功能性磁振影像
A Course of MRI

盧家鋒 助理教授
國立陽明大學 物理治療暨輔助科技學系
alvin4016@ym.edu.tw

本週課程內容-functional MRI

- fMRI造影原理 (principles)
- fMRI處理流程 (pre-processing procedure)
  - 切面時間校正(Slice timing)
  - 移動校正(Realignment)
  - 與結構影像對位(Co-registration)
  - 影像標準化(Normalization)
  - 影像平滑化(Smoothing)
  - 一般線性模型(General Linear Model, GLM)
- fMRI實驗設計 (experimental designs)

Analysis Softwares

- Statistical Parametric Mapping (SPM), SPM8/ SPM12b
  - http://www.fil.ion.ucl.ac.uk/spm/
- FMRIB Software Library (FSL), FSL5.0
  - http://dbm.neuro.uni-jena.de/vbm/download/
- Analysis of Functional NeuroImages (AFNI)
  - http://afni.nimh.nih.gov/afni/
- Brain Voyager
  - http://www.brainvoyager.com/

fMRI造影原理

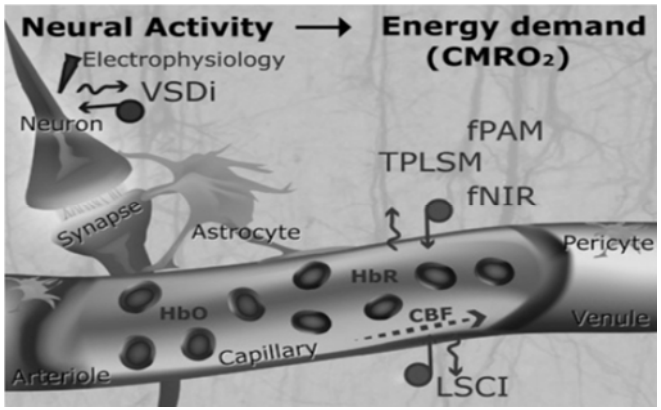
fMRI BOLD signal

- fMRI does not measure neuronal activation directly, but the consequences of metabolic processes associated with activation.
- **Blood Oxygenation Level Dependent (BOLD)** contrast *(Ogawa et al., PNAS, 1990; Turner et al., MRM, 1991)*
- The MR signal in the vicinity of blood vessels and in perfused brain tissue decreased with a decrease in blood oxygenation.

Brain Activity

- Neurovascular coupling
  - Excitatory postsynaptic potentials
  - Inhibitory postsynaptic potentials
  - Cellular action potential

vasodilation

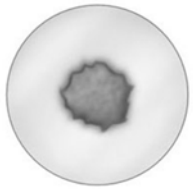


permeability

Liao et al, BioMedical Engineering 2013,12:38.

Hemoglobin

Oxygenated Hemoglobin
- Diamagnetic
- Doesn't distort surrounding magnetic field
- No signal loss…

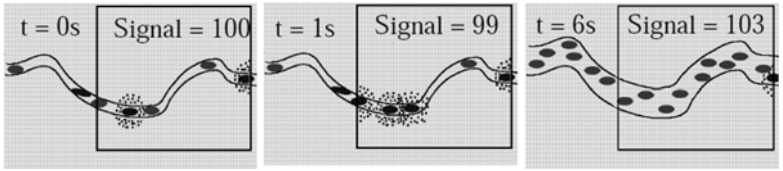


Deoxygenated Hemoglobin
- Paramagnetic
- Distorts surrounding magnetic field
- Signal loss !!!

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

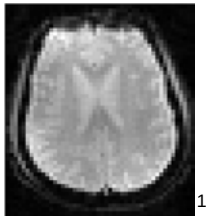
fMRI BOLD signal

- t = 0s, a steady state in which there is an given amount of oxygenated and deoxygenated hemoglobin.
- t = 1s, an increased of deoxygenated hemoglobin due to the oxygen demands of neuronal activation.
- t = 6s, an increased of blood supply and oxygenated hemoglobin "flush away" the deoxygenated ones.



