

# Practice in resting-state fMRI (rs-fMRI) Analysis: PART I

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# Course Arrangement

## PART I

- REST toolbox <http://restfmri.net/forum/index.php?q=rest>
- ReHo, ALFF, fALFF, Statistics

## PART II

- REST toolbox
- Functional connectivity (seed-based, atlas-based)
- FC strength mapping

# Course Arrangement

## PART III

- Large-scale network analysis
- Graph theory: topological properties (degree, strength, efficiency, clustering...)

## PART IV

- Dynamic functional connectivity

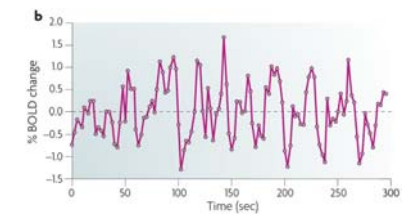
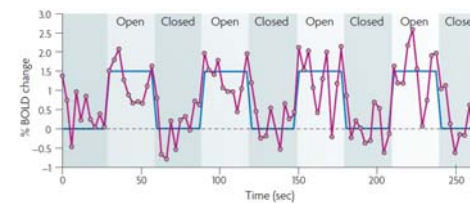
# Spontaneous Fluctuation

## Task-specific fMRI

- ✓ Model-based Analysis
- ✓ Model-free (data-driven) Analysis

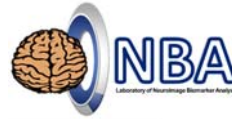
## Resting-state fMRI (rs-fMRI)

- ✓ Model-free (data-driven) Analysis



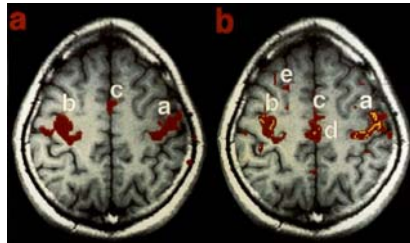
*Nature Reviews Neuroscience* 8.9 (2007): 700-711.

## First rs-fMRI Article (MRM 1995)



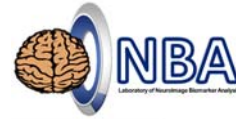
### Functional Connectivity in the Motor Cortex of Resting Human Brain Using Echo-Planar MRI

Bharat Biswal, F. Zerrin Yetkin, Victor M. Haughton, James S. Hyde



a. Functional activation during tasking  
b. rs-fMRI correlation maps  
(red: positive, yellow: negative)

## Rs-fMRI Analyses



### 1. Depicting local features of BOLD signal

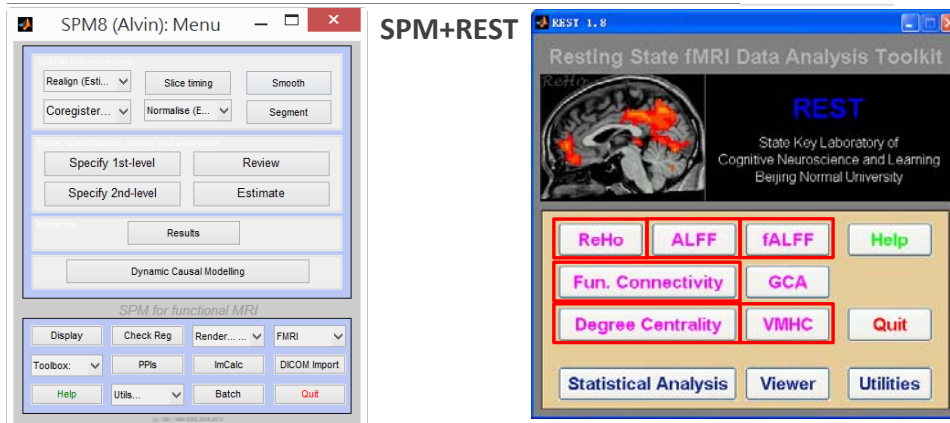
- Regional homogeneity (ReHo; Zang et al., NeuroImage 2004)
- Amplitude of low-frequency fluctuation (ALFF; Zang et al., Brain & Development 2007)
- Fractional ALFF (fALFF; Zou et al., J Neurosci Methods 2008)

