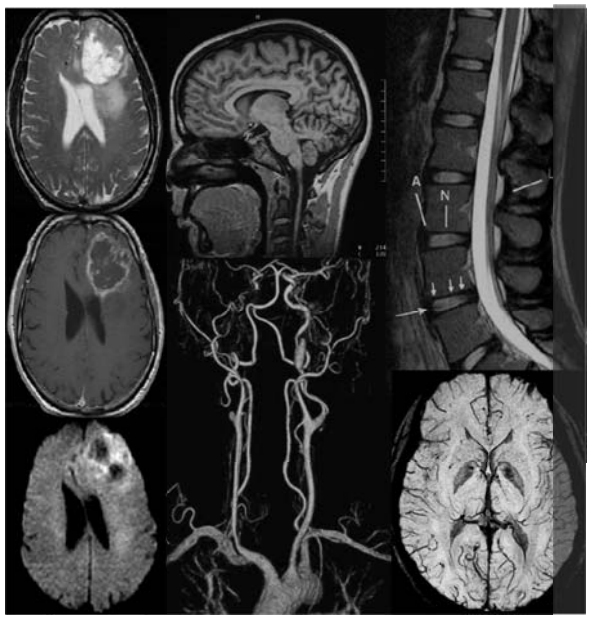

Magnetic Resonance in Medicine
Functional MRI (fMRI)

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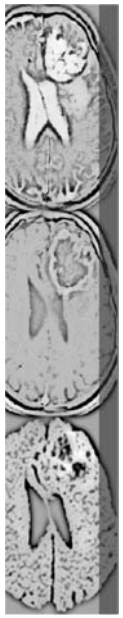


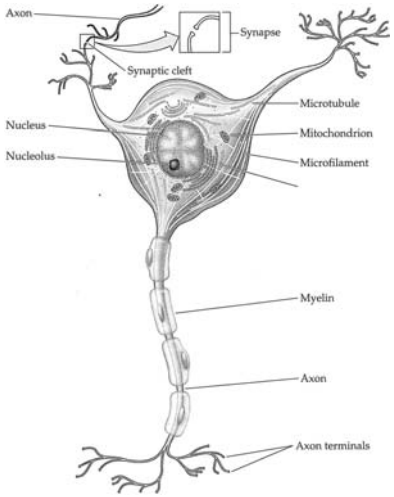
Content http://cflu.lab.nycu.edu.tw/

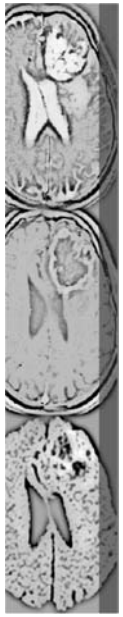
- Physiology of Neural Activity
  - To understand the physiological basis of functional imaging
- Principles of functional MRI (fMRI)
  - To apply and combine neurophysiology with MRI for functional imaging

- Functional Magnetic Resonance Imaging
  - Scott A. Huettel, Allen W. Song, Gregory McCarthy
- Introduction to Functional Magnetic Resonance Imaging (2nd edition)
  - Richard B. Buxton

Physiology of Neural Activity

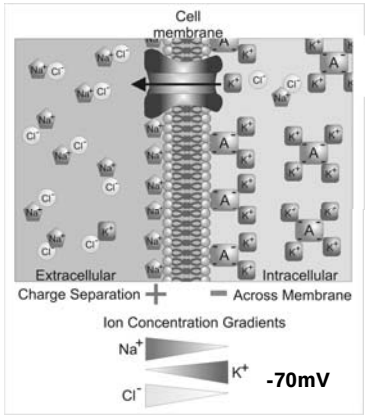
To understand the physiological basis of functional imaging





