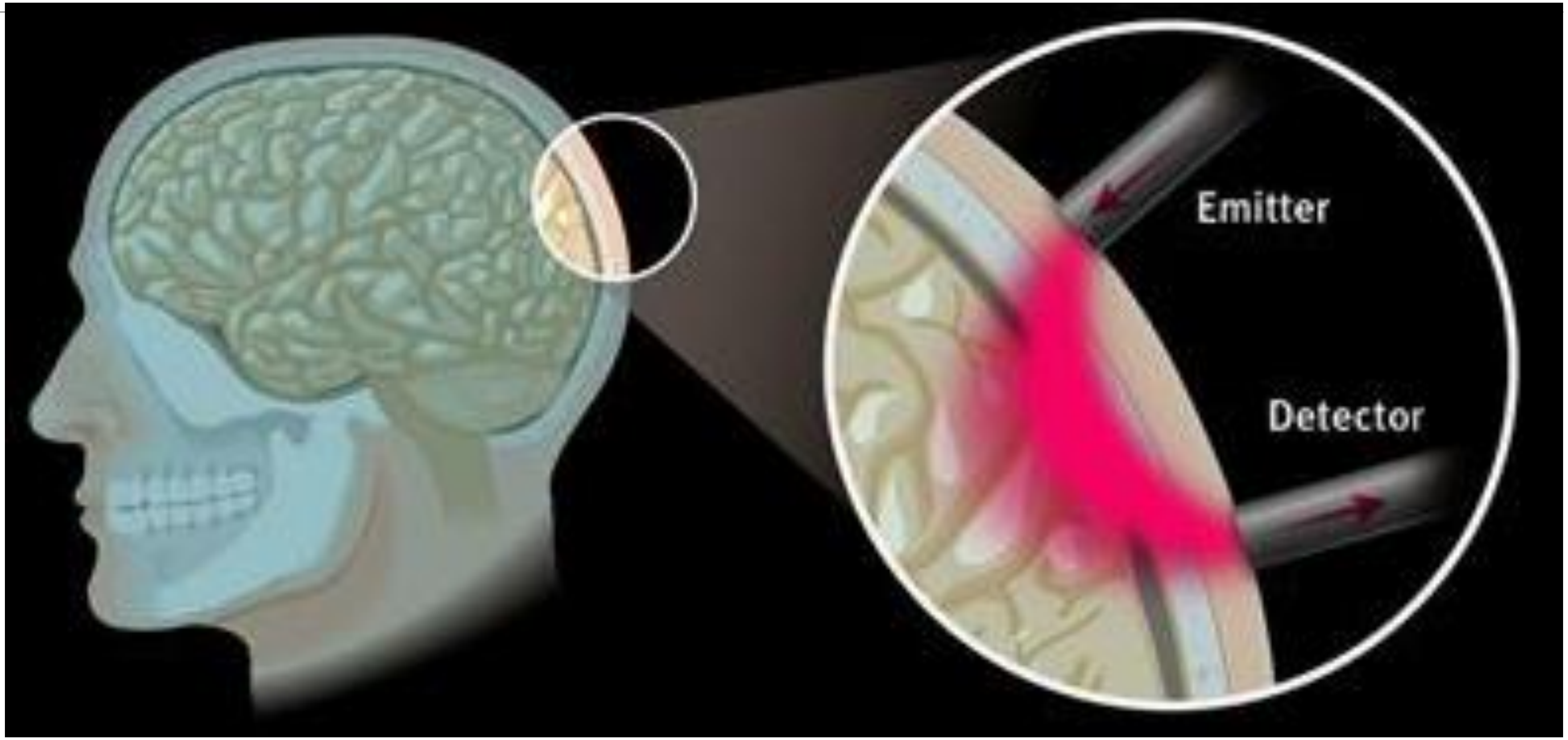
lower absorption within Near-infrared wavelength.



Near-infrared photons perform diffusive motion.