Matthijs Vink, Preprocessing and analysis of functional MRI data, 2007.

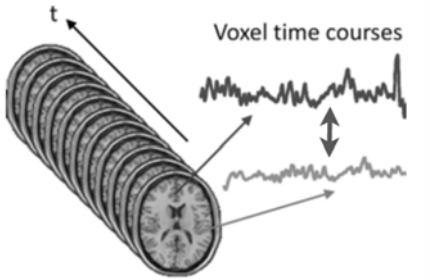
Common fMRI protocol



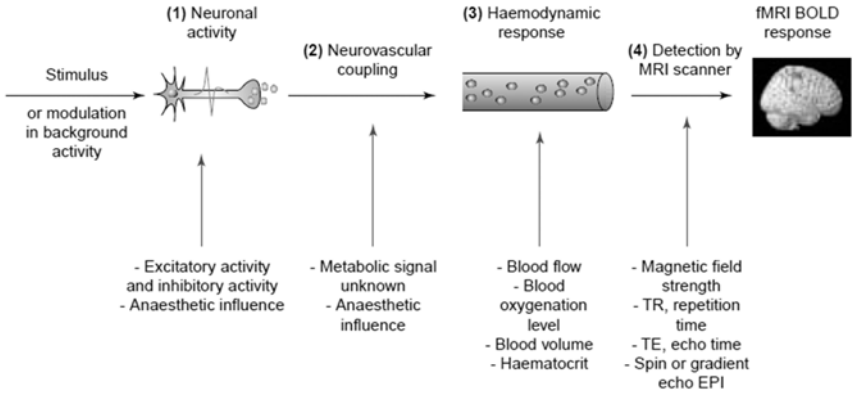
1 voxel ~10^6 neurons

3.44 x 3.44 x 3.40 mm^3

- Single-Shot 2D EPI (GRE-EPI), T2* weighting
- Repetition Time = 2000 ms
- Echo Time = 20 ms
- Flip Angle = 70~90°
- NEX = 1
- Slice thickness = 3.4 mm
- Field of View = 220 x 220 mm^2
- Matrix size = 64 x 64
- Volume number = 240 ~ 360

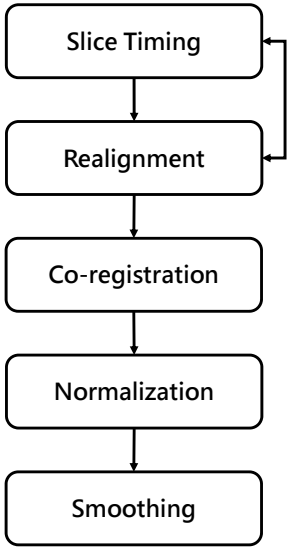


Neuronal activity and BOLD

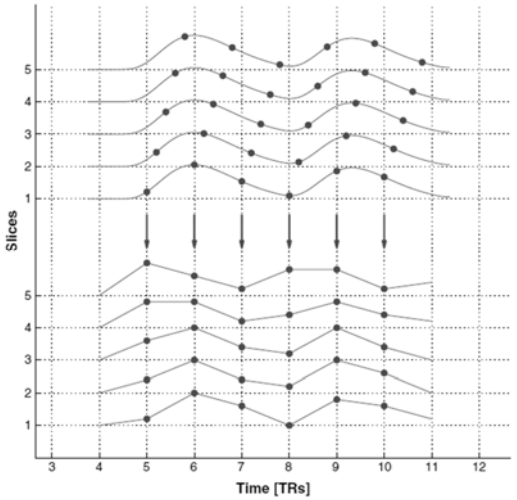


Arthurs et al., How well do we understand the neural origins of the fMRI BOLD signal, 2002.

