Resting-state fMRI and DTI

David C. Zhu, Ph.D.
Associate Professor of Psychology and Radiology
Cognitive Imaging Research Center
Michigan State University, East Lansing, Michigan, USA
Two Main Paths of BOLD (Blood Oxygen Level-Dependent) fMRI

First 1-2 seconds

Stimulation

↓

Neuronal Activity

↓

$\text{CMR}_{\text{glucose}}$

↑

$\text{CMR}_{\text{O}_2}$

↓

Blood Oxygen Level

↓

Deoxygenated hemoglobin: paramagnetic

↓

Blood Magnetic Susceptibility Effects

↓

$T_2^*$ decay

↓

fMRI Image Signal Intensity

Later seconds

Cerebral Blood Flow (CBF)

↓

Blood Oxygen Level

↓

Oxygenated hemoglobin: diamagnetic

↓

Blood Magnetic Susceptibility Effects

↓

$T_2^*$ decay

↓

fMRI Image Signal Intensity
(A) A single short-duration event

(B) A block of multiple consecutive events

FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 7.15 © 2004 Sinauer Associates, Inc.
Modeling of fMRI

Stimuli $f(t)$ → Subsystem 1 → Subsystem 2 → Subsystem n → Measurement $y(t)$

System with impulse response function (IRF) $h(t)$

$y(t) = f(t) \otimes h(t)$

$= \int_{0}^{t} f(\tau)h(t - \tau)d\tau$
The MR signal intensity at a voxel from a 7-min run

Baseline signal + linear trend + IRF

The design matrix (when the stimulus ON and OFF)

Error term

\[ Z = X \beta + \epsilon \]
Using the matrix notation,

\[
Z = \begin{bmatrix}
Z_p \\
Z_{p+1} \\
. \\
. \\
. \\
Z_{N-1}
\end{bmatrix},
\]

\[
X = \begin{bmatrix}
1 & p & f_p & \cdots & f_0 \\
1 & p+1 & f_{p+1} & \cdots & f_1 \\
. & . & . & \cdots & . \\
. & . & . & \cdots & . \\
1 & N-1 & f_{N-1} & \cdots & f_{N-p-1}
\end{bmatrix}
\]

\[
\beta = \begin{bmatrix}
\beta_0 \\
\beta_1 \\
h_0 \\
. \\
. \\
h_p
\end{bmatrix}, \quad
\varepsilon = \begin{bmatrix}
\varepsilon_p \\
\varepsilon_{p+1} \\
. \\
. \\
. \\
\varepsilon_{N-1}
\end{bmatrix}, \quad
\hat{\beta} = \begin{bmatrix}
\hat{\beta}_0 \\
\hat{\beta}_1 \\
\hat{h}_0 \\
. \\
. \\
\hat{h}_p
\end{bmatrix}
= (X^t X)^{-1} X^t Z
Facts

- The brain is only about 2% of total body mass.
- But it consumes about 20% of the body’s total energy at “rest”.
- Engaging in active tasks increases neuronal metabolism less than 5%.

What is this energy at “rest” consumed by?

The on-going spontaneous neuronal activity
Data Acquisition

GE 3T Signa® HDx MR scanner with an 8-channel head coil.

7 minute resting-state fMRI EPI scan (relax and eyes closed):
- 36 3-mm axial slices,
- 22 cm × 22 cm FOV, 64 × 64,
- 27.7 ms TE, 2500 ms TR,
- 80° flip angle, 164 time points.

Alternative fMRI method for people who cannot perform tasks.
Two popular methods of processing for resting-state fMRI

1. Correlation analysis

2. Independent component analysis (ICA)
Correlation analysis

\[ S_{\text{measure}} = S_{\text{intrinsic}} + S_{\text{random}} \]
Resting-state fMRI Analysis in AFNI

Pre-processing:

Slice-timing and motion correction.

Removed baseline, linear and quadratic trends of the data, and the potentially motion-introduced artifacts.

Modeled the brain global mean signal change as the physiological noise assuming that the physiological noise affects the brain globally.