### 2. Functional connectivity analysis

- Linear correlation
- Granger causality analysis (GCA), effective connectivity
- Independent component analysis (GIFT-ICA; Calhoun et al., NeuroImage 2001)

Functional segregation ↔ Functional Integration

## Easier Way to Learn : )



## Employed Software/Package



### 1. SPM preprocessing

- <http://www.fil.ion.ucl.ac.uk/spm/>

### 2. REST functional connectivity, ReHo, ALFF, fALFF, VMHC

- <http://restfmri.net/forum/index.php?q=rest>

**SPM5/8 is required for running REST toolbox!**  
**MATLAB version older than R2013b is recommended.**

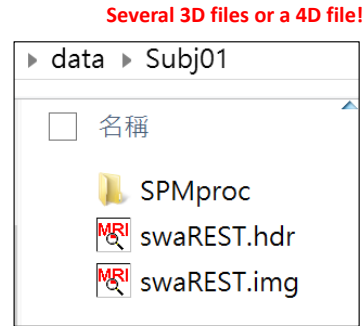
Error using rest\_Fix\_Read\_Write\_Error (line 64)  
Meet error while fixing read write error. Please restart MATLAB, and run "rest\_Fix\_Read\_Write\_Error" before starting anything.

# Organize data folder

Before using REST toolbox,

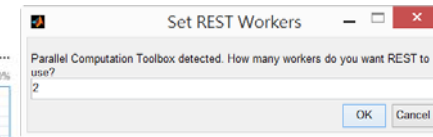
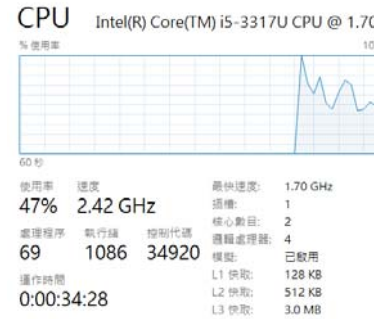
Make sure only pairs of sw\*.img/hdr or sw\*.nii files within a subject directory.

Move all other files (such as anatomical images) to a subfolder.



# Initialize REST environment

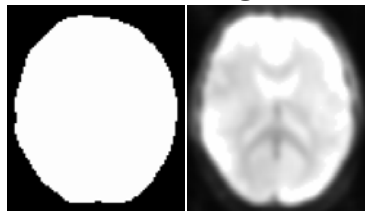
```
>> rest
```



```
Command Window
Welcome: Alvin, 20151002_2312
REST Version: 1.8, Release: 20130615
Citation Information:
Xiao-Wei Song, Zhang-Ye Dong, Xiang-Yu Long, Su-Fang Li, Xi-Nian Zu
Starting matlabpool using the 'local' profile ... connected to 2 workers.
Now REST is Running on 2 workers.
fx >>
```

# Create Brain Mask

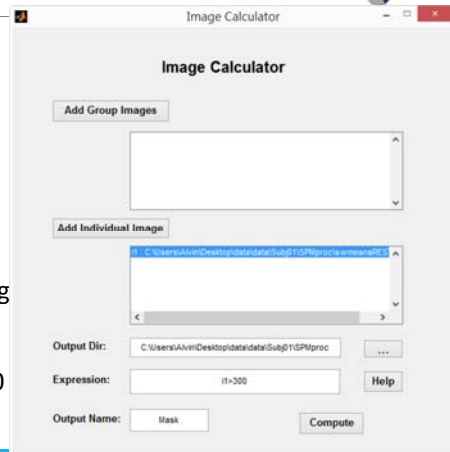
Utilities → REST Image Calculator



Import subject's swmeanREST.img

Can only handle 3D image not 4D!

