Analysis of Functional Magnetic Resonance Imaging (fMRI)

Principles of BOLD fMRI

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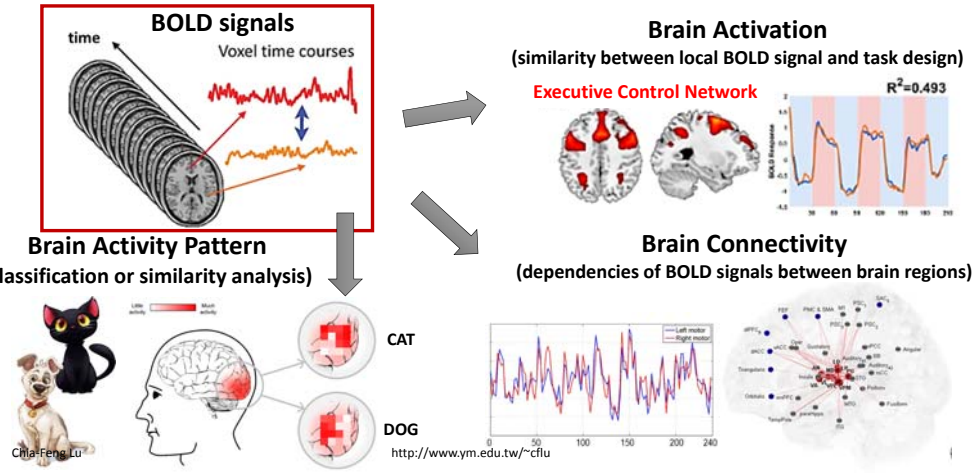
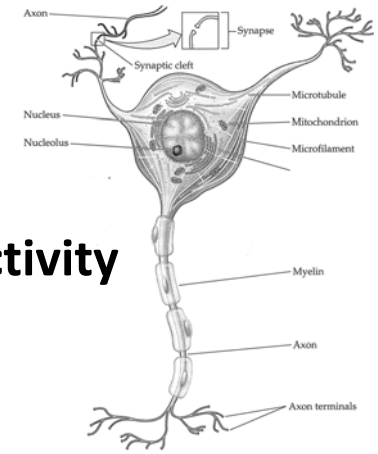
fMRI Analysis

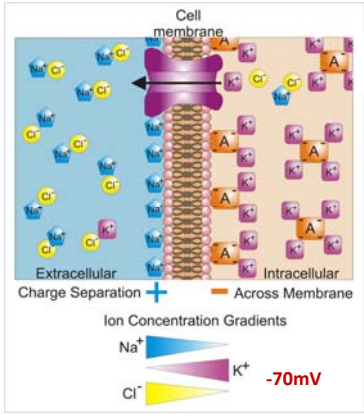


Physiology of Neural Activity



Membrane Potential

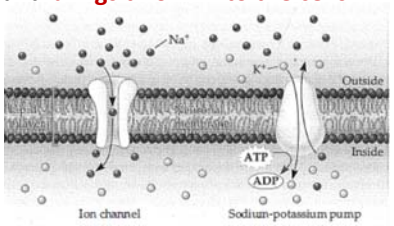
- Neuronal membranes prevent free diffusion of ions.
- A neuron at rest has…
  - a greater concentration of K^+ inside its membrane;
  - a greater concentration of Na^+, Ca^{2+}, and Cl^- outside.
- The difference in electric potential between the interior and the exterior of a biological cell is typically ranged from –40 mV to –80 mV.



https://en.wikipedia.org/wiki/Membrane_potential

Ion Channels and Pumps

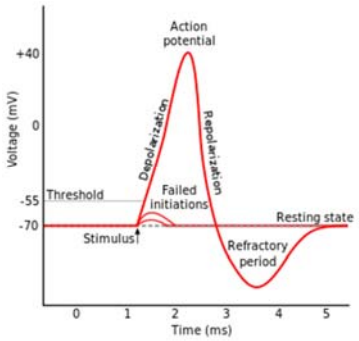
- Ion channels
  - Allow ions to diffuse through the cell membrane
- Sodium-potassium pumps
  - Restores the original distribution of ions
  - Forces **three Na^+ out of the cells** and **brings two K^+ into the cells**
  - Demands ATP