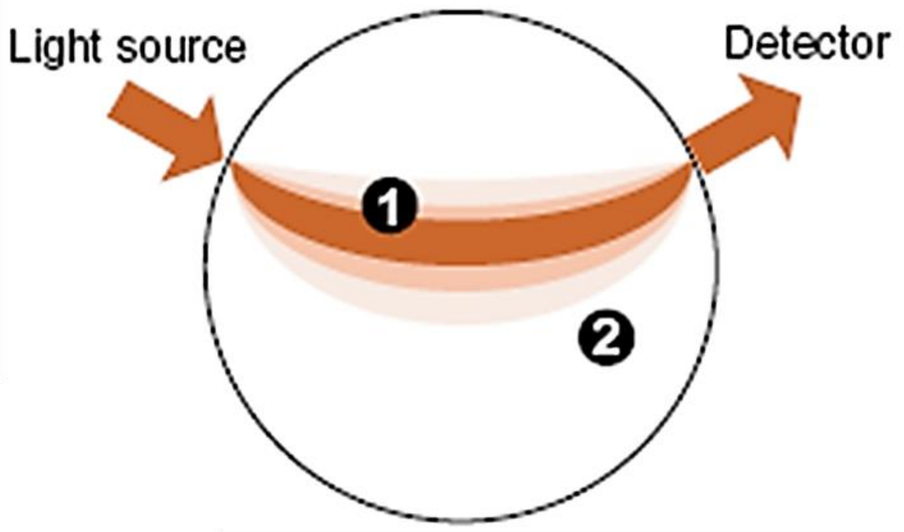
Diffusive Motion



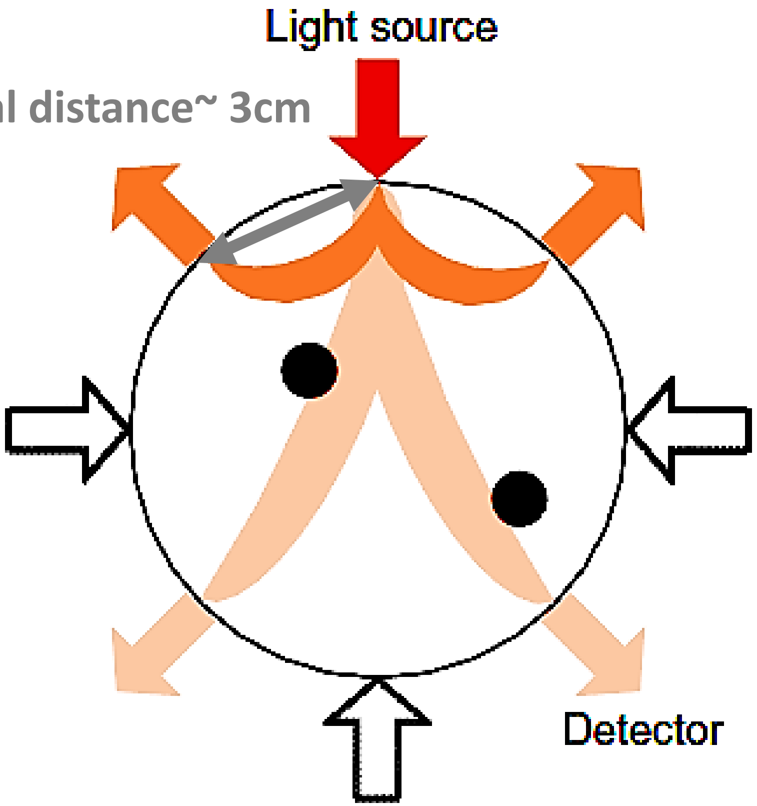


Absorption and scattering

Source-Detector Arrangement

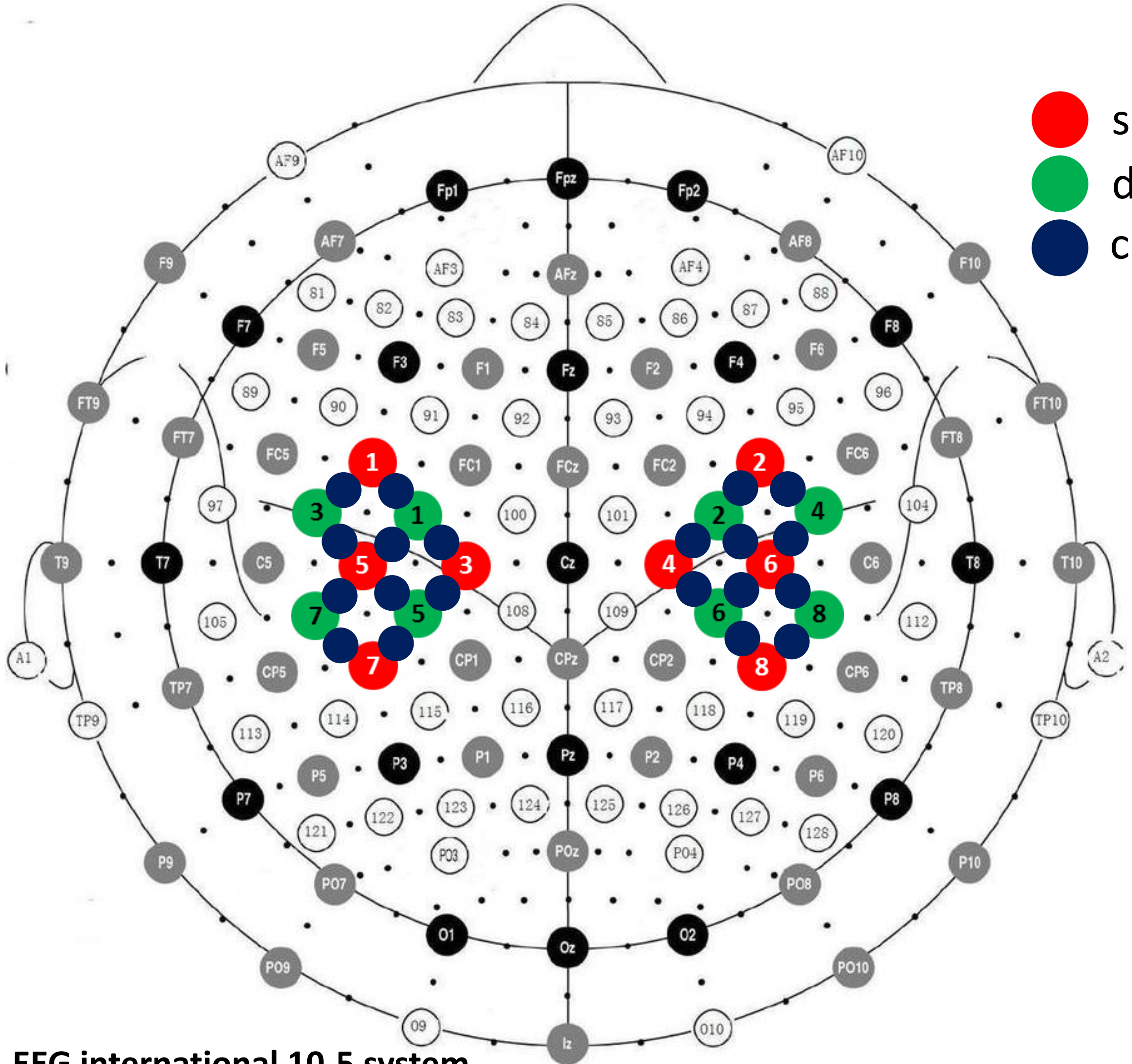


Diffusive motion
Banana-shape distribution



Spatial encoding → fire one source at one cycle

Source-Detector Arrangement

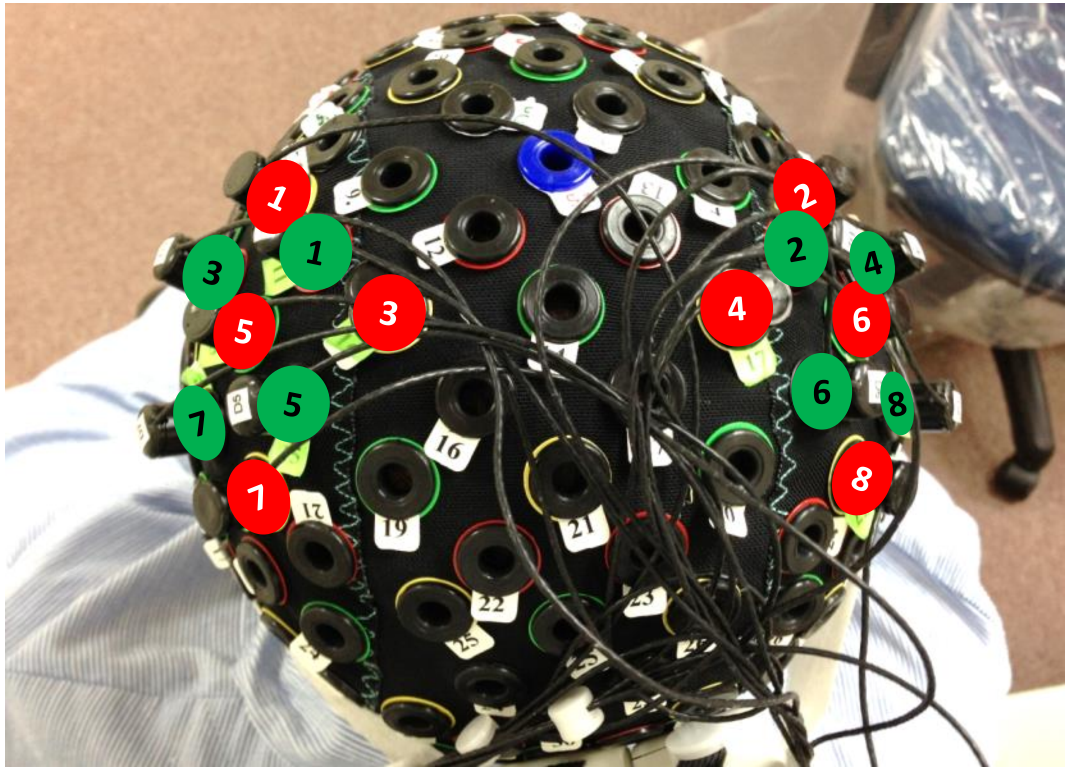


EEG international 10-5 system

sources

detectors

channels

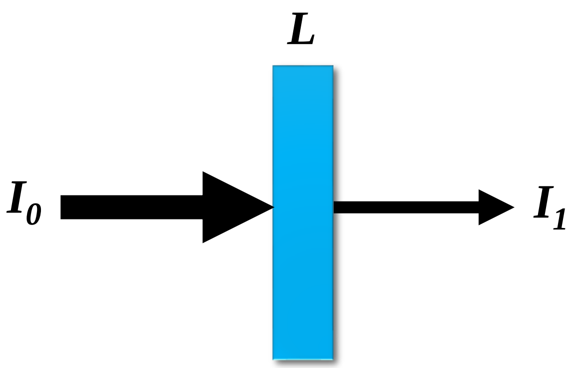


Beer-Lambert Law

Describe the attenuation of light propagating in a homogeneous medium.

$$I_1 = I_0 \exp(-\mu_a(\lambda)L)$$

I_0: the incident light
I_1: the light leaving the medium
L : the propagation path length
μ_a : the absorption coefficient



non-scattering &
homogeneous medium

A Mixture of Chromophore

The sum of the products of the concentration of each chromophore c_n with its molar extinction/absorption coefficient ε_n.

$$\mu_a(\lambda) = \sum_n \varepsilon_n(\lambda) c_n$$

< Blood >

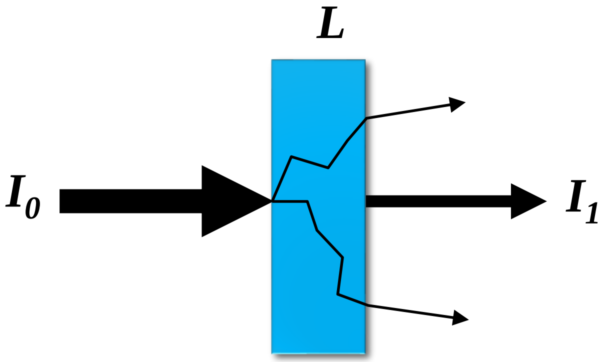
- White blood cells and platelets <1%
- Red blood cells ~44%
- Plasma ~55%

The individual extinction coefficient of each chromophore represent their absorption at a particular concentration ($cm^2 \cdot mol^{-1}$).