i1 > 300



# ReHo approaches

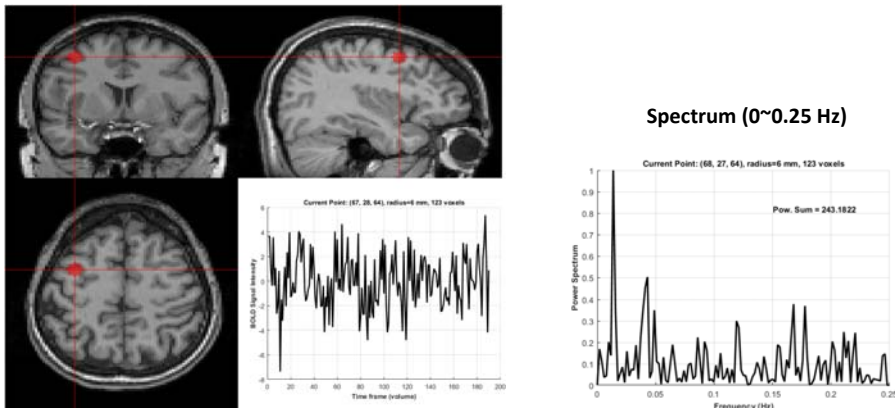
KCC: Kendall's coefficient of concordance,

Cohc: Coherence, linear correlation in frequency domain

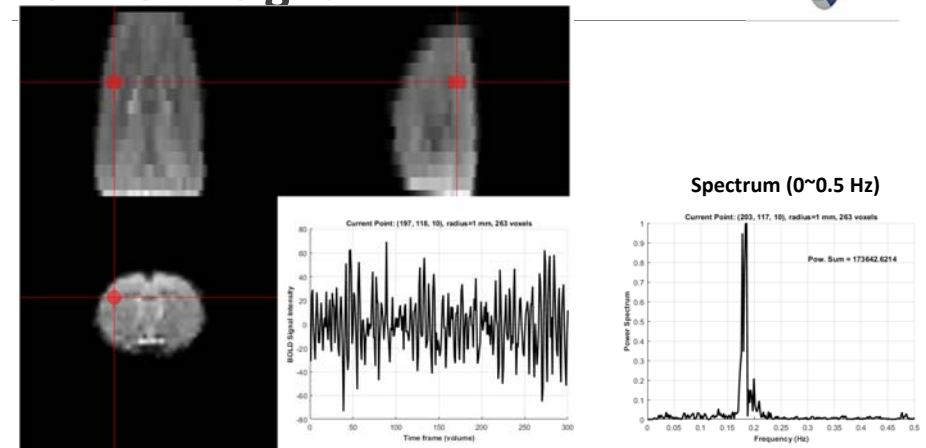


Liu, Dongqiang, et al. "Using coherence to measure regional homogeneity of resting-state fMRI signal." *Frontiers in systems neuroscience* 4 (2010): 24.

# Human BOLD signal



# Rat BOLD signal



## ReHo

# ReHo Setup

Assign folder with Analyze75 image pair (.img/.hdr), smoothed images

Select the user-defined mask

Select output directory and prefix



About 2~6 minutes~

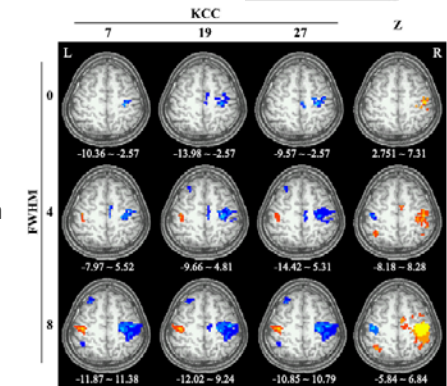
## ReHo

# What does ReHo represent?

Regional homogeneity, temporal similarity between neighbor voxels within a small cluster.

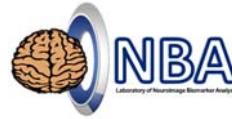
“ReHo supposed that voxels within a functional brain area were more temporally homogeneous when this area is involved in a specific condition.”

Model-free, data-driven ReHo can reflect cortical activation.



Zang et al., NeuroImage 2004.