Membrane Potential

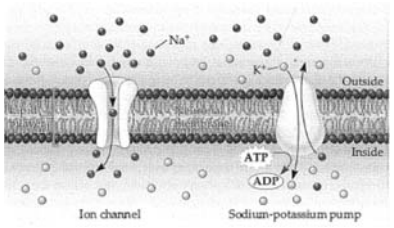
- Neuronal membranes prevent free diffusion of ions.
- A neuron at rest has…
  - a greater concentration of K^+ inside its membrane;
  - a greater concentration of Na^+, Ca^{2+}, and Cl^- outside.
- The difference in electric potential between the interior and the exterior of a biological cell is typically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



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

Ion Channels and Pumps

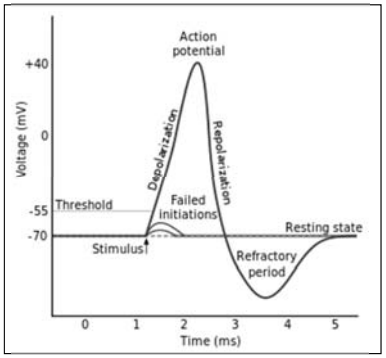
- Ion channels
  - Allow ions to diffuse through the cell membrane
- Sodium-potassium pumps
  - Restores the original distribution of ions
  - Forces three Na^+ out of the cells and brings two K^+ into the cells
  - Demands ATP



ATP: adenosine triphosphate
ADP: adenosine diphosphate

Action Potential

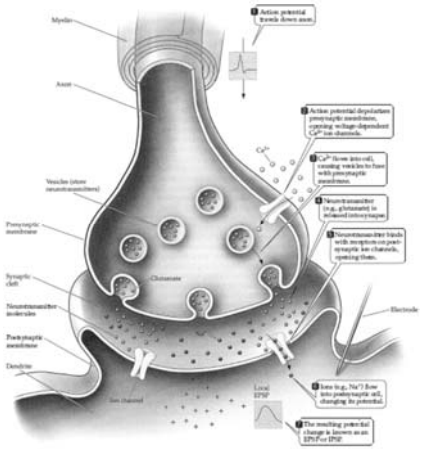
- All-or-none principle
  - Action potentials are said to be all-or-none signals, since either they occur fully or they do not occur at all.
- Depolarization
  - At the beginning of the action potential, the Na^+ channels open and Na^+ moves into the axon, causing depolarization.
- Repolarization
  - 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.



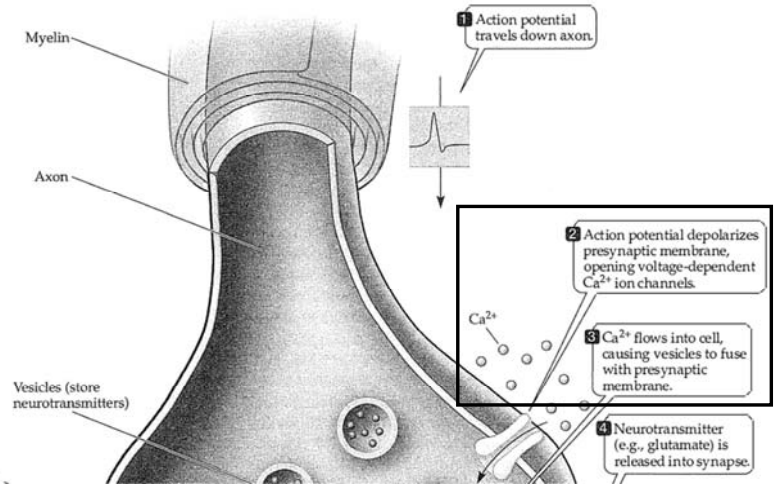
The resting potential is around –70 millivolts (mV) and the threshold potential is around –55 mV.

