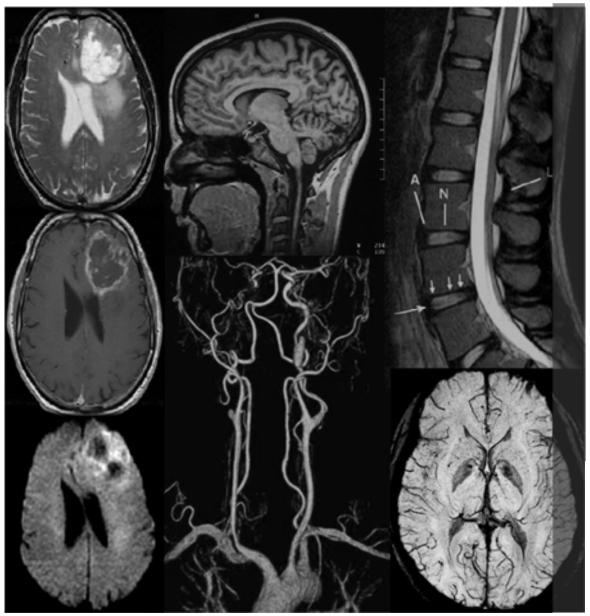


醫用磁振學MRM
功能性磁振造影II
functional MRI - Analyses

盧家鋒 助理教授

國立陽明大學 生物醫學影像暨放射科學系
alvin4016@ym.edu.tw

本週課程內容 http://www.ym.edu.tw/~cflu

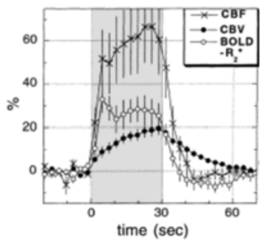
- 功能性磁振造影原理回顧
- fMRI實驗設計
- 影像前處理流程/一般線性模型

- Functional Magnetic Resonance Imaging
  - Scott A. Huettel, Allen W. Song, Gregory McCarthy
- Introduction to Functional Magnetic Resonance Imaging (2nd edition)
  - Richard B. Buxton

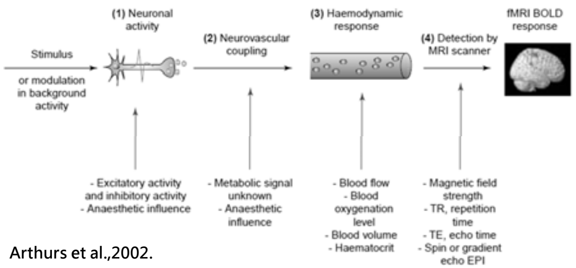
功能性磁振造影原理回顧
Review of fMRI Principles

Neuronal activity and BOLD

- Blood-oxygenation level dependent (BOLD)
- BOLD fMRI detects the alterations in
  - The level of deoxygenated hemoglobin
  - Cerebral blood volume



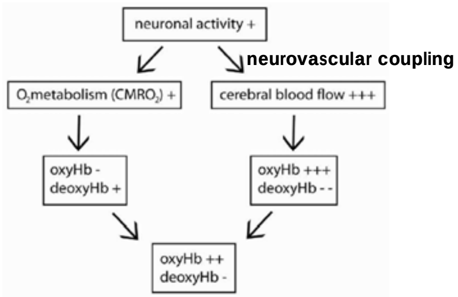
Mandeville et al.,MRM 1999.



Arthurs et al.,2002.

