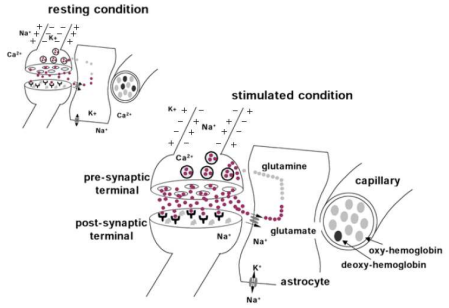
Technical aspects and safety of functional MRI

Associate Professor
Jun-Cheng Weng, Ph.D.
Chang Gung University
16 Jan 2019

Outline

- BOLD fMRI review
- Imaging method
- Imaging parameter
- Temporal resolution limitation
- Spatial resolution limitation
- Other issues
- Safety

Physiology during neural activation

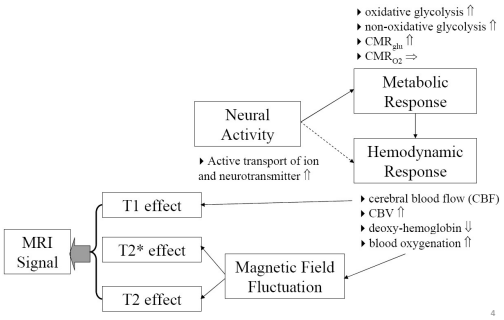


Kida and Hyder, Magnetic Resonance Imaging Methods and Biologic Applications 2006; chapter 7.

Energy during neural activation

- **Neuronal firing: electrical activity**
  - Excitatory and inhibitory
    - Neurotransmitter release and uptake
  - Action & graded potential
    - Ion flow
  - Hormone
- **Biochemical reaction: metabolic activity**
  - Active transport of ion pumps
  - Oxidative / non-oxidative glycolysis
- **Vascular response: hemodynamic activity**
  - Energy demand, clean up waste
  - Blood flow, blood volume, blood oxygenation

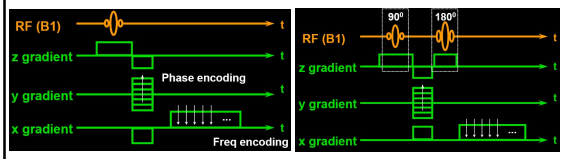
BOLD fMRI physiology



Imaging method - contrast type

- **Gardient echo (GE) vs. spin echo (SE)**
  - Contrast: T2* vs. T2 sensitive
  - Singal: GE > SE (3-4 folds)
    - $\Delta R2^*/R2^* > \Delta R2/R2$
  - Localization: SE > GE
    - SE: micro-vascularture (capillary)
    - GE: macro-vascularture (draining vien, capillary)
  - Artifacts: GE > SE
    - susceptibility, distortion
  - Acquistion time: SE > GE

Gradient-echo vs. spin-echo sequence



6

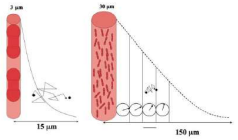
Blood vessel effect

- **Capillary**
  - Diffusion distance > gradient difference
  - Irreversible dephasing
  - T2 shorten by diffusion
  - Stronger T2 effect => SE

$$S(t) = S_0 e^{-t/T2}$$

- **Large blood vessel**
  - Diffusion distance << gradient difference
  - Reversible dephasing
  - T2* shorten by average of spin
  - Stronger T2* effect => GE

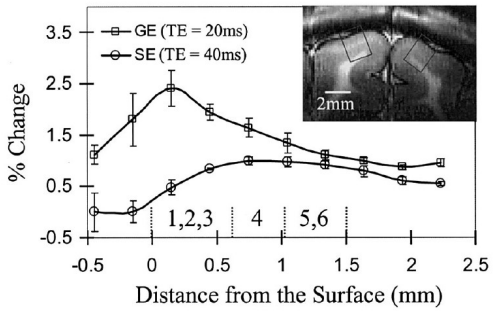
$$S(t) = \sum_j S_{0j} e^{-t/T2_j} (e^{-i\omega_j t_j})$$



- Kim et al., Methods 2003; 30: 28-41.

7

GE vs. SE BOLD fMRI



- Zhao, et al., MRM 2004; 51: 518-524.