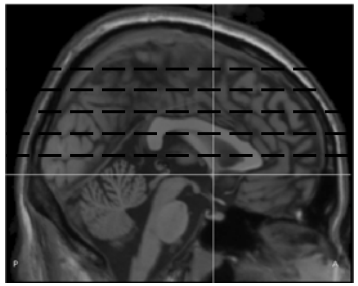
fMRI處理流程



Slice timing



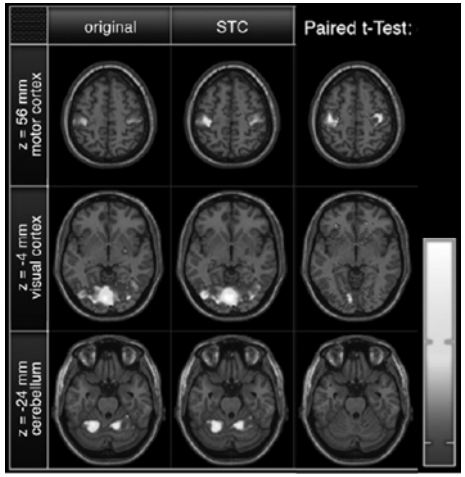
For example:
Acquire 5 slices in 1 TR
➔ Temporal offset between slices



Sladky et al, NeuroImage 2011,58:588-594.

Slice-timing correction

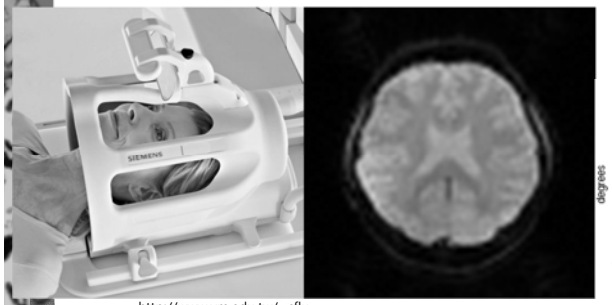
- Interpolation (TR < 3s)
  - Linear interpolation
  - Sinc interpolation (SPM8 default)
  - Cubic interpolation
- Choose the mid-slice as a reference slice
  - Only need TR/2 time shift
  - All regressors in the GLM also need to be adjusted for this time shift by TR/2



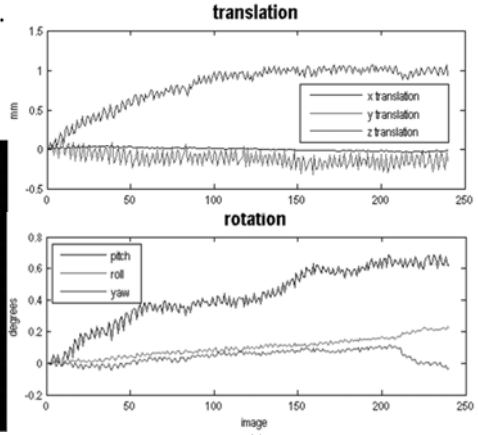
Sladky et al, NeuroImage 2011,58:588-594.

Realignment of head motion

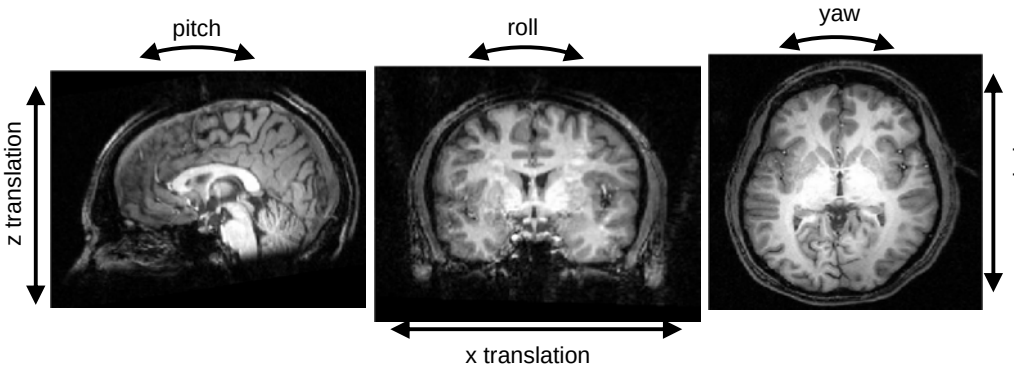
- The signal variation from movement is larger than hemodynamic response.
- Must be performed before normalization.