Scattering Events

Refractive index mismatches at boundaries.

$$I_1 = I_0 \exp(-\mu_s(\lambda)L)$$



μ_s : the scattering coefficient

The scattering path length, defined as $1/\mu_s$, is the expected value of distance that a photon travels between scattering events.

Optical Density (OD)

OD is the amount of attenuation that occurs when light passes through an optical component.

- comes from both the absorption and scattering of light.

Transmission, $T = I_1/I_0$

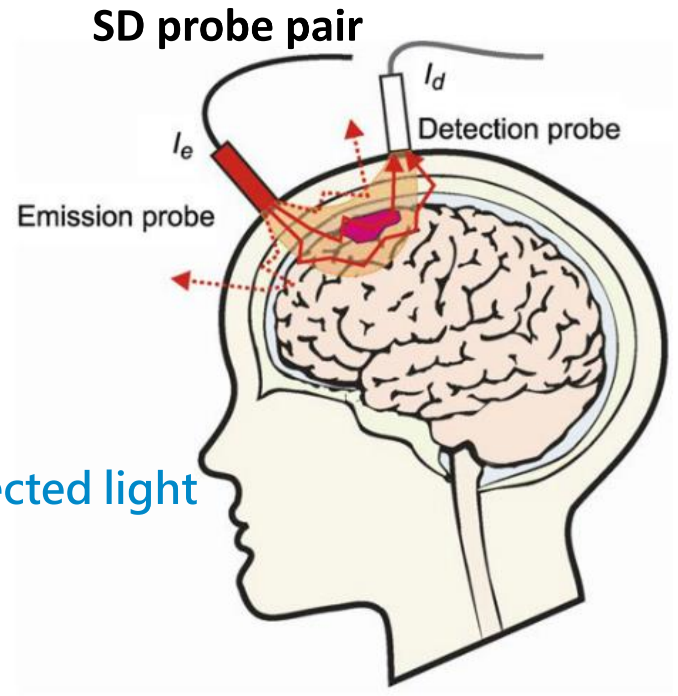
$$OD = log_{10}(1/T) = -log_{10}(T)$$

< Example >
Attenuate light by a factor of 10^3,
$T = 10^{-3}$,
$OD = -log_{10}(10^{-3}) = 3$

Photon Migration in Brain

Modified Beer-Lambert Law

$$OD = \ln\left(\frac{I_e}{I_d}\right) \approx \mu_{a\ head}\langle L_{head}\rangle + G$$



$\boldsymbol{\mu_{a\ head}}$: assume the absorption in the head is homogeneous

$\langle \boldsymbol{L_{head}} \rangle$: the mean optical path length of the detected light

G: the scattering loss (cannot be measured)

Modified Beer-Lambert Law

Based on an assumption that the scattering loss does not change during the measurement period.

$$\Delta OD = ln\left(\frac{I_e}{I'_d}\right) - ln\left(\frac{I_e}{I_d}\right) = ln\left(\frac{I_d}{I'_d}\right) = \Delta\mu_{a\ head}\langle L_{head}\rangle$$

Change caused by brain activations
(dynamics of HbO and HbR)

Brain Activation

Assumption:

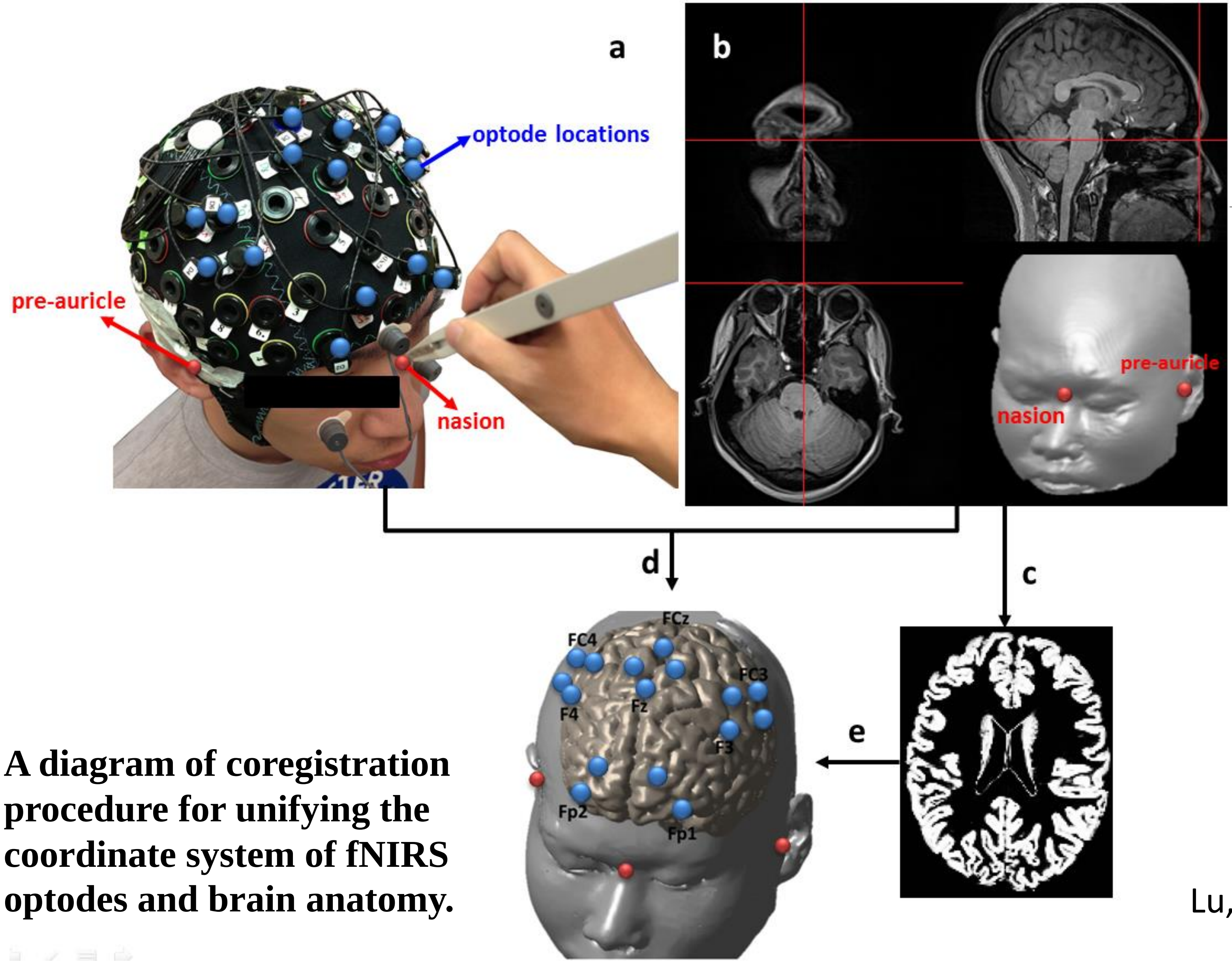
- the concentration of hemoglobin is only changed during the measurement period by brain activation.

$$\Delta\mu_{a\ head}(\lambda) = \varepsilon_{HbO}(\lambda)\Delta c_{HbO} + \varepsilon_{HbR}(\lambda)\Delta c_{HbR}$$

Measurements under two or more wavelengths (760 and 850 nm) are demanded.