Modeled the noise in the correlation analysis.

**Correlation analysis** was done on every voxel of the brain against the time course from the average signal within the seed region.

**Group Analysis** after Fisher's Z transformation on correlation coefficients.
Additional nuisance signal removal with regressors:

CSF
White matter

Band-pass filtering: 0.009 Hz – 0.08 Hz
Time courses of correlated and uncorrelated regions
Independent Component Analysis

http://www.fmrib.ox.ac.uk/fsl/melodic/index.html
http://www.fmrib.ox.ac.uk/fsl/melodic/index.html
\[ Z = X \beta + \varepsilon \]

- The MR signal intensity at a voxel from a 7-min run
- Baseline signal + linear trend + IRF
- Error term
- The design matrix (when the stimulus ON and OFF)

\[ \hat{\beta} = (X^t X)^{-1} X^t Z \]
The MR signal intensity at a voxel \(i\) from a 7-min resting-state fMRI scan.

Solving the blind separation problem, the source signals can be decomposed to

\[
\hat{S} = \mathbf{W}x
\]

Example in a party

People at Table 1: make sound “ga”, $s_1$

= $a_{11} s_1 + a_{21} s_2 + a_{31} s_3 + \text{noise}_1$

People at Table 2: make sound “da”, $s_2$

= $a_{12} s_1 + a_{22} s_2 + a_{32} s_3 + \text{noise}_2$

People at Table 3: make sound “ba”, $s_3$

= $a_{13} s_1 + a_{23} s_2 + a_{33} s_3 + \text{noise}_2$
ICA example results with MELODIC

cd /export/data2/PI/training/davidzhu/ForLiuClass2011/RS_001/ICA_analy/report/

firefox 00index.html &

IC 1: Default Mode Network
IC 25: Visual Network
Independent Component Analysis

http://www.fmrib.ox.ac.uk/fsl/melodic/index.html
Introduction to Diffusion Tensor Imaging (DTI)
Fick’s Law describes particle movement

Net flux (mole mm$^2$/s): \[ J = -D \frac{\Delta C}{\Delta x} \]

Diffusion coefficient D is in mm$^2$/sec

\[ \frac{\Delta C}{\Delta x} = \text{concentration gradient in mole/mm}^4 \]

High concentration \[ J \] Low concentration
Figure 5.20 Diffusion

- Start location
- End location

Time
Stejskal-Tanner Diffusion-weighted Sequence
Isotropic Diffusion

Signal attenuation due to diffusion coefficient $D$

\[ A = \frac{S}{S_0} = e^{-bD} \]

Where $b = \text{commonly called \textit{“b factor”}, which characterizes the gradient pulses (timing, amplitude, shape)} = \text{clinical practice, 1000 s/mm}^2
Stejskal-Tanner Diffusion-weighted Sequence

\[ b = \gamma^2 G^2 \delta^2 (\Delta - \frac{\delta}{3}) \]
Anisotropic Case (for example, axons)

\[ b = \begin{bmatrix} b_{xx} & b_{xy} & b_{xz} \\ b_{yx} & b_{yy} & b_{yz} \\ b_{zx} & b_{zy} & b_{zz} \end{bmatrix} \]

\[ D = \text{diffusion tensor} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} \]

\[ A = e^{-bD} \]

\[ A = e^{-\left( b_{xx} D_{xx} + b_{yy} D_{yy} + b_{zz} D_{zz} + 2b_{xy} D_{xy} + 2b_{xz} D_{xz} + 2b_{yz} D_{yz} \right)} \]
Diagonalization

$\mathbf{DE} = \mathbf{E} \Lambda$

$\mathbf{E} = \text{eigen vector (unit vector)}$

$\Lambda = \text{eigen value} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$

Laboratory frame Diffusion ellipsoid
Mean diffusivity $= \lambda_{\text{mean}} = (\lambda_1 + \lambda_2 + \lambda_3)/3$