Metabolic and hemodynamic changes

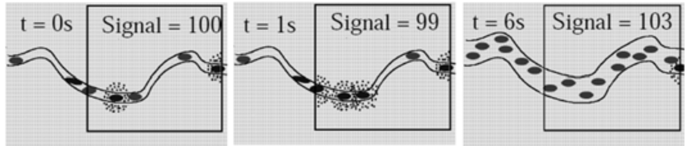
- Mismatch between CBF and O_2 consumption
- Neural/Brain activation
  - Elevated oxy-Hb fraction
  - Decrease deoxy-Hb fraction



Neuroimaging – Methods, pp.53.

fMRI BOLD signal

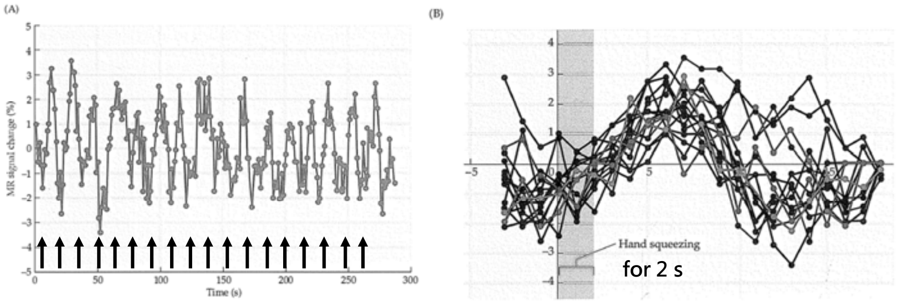
- t = 0s, a steady state in which there is an given amount of oxygenated and deoxygenated hemoglobin.
- t = 1s, an increased of deoxygenated hemoglobin due to the oxygen demands of neuronal activation.
- t = 6s, an increased of blood supply and oxygenated hemoglobin "flush away" the deoxygenated ones.



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

fMRI signal example

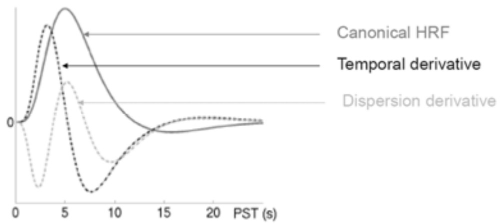
- A sample fMRI time course from a single voxel in the motor cortex during a task in which the subject squeezed her hand for 2 s every 16 to 18 s.



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)

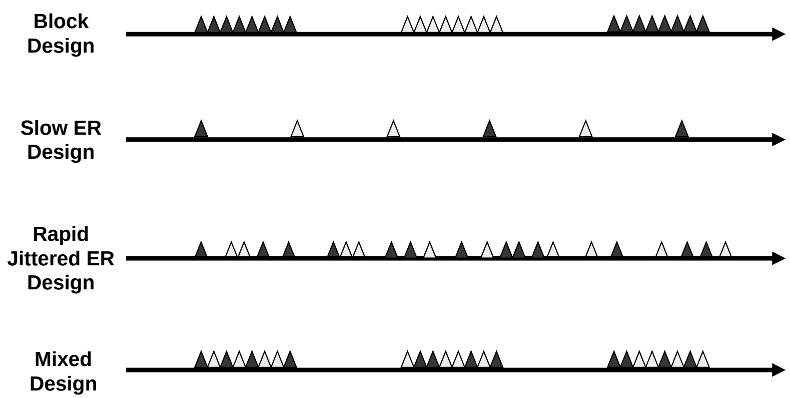
Experimental design

- 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*.

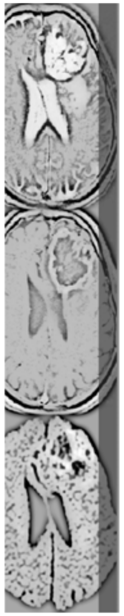
Design Types

▲ = trial of one type

△ = trial of another

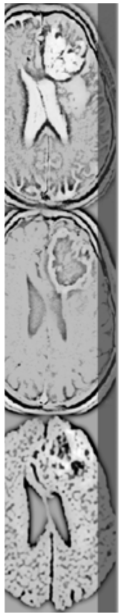


fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html



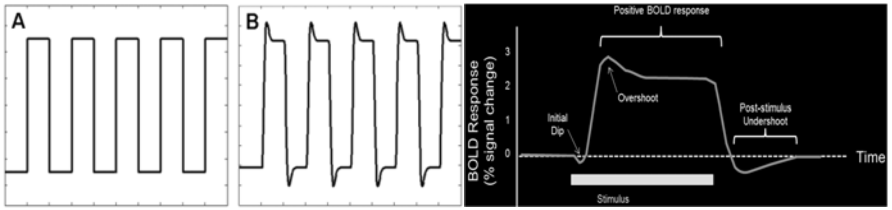
Block designs

- 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.