Synapses

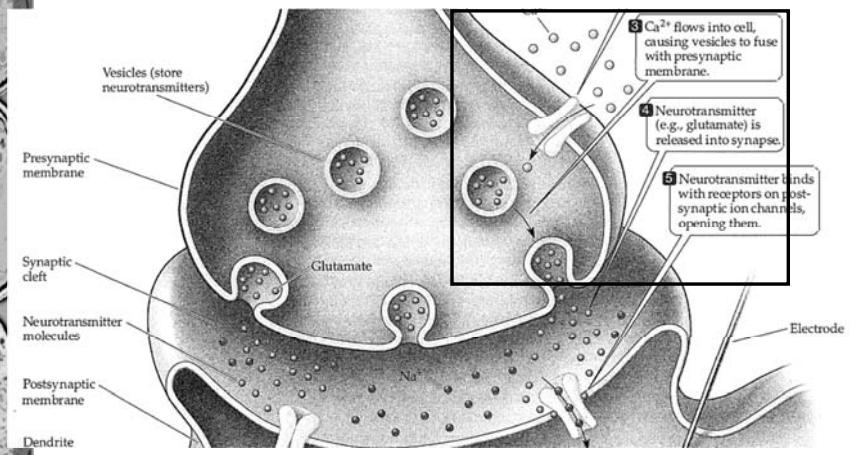
- Glutamate: One of the most important excitatory neurotransmitters.
- excitatory postsynaptic potential (EPSP): A depolarization of the postsynaptic cell membrane.
- γ-aminobutyric acid (GABA): One of the most important inhibitory neurotransmitters.
- inhibitory postsynaptic potential (IPSP): A hyperpolarization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



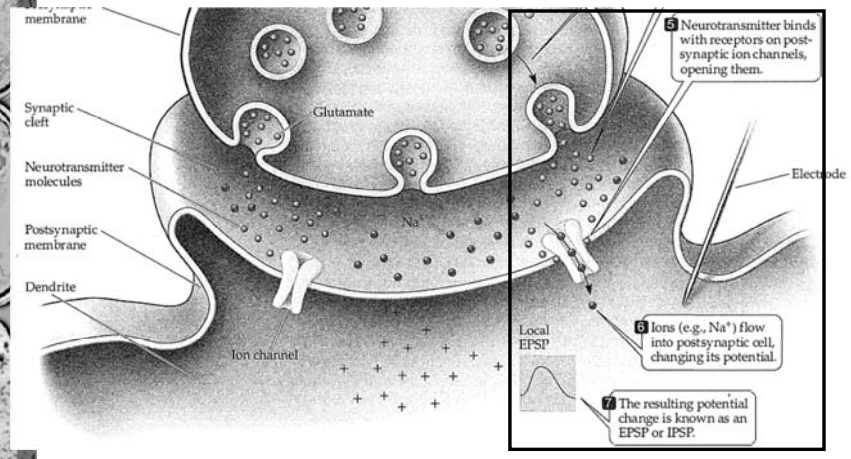
Synapse, part 1/3



Synapse, part 2/3

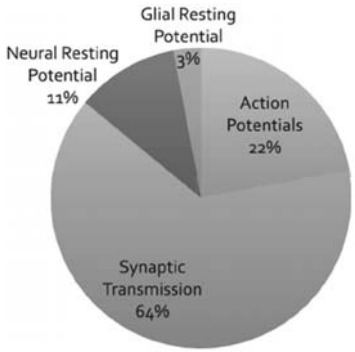


Synapse, part 3/3



Energy budget for signaling

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



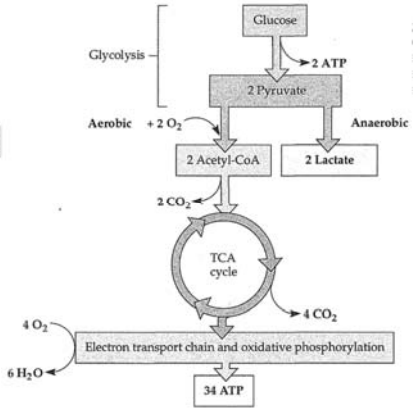
Information and Efficiency in the Nervous System—A Synthesis (Rat)

Based on the process of neural activity, what can be the potential probes to observe brain function?

