Introduction of fMRI Analysis
功能性磁振造影：影像分析簡介

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

2019.7.4

Answers to the Questions

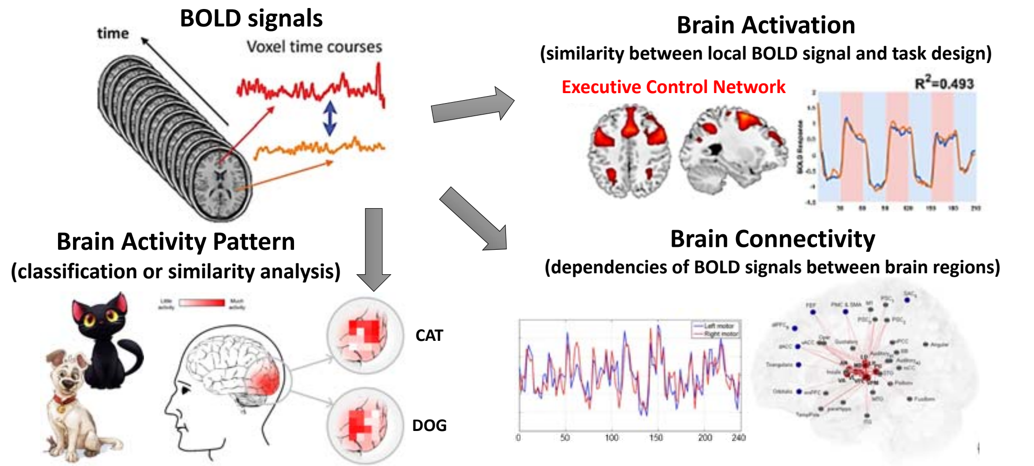
Specialization
Representation
Integration

Brain activation to the corresponding task.
- Where is the motion area?
- Where is the face recognition area?

Brain encoding to the representation of stimulus classes.
- What are the varying brain states in an area?
- How do brain cortices encode different types of information?

Brain connectivity to the integration of neural networks.
- How do neurons and neural networks process information?

fMRI Analysis



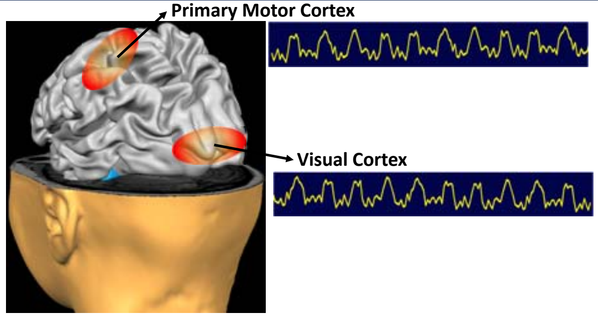
fMRI Analysis

- **Brain Activation Analysis**
  - General Linear Model (GLM)
- **Brain Decoding:**
  - Multivariate Pattern Analysis (MVPA)
  - Classifier-based MVPA, pattern similarity analysis
- **Brain Connectivity:**
  - Statistical dependency
  - Independent Component Analysis (ICA)
  - Network analysis

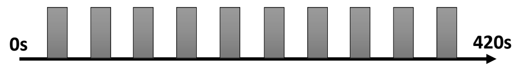
Brain Activation Analysis

General Linear Model (GLM)

Data Acquisition



Block Design



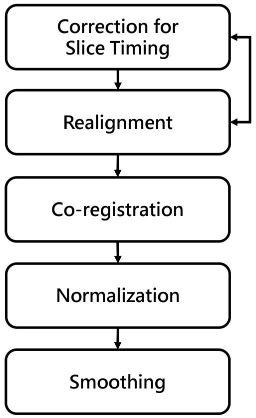
10 tasking blocks (duration = 20s) with resting interval (20s)

MRI

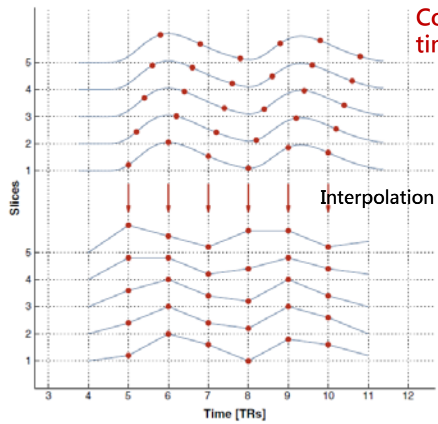
- 3D MPRAGE (3D T1W)
- BOLD fMRI:
  10 blocks in one task run
  (visual stimuli)