6-parameter Rigid body registration & transformation



3 translations and 3 rotations



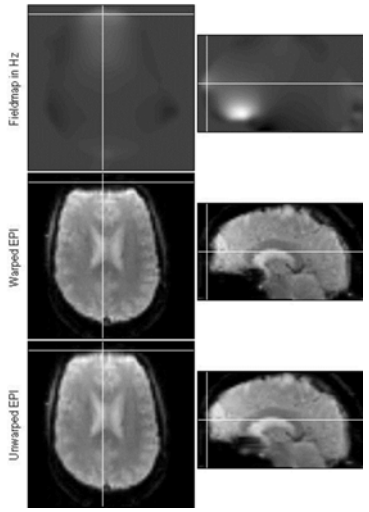
fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Slice timing ⇔ realignment

- For interleaved acquisitions
  - Slice timing correction first, and then realignment
- For sequential acquisitions
  - Realignment first, and then slice timing correction

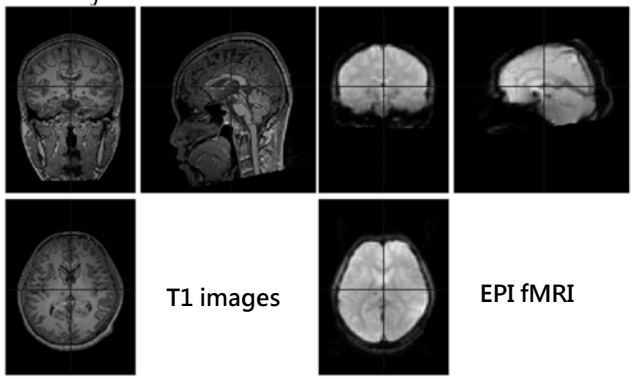
EPI undistortion/unwarp

- Magnetic inhomogeneity can cause
  - Signal loss
  - Spatial distortion
- Magnetic field warps at tissue boundaries
  - The frontal pole, orbito-frontal cortex
  - Medial temporal lobe (hippocampus)
- The benefit of undistortion/unwarp
  - Make the shape of an individual's fMRI data more similar to their anatomical images.



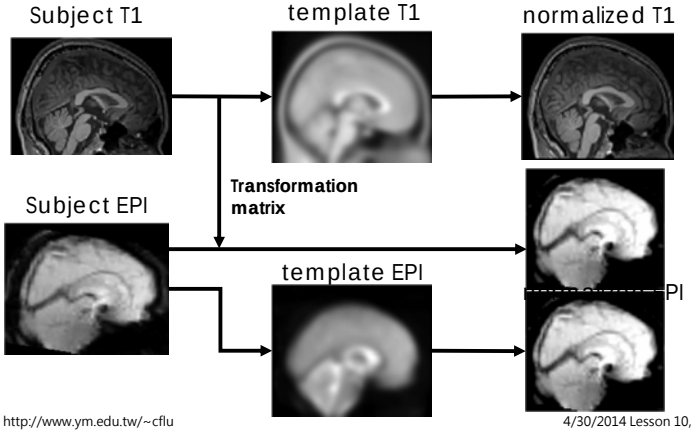
Co-registration

- Align fMRI (EPI) data with structural (T1) images.
  - Rigid body transformation using mutual information
  - Manual adjustment



Normalization

- We can perform spatial normalization using either anatomical (T1) images or fMRI (EPI) data.



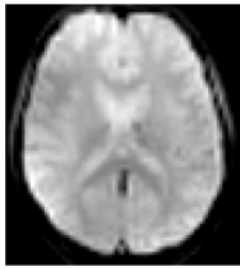
Problems with normalization

- The structural alignment does not guarantee the functional alignment.
- Differences between individuals in cortex anatomy and physiology can not be perfectly registrated
  - Over-warping lead to meaningless distortion and unwanted features.
- Brain pathology (e.g. atrophy, brain injury, tumor) may confuse the normalizing procedure.