The level of tissue constraint

Fractional Anisotropy $= FA = \frac{\sqrt{3[(\lambda_1 - \lambda_{\text{mean}})^2 + (\lambda_2 - \lambda_{\text{mean}})^2 + (\lambda_3 - \lambda_{\text{mean}})^2]}}{\sqrt{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$

the directionality of diffusion

Axon fiber integrity

Mean diffusivity map

FA map
Table 1
Diffusion Coefficients of Water in Human Brain ($\times 10^{-3}$ mm$^2$/s)*

<table>
<thead>
<tr>
<th></th>
<th>Mean diffusivity</th>
<th>Anisotropy (1-volume ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrospinal fluid (CSF)</td>
<td>3.19 ± 0.10</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td>Gray matter (frontal cortex)</td>
<td>0.83 ± 0.05</td>
<td>0.08 ± 0.05</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>0.67 ± 0.02</td>
<td>0.08 ± 0.03</td>
</tr>
<tr>
<td>White matter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyramidal tract</td>
<td>0.71 ± 0.04</td>
<td>0.93 ± 0.04</td>
</tr>
<tr>
<td>Corpus callosum (splenium)</td>
<td>0.69 ± 0.05</td>
<td>0.86 ± 0.05</td>
</tr>
<tr>
<td>Internal capsule</td>
<td>0.64 ± 0.03</td>
<td>0.70 ± 0.08</td>
</tr>
<tr>
<td>Centrum semiovale</td>
<td>0.65 ± 0.02</td>
<td>0.27 ± 0.03</td>
</tr>
</tbody>
</table>

*Measurements were obtained in normal volunteers using diffusion tensor MRI (from ref. 31).

Fiber Tracking

(A)  (B)  (C)  (D)

*Functional Magnetic Resonance Imaging 2e, Box 5.1, Figure 2*
Deterministic approach:
Answer Yes/no.

Software: (1) DTI Studio
(2) MedINRIA

Probabilistic approach:
How probable two voxels/regions connected together
Software: FSL
Probabilistic tracking at Right Fornix
Data Acquisition

GE 3T Signa® HDx MR scanner with an 8-channel head coil.

12 minute and 6 second DTI scan (full-brain coverage):
Dual spin echo EPI sequence,
48 2.4-mm axial slices,
22 cm × 22 cm FOV, 128 × 128, 2 NEX,
75 ms TE, 13.7 s TR,
parallel imaging acceleration factor = 2,
b = 1000 s/mm², 25 directions
DTI Analysis with the Diffusion Toolbox (FDT v2.0) in FSL software package

Eddy-current distortion and motion correction.

Applied Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques with the crossing fibers \( n = 2 \) modeled (BEDPOSTX).

Applied probabilistic tractography (PROBTRACKX) to each seed region to calculate the corresponding connectivity distributions.

The connectivity distributions were then normalized by the total number of generated tracts from the seed region.

Integration

- Resting-state fMRI allows the examination of brain function connectivity (1).

- Diffusion tensor imaging (DTI) fiber tracking allows the evaluation of structural connection between cortical regions (2).

1. Fox MD, Raichle ME. Nat Rev Neurosci. 2007; 8:700-711.
Test both functional and structural connectivity.
Example of Integration
Seed Region #1: pC/rsp (posterior cingulate/retrosplenial cortex)

**Group Integration**
(17 subjects):
Whole-brain corrected $P < 0.0325$.
Mean structural normalized connectivity distribution $> 10^{-4}$.

**MeFC/ACC (Medial Frontal Cortex/Anterior Cingulate Cortex)**

Individual subject cases: functional $P < 10^{-5}$, structural normalized connectivity distribution $> 10^{-4}$

MeFC/ACC (mainly MeFC)

Successful Integration in 8/17 subjects

2/17 subjects

Fibers clearly failed to track in 7/17 subjects
Seed Region #3: Left Cuneus

**Group Integration**
(17 subjects):
Whole-brain corrected $P < 0.0325$.
Mean structural normalized connectivity distribution > $10^{-4}$.

Individual subject cases: functional $P < 10^{-5}$, structural normalized connectivity distribution > $10^{-4}$

Successful Integration in 16/17 subjects

Fibers clearly failed to track in 1/17 subject