Critical Issues of fNIRS

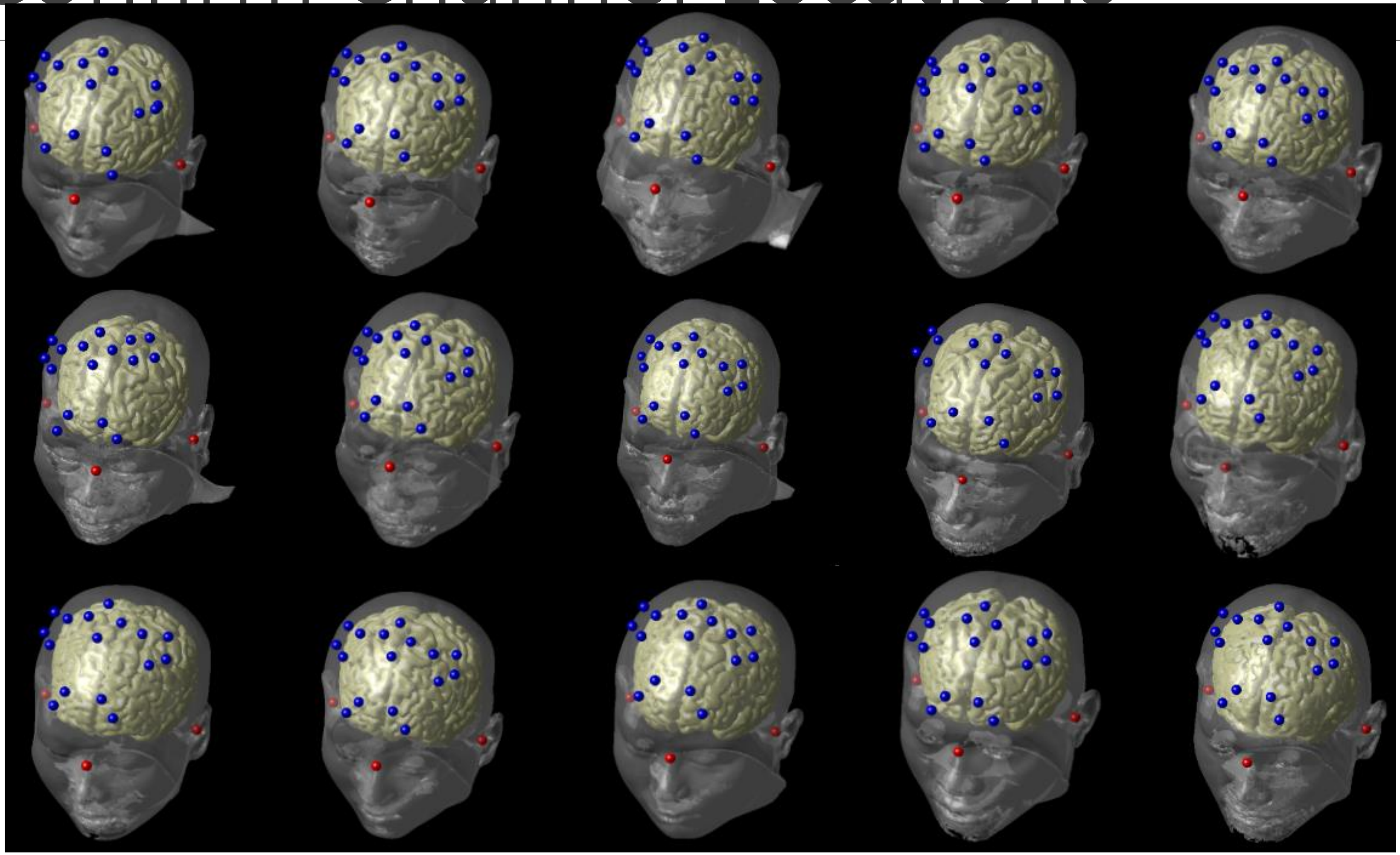
1. Validation of optodes/channels locations
   (coverage of brain area)
2. Signal quality: motion artifacts and physiological noise
3. Removal of contaminations from superficial tissues



A diagram of coregistration procedure for unifying the coordinate system of fNIRS optodes and brain anatomy.

Lu, et al. PLoS One, 2015.

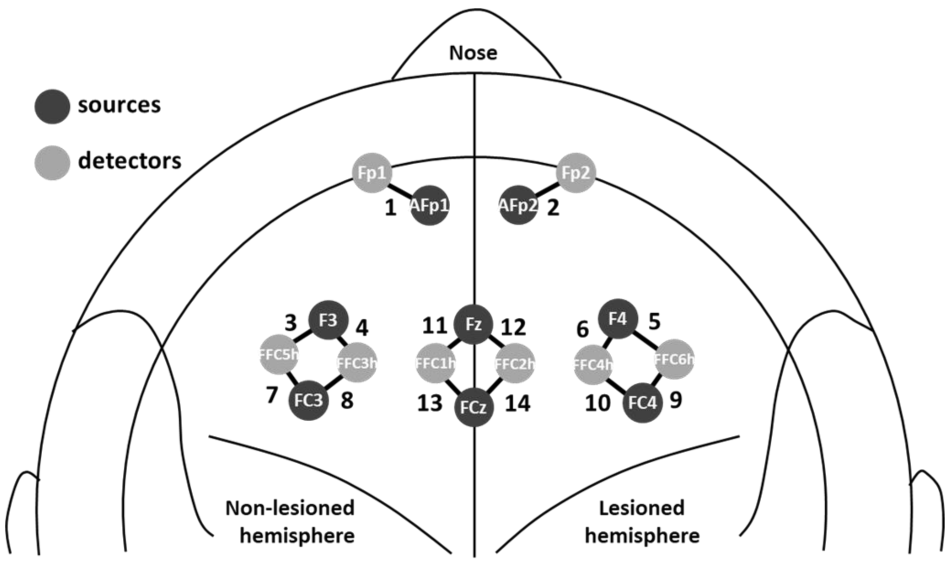
Confirm Channel Locations



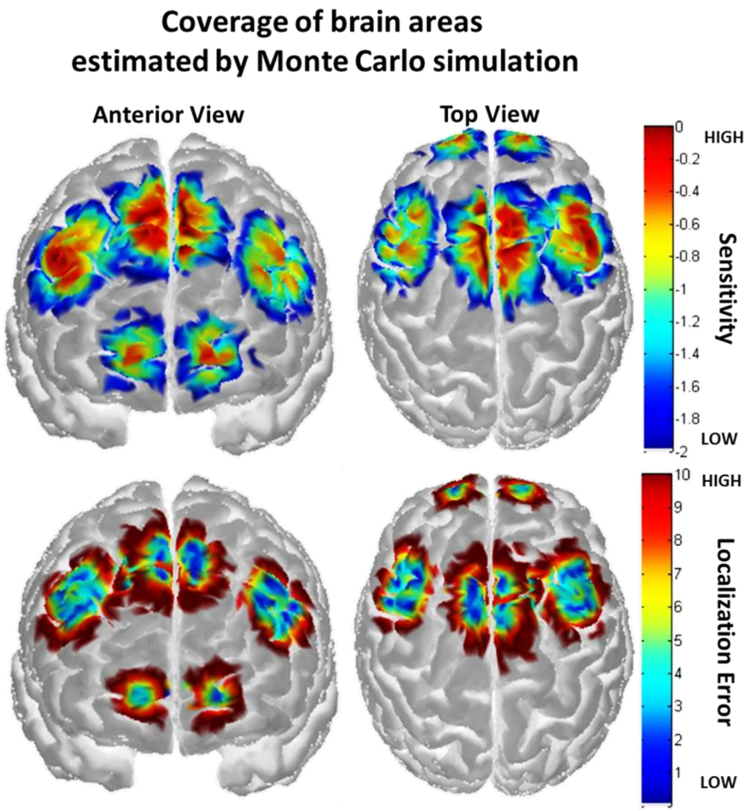
S-D Arrangement & Brain Coverage

Using Monte Carlo simulation to check the coverage of brain areas.