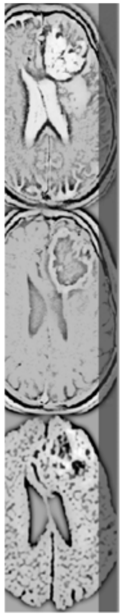


Block designs

- 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.

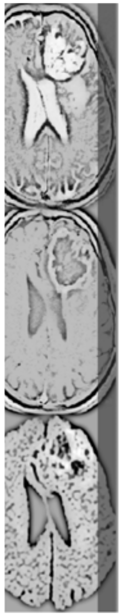


Pros & Cons of Block Designs

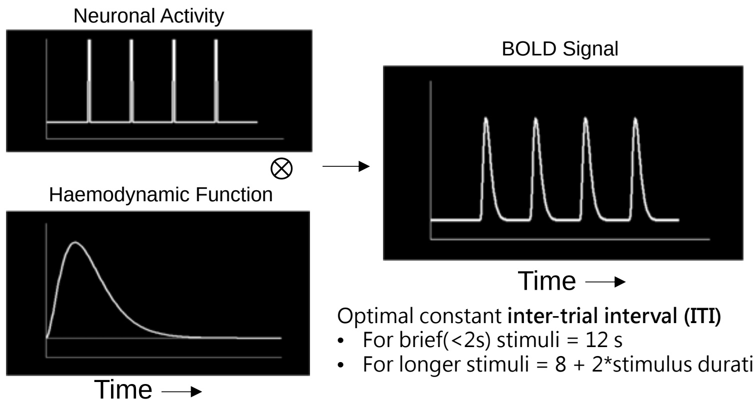
- high detection power of activated voxel/region
- has been the most widely used approach for fMRI studies
- accurate estimation of hemodynamic response function is not as critical as with event-related designs

- 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

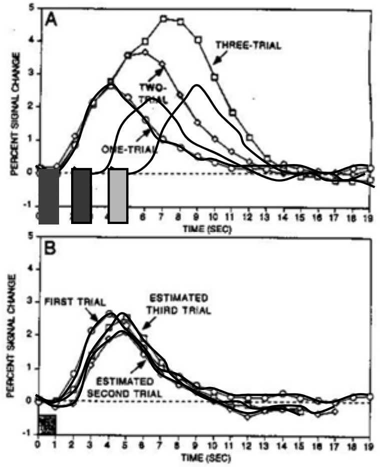
- excellent estimation of BOLD changes
- useful for studies with delay periods
- very useful for designs with motion artifacts because you can tease out artifacts

- 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

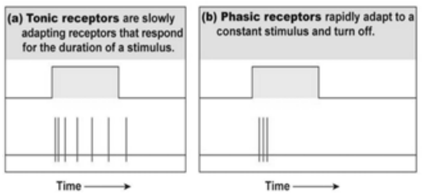
Not quite linear but good enough!

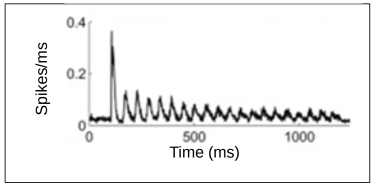
Dale & Buckner, 1997
fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/

BOLD isn't totally linear

- Linearity of BOLD is sufficient for events with at least 4s of ITI.