ATP: adenosine triphosphate
ADP: adenosine diphosphate

Action Potential

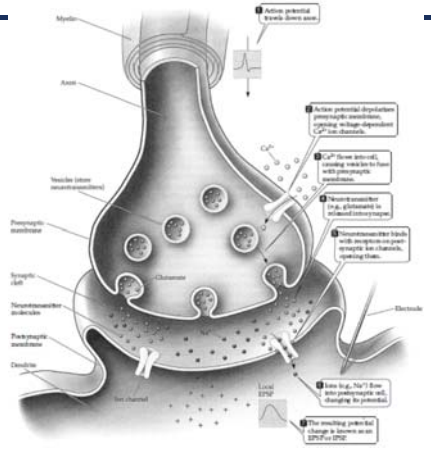
- **All-or-none** principle
  - Action potentials are said to be all-or-none signals, since either they occur fully or they do not occur at all.
- **Depolarization**
  - At the beginning of the action potential, the Na^+ channels open and Na^+ moves into the axon, causing depolarization.
- **Repolarization**
  - Repolarization occurs when the K+ channels open and K^+ moves out of the axon. This creates a change in polarity between the outside of the cell and the inside.



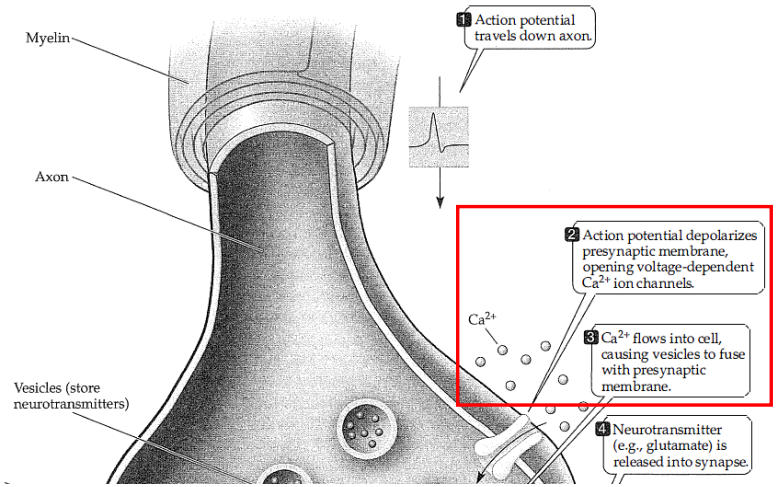
The resting potential is around –70 millivolts (mV) and the threshold potential is around –55 mV.

Synapses

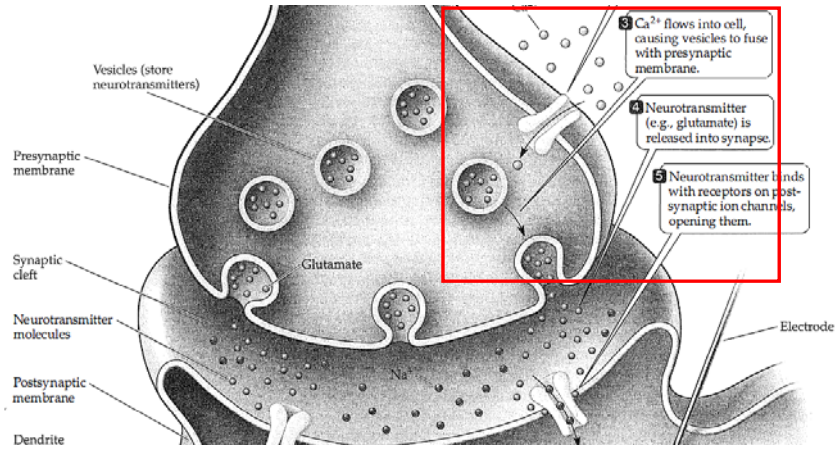
- Glutamate: One of the most important excitatory neurotransmitters.
- excitatory postsynaptic potential (EPSP): A depolarization of the postsynaptic cell membrane.
- γ-aminobutyric acid (GABA): One of the most important inhibitory neurotransmitters.
- inhibitory postsynaptic potential (IPSP): A hyperpolarization of the postsynaptic cell membrane.