# An example of ReHo (KCC)



**OBJECTS**  
i: 5 time points (number of ranks) n=5

**JUDGES**  
j: 3 voxels within a cluster

K=3

4	3	1	5	2
4	3	1	5	2
4	3	1	5	2

$R_1=12, R_2=9, R_3=3, R_4=15, R_5=6,$

$$R_i = \sum_{j=1}^K r_{i,j}$$

$$\bar{R} = \frac{1}{n} \sum_{i=1}^n R_i$$

$$S = \sum_{i=1}^n (R_i - \bar{R})^2$$

$$W = \frac{12S}{K^2(n^3 - n)}$$

$\bar{R} = 9, S = 90$

$W = \frac{12 \times 90}{9(125 - 5)} = 1 \rightarrow$  **unanimous measurements**

# An example of ReHo (KCC)



**OBJECTS**  
i: 5 time points (number of ranks) n=5

**JUDGES**  
j: 3 voxels within a cluster

K=3

4	3	1	5	2
5	1	2	3	4
3	2	4	1	5

$R_1=12, R_2=6, R_3=7, R_4=9, R_5=11,$

$$R_i = \sum_{j=1}^K r_{i,j}$$

$$\bar{R} = \frac{1}{n} \sum_{i=1}^n R_i$$

$$S = \sum_{i=1}^n (R_i - \bar{R})^2$$

$$W = \frac{12S}{K^2(n^3 - n)}$$

$\bar{R} = 9, S = 24$

$W = \frac{12 \times 24}{9(125 - 5)} = 0.27 \rightarrow$  **Lower concordance**

# An example of ReHo (KCC)



**OBJECTS**  
i: 5 time points (number of ranks) n=5

**JUDGES**  
j: 3 voxels within a cluster

K=3

4	3	1	5	2
3	5	4	1	2
2	1	4	3	5

$R_1=9, R_2=9, R_3=9, R_4=9, R_5=9,$

$$R_i = \sum_{j=1}^K r_{i,j}$$

$$\bar{R} = \frac{1}{n} \sum_{i=1}^n R_i$$

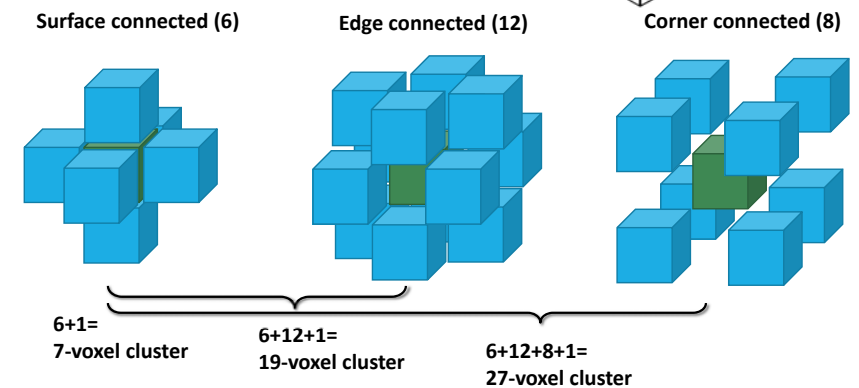
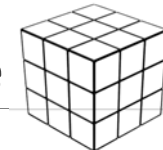
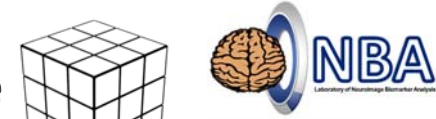
$$S = \sum_{i=1}^n (R_i - \bar{R})^2$$

$$W = \frac{12S}{K^2(n^3 - n)}$$

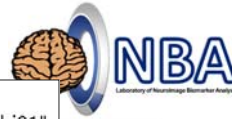
$\bar{R} = 9, S = 0$

$W = \frac{12 \times 0}{9(125 - 5)} = 0 \rightarrow$  **Total disagreement**

# Neighbors & Cluster size



## ReHo Computation time: 2 ~6 mins



```

Ideal rectangular filter: "C:\Users\Alvin\Desktop\NCKU-REST\data\Subj01"
Read 3D EPI functional images: "C:\Users\Alvin\Desktop\NCKU-REST\data\Subj01".

Load mask "".
Band Pass Filter working. Wait.....
Saving filtered images. Wait...
Band pass filter over.
Elapsed time is 194.178927 seconds.

ReHo :

Read these 3D EPI functional images. wait...
Read 3D EPI functional images: "C:\Users\Alvin\Desktop\NCKU-REST\data\Subj01_filtered".

Rank calculating.....
Calculate the kcc on voxel by voxel for the data set.....

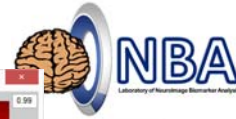
Regional Homogeneity computation over, elapsed time: 167.781 seconds
    
```