(a)

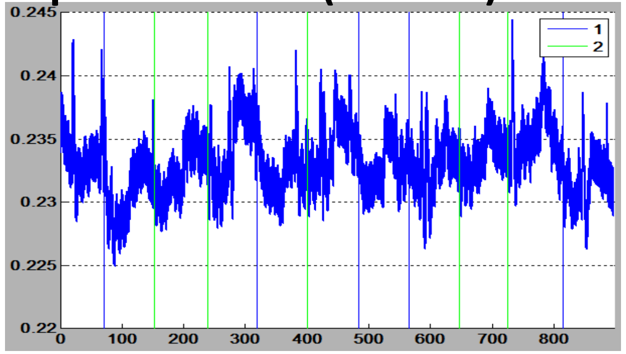


(b)

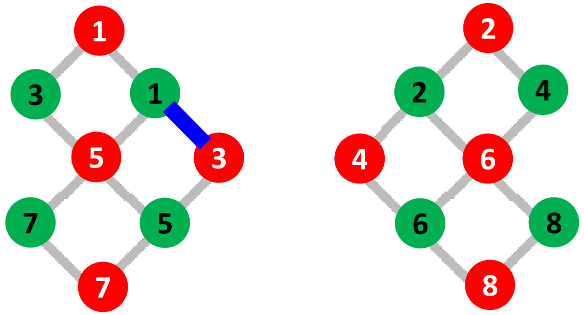


Signal Processing & Analysis

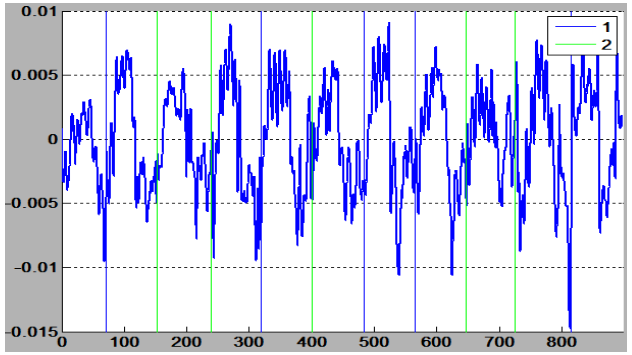
Step 1: raw data (760 nm)



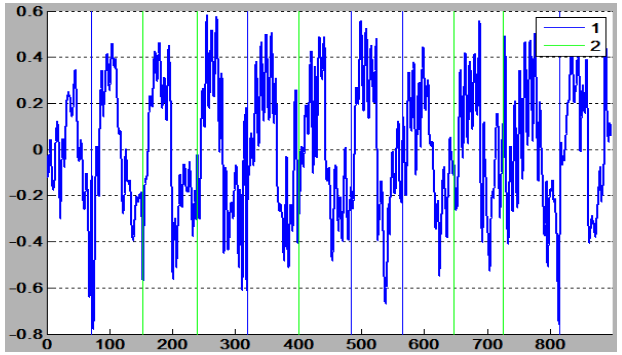
S-D arrangement



Step 2: optical density and filtering



Step 3: Motion correction & HbO/HbR conc.



NBA
Laboratory of Neuroimage Biomarker Analysis

實驗設計
Experimental Design

Reference: *Basics of Experimental Design for fMRI: Block Designs & ER designs* http://www.fmri4newbies.com

Concept of Exp. Design

If neuroimaging is the answer, what is the question?

- Stephen M. Kosslyn (1999). *Phil Trans R Soc Lond B*.

Is your study designed to answer questions about the functioning of the brain?

Does your study bear on specific questions about the roles of particular brain regions?

Considerations in fNIRS

The foreknowledge of the location

The expected characteristics of the activation signal

The specific hypothesis addressed by the study

➔ Block design or Event-related (ER) design ?

Location of activation

Limited source and detector optodes

Limited to the outer layers of the brain (approximately 5-8 mm)

The depth sensitivity may be adjusted based on the source-to-detector distance

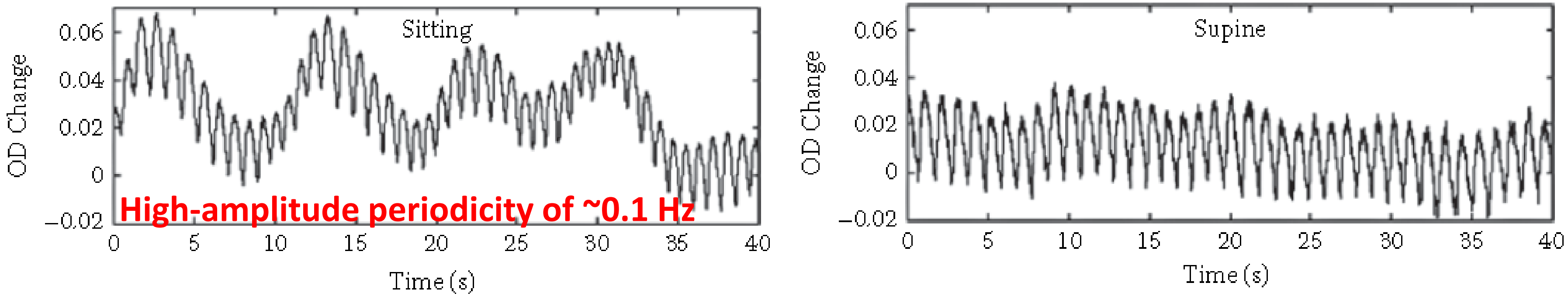
- Visual cortex vs. prefrontal cortex

Baseline Recording

without stimulation

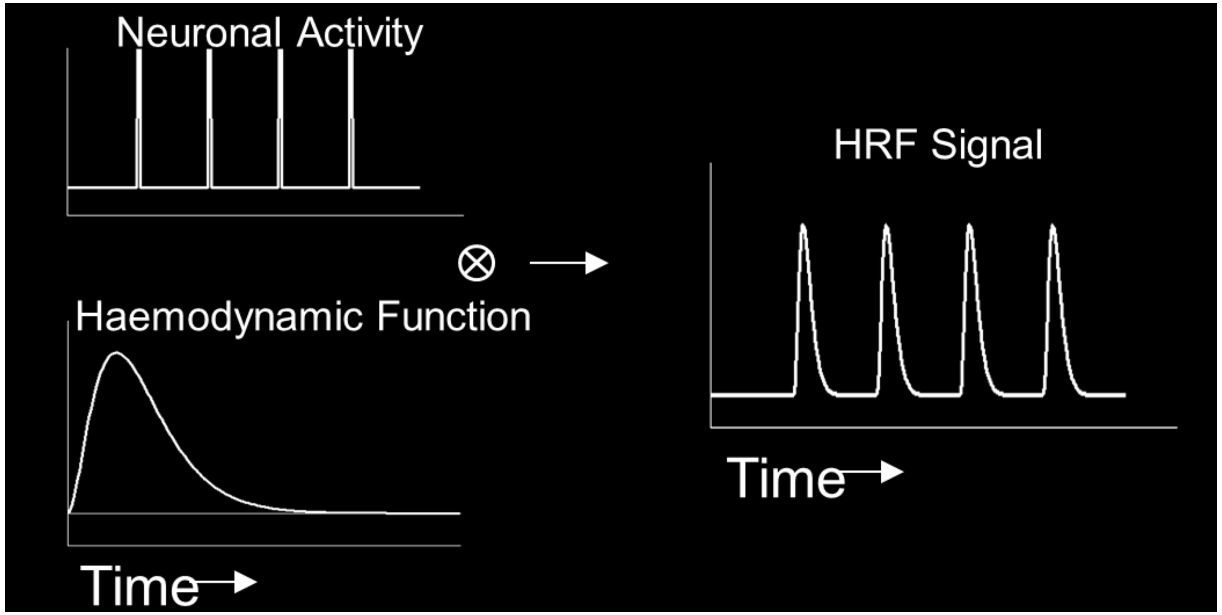
Eye-closed resting for a subject

- 830nm, at C3 location
- The Mayer wave (~0.1 Hz), a systemic blood pressure oscillation, is more prominent when stand ing or sitting
- Vascular physiology, vasomotion or autonomic regulation