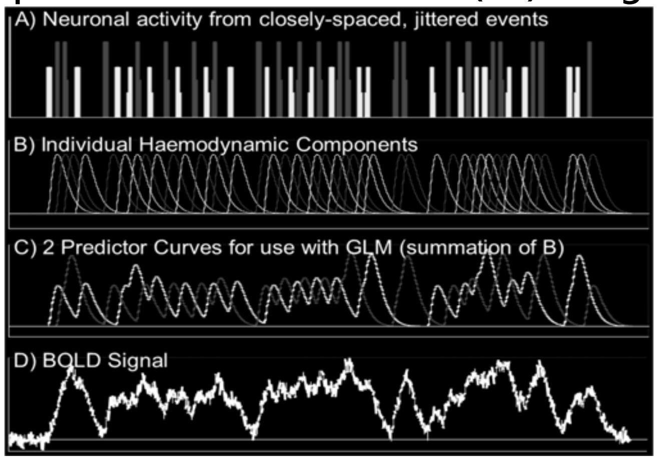
- Phasic neural responses
- Adaption or habituation depends on stimulus duration and intensity.





Ganmor et al., 2010, Neuron

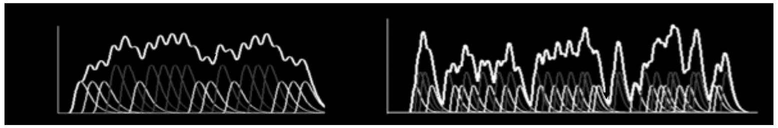
Rapid Jittered Event-Related (ER) designs



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

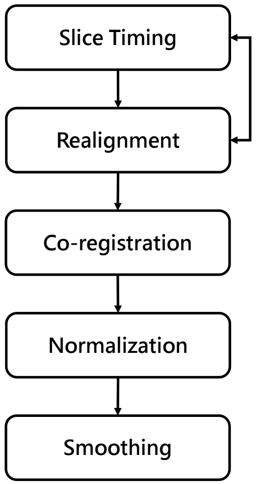
Pros & Cons of Rapid-ER Designs

- 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

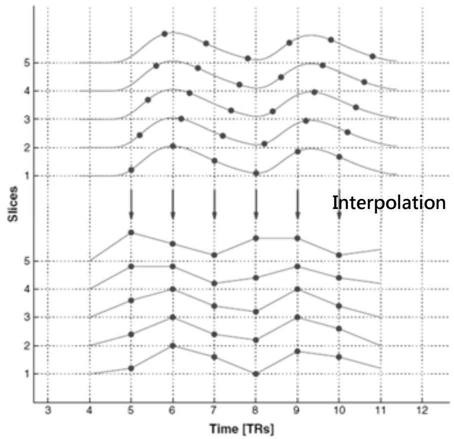
fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

fMRI前處理流程

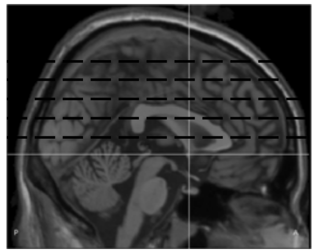


Slice timing

Correction for slightly different imaging timing for multi-slice acquisition in a TR.



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

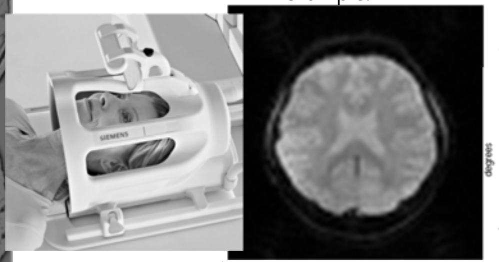


Sladky et al, NeuroImage 2011,58:588-594.

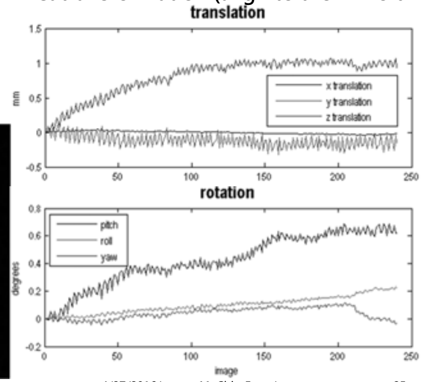
Realignment of head motion

- The signal variation from movement is larger than hemodynamic response.

