功能性近紅外光實驗設計
fNIRS Experiment Design

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本週課程內容

- Experimental design
- Design examples

- **In Vivo Optical Imaging of Brain Function.** CRC Press, 2009.
  - Noninvasive Imaging of Cerebral Activation with Diffuse Optical Tomography (chap 14), TJ Huppert, MA Franceschini, DA Boas
- **Basics of Experimental Design for fMRI: Block Designs & ER designs**
  - http://www.fmri4newbies.com

實驗設計
Experimental Design

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 ?

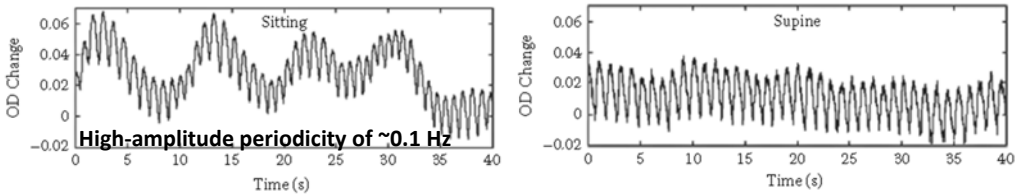
Location of activation

- 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

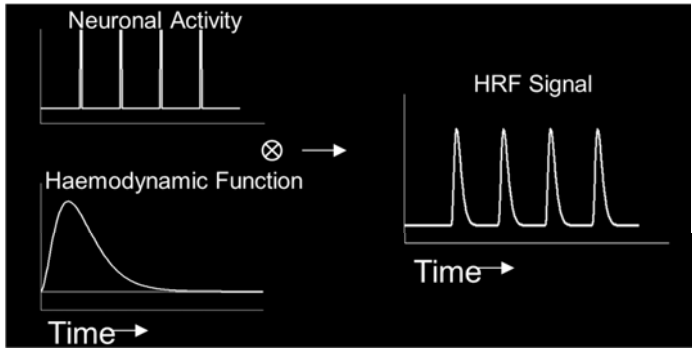
without stimulation

- 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

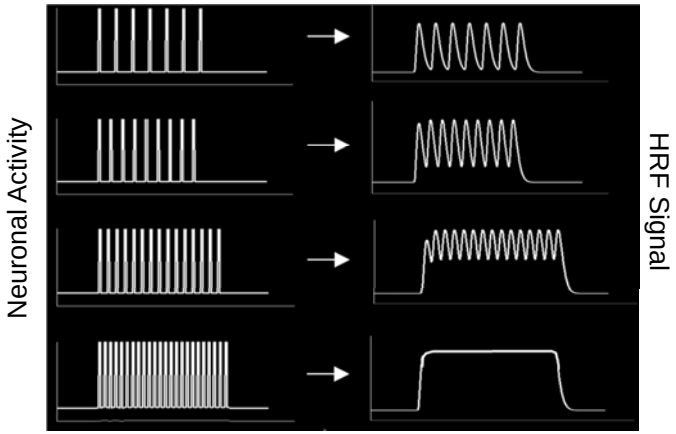


Convolution of Single Trials

- Anticipated temporal profile of HRF

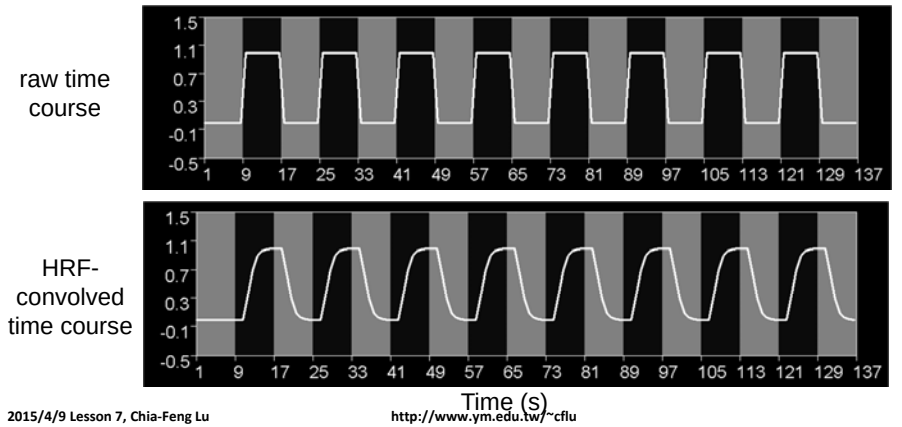