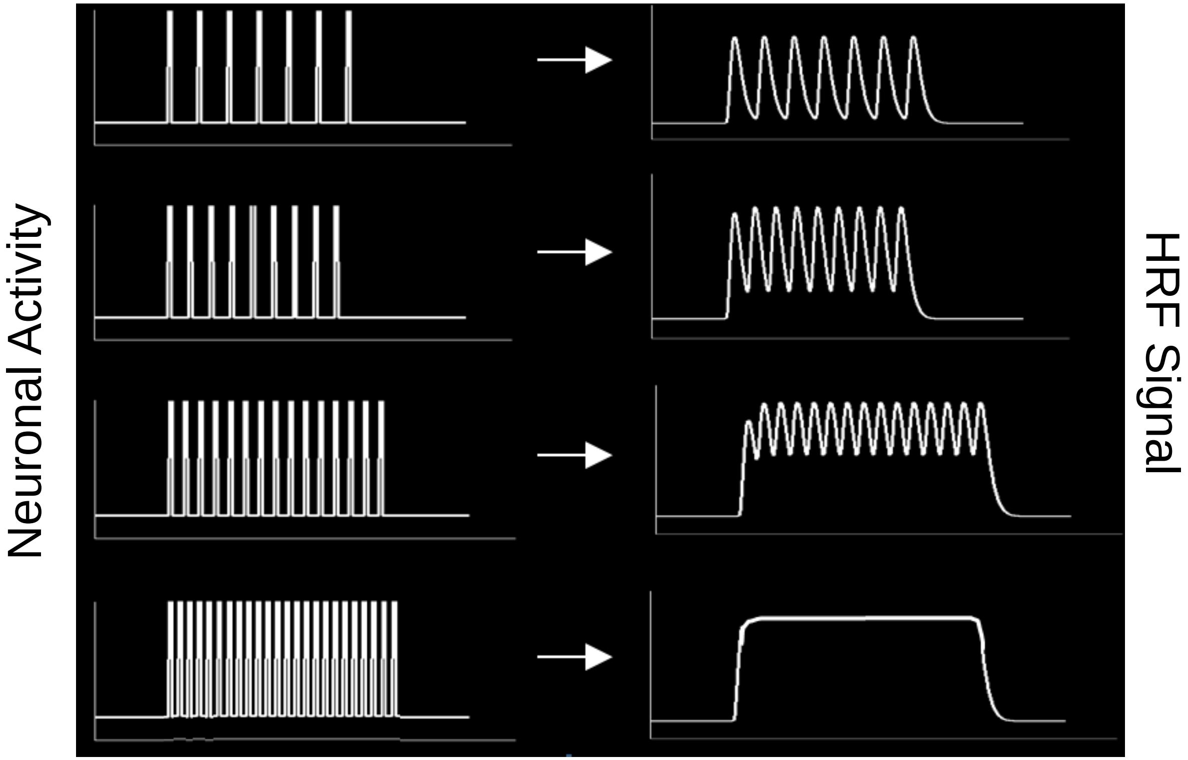


Convolution of Single Trials

Anticipated temporal profile of HRF

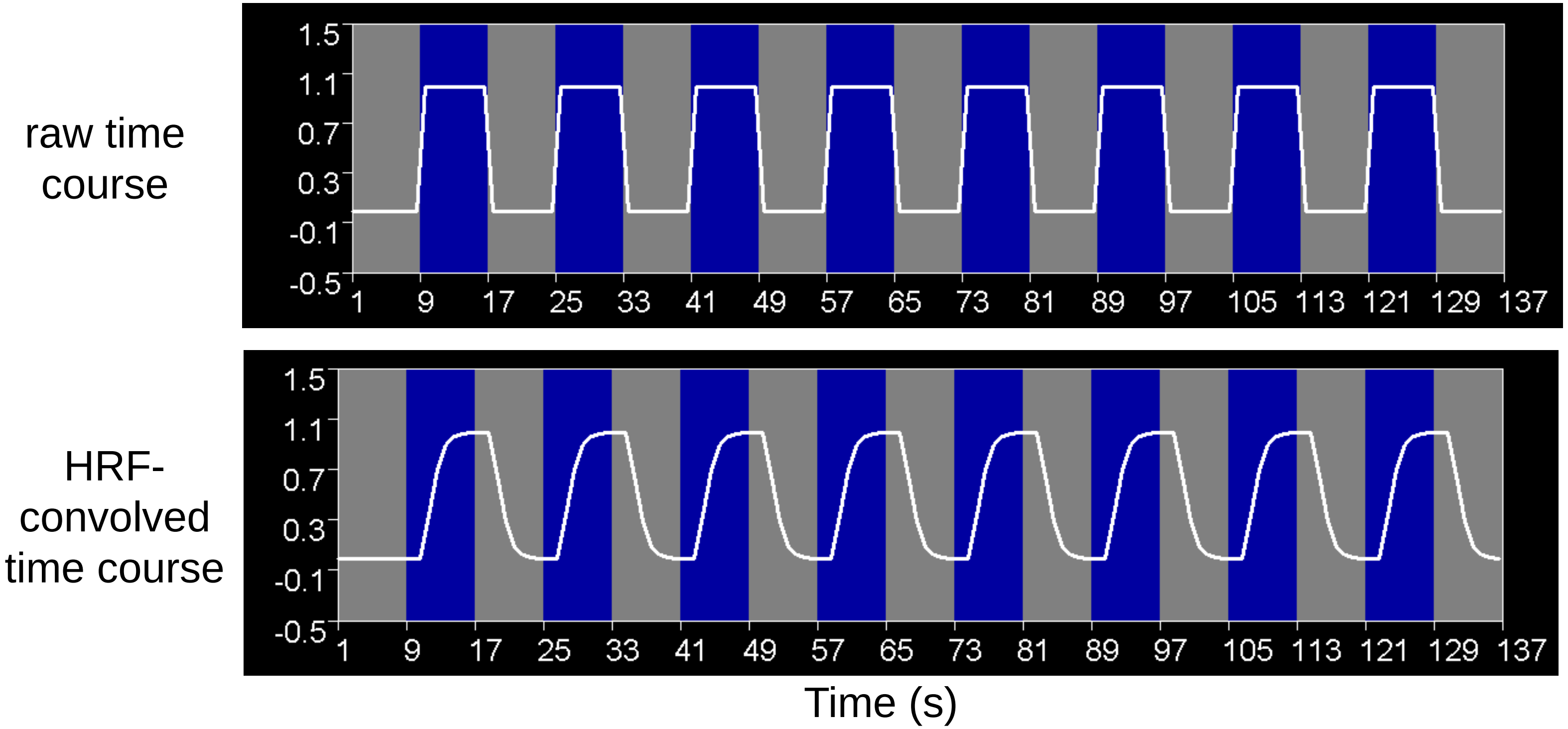


Convolution of Single Trials



Temporal dynamics of signal

Block design



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Statistical Power

The probability of rejecting the null hypothesis when it is actually false

- if there's an effect, how likely are you to find it?

Effect size

- More trials/blocks

Sample size

- More subjects, more runs

Signal to noise ratio

- Careful setup, fewer artifacts

➔ increase power

Put conditions in a run

As far as possible, put the two/all conditions you want to compare within the same run.

Why?

- subjects get drowsy and bored
- Instrumentation may have different amounts of noise from one run to another (e.g., baseline shift)
- May cause stats differently between runs

Experiment Duration

Short enough that the subject can remain comfortable without unnecessary moving or distraction

Long enough that studied condition can be included in run

- Simplify the task condition, usually 2~6 conditions
- At least 3 repetition for each condition

Ideal duration is between 10 to 30 minutes

Block Design

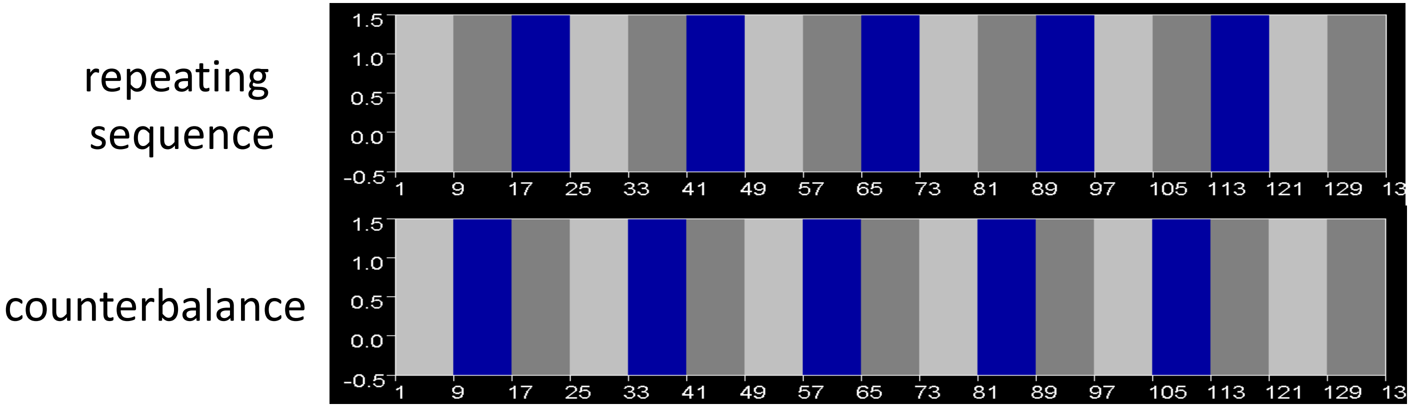
Repeating Sequence

We could just order the epochs in a repeating sequence…

Problem: There might be order effects (especially for cognitive study)

Solution: Counterbalance with another order

Caution: remember the order !