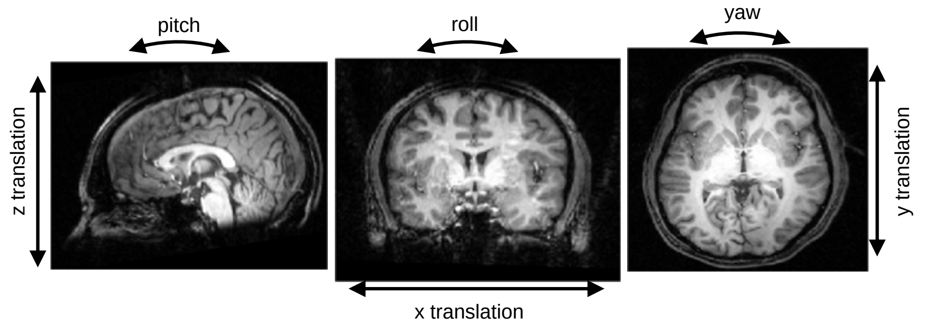
An example:



6-parameter Rigid body registration & transformation (align to the 1st volume)



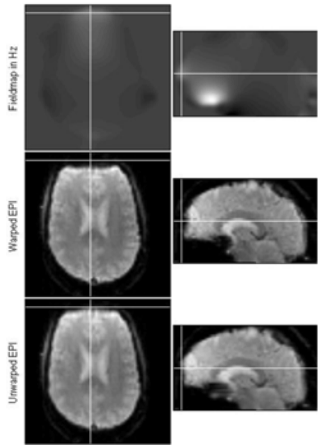
3 translations and 3 rotations



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

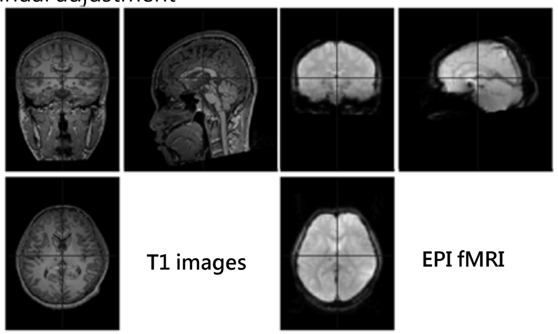
EPI undistortion/unwarp

- 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.



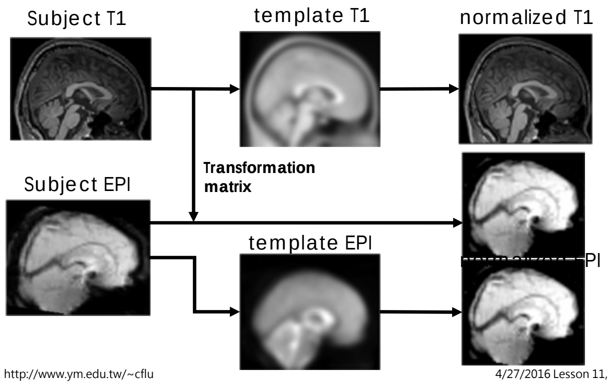
Co-registration

- 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.

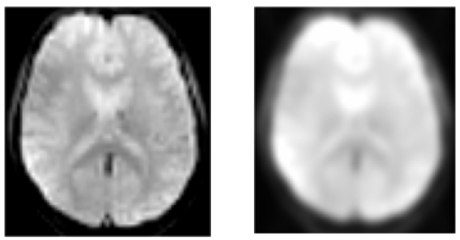


Problems with normalization

- The structural alignment does not guarantee the functional alignment.
- Differences between individuals in cortex anatomy and physiology can not be perfectly registered
  - 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