Convolution of Single Trials



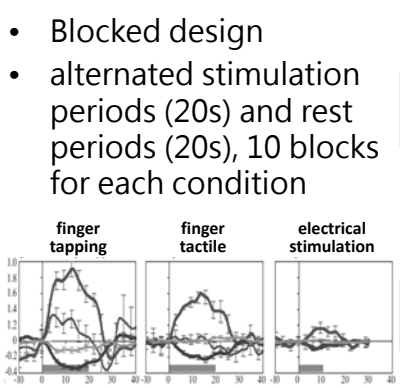
Temporal dynamics of signal

Block design

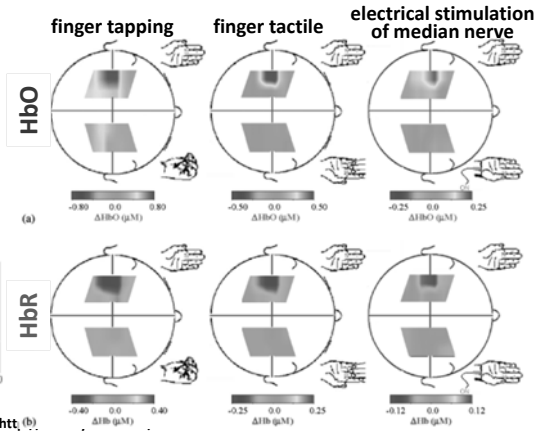


fNIRS evoked response

- Blocked design
- alternated stimulation periods (20s) and rest periods (20s), 10 blocks for each condition



Franceschini et al., 2003



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

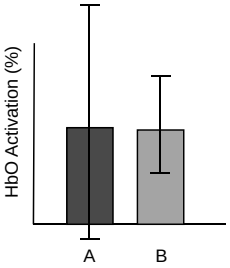
➔ increase power

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

Common flawed logic

- Run1: A – baseline
- Run2: B – baseline
- A – 0 was significant, B – 0 was not
  - Area X is activated by A more than B ??



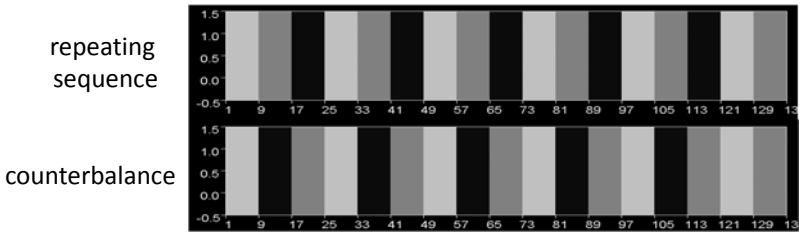
Experiment Duration

- 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

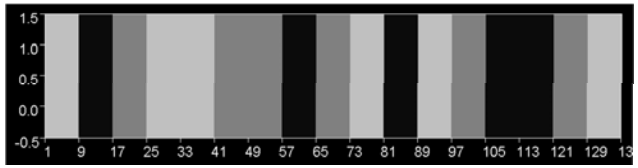
Repeating Sequence

- 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 !