(5-min discussion)

Neurovascular Coupling

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

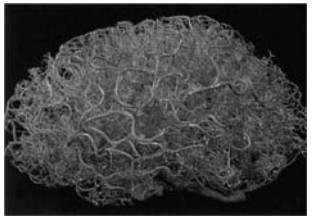


ATP: adenosine triphosphate

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

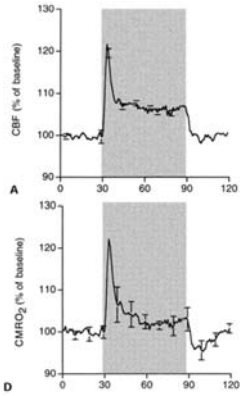
Brain vascular system: glucose and oxygen



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.

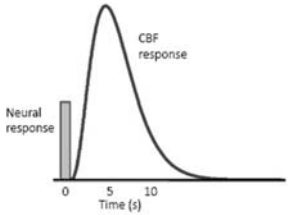


CMRO2: cerebral metabolic rate of oxygen

Ances et al., JCBFM 2001.

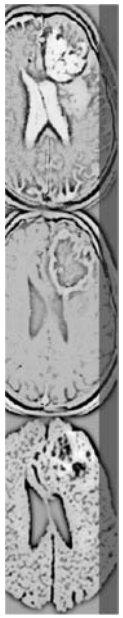
Coupling Properties

- Use of vascular responses to infer neural activity
  - Time: CBF vs. neural activation
    - Delayed by 1 ~ 2 s
    - Peaks 4 ~ 6 s after the neural response
  - Space: focal activation of neurons → 1~5 mm point spread function
  - Amplitude: linear relationship?
    - In general, amplitude coupling appears to be largely linear.
    - 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.

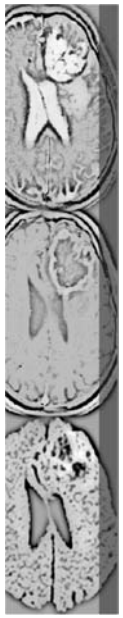


Short Summary

- Neural activity causes energy consumption
  - Action potentials
  - Synaptic Transmission
  - Maintenance of resting state
- Neural activity requires blood supply
  - regional cerebral blood flow (rCBF) ↑
  - regional cerebral blood oxygenation (rCBO) ↑
- Vascular response based on neurovascular coupling is an indirect probe of neural activity.

Principles of fMRI

To apply and combine neurophysiology with MRI for functional imaging

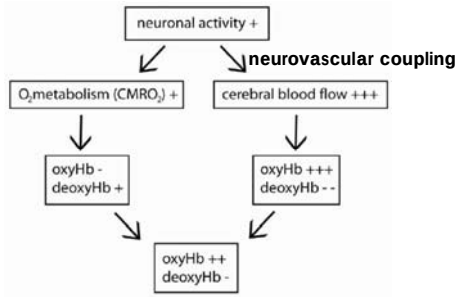


fMRI BOLD signal

- 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

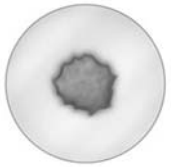
- Mismatch between CBF and O_2 consumption
- Neural/Brain activation
  - Elevated oxy-Hb fraction
  - Decrease deoxy-Hb fraction



Neuroimaging – Methods, pp.53.

Hemoglobin

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

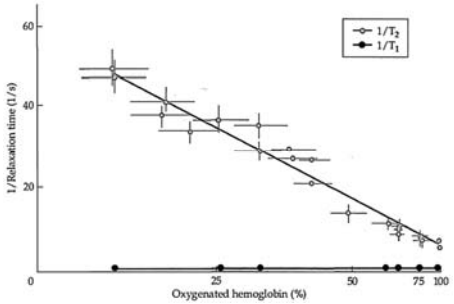


Deoxygenated Hemoglobin
- Paramagnetic
- Distorts surrounding magnetic field
- Signal loss in BOLD signal !!!