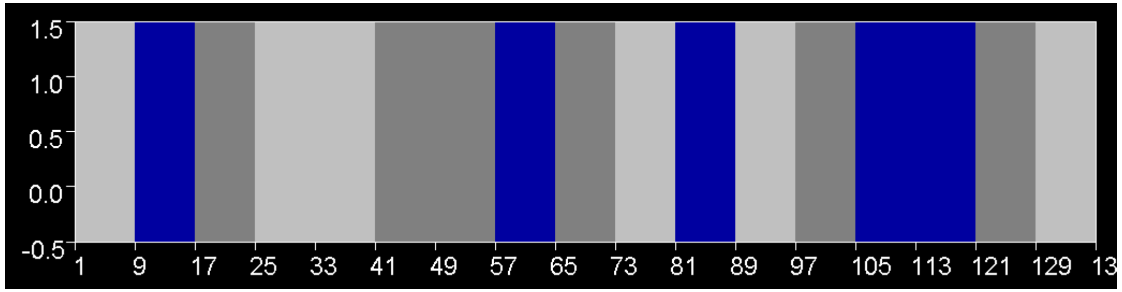


Block Design

Random Sequence

We could make multiple runs with the order of conditions randomized…

Problem: To avoid flukiness, you'd want to have different randomization for different runs and different subjects, but then you're going to spend ages defining protocols for analysis



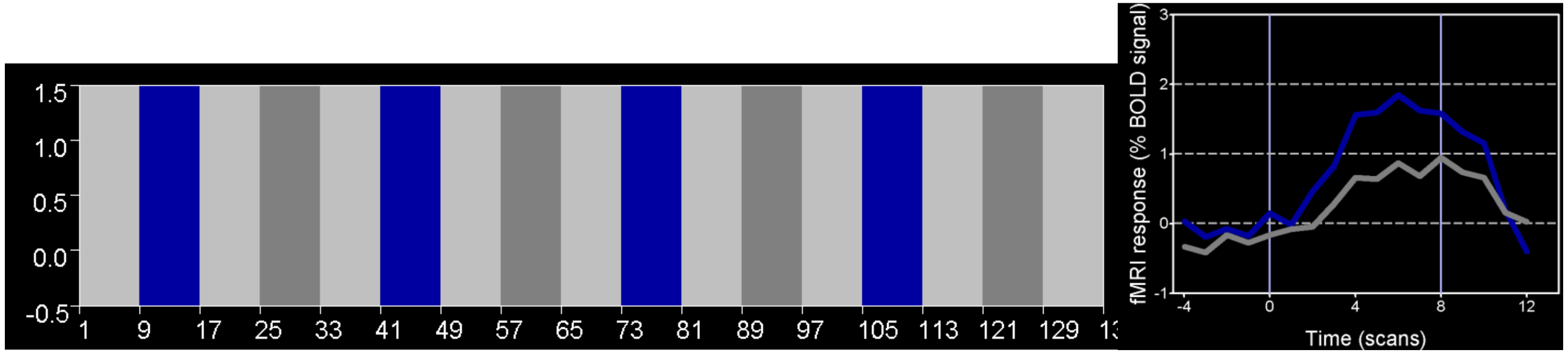
Block Design

Regular Baseline

A fixation baseline between all stimulus conditions (either with regular or random order)

Benefit: With event-related averaging, this regular baseline design provides nice clear time courses, even for a block design

Problem: Spending half of scan time collecting the condition you care the least about



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Block Designs

Pros & Cons

Pros

- high detection power (identify channels of activation)
- has been the most widely used approach
- accurate estimation of hemodynamic response function is not as critical as with event-related designs

Cons

- poor estimation power (measure the time course of Hb)
- subjects get into a mental set for a block
- very predictable for subject
- can't look at effects of single events (e.g., correct vs. incorrect trials, remembered vs. forgotten items)
- long experiment duration with too many conditions (e.g., more than 4 conditions + baseline)

Slow Event-Related Designs

Pros & Cons

Pros

- excellent estimation
- useful for studies with delay periods
- very useful for designs with motion artifacts (grasping, swallowing, speech) because you can tease out artifacts
- analysis is straightforward

Cons

- poor detection power because you get very few trials per condition by spending most of your sampling power on estimating the baseline
- subjects can get VERY bored and sleepy with long inter-trial intervals

Design Steps

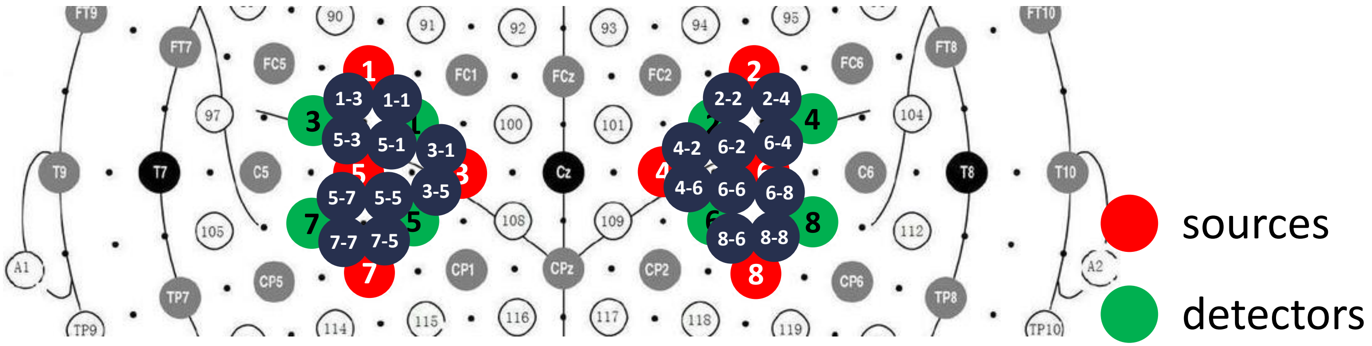
Participants' tolerance
- Age, disease …

Study aims
- Target Locations
- Number of conditions
- Anticipated signals

Experiment paradigm
- S-D arrangement, number of channel
- Block design or event-related design
- Task instruction & stimulation delivery

Log sheet
- Name, gender, age, history number/ID, habitual hand, study group
- Experiment paradigm and notation