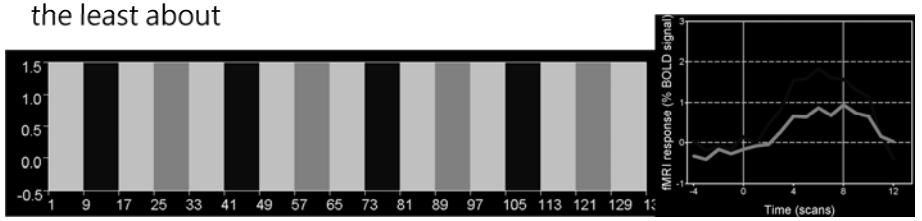
Block Design
Random Sequence

- 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

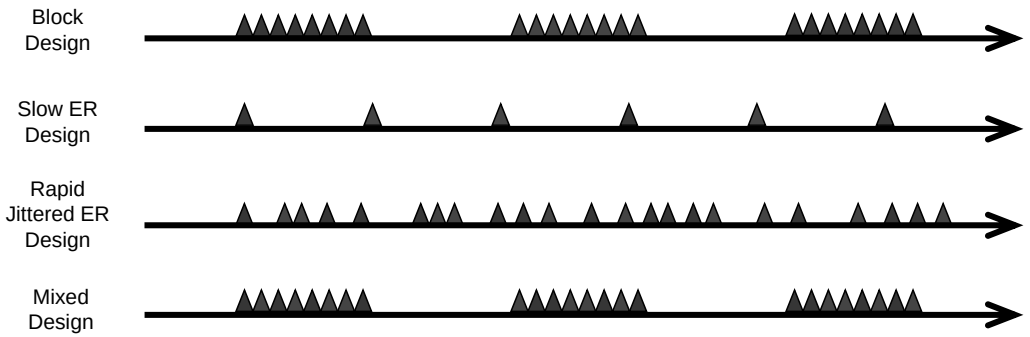


Block Design
Regular Baseline

- 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



Design Types



Block Designs
Pros & Cons

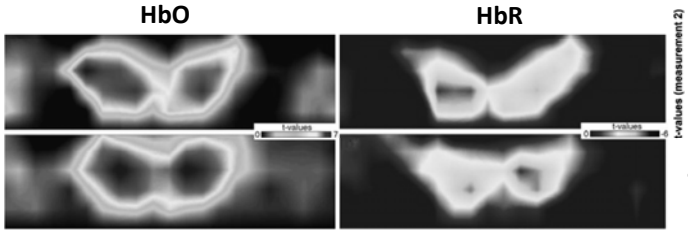
- **Pros**
  - high detection power (identify channels of activation)
  - has been the most widely used approach
  - accurate estimation of hemodynamic response function is not as critical as with event-related designs
- **Cons**
  - poor estimation power (measure the time course of Hb)
  - subjects 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)

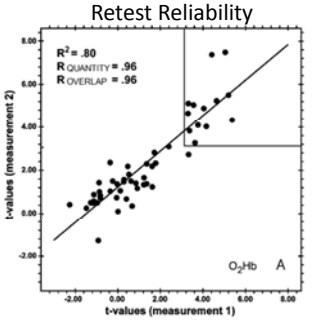
Slow Event-Related Designs
Pros & Cons

- **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

Reliability of ER fNIRS

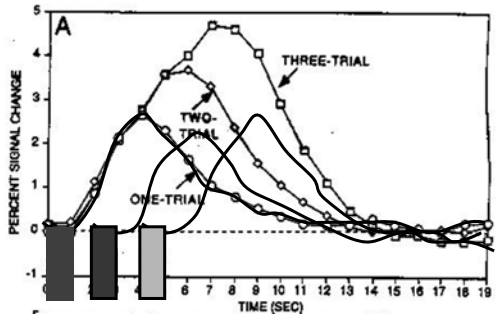
- a simple checkerboard for 1200 ms reversing in contrast at 6 Hz followed by 13.8 s of a black screen presentation
- number of trials was set to n = 60
- retest interval = 3 weeks





Plichta et al., 2006

Linearity of BOLD signal



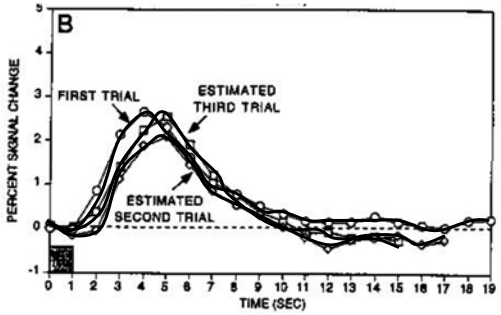
Linearity:
"Do things add up?"

red = 2 - 1

green = 3 - 2

Dale & Buckner, 1997

Linearity of BOLD signal



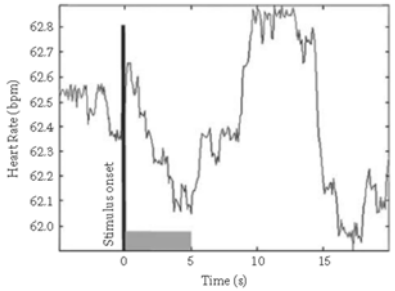
Sync each trial response to start of trial