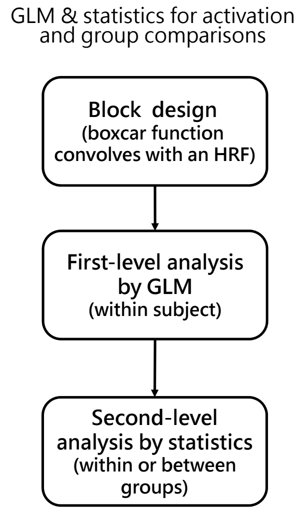


2 x 2 x 2 mm^3

normalization

Normalization+smoothing

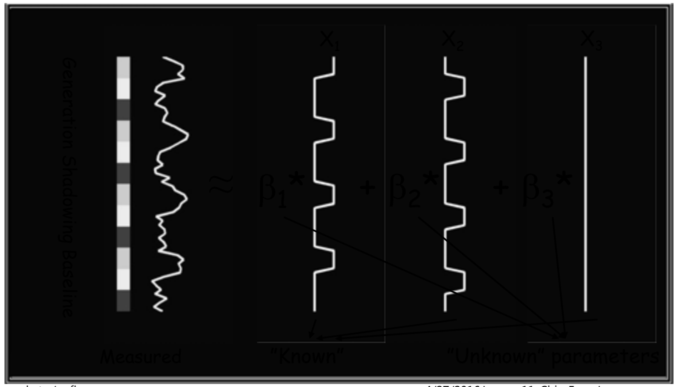
一般線性模型
General Linear Model, GLM



The Model

We have our set of hypothetical time-series

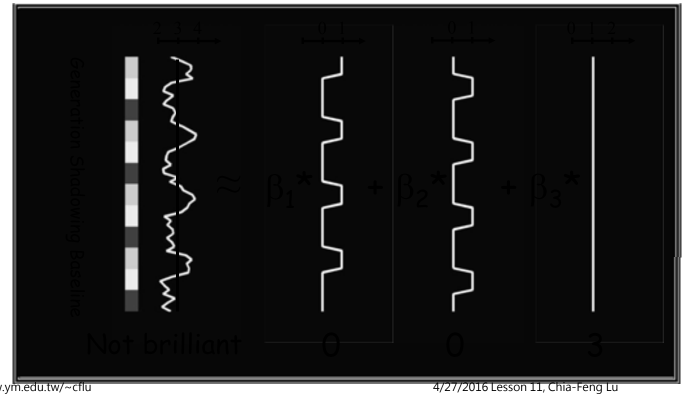
The estimation entails finding the parameter values such that the linear combination of these hypothetical time series "best" fits the data.



Parameter Estimation

Finding the "best" parameter values

For a given voxel (time-series) we try to figure out just what type of voxel this is by "modelling" it as a linear combination of the hypothetical time-series.

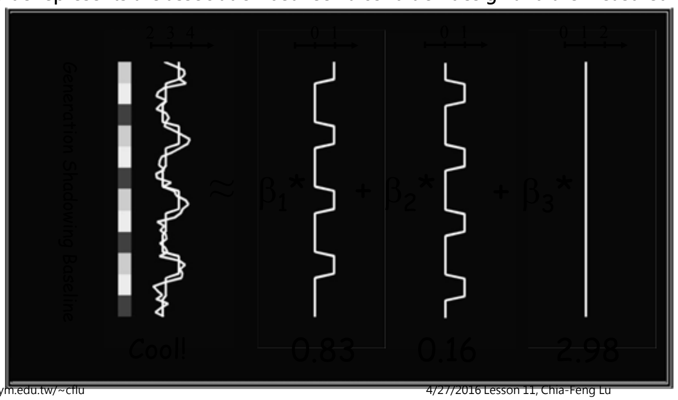


Parameter Estimation

Finding the "best" parameter values

For a given voxel (time-series) we try to figure out just what type of voxel this is by "modelling" it as a linear combination of the hypothetical time-series.