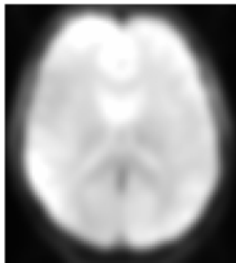
Gaussian Smoothing

- Each voxel becomes weighted average of surrounding voxels.
- Render the data more normally distributed.
- Compensate for inaccuracies in normalization between individuals.
- Increase signal-to-noise ratio

2 x 2 x 2 mm^3



normalization

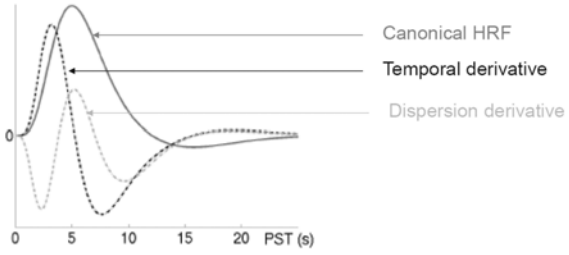


Normalization+smoothing

fMRI實驗設計

BOLD and HRF characteristics

- The relationship between neural activation and BOLD signal
  - Neuronal firing and postsynaptic potentials occur very soon (tens to hundreds of milliseconds)
  - BOLD: initial dip (~1s) → maximal value (~6s) → return to baseline (~20s)
- **Hemodynamic response function (HRF)**



Friston et al, Neuroimage, 1995, 1998.

HRF and its derivatives

- The HRF characteristics can differ between
  - Brain regions within one subject (inter-region difference)
  - Subjects (inter-subject difference)
- The adaption of HRF in
  - The onset time (time derivative)
  - Dispersion/width of curve (dispersion derivative)

Experimental design

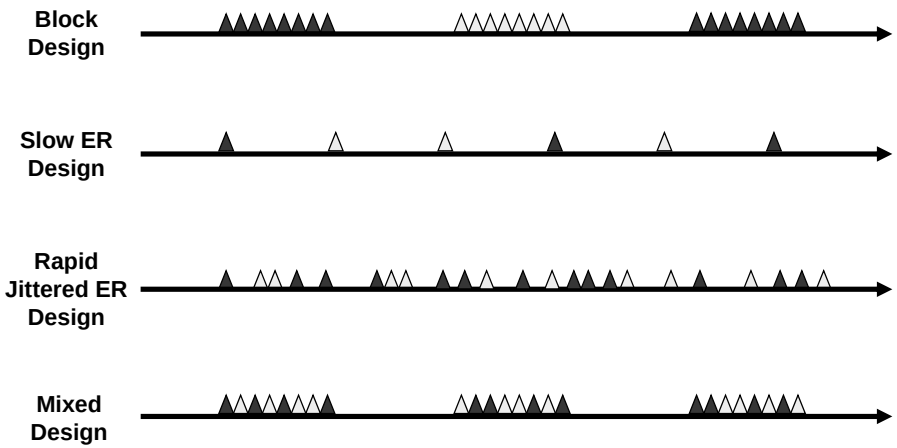
- Block designs
  - Combine BOLD response to a number of continuous trials (events)
- Event-related (ER) designs
  - Obtain the BOLD response to a single event

- The more *efficient* a design, the less scan time is needed to achieve sufficient *power*.