Not quite linear but good enough!
(with interval of 2~4 s)

Dale & Buckner, 1997

Other considerations

- The potential contamination from background physiological signals.
  - Heart-rate increase
  - Motion artifacts
- Post-processing

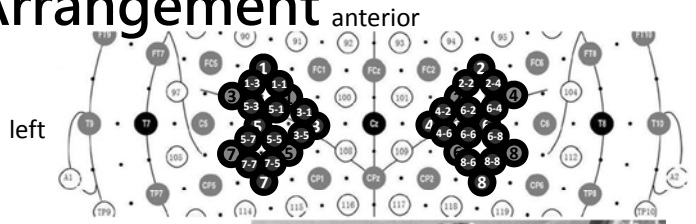


實驗設計實例
fNIRS Examples of Exp Design

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

S-D Arrangement

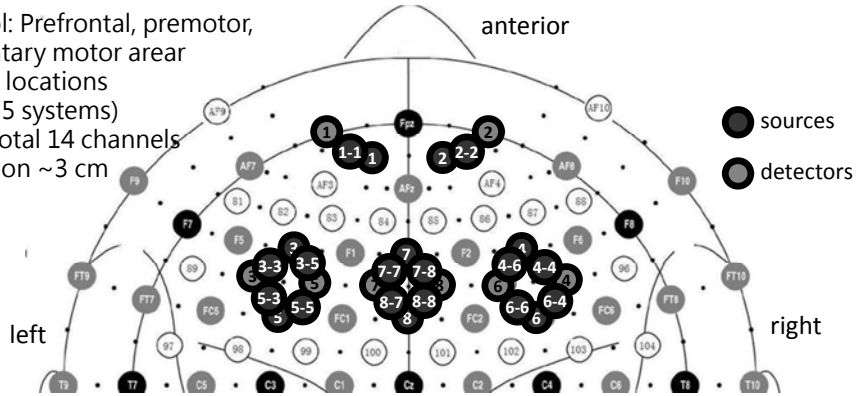


Bilateral arm lifting:
Sensorimotor area
➔ FC, C, CP locations (EEG 10-5 systems)
➔ 8S-8D, total 20 channels
separation ~3 cm

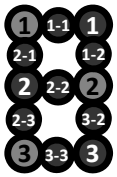
sources
detectors

S-D Arrangement

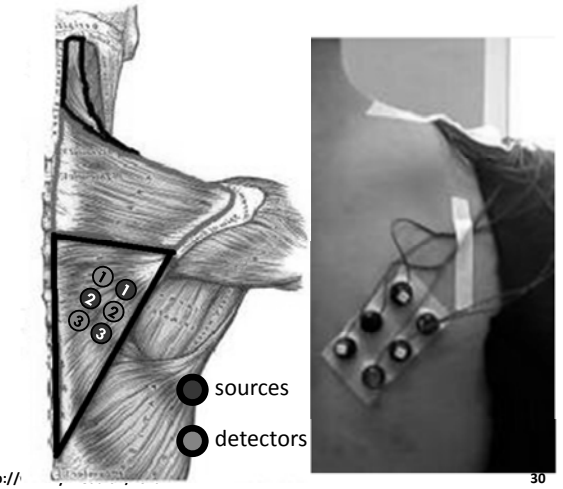
Gait control: Prefrontal, premotor, supplementary motor arear
➔ Fp, F, FC locations (EEG 10-5 systems)
➔ 8S-8D, total 14 channels separation ~3 cm



