What influences the fMRI signal?

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Inhibition
Excitation
Frequencies
Coherence
Transients
Subthreshold potential

Neuronal Activation

Hemodynamics

Measured Signal

Magnitudes
Latencies
Correlations
Fluctuations
Transients
Undershoots

tSNR ≈ 100
fCNR ≈ 10 to < 1

Noise

Thermal
System
Motion
Physiologic
Respiration
Cardiac

layer
voxel
region
What Measures Can we Obtain with fMRI and MRI?

fMRI Signal: (BOLD, volume, perfusion):
- Location
- Extent
- Magnitude
- Width or shape
- Latency
- Post undershoot
- Transients within activation response
  - (pre undershoot, initial transient, post transient, post undershoot)
- Changes in activation over time/repeats/task intensity...
- Multi-voxel pattern
- Connectivity
- Mutual information
- Decode-ability
- Resting state: resting state correlation magnitude and extent
- Resting state: dynamics of resting state (i.e. windowed correlation)
- Resting state: Spatial or temporal components
  - (overall latency, pulsatility, entropy, information, etc.)
- BOLD/flow ratio -> CMRO2
- SE/GE ratio -> vessel geometry

Anatomy:
- White matter
- Gray matter density & volume
- CSF
- Mylenation
- Gyrification
- Fractal Dimension
- Fractional anisotropy
- Susceptibility weighted measurements (blood volume and iron)
- Magnetization transfer, spin-locking, etc...
What Physical Parameters Influence the fMRI signal?

- **TR**: inflow, tissue signal
- **TE**: BOLD, IV signal
- **Field Strength**
- **Flip Angle**
- **Diffusion weighting**
- **MT**: macromolecules
- **Slice Thickness**
- **Voxel Dimension**
- **Readout Direction**
Shorter TR:

- Increases samples per unit time
- Increases inflow effects on outer slices
- Decreases SNR
- Allows physiologic fluctuations to be better characterized and remove.
**TE**

- $R_2^* = 15.12 \pm 0.03$
  $S_{a_0} = 547.8 \pm 0.2$
- $R_2 = 7.76 \pm 0.06$
  $S_{r_0} = 347.2 \pm 0.5$
- $\Delta R_2^* = -0.81 \pm 0.02 \text{ s}^{-1}$
  $\Delta S_{r_0} (GE) = 3.8 \pm 0.5$
- $\Delta R_2 = -0.19 \pm 0.02 \text{ s}^{-1}$
  $\Delta S_{r_0} (SE) = 1.0 \pm 1.0$

### GE

- Ln (Signal)
- Resting $R_2^* = 15.92 \pm 0.04$
  $S_{r_0} = 544.0 \pm 0.3$
- Active $R_2 = 7.95 \pm 0.06$
  $S_{a_0} = 346.2 \pm 0.5$

### Percent Change

- GE int. = 0.64 ± 0.15 %
- SE int. = 0.24 ± 0.38 %

### SA - Sr

- GE
- SE

- $S_{r_0} \neq S_{a_0}$
- $S_{r_0} = S_{a_0}$

### TE (ms)

- GE
- SE
Field Strength

Contrast at 1.5T (dR2* = -0.8 1/s)

Contrast at 3T (dR2* = -1.6 1/s)

SNR↑
%change↑
Physio noise↑
CNR↑ (depends on physio/thermal)
Off-resonance artifacts↑
RF power deposition↑

Functional Contrast at Optimal TE

SNR (% change)

Physio noise

CNR (depends on physio/thermal)

Off-resonance artifacts

RF power deposition
Physiologic Fluctuations
Temporal SNR vs Individual Image SNR

Flip Angle

J. Gonzalez-Castillo, V. Roopchansingh, P. A. Bandettini, J. Bodurka,
Physiological noise effects on the flip angle selection in BOLD fMRI.
Diffusion Weighting

Diffusion Weighting in GRE and SE

Spin Echo

Gradient Echo

Bernstein et al. (2004) Handbook of MRI Pulse Sequences
Diffusion Weighting

Magnetization Transfer Pulses

Removes extravascular (macromolecule) signal

Magnetization transfer. An specially designed RF pulse (called an MT Pulse) is applied which selectively injects energy into the bound pool of protons (macromolecules and bound water). This energy is then transferred (primarily by dipolar interactions) to the free water pool, partially saturating it.

http://mriquestions.com/magnetization-transfer1.html
Magnetization Transfer Pulses

Kim, Hendrich, Kim, MRM 2008
Slice Thickness

[Graph showing signal vs voxel volume with a linear relationship.]