BOLD-fMRI Preprocessing

- Standard preprocessing steps for fMRI
  - Slice timing
  - Realignment
  - Co-registration (with anatomical images)
  - Normalization
  - Smoothing
  - Segment (tissue classification; optional)

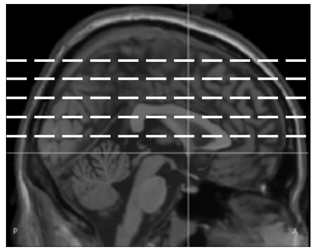


Correction for Slice Timing



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

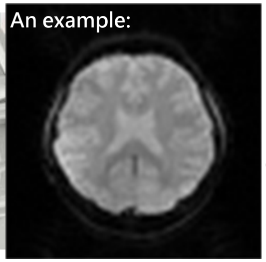


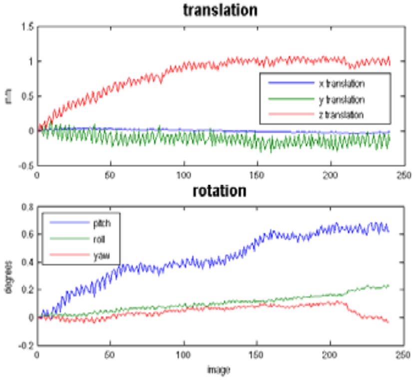
Sladky et al, NeuroImage 2011,58:588-594.

Realignment of head motion

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

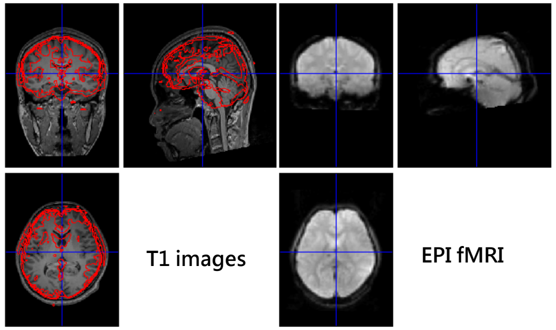
6-parameter Rigid body registration
& transformation (align to the 1st volume)
➔ 6 co-variates for rs-fMRI analysis





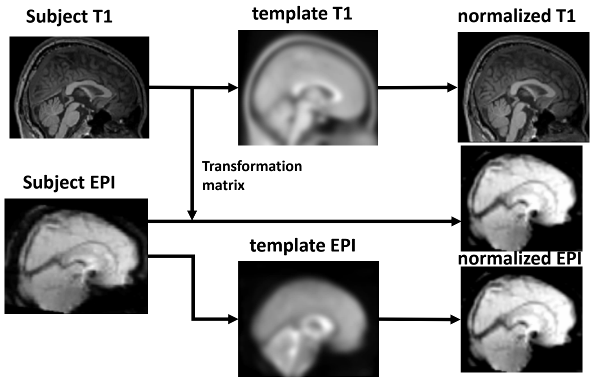
Co-registration

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



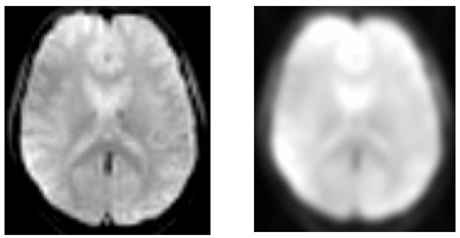
Spatial Normalization

- Perform spatial normalization using either anatomical (T1) images or fMRI (EPI) data.



3D Gaussian Smoothing

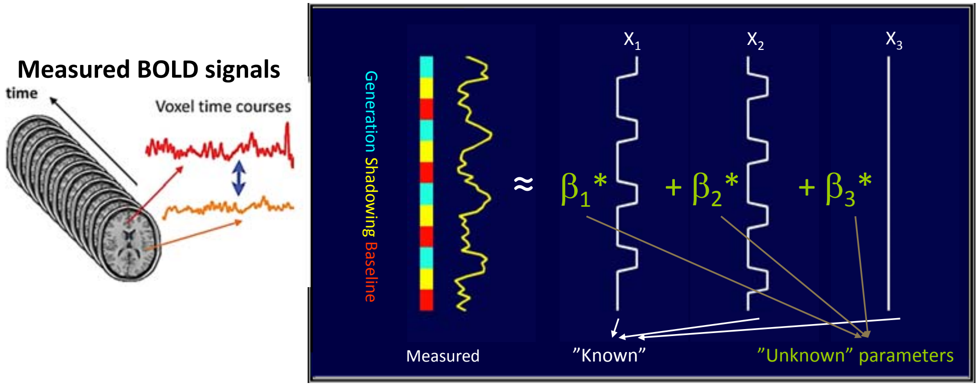
- Each voxel becomes weighted average of surrounding voxels.
- Render the data more normally distributed.
- Compensate for inaccuracies in normalization between individuals.
- Increase signal-to-noise ratio