S-D Arrangement



Trapezius muscle
➔ 3S-3D, total 7 channels separation 2~2.5 cm

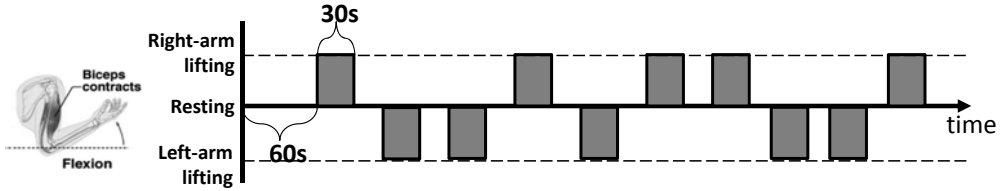


Block design diagram

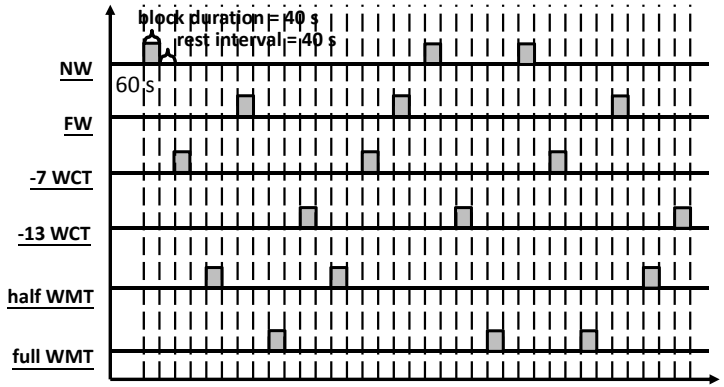
Baseline	Relax and sit on an armchair (~1 min)
Experiment I	Right-arm lifting (~30 s)
Rest interval	Relax and sit on an armchair (~30 s)
Experiment II	Left-arm lifting (~30 s)

(Overall ~11 mins)

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



Block design diagram



time (overall 40s x (18 blocks + 18 rest intervals)+60s = 1500 s = 25mins)

Task Instruction

語意流暢度測試

我們會給予您一個注音符號，例如 ㄈ
請您說出以此開頭的語詞

風車、鳳凰、發現
富裕、廢料、非常

Log sheet

fNIRS cerebral Hb monitoring sheet for dual task

Test date and time：_____

Subject name：_____

Subject ID：_____ Gender：_____

Birthday：_____ Habitual hand：_____

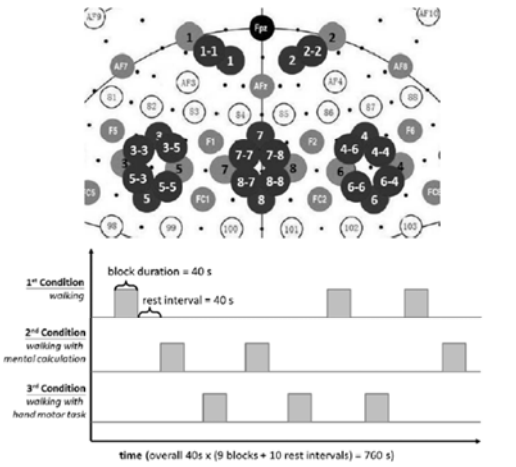
NOTE：_____

_____

_____

Log sheet

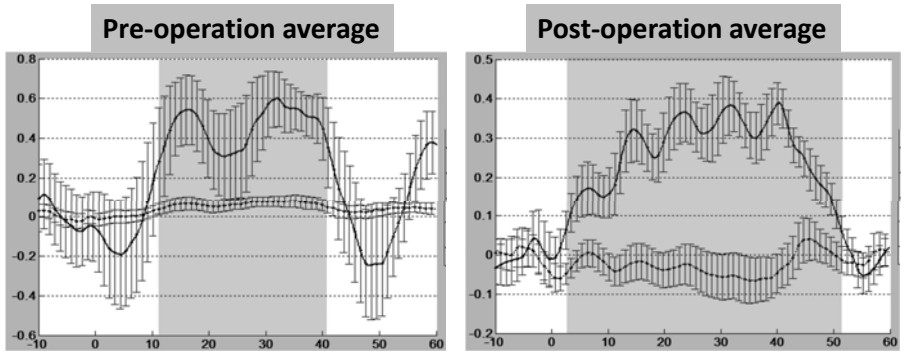
〔 Pre-Training 〕



※Experiment States were marked by "F1(2^0)" and "F3(2^2)", turning by "F2(2^1)"

Evaluation Outcome

- Change percentage, activation interval, slop



THE END

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