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

Effects of blood deoxygenation

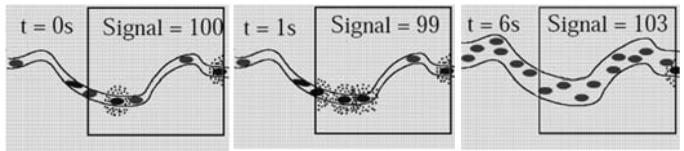
- The more deoxygenated hemoglobin that is present, the shorter the T2.
  - Loss of phase due to both spin-spin interactions and local field inhomogeneities.
- Note that T1 is not affected by blood oxygenation level.



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.

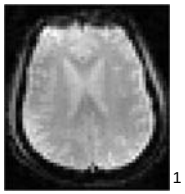


Matthijs Vink, Preprocessing and analysis of functional MRI data, 2007.

Common fMRI protocol

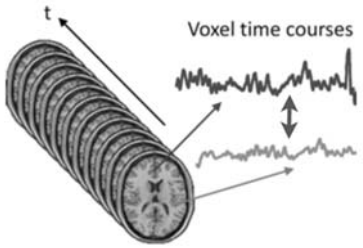
- Single-Shot 2D EPI (GRE-EPI), T2* weighting
- Repetition Time = 2000 ms
- Echo Time = 20 ms
- Flip Angle = 70~90^{o}
- NEX = 1
- Slice thickness = 3.4 mm
- Field of View = 220 x 220 mm^2
- Matrix size = 64 x 64
- Volume number = 240 ~ 360

  (depends on experiment design)



1 voxel ~10^6 neurons

3.44 x 3.44 x 3.40 mm^3

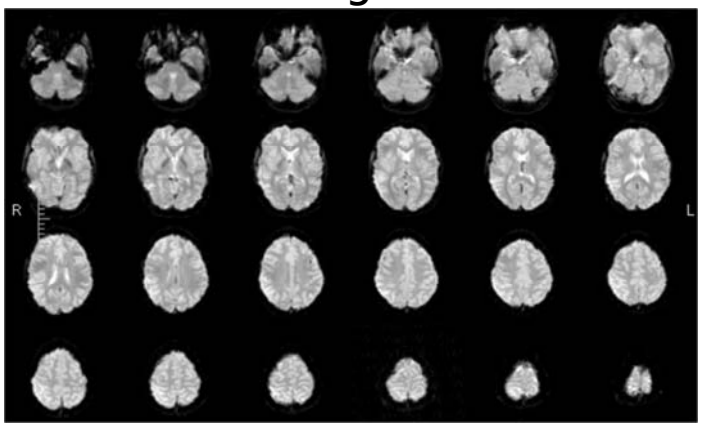


Please discuss why these BOLD-fMRI parameters are applied?

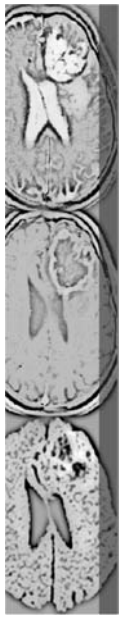
(GRE-EPI, spatial resolution, TR)

(5-min discussion)

EPI BOLD raw images

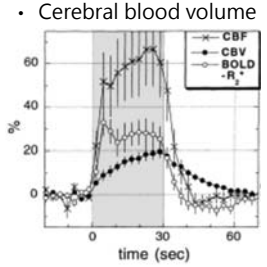


http://practicalfmri.blogspot.tw/2012/05/rare-intermittent-epi-artifacts-spiking.html