Bilateral Arm lifting



No. Rows 4

No. Columns 6

Clear Table

Export to NILAB

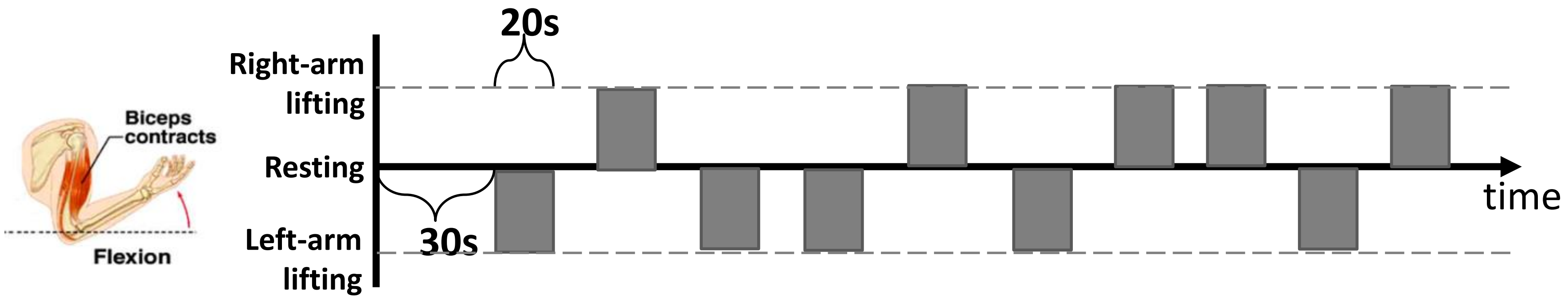
1-3	1-1			2-2	2-4
5-3	5-1	3-1	4-2	6-2	6-4
5-7	5-5	3-5	4-6	6-6	6-8
7-7	7-5			8-6	8-8

Block design diagram

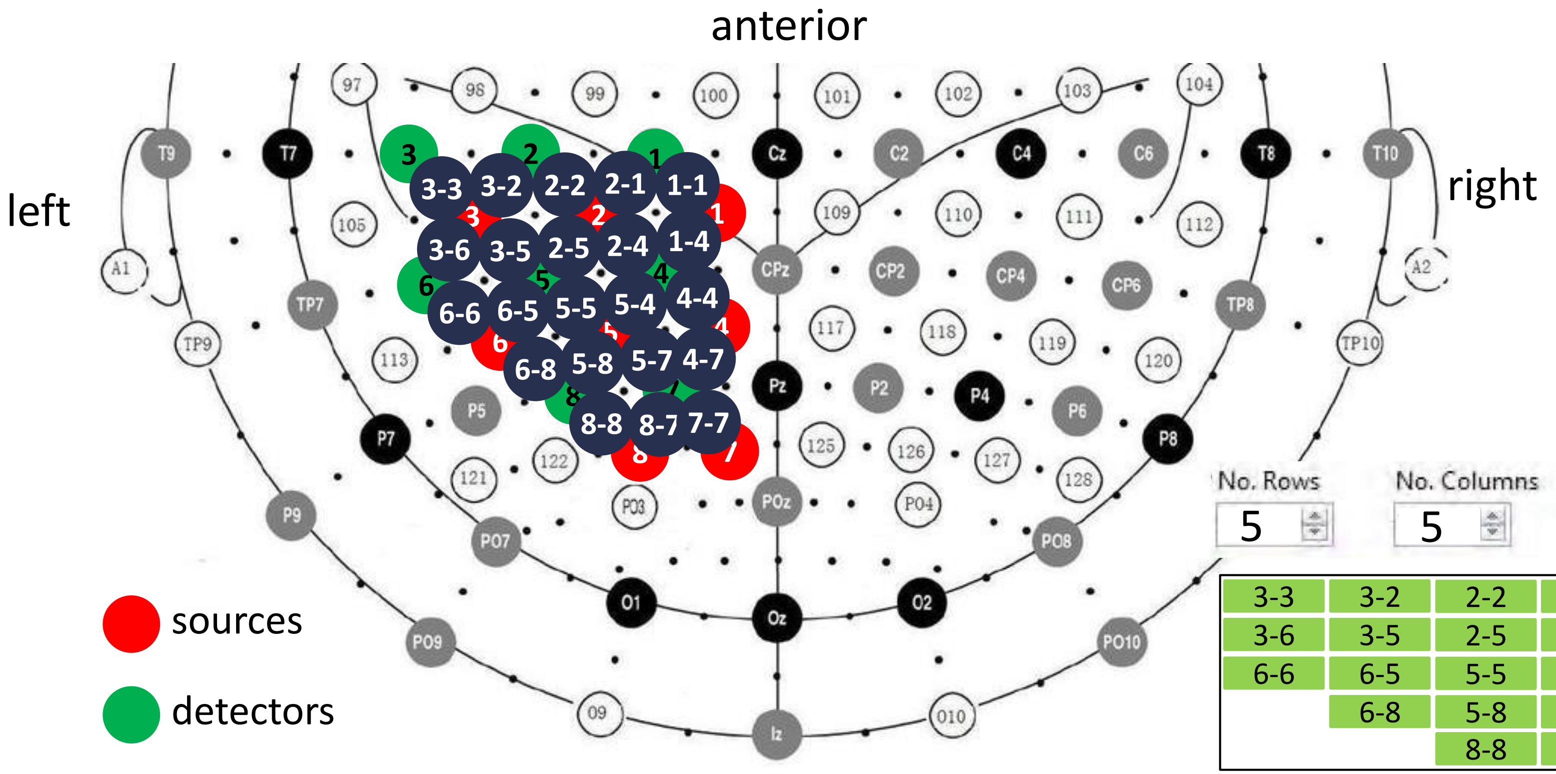
Baseline Relax and sit on an armchair (30s)
Experiment I Right-arm lifting (20 s)
Rest interval Relax and sit on an armchair 20 s)
Experiment II Left-arm lifting (20 s)

(Overall ~7.2 mins)

※Experiment States were marked by “**F1**” and Rest intervals were marked by “**F3**”



Oddball task



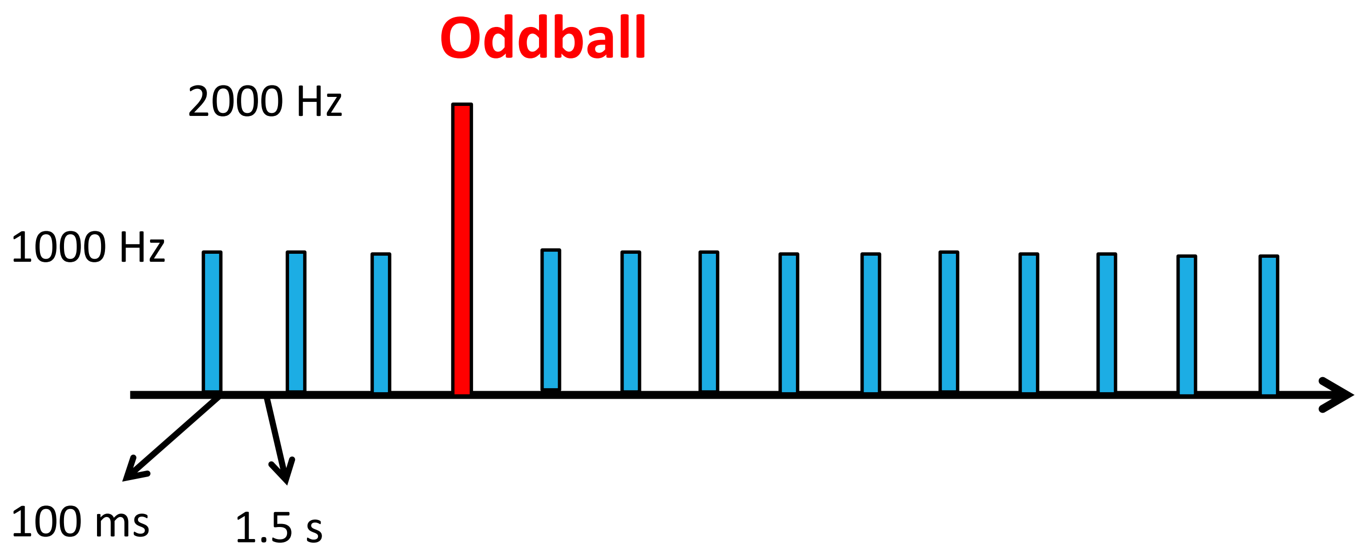
No. Rows 5 | No. Columns 5 | Clear Table

3-3	3-2	2-2	2-1	1-1
3-6	3-5	2-5	2-4	1-4
6-6	6-5	5-5	5-4	4-4
	6-8	5-8	5-7	4-7
		8-8	8-7	7-7

Event-Related design

12 oddball events (8% of total number)

3~6 regular tones before, and 10 after oddball



盧家鋒 **Chia-Feng Lu, PhD**

Q & A

Thanks for your attention :)