Design Types

▲ = trial of one type

△ = trial of another



fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

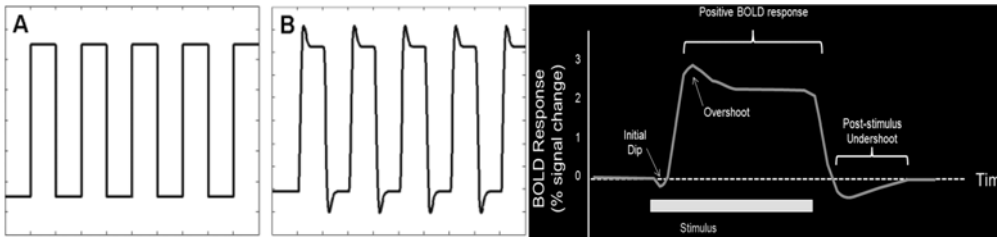
Block designs

- A design in which the task is presented in so-called blocks (15~30s), alternated with resting blocks.

- The number of scans should be equal in all conditions, so that the variance in all factors is the same.
- The longer the blocks are, the more chance there is for a correlation with low-frequency noise.
- The strength of the brain signal can decrease over time.

Block designs

- Box-car function
  - A 0 for no-task and a 1 for task period
- Hemodynamic (BOLD) changes don not suddenly activate and stop activating in the way modelled by the box-car function
  - A better estimation by convolving the box-car input function with an hrf.



Matthijs Vink, Preprocessing and analysis of functional MRI data, 2007.

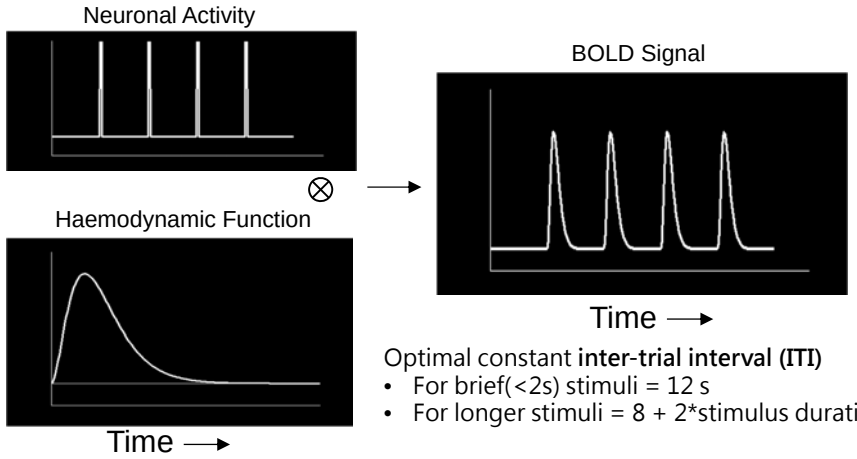
Pros & Cons of Block Designs

- high detection power of activated voxel/region
- has been the most widely used approach for fMRI studies
- accurate estimation of hemodynamic response function is not as critical as with event-related designs

- poor estimation power to differentiate the time courses in response to different conditions
- very predictable for subject
- Can't look at effects of single events
- becomes unmanagable with too many conditions (e.g., more than 4 conditions + baseline)

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Slow Event-Related (ER) designs



Optimal constant **inter-trial interval (ITI)**
- For brief(<2s) stimuli = 12 s
- For longer stimuli = 8 + 2*stimulus duration

Pros & Cons of Slow ER Designs

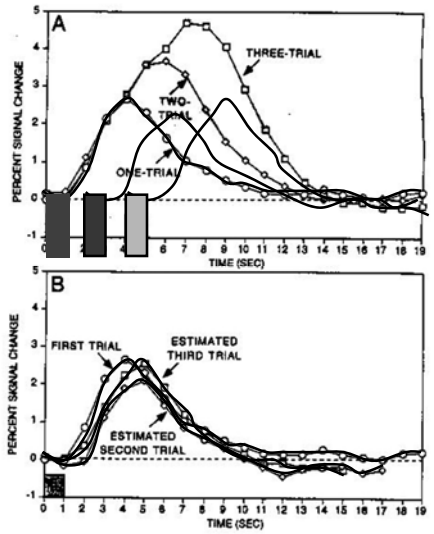
- excellent estimation of BOLD changes
- useful for studies with delay periods
- very useful for designs with motion artifacts because you can tease out artifacts

- poor detection power because of very few trials per condition
- subjects can get VERY bored and sleepy with long ITI.