2 x 2 x 2 mm³ **normalization** **Normalization+smoothing**

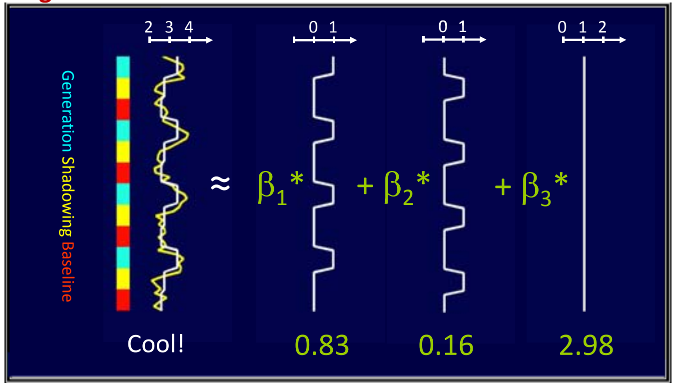
The Model of GLM

Finding the linear combination of these hypothetical time series "best" fits the data.



Parameter Estimation

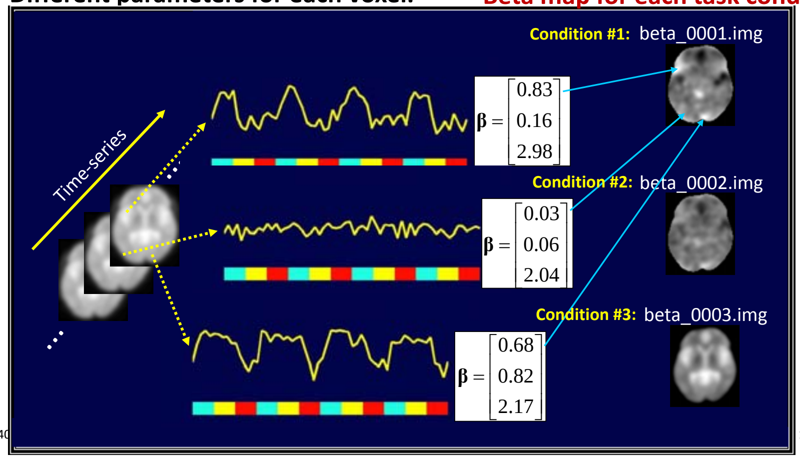
Beta value represents the association between a condition design and the measured BOLD signal.



Parameter Estimation

Same model for all voxels.

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



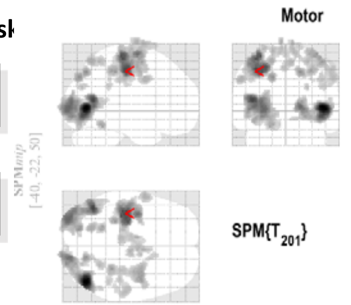
T-test: a simple example

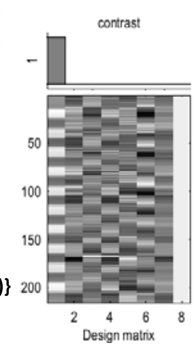
Right hand grasping task

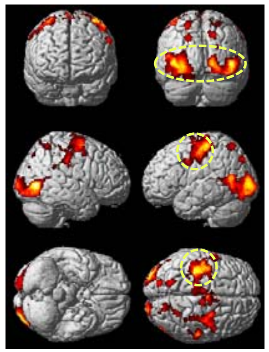
Q: activation during grasping?

Null hypothesis: $\beta_1 = 0$

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







SPMresults:
Height threshold T = 5.4989 {p<0.01 (FWE)}
Extent threshold k = 30 voxels

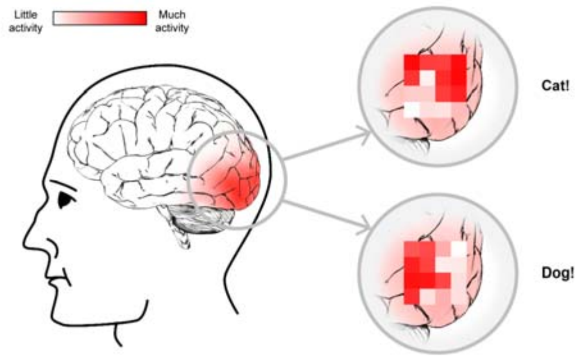
Available Softwares

- Statistical Parametric Mapping, SPM
  - https://www.fil.ion.ucl.ac.uk/spm/
- Analysis of Functional NeuroImages, AFNI
  - https://afni.nimh.nih.gov/
- FSL-FEAT
  - https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT