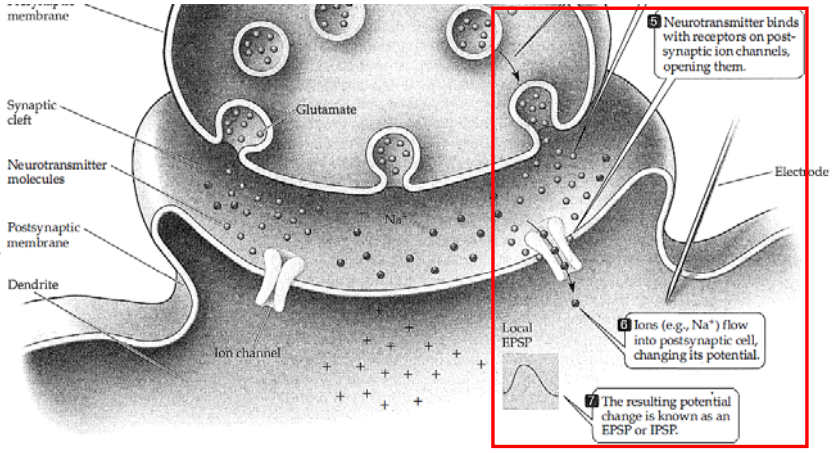
Synapse, part 1/3



Synapse, part 2/3

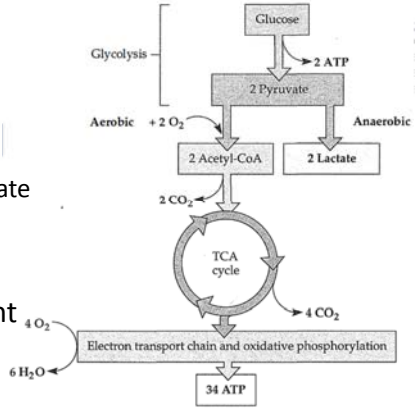


Synapse, part 3/3



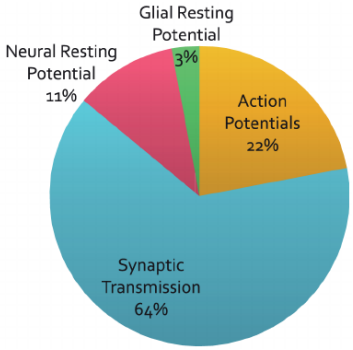
Neurovascular Coupling

- ATP is essential for neural activity
  - Restoration of ionic gradients
  - neurotransmitter recycling
- Glycolysis
  - a small amount of ATP (2 ATP) → produce lactate
- Oxidative glucose metabolism (90% in brain)
  - a large amount of ATP (34 ATP)
- Cerebral metabolism depends on a constant supply glucose and oxygen



Energy budget for signaling

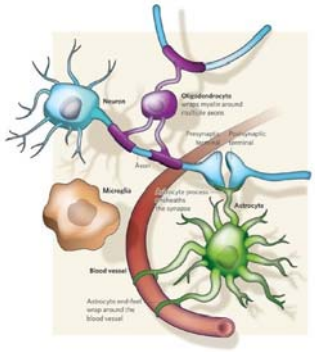
- Synaptic Transmission
  - Restoring Ca^{2+} flux
  - Recycling of glutamate
  - Restoration following IPSPs/EPSPs
- Action potentials
  - Restoration following action potential
- Maintenance of resting potential



Information and Efficiency in the Nervous System—A Synthesis (Rat)

Neurovascular Coupling

- Multiple mechanisms…
  - Astrocytes links neurotransmitter activity (glutamate cycling) to vascular responses.
  - Direct neuronal innervation of smooth muscle cells can also control blood flow.
- Requirement of metabolic nutrients
- Elimination of waste products
  - CO_2 and excessive heat



Neurovascular Coupling

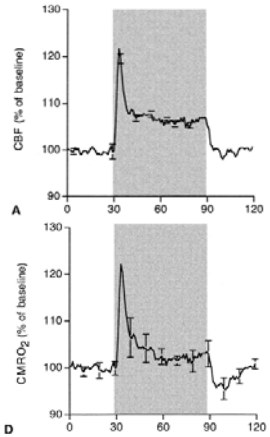
- A continuous supply of energy substrates is maintained by CBF
- Neural activity
  - Blood perfusion via capillaries ↑
  - regional cerebral blood flow (rCBF) ↑
  - regional cerebral blood oxygenation (rCBO) ↑
- Changes in rCBF or rCBO can be used to map brain activity
  - Functional neuroimaging

Brain vascular system: glucose and oxygen

Zlokovic & Apuzzo, 1998.