How about making it fast?

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Linearity of BOLD signal



Linearity:
"Do things add up?"

red = 2 - 1

green = 3 - 2

Sync each trial response to start of trial

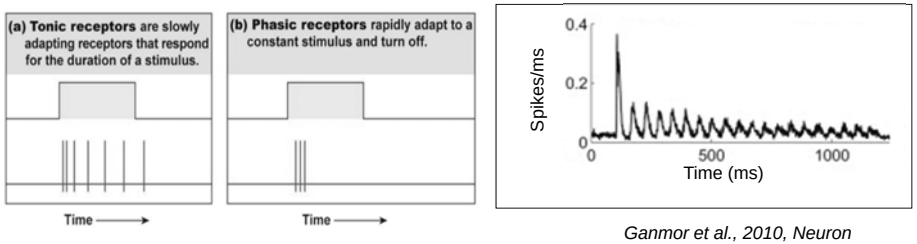
Not quite linear but good enough!

Dale & Buckner, 1997

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbi

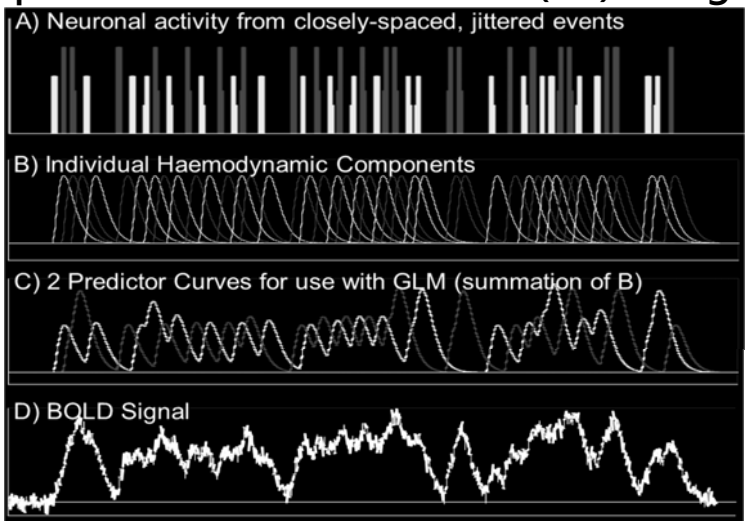
BOLD isn't totally linear

- Linearity of BOLD is sufficient for events with at least 4s of ITI.
- Phasic neural responses
- Adaption or habituation depends on stimulus duration and intensity.



Ganmor et al., 2010, Neuron

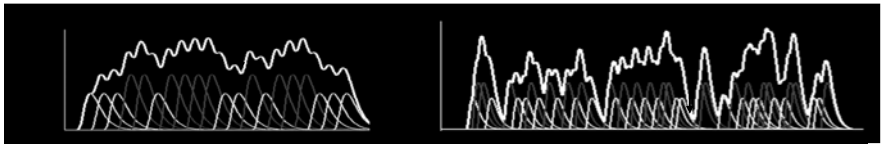
Rapid Jittered Event-Related (ER) designs



fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Why jitter?

- Yields larger fluctuations in signal



When pink is on, yellow is off
→ pink and yellow are anticorrelated

Includes cases when both pink and yellow are off
→ less anticorrelation

- Without jittering predictors from different trial types are strongly anticorrelated
  - As we know, the GLM doesn't do so well when predictors are correlated (or anticorrelated)

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Pros & Cons of Rapid-ER Designs

- high detection power
- trials can be put in unpredictable order
- subjects don't get so bored

- reduced detection compared to block designs
- requires stronger assumptions about linearity
  - BOLD is non-linear with inter-event intervals < 4 sec.
  - Nonlinearity becomes severe under 2 sec.
- errors in HRF model can introduce errors in activation estimates

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

THE END

alvin4016@ym.edu.tw