Brain Decoding

Multivariate Pattern Analysis (MVPA)

Decoding Activity Pattern of Brain



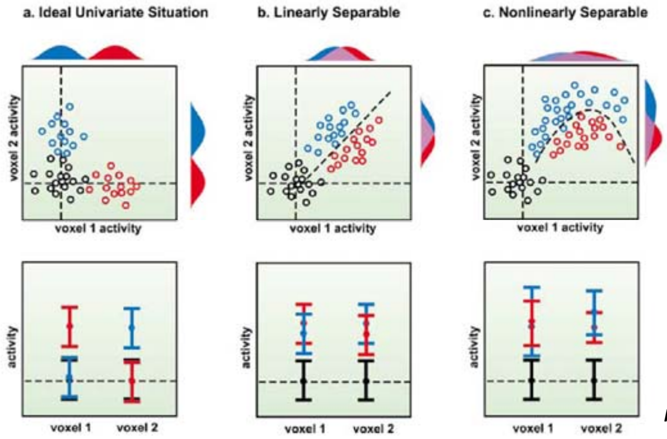
Looking at the pattern of activation within a brain area allows us to answer what the person is seeing.

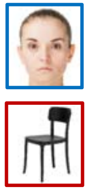
Illustration by Pim Mostert http://blog.donders.ru.nl/?p=4361&lang=en

Brain Activation → Brain Decoding

- **Mass-univariate model-based analysis**
  - Analyze every voxel (~50,000) one at a time
  - General Linear Model, GLM (since 1995)
- **Multivoxel Pattern Analysis, MVPA**
  Multivariate Pattern Analysis, MVPA
  - Original version: correlation analysis
  - Machine learning: Support Vector Machine, SVM

Why we need multivariate analysis?





A: Human face

B: Chair

Neuroimage, *19*(2), pp.261-270, 2003.

Major limitations of GLM

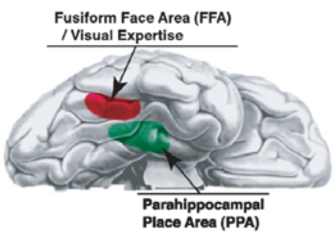
- The basic assumption that the covariance across neighboring voxels is not informative about the cognitive function under examination.
- Such covariance is considered as uncorrelated noise and normally reduced using spatial filters that smooth BOLD signals across neighboring voxels.
- Additionally, the GLM approach is inevitably limited by the model used for statistical inference.

➔ **Fail to capture "distributed" neural codes.**

Origin of MVPA

Three hypothesis made by **James V. Haxby**, 2001.

- Each object category would evoke a distinct pattern of response in ventral temporal cortex.
- These distinctive patterns would not be restricted to category-selective regions, such as the FFA (face) and PPA (other objects).
- Neural activity patterns within category-selective regions would carry information that discriminates between categories.

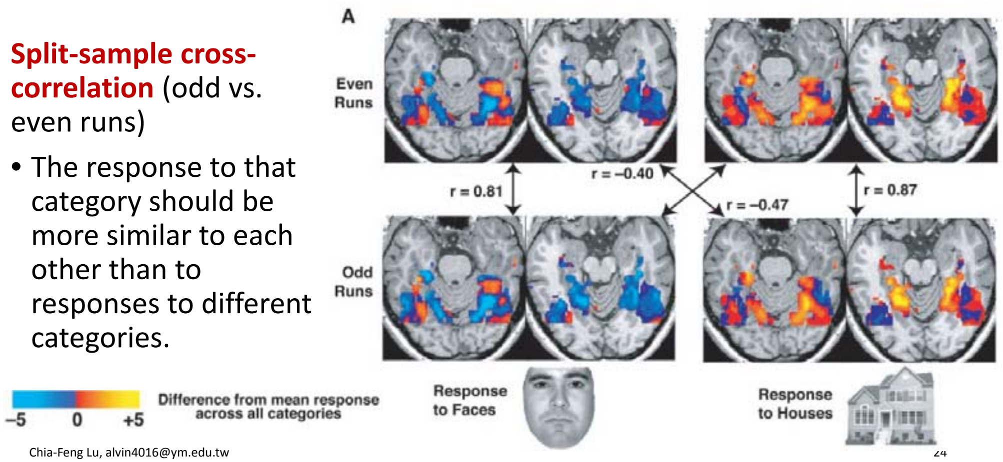


Origin of MVPA

Science, ***293***(5539), 2425-2430, 2001.