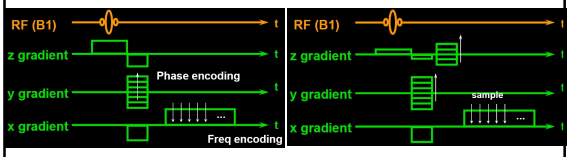
8

Imaging method - pulse sequence

- **k-trajectory**
  - Fast (s per slice): FLASH / FSE
    - Higher SNR, less off-resonance artifacts
  - Ultra-fast (0.1s per slice): EPI
    - Highly sensitive to T2* - > high BOLD signal
    - Subsecond resolution -> whole brain
    - Less physiological fluctuation
    - Less motion artifact
    - Less inflow artifact (infinite TR)
  - 2D /3D

9

2D vs. 3D imaging pulse sequence



- 3D: Gz & Gy form two inner/outer loops

10

Imaging method – 2D / 3D

- 2D multi-slice vs. 3D

	3D	2D
Benefit	• Rectangular slice profile • Thin slice / high resolution • Can generate arbitrary view from data • High SNR due to signal averaging of z axis (phase encoding)	• Faster • Less motion artifact
Pitfall	• Long scan time • Motion artifact • Aliasing artifact in z	• Imperfect slice profile (slice crosstalk) • Hard to get thin slice (anisotropic resolution)

11

Imaging parameters

- Important parameters:
  - TR, TE, slice thickness, matrix size, field-of-view, bandwidth, slice order, slice gap, flip angle
- Tradeoff among SNR, CNR, spatial/temporal resolution
  - BOLD contrast, imaging speed, volume coverage, spatial resolution, image SNR, sensitivity to physiological activity, motion

12

Tradeoff among SNR, CNR, resolution

- **TR:** temporal resolution, inflow effect, SNR, slice number
- **TE:** =T2*
- **FA:** inflow effect
- **BW:** SNR, image acquisition time; EPI: T2* blur, distortion, chemical shift
- **FOV:** spatial resolution, SNR
- **Matrix size:** spatial resolution, SNR, imaging time
- **Slice thickness:** spatial resolution, SNR, volume coverage, partial volume
- **Slice number:** volume coverage, temporal resolution
- **Slice order/gap:** slice cross-talk

13

SNR and CNR

- **Signal-to-noise ratio (SNR)**
  - The most critical concern
  - Voxel size, BW, matrix, TR, FA
  - Optimal flip angle: Ernst angle $\alpha = cos^{-1}(e^{-TR/T1})$
- **Contrast-to-noise ratio (CNR)**
  - Voxel size: partial volume effect
  - Optimal TE = T2* of gray matter (30-40 ms @ 3T)

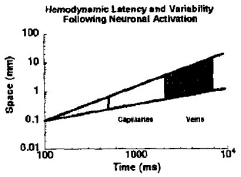
$\frac{\Delta S}{N} = \frac{S_0}{N} e^{-TE\ R2^*}(TE\ \Delta R2^*)$

$\propto \Delta R2^*/R2^*$ (when TE = T2*)

14

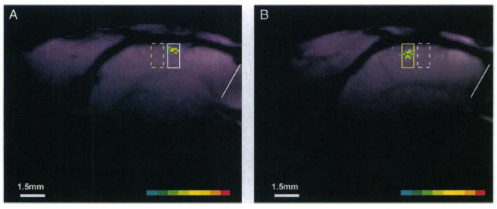
Limitations

- Temporal
  - The shortest neural activity
- Spatial
  - The accuracy of spatial localization



15

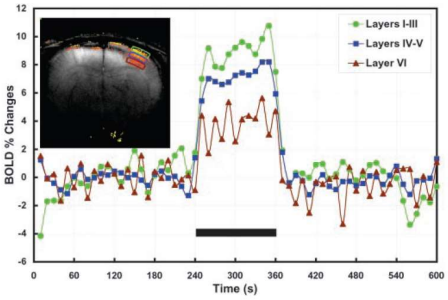
BOLD fMRI: rat whisker



- Yang, et al., PNAS 1996: 93: 473-478.

16

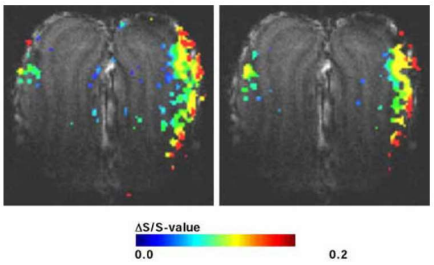
BOLD fMRI: laminar layers



- Silva and Koretsky, PNAS 2002; 99(23): 15182-15187.