CBF and O_2 Consumption Mismatch

- During neural activity…
  - The fractional increases in CBF and glucose consumption are similar in magnitude.
  - Oxygen consumption increases much less than CBF.
- ➔ A net increase of oxygen in the blood and tissue.

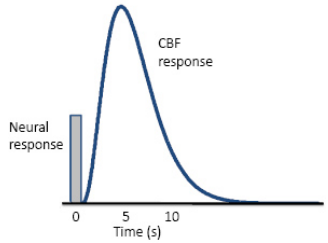


CMRO2: cerebral metabolic rate of oxygen

Ances et al., JCBFM 2001.

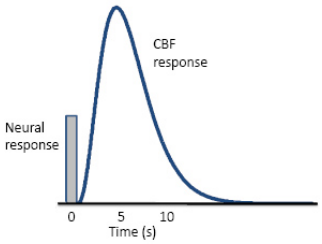
Coupling Properties

- Use of vascular responses to infer neural activity
  - **Time**: lack of temporal information in vascular response
  - **Space**: focal activation of neurons ⇔ local vascular response?
  - **Amplitude**: linear relationship?



Coupling Properties: Time

- CBF vs. neural activation
  - Delayed by 1 ~ 2 s
  - Peaks 4 ~ 6 s after the neural response
- Fast modulation of neural activity is unlikely to be reflected in the vascular response.



- **slow reaction of smooth muscle cells**
- **slow diffusion and uptake of neurovascular mediators**

Coupling Properties: Space

- Spatial resolution of the vascular response
- Vascular point spread function (PSF)
  - 1~5 mm
  - Depends on imaging conditions: monitoring tech., magnetic field, pulse sequence, species, and brain regions.
- Gray matter,
  - densest network of capillaries, intervessel distance of ~ 25 μm

Coupling Properties: Amplitude

- In general, amplitude coupling appears to be largely linear.
  - For stimulus durations larger than 4 s
- Various nonlinearities have been noted
  - neural responses below a certain amplitude may not evoke a CBF response
  - neural responses may saturate, while vascular responses continue to increase

Alteration Factors

- Disease
  - the chemical mediators
  - the dynamics of the vascular system
  - hypertension, diabetes, and AD alter Ionic channels on vascular smooth muscle
- Aging
  - change the vascular system
  - increasing tortuosity or reducing elasticity of the blood vessels
- Pharmacology
  - Diazoxide is used as a vasodilator →large vascular responses with little or no change in neural activity.
  - Hypercapnia (the concentration of CO_2 in the blood ↑) → vasodilation.

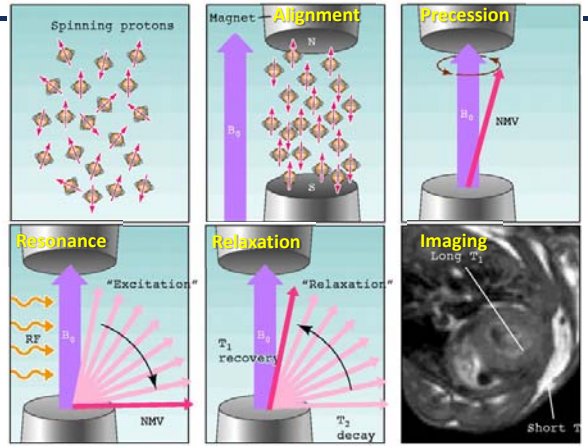
Principles of fMRI

Principles of MR imaging

Nuffield Health

https://youtu.be/2COPkX5FUAI

Principles of MR imaging



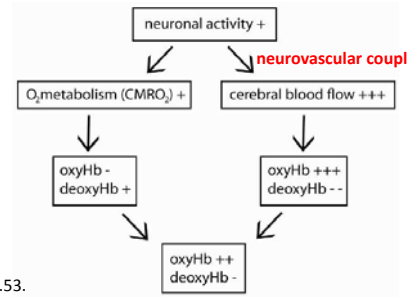
http://physiologyonline.physiology.org/content/19/4/168