Split-sample cross-correlation (odd vs. even runs)

- The response to that category should be more similar to each other than to responses to different categories.

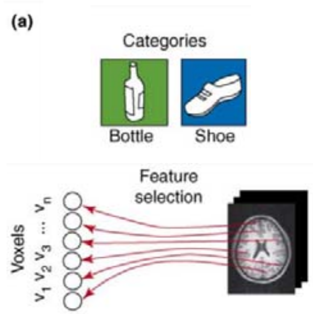


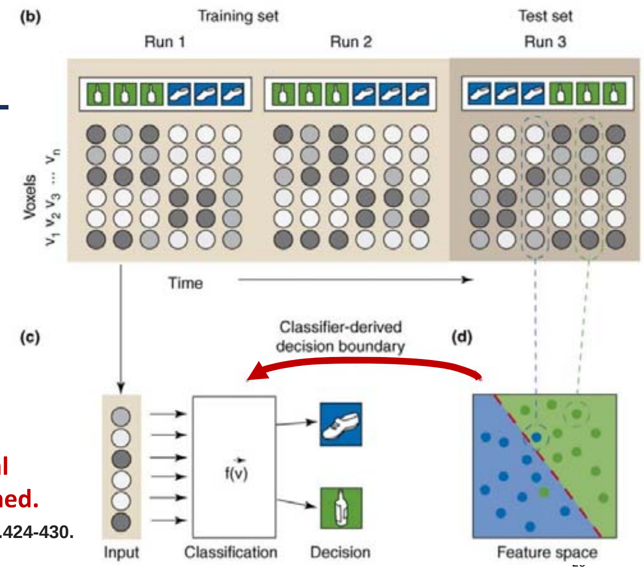
MVPA: A Classification Problem

- Classification consists in determining a decision function f that takes the values of various “features” in a data “example” x and predicts the class of that “example.”

- An “**example**” may represent a given trial in the experimental run.
- The “**features**” may represent the corresponding fMRI signals in a cluster of voxels.
- The experimental conditions may represent the different “**classes**”.

MVPA Diagram





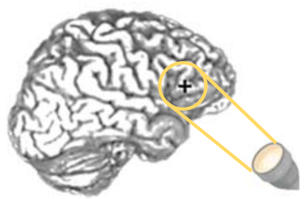
No explicit temporal or spatial smoothing should be performed.

***Trends in cognitive sciences*, *10*(9), pp.424-430.**

Searchlight Approach

- Kriegeskorte, N., Goebel, R. and Bandettini, P., 2006. Information-based functional brain mapping. ***Proceedings of the National Academy of Sciences***, *103*(10), pp.3863-3868.

- **Where in the brain does the activity pattern contain information about the experimental condition?**
  - Rather than asking where in the brain does the average activity changes across experimental condition.

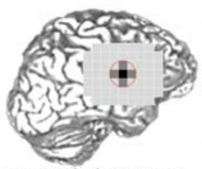


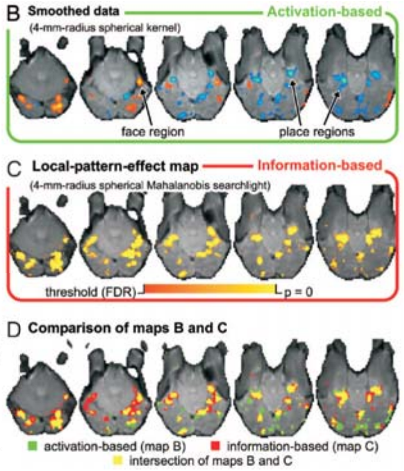
Searchlight Approach

When the **target** is to find…	**Assumption**	**Combination** of local signals
Activated Regions →	**Activate a region as a whole** →	**Local averaging** (spatial smoothing)
	V.S.	
Informative Regions →	**Activity patterns as distributed representations** →	**Multivariate statistics** (compare activity patterns among conditions)
	Salt-and-pepper fine structure	

Searchlight Approach

- Scan the brain with a **spherical multivariate "searchlight"** centered on each voxel in turn.
  - An optimal radius of 4mm contains 33 2-mm-isotropic voxels.
- The resulting map shows **how well the multivariate signal in the local spherical neighborhood differentiates the experimental conditions.**
  - Average absolute t value
  - Mahalanobis distance