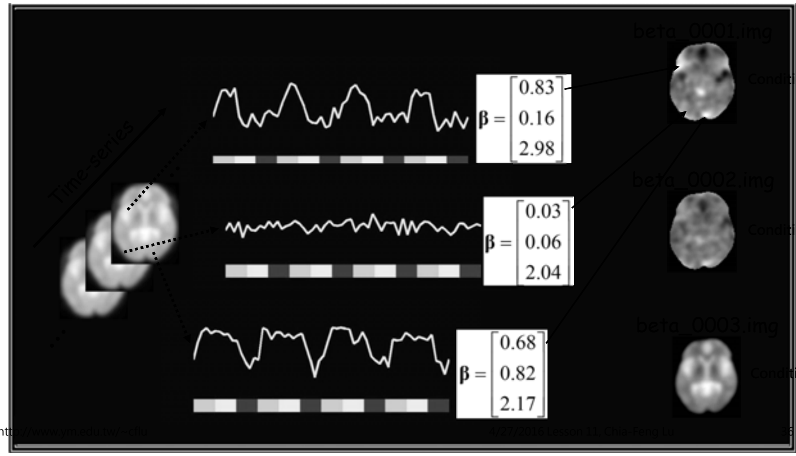
Beta value represents the association between a condition design and the measured BOLD signal.

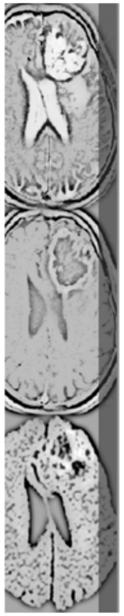


Parameter Estimation

Same model for all voxels.

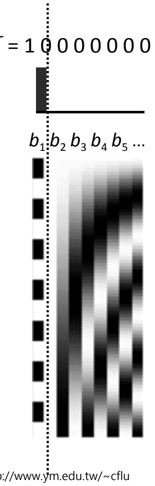
Different parameters for each voxel. Beta map for each task condition





T-test - one dimensional contrasts – SPM{*t*}

$c^T = 1\ 0\ 0\ 0\ 0\ 0\ 0\ 0$

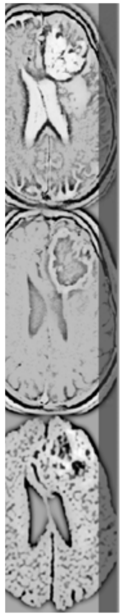


Question: box-car amplitude > 0 ? = $b_1 = c^T b > 0$?

Null hypothesis: H_0: $c^T b = 0$

Test statistic: $T = \dfrac{\textit{contrast}\text{ of estimated parameters}}{\sqrt{\text{variance estimate}}}$

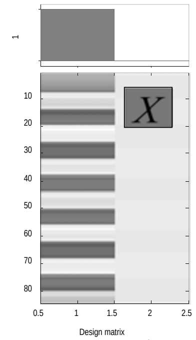
$$T = \frac{c^T \hat{\beta}}{\sqrt{\mathrm{var}(c^T \hat{\beta})}} = \frac{c^T \hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T \left(X^T X\right)^{-1} c}} \sim t_{N-p}$$



T-test: a simple example

Passive word listening versus rest

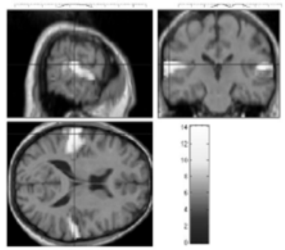
$c^T = [\ 1\quad 0\ ]$



Q: activation during listening?

Null hypothesis: $\beta_1 = 0$

$$t = \frac{c^T \hat{\beta}}{Std(c^T \hat{\beta})}$$



SPMresults:
Height threshold T = 3.2057 {p<0.001}

voxel-level			mm mm mm		
T	$(Z_{\equiv})$	$p_{uncorrected}$			
13.94	Inf	0.000	-63	-27	15
12.04	Inf	0.000	-48	-33	12
11.82	Inf	0.000	-66	-21	6
13.72	Inf	0.000	57	-21	12
12.29	Inf	0.000	63	-12	-3
9.89	7.83	0.000	57	-39	6
7.39	6.36	0.000	36	-30	-15
6.84	5.99	0.000	51	0	48
6.36	5.65	0.000	-63	-54	-3
6.19	5.53	0.000	-30	-33	-18
5.96	5.36	0.000	36	-27	9
5.84	5.27	0.000	-45	42	9
5.44	4.97	0.000	48	27	24
5.32	4.87	0.000	36	-27	42

THE END

alvin4016@ym.edu.tw