fMRI BOLD signal

- fMRI does not measure neuronal activation directly, but the consequences of metabolic processes associated with activation.
- **Blood Oxygenation Level Dependent (BOLD)** contrast
  (Ogawa et al., PNAS, 1990; Turner et al., MRM, 1991)
- The MR signal in the vicinity of blood vessels and in perfused brain tissue decreased with a decrease in blood oxygenation.

Metabolic and hemodynamic changes

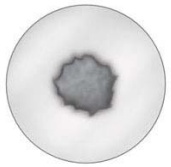
- Mismatch between CBF and O_2 consumption
- Neural/Brain activation
  - Elevated oxy-Hb fraction
  - Decrease deoxy-Hb fraction



Neuroimaging – Methods, pp.53.

Hemoglobin

Oxygenated Hemoglobin
- Diamagnetic
- Doesn't distort surrounding magnetic field
- No signal loss in BOLD signal

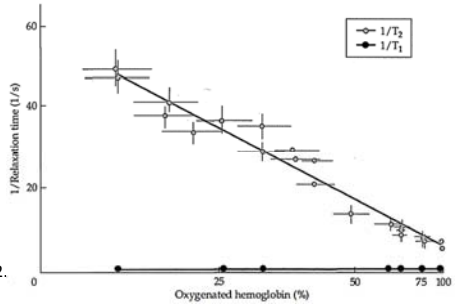


Deoxygenated Hemoglobin
- Paramagnetic
- Distorts surrounding magnetic field
- Signal loss in BOLD signal !!!

fMRI slides from http://culhamlab.ssc.uwo.ca/fmri4newbies/Tutorials.html

Effects of blood deoxygenation

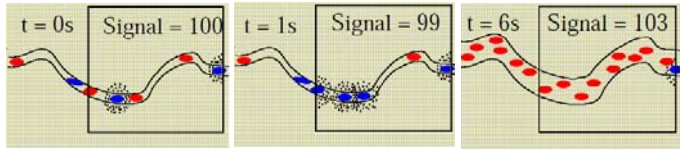
- **The more deoxygenated hemoglobin that is present, the shorter the T2.**
  - Loss of phase due to both spin-spin interactions and local field inhomogeneities.
- Note that T1 is not affected by blood oxygenation level.



Thulborn et al., 1982.

fMRI BOLD signal

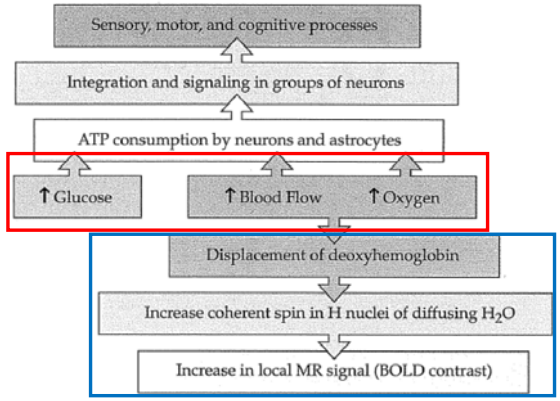
- t = 0s, a steady state in which there is an given amount of oxygenated and deoxygenated hemoglobin.
- t = 1s, an increased of deoxygenated hemoglobin due to the oxygen demands of neuronal activation.
- t = 6s, an increased of blood supply and oxygenated hemoglobin "flush away" the deoxygenated ones.



Matthijs Vink, Preprocessing and analysis of functional MRI data, 2007.