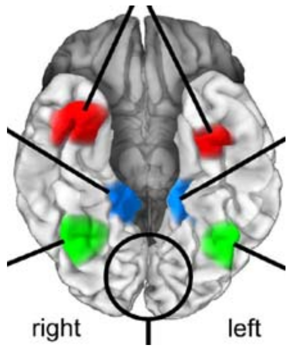


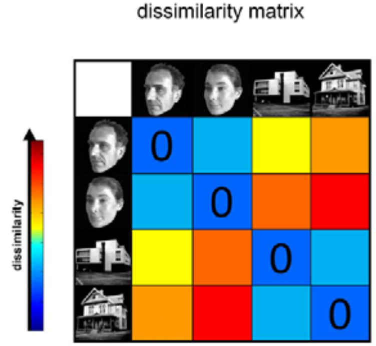


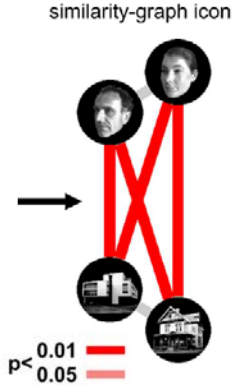
PNAS, 103(10), 3863-3868.

Pattern Similarity Analysis

Compared between regions, species, mental states, and diseases.







Frontiers in systems neuroscience, *2*, p.4, 2008

Toolbox of MVPA

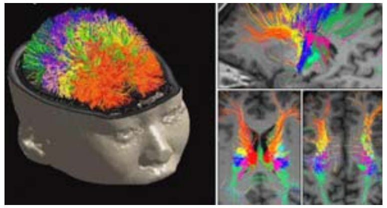
- Hanke, M., Halchenko, Y.O., Sederberg, P.B., Hanson, S.J., Haxby, J.V., Pollman, S., 2009. PyMVPA: a Python toolbox for multivariate pattern analysis of fMRI data. ***Neuroinformatics*** 7, 37–53.
- An MVPA toolbox using Matlab (the Princeton MVPA toolbox) (http://code.google.com/p/princeton-mvpa-toolbox/).
- Oosterhof, N.N., Connolly, A.C. and Haxby, J.V., 2016. CoSMoMVPA: multi-modal multivariate pattern analysis of neuroimaging data in Matlab/GNU Octave. ***Frontiers in neuroinformatics***, *10*, p.27.

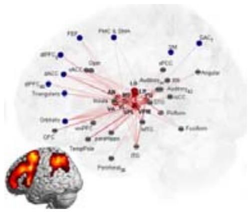
Brain Connectivity

Statistical Dependency and Network Analysis

Brain Connectivity

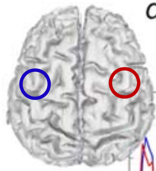
- **Structural connectivity**
  - Anatomical links (neuronal fibers)
- **Functional connectivity**
  - Statistical dependency
- **Effective connectivity**
  - Causal interactions between distinct units

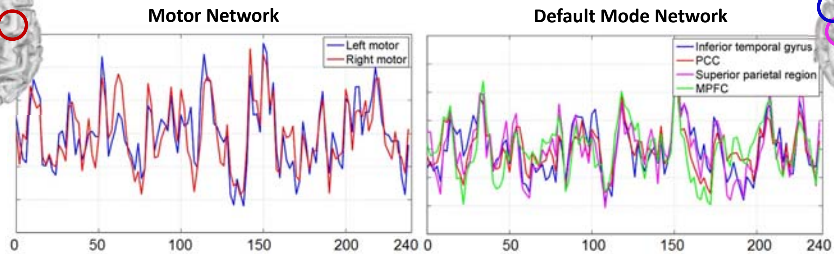


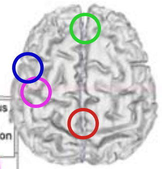


Functional connectivity

- Functional connectivity (FC) is defined as the statistical association or dependency *among two or more anatomically distinct time-series*.



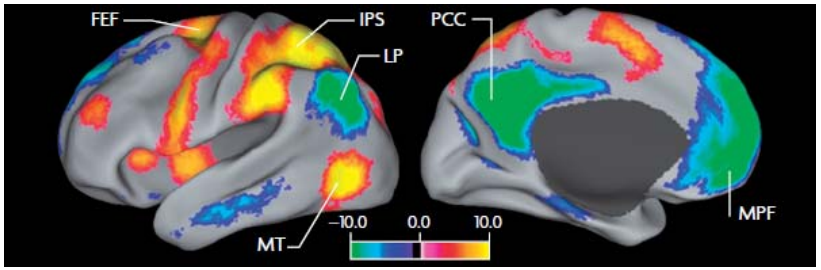




(Friston 1994, HBM 20, 56-78 & Friston et al., 1996,Cereb Cortex, 60 156-164)

Default Mode Network

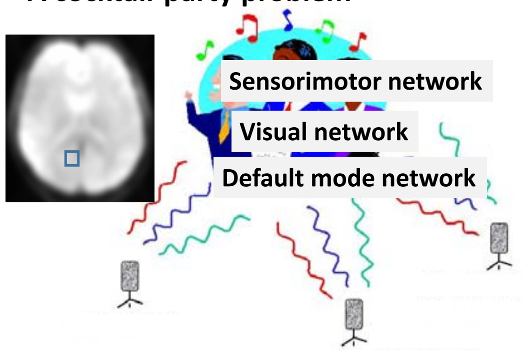
- During resting state scans, there are two networks in which areas are correlated with each other and anticorrelated with areas in the other network



Fox and Raichle, 2007, Nat. Rev. Neurosci.