data ▶ Subj01

名稱

- ReHoMap
- SPMproc
- waREST.hdr
- waREST.img

## ReHo Slice Viewer



Underlay: manat.img  
 overlay: ReHoMap\*.nii  
 Adjust threshold

## ALFF

### What does ALFF represent?



Regional activation (regional activity during resting state).

Regional spontaneous neural activity

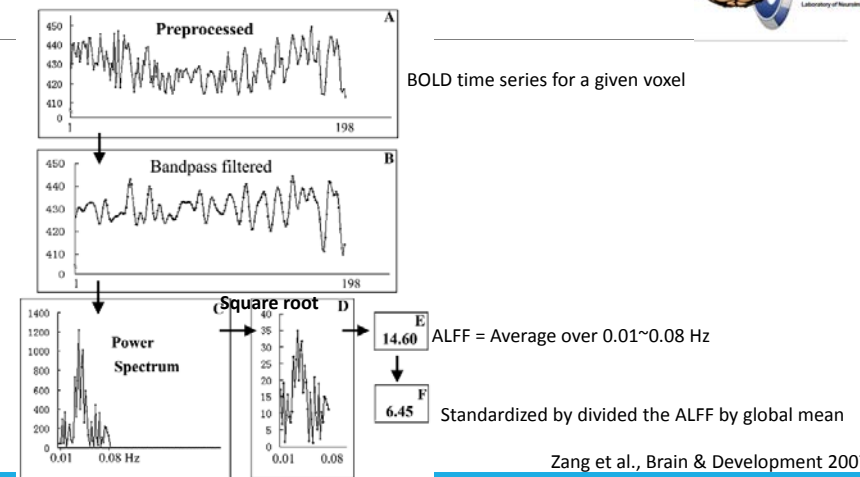
- ALFF is higher in grey matter than in white matter (Biswal et al., 1995).
- Kiviniemi et al. [22] reported activation in the visual cortex due to low-frequency fluctuations at about 0.034 Hz using the power spectrum method.

ReHo and functional connectivity analyses focus on the similarities of intra- and inter-regional time series, respectively, and ALFF measures the amplitude of regional activity.

Zang et al., Brain & Development 2007

## ALFF

### ALFF flowchart



Zang et al., Brain & Development 2007

## Fractional ALFF

However, it has been indicated that the ALFF is also sensitive to the physiological noise.

