Combining physics and physiology to measure brain function

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Learning objectives

At the end of this lecture attendees should be able to:

1. Describe basic physics underlying MRI
2. Describe physiological changes when brain becomes active
3. Describe form of fMRI data and application of the general linear model
MRI

EUROPEAN MRI SCANNERS

YEAR

2001 2002 2003 2004 2005 2006 2007 2008 2009

0 500 1000 1500 2000 2500 3000 3500 4000
MRI

EUROPEAN MRI SCANNERS

YEAR

Friday, 16 August, 13
NMR

radio frequency (RF)
energy

\[ \omega = \gamma B \]

Bloch & Purcell
Nobel Prize in Physics (1952)
Imaging

- Clever bit: working out which bit of signal came from where
- Different tricks for each of three dimensions
- All based on applying "gradients" in magnetic field

Mansfield & Lauterbur
Nobel Prize in Physiology or Medicine (2003)
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MR pulse sequences

- RF
- Gradient in z (Slice select)
- Gradient in x (Frequency encode; readout)
- Gradient in y (Phase encode)
- Record at TE

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MRI of the brain

**Structural image**
T1 weighted for contrast between grey and white matter
Resolution 1x1x1mm; 256x256x256 voxels
3 Tesla MRI, spin-echo MPRAGE, 4 minutes
(17 Megapixels)

**Functional image (fMRI)**
T2* weighted for sensitivity to brain activity
Resolution 3x3x4 mm; 64x64x21 voxels
3 Tesla MRI, gradient-echo BOLD EPI, 2 seconds
(0.1 Megapixels)
7T MRI of the brain

Venous imaging
Susceptibility-weighted imaging
Resolution 0.3x0.3x1 mm; 1414x1037x256 voxels
7 Tesla MRI, gradient-echo, 6 minutes
(375 Megapixels)
MRI of the brain

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Physiology & fMRI
Brain activity

- Neurons become active & consume energy
- Muscles on arterioles release; blood flow increases; veins swell; over-supply of blood leads to reduced deoxyhemoglobin
Blood Oxygen Level Dependent (BOLD) fMRI

- Reduced deoxyhemoglobin in veins; change in volume
  - Net effect of activation is signal increase

Ogawa et al (1990)
Blood Oxygen Level Dependent (BOLD) fMRI

- Not triggered by oxygen depletion but by neurotransmitters
- Not clear what neural measure best predicts BOLD (e.g., local field potentials vs. spiking)
  - Causality of neuronal activity & hemodynamic changes not always clear
- But, BOLD has survived many challengers (e.g., perfusion, diffusion fMRI)
  Not simple, but useful
Hemodynamic response

- Neuro-vascular coupling
- Vascular transit times
Acquiring fMRI data

- Volunteers typically watch/listen and perform a task
- Acquire snapshot of brain activity every 2 seconds for 5-50 minutes
Pre-processing of fMRI data

- Correct for artefacts in data
  - e.g., head motion, timing of different slices, low-frequency drift
- To do group studies, or compare locations with literature, often transform individual brains to a standard space
- Computationally & storage intensive
GLM

CONVOLVE WITH HDR
GLM

$Y(v,t)$

$X_1(t)$

$X_2(t)$

$X_3(t)$
GLM

\[ Y(v,t) = X_1(t) \cdot \beta_1(v) + X_2(t) \cdot \beta_2(v) + X_3(t) \cdot \beta_3(v) \]
GLM

\[ Y(v,t) = X_1(t) \beta_1(v) + X_2(t) \beta_2(v) + X_3(t) \beta_3(v) + \epsilon \]
GLM (matrix form)

$$Y = X\beta + \varepsilon$$

$$(v \times t), (t \times r), (v \times t)$$

$X$ is usually called “design matrix”

Often shown graphically
Statistics

- “Mass univariate” - each voxel tested independently
- First-level (single subject) statistics: compare \( \beta \)-values to noise \( \epsilon \)
- Second-level (group) statistics: test \( \beta \)-values across subjects
Multiple comparisons

- Tens of thousands of voxels -> lots of tests
  - test each one at some alpha level (e.g., p<0.05)
  - multiple tests will lead to lots of false positives

- Need to use more stringent threshold
  - Bonferroni too conservative, as voxels not independent

- Several strategies in use
  - random-field theory (measure smoothness)
  - voxel-based false discovery rate (FDR)
  - cluster-based FDR (with/without a priori threshold)

Beware uncorrected stats/ arbitrary ROI selection

http://www.danielbor.com/dilemma-weak-neuroimaging/
Be excited, but beware

- fMRI has tremendous potential
- A single well-designed experiment can reveal something new about the healthy or injured human brain
- Dynamic academic, clinical & commercial research field
- Expensive (compared to cognitive science)
- Hard: >50% failure rate is typical
- Many analysis options
- Lack of geek skills
- Easily spun
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