Independent Component Analysis

- **A cocktail-party problem**



Number of microphones>=number of speakers

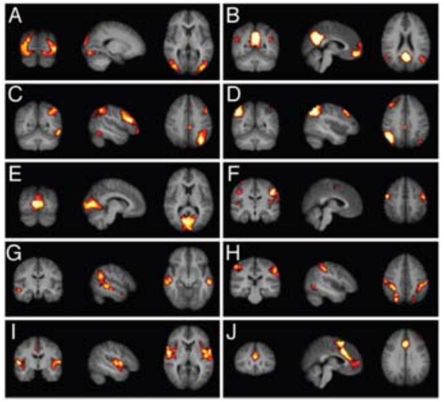
$$x_1(t) = 0.7s_1(t) + 0.2s_2(t) + 0.1s_3(t)$$
$$x_2(t) = 0.3s_1(t) + 0.4s_2(t) + 0.3s_3(t)$$
$$x_3(t) = 0.1s_1(t) + 0.2s_2(t) + 0.7s_3(t)$$

$$\begin{bmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_m(t) \end{bmatrix} = \mathbf{A} \begin{bmatrix} s_1(t) \\ s_2(t) \\ \vdots \\ s_k(t) \end{bmatrix}$$

A is the mixing matrix

Independent Components

- A. parts of visual cortex
- B. default mode network
- C & D. left and right memory function
- E. visual cortex
- F. sensorimotor cortex
- G. occipitotemporal pathway (ventral stream)
- H. superior parietal cortex
- I. auditory cortex
- J. executive control & working memory

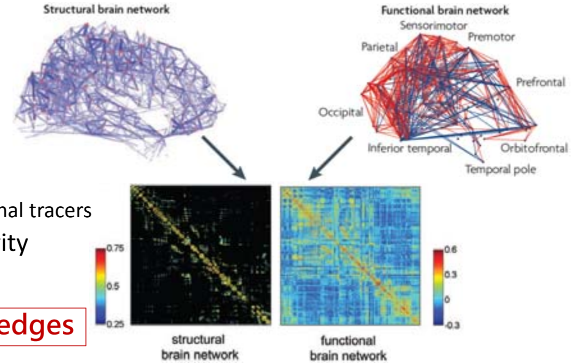


Consistent resting-state networks across healthy subjects. PNAS 2006, 103 37): 13848-13853.

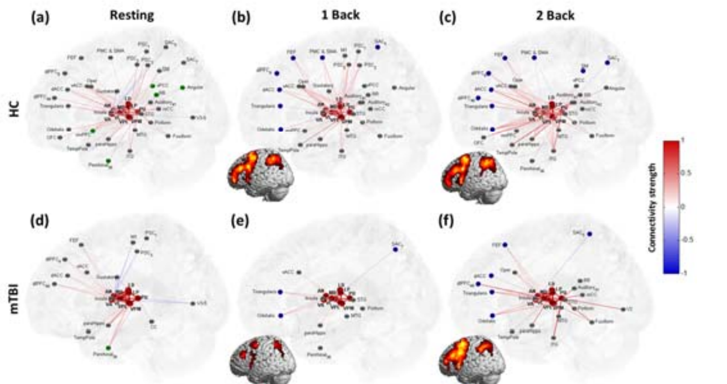
Network construction

- **Nodes**
  - Cortical regions
- **Edges**
  - Cortical thickness correlations
  - Fiber connections
    - DSI, DTI, transneuronal tracers
  - Functional connectivity
    - fMRI, EEG, MEG

Network = nodes + edges



Concussion-related alterations of FC

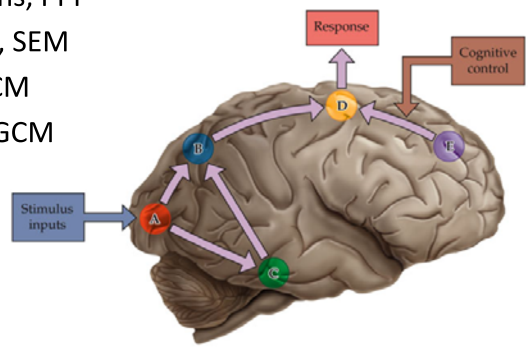


Lu et al., 2017 ISMRM.