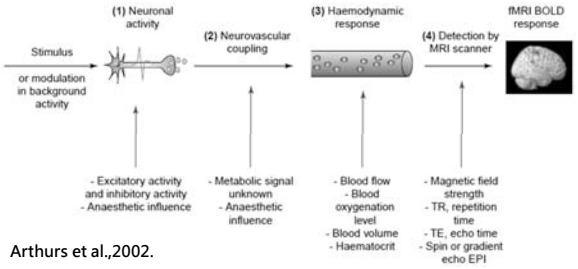


Neuronal activity and BOLD

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



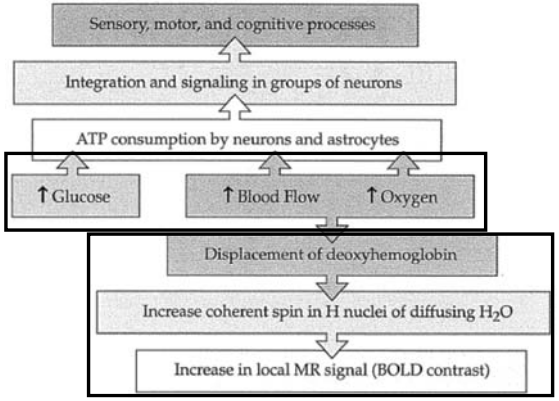
Mandeville et al.,MRM 1999.



Arthurs et al.,2002.

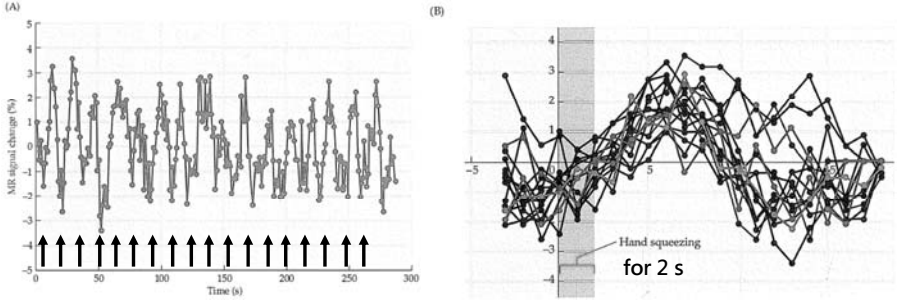
Biomarkers of brain activation

- 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

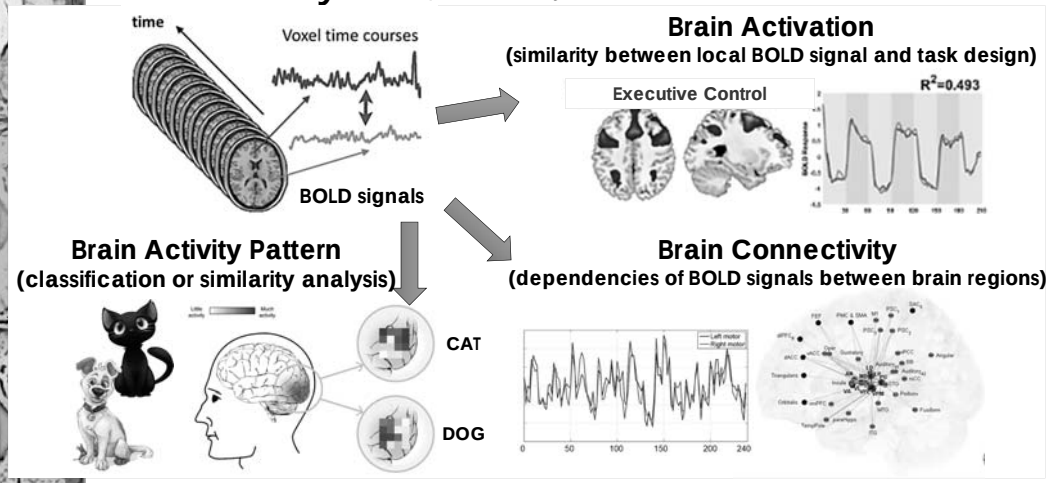


fMRI signal example

- 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.



fMRI Analysis http://cflu.lab.nycu.edu.tw/CFLu_course_fMRIana.html



THE END

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