BOLD fMRI

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Lecture ‘series’

• Week 1: Biological basis: where’s the signal coming from?
• Week 2: Physical basis: what is the signal, how is it measured?
• Week 3: Imaging basics: imaging sequences, noise and artifacts.
• Week 4: The specific case of BOLD fMRI.
• Week 5: BOLD analysis: what’s significant and what’s not?
• Week 6: Spikes vs. BOLD: neural activity in visual areas
Biological basis

• fMRI measures blood oxygenation and/or flow

• How are blood oxygenation and flow related to neural activity?
  – Oxygen consumption
  – Metabolism
  – Blood flow
  – Energy budgets

• Things to consider:
  – Spatial resolution
  – Temporal resolution
  – Spatial specificity
  – Neural specificity
Terms

- **BOLD**: blood oxygenation level-dependent
- **CBF**: cerebral blood flow
- **CBV**: cerebral blood volume
- **CBv**: cerebral blood velocity
- **CMRO$_2$**: cerebral metabolic rate, oxygen
- **CMRglu**: cerebral metabolic rate, glucose
Primary visual cortex: layers and columns

The Primary Visual Cortex
by Matthew Schmolesky
www.webvision.med.utah.edu/VisualCortex.html
What happens when one neuron is active?

- Activity ≡ increased firing rate
- Increased firing rates run down membrane potential
- Membrane potential results from high [K+] in the cell and high [Na+] outside the cell
- ATP is consumed to restore membrane potential (Na/K-ATPase)
- ATP is also required to restore equilibrium at synaptic sites

http://www.bae.ncsu.edu/bae/research/blanchard/…/neuron.gif
Energy budget

Distribution of ATP consumption for a mean action potential rate of 4 Hz

- action potentials 47%
- resting potentials 13%
- glu recycling 3%
- presynaptic Ca\(^{2+}\) 3%
- postsynaptic receptors 34%

A brief digression into cell biology

ATP is generated by aerobic glycolysis and anaerobic TCA cycle.
What happens when many neurons are active?

• The population needs increased CBF to provide glucose and oxygen
  – Excitatory vs. inhibitory activity
    • 90% of neurons are glutamatergic/excitatory
    • 10% GABAergic/inhibitory
  – It’s not just neurons doing the signaling (neurons and glia exist in ~1:1 ratio)

• Possible signals for increased blood flow:
  – Increased extracellular potassium (direct or indirect effect)
  – NO: range and timing match well
  – Other signals transmitted along capillaries or glia?
Link to blood flow

1. Incoming signal
2. Synaptic activity
3. Accumulated ions, neurotransmitters, signaling molecules
4. Arteriolar relaxation
5. Flow changes at a larger scale and
6. Increased blood volume in venuole

Figure 12, from Woolsey, T. A et al. (1996). “Neuronal units linked to microvascular modules in cerebral cortex: response elements for imaging the brain.” Cerebral Cortex 6: 647-660.
Decoupling of CBF, CMRglu and CMRO$_2$

- PET studies by Fox and Raichle demonstrated 40% increase in CBF and CMRglu, but only 5% increase in CMRO$_2$

- Positive BOLD signal confirms this!

- Is neural activity anaerobic? Is oxygen consumption delayed? Is CBF much more widespread than CMRO$_2$?
The Balloon model (Buxton)

- Two main features
  - CBF and CMRO$_2$ are coupled
  - Limitation is rate at which O$_2$ is extracted from capillaries
- Also
  - Undershoot after stimulus is increased CBV, not delayed oxygen consumption
  - Not ‘watering the garden for the sake of one thirsty flower’ (in original context, Malonek and Grinvald, 1996)

**FIG. 3.** Fractional change in cerebral blood flow required to produce a given fractional change in the rate of delivery of O$_2$ to the tissue, calculated from Eq. 5 for three values of the resting oxygen extraction fraction. Tight coupling of flow and metabolism requires a large change in flow in order to produce a much smaller change in oxygen metabolism, but the exact relationship depends strongly on the resting OEF.

*From: Buxton J Cereb Blood Flow Metab, Volume 17(1), January 1997:64-72*
Spatial specificity

Cortical territory for a large venuole is about the size of a barrel, but … … not in register with barrels … not in register with feeding arterioles, where CBF is regulated

Figure 10, from Woolsey, T. A et al. (1996). “Neuronal units linked to microvascular modules in cerebral cortex: response elements for imaging the brain.” Cerebral Cortex 6: 647-660.