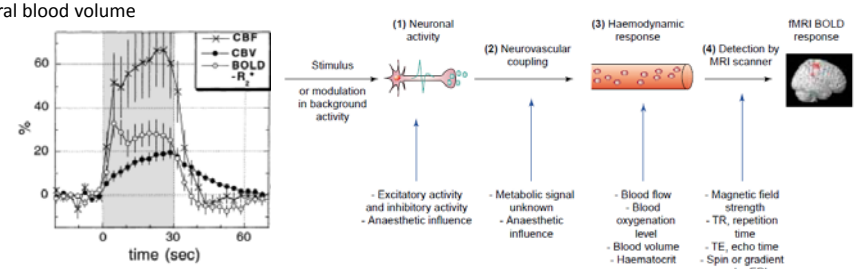
Biomarkers of brain activation

- Oxygen
  - **BOLD fMRI**
  - Functional near-infrared spectroscopy (fNIRS)
  - Positron emission tomography (PET)
- Blood Flow
  - Arterial spin labeling (ASL)
- Glucose (still impractical now)
  - PET
  - MR CEST techniques



Neuronal activity and BOLD

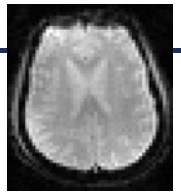
- Blood-oxygenation level dependent (BOLD)
- BOLD fMRI detects the alterations in
  - The level of deoxygenated hemoglobin
  - Cerebral blood volume



Mandeville et al.,MRM 1999.

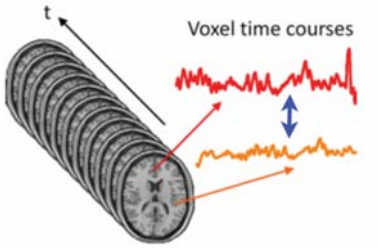
Common fMRI protocol

- Single-Shot 2D EPI (GRE-EPI), T2* weighting
- Repetition Time = 2000 ms
- Echo Time = 20 ms
- Flip Angle = 70~90°
- NEX = 1
- Slice thickness = 3.4 mm
- Field of View = 220 x 220 mm^2
- Matrix size = 64 x 64
- Volume number = 240 ~ 360
  (depends on experiment design)

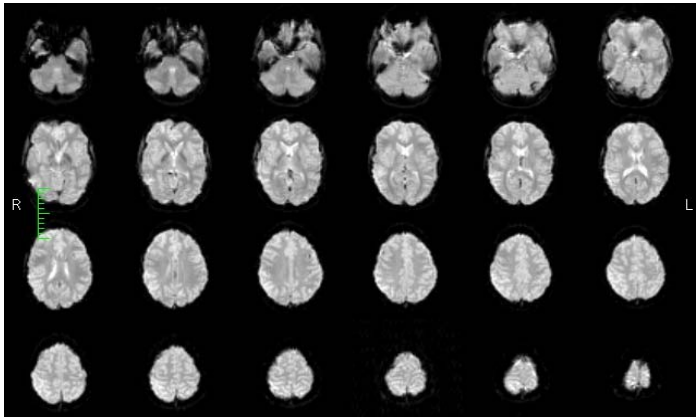


1 voxel ~10^6 neurons

3.44 x 3.44 x 3.40 mm^3



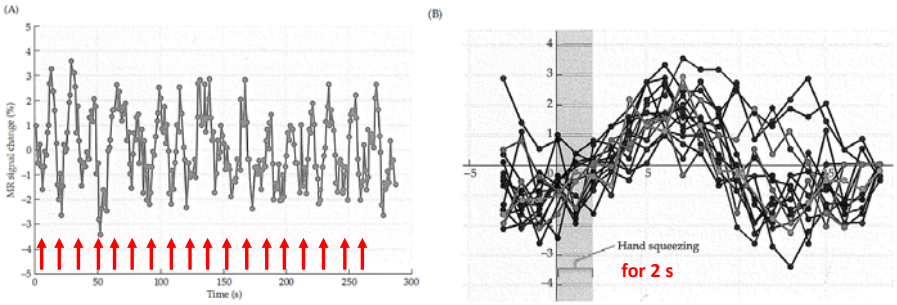
EPI BOLD raw images



http://practicalfmri.blogspot.tw/2012/05/rare-intermittent-epi-artifacts-spiking.html

fMRI signal example

- A sample fMRI time course from a single voxel in the motor cortex during a task in which the subject squeezed her hand for 2 s every 16 to 18 s.



THE END

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Teaching Materials: http://www.ym.edu.tw/~cflu/CFLu_course_fMRIana.html