[Graph showing average percent change vs number of contiguous slices used.]

[Graphs on the right showing percent change for different slice thicknesses (2 mm, 4 mm, 5 mm, 10 mm, 20 mm).]
Readout Direction
Readout Direction

Spiral out imaging with TE = 25 ms, 0.8 mm nominal resolution. The bottom panel displays the central 9 of 36 slices.
What Physiological Parameters Influence the fMRI signal?

- Hematocrit
- Blood pressure
- Blood volume in each voxel
- Neurovascular responsivity
- Drug effects
Hematocrit

Blood pressure

Blood pressure

Sodium Nitroprusside

Nagaoka, et al. JCBFM 2006
Blood pressure

Table 1 Vascular physiological variables (mean ± s.d., n = 5)

<table>
<thead>
<tr>
<th></th>
<th>BOLD studies</th>
<th>CBV studies</th>
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<tbody>
<tr>
<td></td>
<td>Normal BP</td>
<td>Low BP</td>
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<tr>
<td>Systolic</td>
<td>ABP</td>
<td></td>
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<tr>
<td></td>
<td>128.6 ± 6.9</td>
<td>64.4 ± 7.7*</td>
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<tr>
<td>Diastolic</td>
<td>ABP</td>
<td></td>
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<td></td>
<td>82.0 ± 9.8</td>
<td>38.6 ± 2.3*</td>
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<tr>
<td>Mean</td>
<td>ABP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>97.5 ± 8.5</td>
<td>47.2 ± 3.9*</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>ABP</td>
<td></td>
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<td></td>
<td>179.8 ± 11.9</td>
<td>173.6 ± 15.3</td>
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Arterial blood pressure (ABP) is in units of mm Hg, and heart rate is beats/min. Heart rate was obtained from arterial blood pressure data. *Significant differences (single-factor ANOVA) among the six experiments with P < 0.01.
Respiration

Breath-holding

Cued Depth changes

Cued Rate changes

Birn et al. NeuroImage 2008
Blood Volume

Anatomical

12% O2 (Trial 1)

5% CO2 (Trial 3)

A

B

C

D

E

F

Finger Movement (Trial 5)

12% O2 (Trial 2)

5% CO2 (Trial 4)
Blood Volume

Bandettini et al. NMR in Biomedicine 1997
Age dependence of hemodynamic response characteristics in human functional magnetic resonance imaging

Claudine J. Gauthier a, b,*, Cécile Madjar b, Laurence Desjardins-Crépeau b, c, Pierre Bellec b, d, Louis Bherer b, c, Richard D. Hoge a, b

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Neurovascular Responsivity

Aging

Response to modified Stroop task

...leads to a potential underestimation of neuronal activity in older adults
Neurovascular Responsivity

Stroke
Drug Effects

Drug-Induced Changes in Brain Activity

In the first approach, BOLD signal can conceivably be modified by any pharmacological influence on cerebral blood flow, cerebral blood volume, and cerebral metabolic oxygen consumption. There are four principal drug effects which may be seen individually or in combination:

1. Regional changes associated with modified neuronal activity mediated by intact neurovascular coupling.

2. Regional changes associated with modified non-neuronally-induced metabolic activity, such as may result from local drug binding.

3. Regional or global changes in vascular tone and hence cerebral blood flow and volume.

4. Global changes in cerebral blood flow or volume arising from altered heart rate, blood pressure, or breathing.
Caffeine

Drug Effects

Liau, Perthen, Liu, NeuroImage 2008

Addicott, et al. HBM 2010