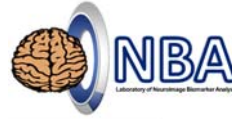
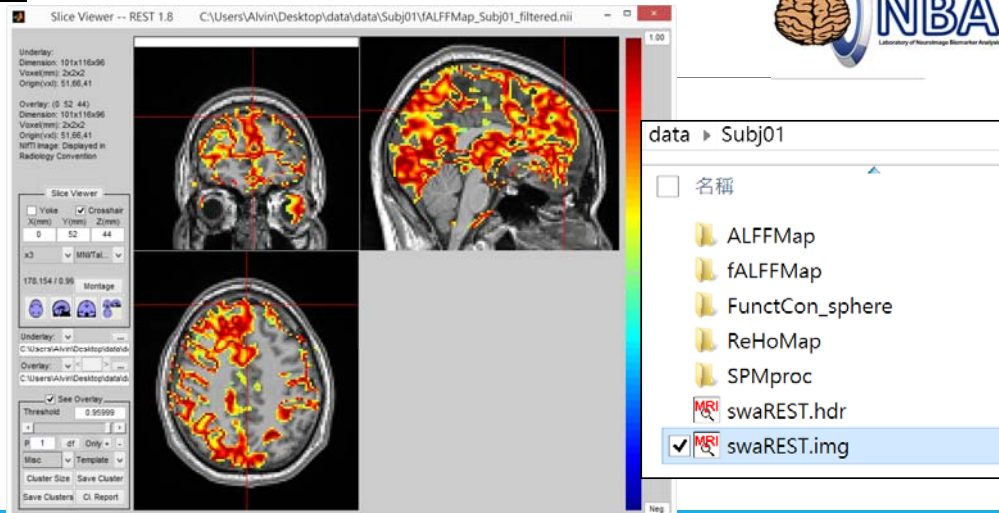
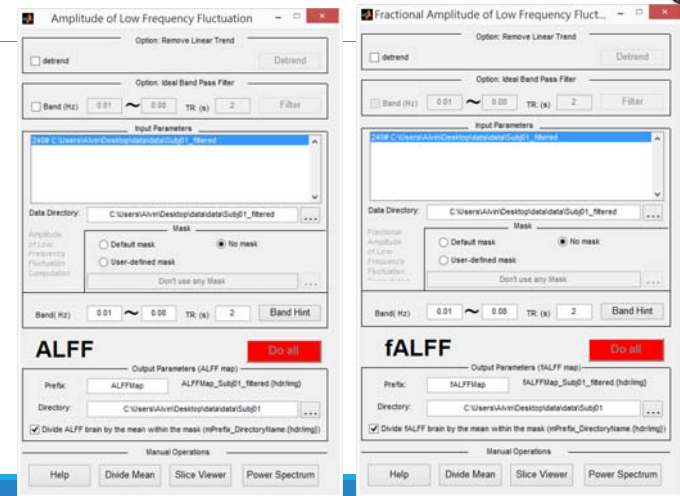
A fractional ALFF (fALFF) approach, i.e., the ratio of power spectrum of low-frequency (0.01–0.08 Hz) to that of the entire frequency range.

The non-specific signal components in the cistern areas in resting-state fMRI were significantly suppressed, indicating that the fALFF approach improved the sensitivity and specificity in detecting spontaneous brain activities.

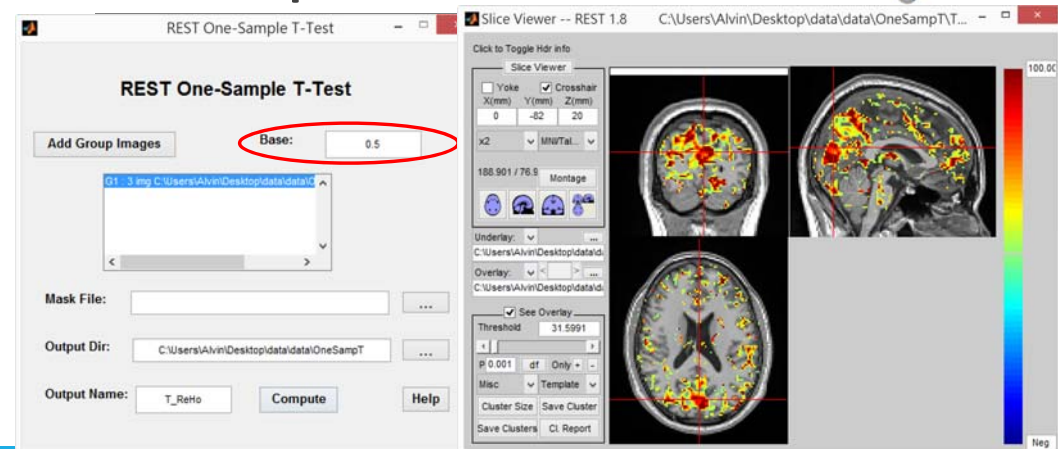
Zou et al., J Neurosci Methods 2008



## ALFF/fALFF Setup



## One sample T-test - ReHo



# Two-sample T-test

Patients vs Healthy Volunteers  
Males vs Females  
Young vs Old



# Q & A