Brain Functional Imaging: Alternatives to BOLD contrast

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Review

• NMR Signal
• MR Imaging
• MRI Contrast
• Functional MRI
Physiology during Neural Activation

- **Neural Firing:** Electric Activity
  - EEG/ERP, MEG, TMS
- **Biochemical Reaction:** Metabolic Activity
  - PET, MRS
- **Vascular Response:** Hemodynamic Activity
  - PET, Optical Imaging, fMRI
  - Cerebral Blood Oxygenation: BOLD
  - Cerebral Blood Flow (CBF): Arterial Spin Labeling
  - Cerebral Blood Volume (CBV): Bolus Injection

BOLD Contrast Review

Blood has magnetic properties:
- Red blood cells: hemoglobin carries O₂
- Deoxy-hemoglobin is paramagnetic

So:
- Neuronal activation changes
- ⇒ Metabolic changes ⇒ deoxy-hemoglobin changes
- ⇒ Microscopic field gradient around vessels
- ⇒ \( T_2 \) and \( T_2^* \) changes (water inside/close to vessels)
- ⇒ Signal changes in \( T_2 / T_2^* \) weighted MRI

**BOLD:** complex function of CBF, CBV, CMRO₂
BOLD Contrast Review

Summary: if activation ↑ then MR signal ↑ in T2 / T2* weighted MRI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow</td>
<td>↑↑</td>
</tr>
<tr>
<td>O2 utilization</td>
<td>↑</td>
</tr>
<tr>
<td>Blood O2 level</td>
<td>↑↑</td>
</tr>
<tr>
<td>Deoxy-hemoglobin level</td>
<td>↓↓</td>
</tr>
<tr>
<td>Distortions in B (ΔB)</td>
<td>↓↓</td>
</tr>
<tr>
<td>Phase dispersal of M</td>
<td>↓↓</td>
</tr>
<tr>
<td>Effective transverse relaxation (T2*)</td>
<td>↑↑</td>
</tr>
<tr>
<td>T2*-weighted signal</td>
<td>↑↑</td>
</tr>
</tbody>
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BOLD Review: Spatial Resolution

• Both T2 and T2* changes detect BOLD changes
• But signal comes from different spins populations
  - T2* effects: dephasing from static + dynamic ΔB
  - T2 effects: dephasing from dynamic ΔB

Red blood cell  Capillary  Large blood vessel

Water diffusion path

Diffusion path > gradient difference  ⇒ spin ‘feels’ dynamic ΔB (T2)
Diffusion path << gradient difference  ⇒ spin ‘feels’ static ΔB (T2*)
BOLD: GE vs SE fMRI

- **T₂-weighted fMRI**
  - insensitive to macroscopic extravascular component
  - sensitive to microscopic extravascular component
  - sensitive to intravascular components all vessels

- **T₂*-weighted fMRI**
  - sensitive to extravascular components all vessels
  - sensitive to intravascular components all vessels

- **Spin-Echo** theoretically more spatially precise than Gradient-Echo
  (because large vessels downstream from activation don’t contribute to signal changes)

- But, **Spin-Echo has a lower magnitude response**
  (factor of 5 or more)
**BOLD: The MRI Sequence**

Echo Planar Imaging (EPI)

- RF
- $G_z$
- $G_y$
- $G_x$
- $S(t)$ (no grads)
- $T_2^*$

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**BOLD: using EPI**

- MR Signal ($M_{xy}$)
- RF
- $T_2^*$
- $T_2$
- $T_{2^*}$ & $T_2$

- GE-EPI
- $T_{2^*}$
- SE-EPI
- $T_2$
- ASE-EPI
- $T_{2^*}$ & $T_2$
BOLD vs Perfusion fMRI

- BOLD signal reflects changes in local [deoxy-Hb]
- BOLD signal depends on: CBF, CBV, CMR$_{O_2}$
- Perfusion (CBF): rate of delivery of metabolic substrates
- Regional $\Delta$CBF closer to neural activity than $\Delta$BOLD
- **Perfusion fMRI**: potential for better spatial localization potentially absolutely quantitative
- **However**: less sensitive + lower temporal resolution

MR Perfusion: Arterial Spin Labeling (ASL)

**MOTIVATION:**
Measure flow changes directly ...

i.e., images of blood water that flows into the capillary bed AND exchanges into the tissue
Arterial Spin Labelling Techniques

- Track a bolus of exogenous tracer
  - paramagnetic contrast agent
  - intra-vascular, non diffusible

- Track ‘magnetically labelled’ water
  - non-invasive

Arterial Spin Labeling (ASL) Perfusion Sequences (magnetic tracers)

image slice

in flowing blood

wash in

tissue water in image

wash out (or relaxation)
How to create a magnetic tracer: Arterial Spin Labeling

- **Image slice(s)**
- **Magnetic field** $B_0$
- **Invert the inflowing magnetization**
- **Magnetic “tagging” or “labeling” of the spins**

**Pulsed ASL: The Label**

- **Image slice**
- **Inversion slab**
- **$180$**
- **$90$**
- **$\sim 1$ s**
- **EPI acq.**

- **T1 is important**
- **Thru slice arteries relatively dark**
- **Large inversion slab is important**
Arterial Spin Labelling

- Perfusion image = control image - labelled image
- Perfusion signal changes < 3% intensity reduction
- Averaging to improve SNR:
  control - label - control - label - control - label - ...
  ⇒ lower temporal resolution than BOLD
- Motion: big problem

Direct measurement of CBV for fMRI

MOTIVATION:
If CBF and CBV measured independently
⇒ estimation of CMRO$_2$
Bolus Gd(DTPA) MR CBV (Intravascular T2* agent)

- Agent stays in brain vessels
- Susceptibility effects ⇒ $T_2^*$ ⇒ signal drop
- Signal drop ⇒ concentration agent
- Integral of concentration timecourse $\propto rCBV$

CBV: Bolus tracking

Signal time course in perfused voxel

MR Signal Intensity

baseline 1st passage recirculation

Time
CBV: Bolus tracking

Concentration time curve in perfused voxel

- Tracer Concentration
- Area under curve Proportional to CBV
- Arrival time
- Time

Summary: Brain fMRI Contrasts

- **BOLD**: the most sensitive, but complex link to sources of neural activation
- **Alternatives to BOLD**: CBF, CBV, CMRO$_2$
- **Alternatives to BOLD**: - used for better understanding BOLD
  - for complement BOLD, potentials, less sensitivity
  - under development