$p < 0.05$ with FDR correction

Correlation ≠ Causality

- Psychophysiological Interactions, PPI
- Structural Equation Modelling, SEM
- Dynamic Causal Modelling, DCM
- Granger Causality Modelling, GCM

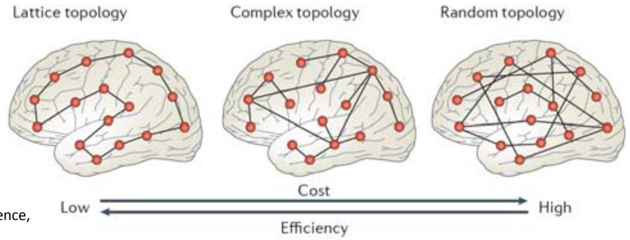


Functional Magnetic Resonance Imaging 2e, Figure 11.10

Human brain networks

Wiring costs ⇔ efficiency

- Clusters of lattice-like short-distance connections between spatially neighboring nodes
- Topologically direct interconnections between spatially remote brain regions → increase efficiency of information processing
- Nodes aggregated topologically and anatomically as modules → minimize wiring cost

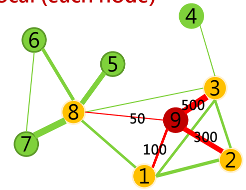


Nature Reviews Neuroscience, 13: 336-349, 2012.

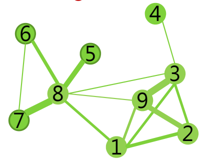
A small-world architecture

Graph theory: topological properties

Local (each node)



Global (average over all nodes)



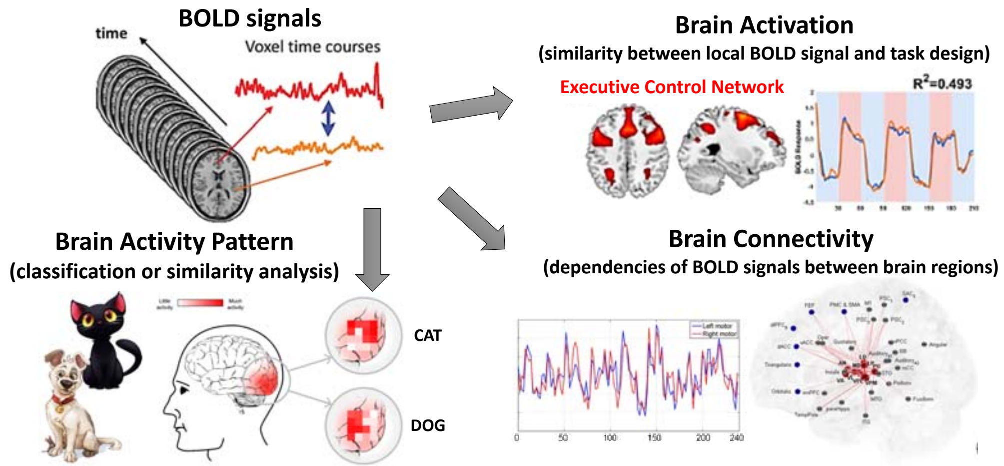
- **degree** (the number of neighbors)
  e.g. degree of node 9 = 4
- **strength** (the connected fiber number*FA)
  e.g. strength of node 9
  = (50+100+300+500)/4 =
  237.5
- **clustering coefficient**
  (the connection between neighbors, [0~1])
  e.g. clustering coefficient of node 9
  = 5/6 = 0.83
- **path length (separation)**
  (the minimal steps for connection)
  e.g. path length from node 9 to node 6
  = 2 steps (9 → 8 → 6)

Philos Trans R Soc Lond B Biol Sci, 360, 937-946, 2005

Available Softwares

- Group ICA of fMRI Toolbox, GIFT
  - http://mialab.mrn.org/software/gift/
- FSL-MELODIC
  - https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/MELODIC
- Statistical Parametric Mapping, SPM
  - https://www.fil.ion.ucl.ac.uk/spm/
- Data Processing & Analysis for Brain Imaging (DPABI)
  - http://rfmri.org/dpabi
- GRETNA Toolbox
  - https://www.nitrc.org/projects/gretna/
- Brain Connectivity Toolbox
  - https://sites.google.com/site/bctnet/

fMRI Analysis



THE END

alvin4016@ym.edu.tw

fMRI Teaching Materials:
http://www.ym.edu.tw/~cflu/CFLu_course_fMRIana.html