17

BOLD fMRI: olfactory bulb

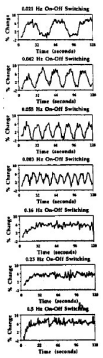


- Xu, et al., PNAS 2003; 100: 11029-11034.

18

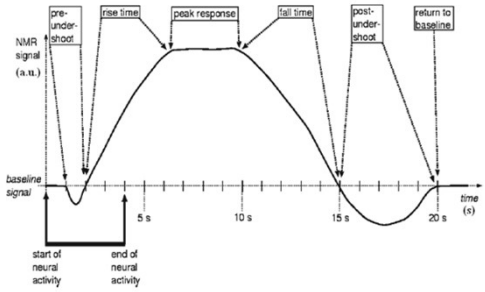
Temporal resolution

- **Physiology**
  - Hemodynamic response resembles a low-pass filter
  - Time constant of the response function
  - Limit of stimulus duration
  - Detectability of difference in latency
    - Within one ROI
      - Deconvolution of HRF
      - Linear system assumption
    - Across ROIs
- **Hardware**
  - Image acquisition rate: tradeoff



19

Hemodynamic response function



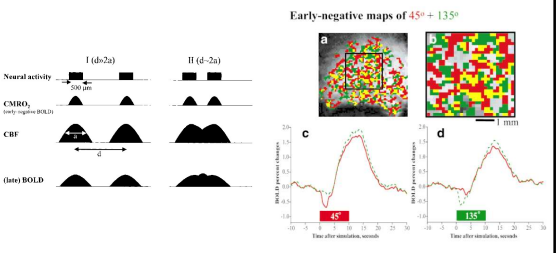
20

Variability of hemodynamics

- Temporal variability
  - Noise
    - 1% baseline fluctuation
  - HRF time constant variation
    - entire: 650ms; rise: 450ms; fall: 1250ms
  - Variation over space
    - +/- 2.5s

21

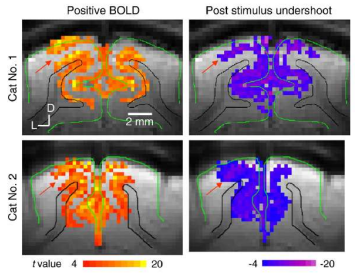
Initial dip: orientation columns in cat visual area



- Duong, et al., MRM 2000; 44:231-242

22

Undershoot: cat visual cortex



- Zhao, et al., NeuroImage 2007; 34: 1084-1092.

23

What's the temporal limit of

- Maximum on-off switch rate
- Minimum detectable activation duration
- Minimum detectable difference in activation duration or onset in same region
- Minimum detectable activation interval across separate brain regions
- Maximum image acquisition rate

24

Current temporal limit

- Maximum on-off switch rate
  - 4 s to 8 s duration cycles
- Minimum detectable activation duration
  - 30 ms
- Minimum detectable difference in activation duration or onset in same region
  - 100 ms
- Minimum detectable activation interval across separate brain regions
  - 100 ms with normalization
- Maximum image acquisition rate
  - 64 images per sec

25

Spatial resolution

- Consideration
  - CNR & SNR
  - Large vessel
    - Vessels that can not resolved by high resolution image
    - Large vein has larger signal change
      -> significant at low CNR/SNR
  - Spatial limitation of hemodynamic response
    - Point spread function

26

Spatial limit - CNR

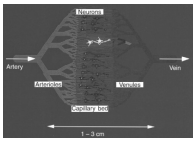
- **Signal**
  $\Delta S = \rho S_0 (e^{-TE\Delta R2^*} - 1)$
  - S_0: control state signal
    - Proportional to voxel volume
  - ρ: active volume < 1
  - Solution: coil, higher-field
- **Noise**
  - Random noise
  - Physiological
  - Head motion
  - System instability

  } location-dependent

27

Spatial limit - macrovasculature

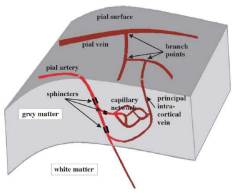
- **Inflow effect**
  - Esp for sequence using multiple excitation
  - Solution
    - Longer TR (full relaxation)
    - Shorter flip angle
    - Spin echo
- **BOLD (T2* effect)**
  - Venous T2/T2* will change during activation
    -> spin-echo also affected
  - Draining/large vein effect
  - Solution
    - Bipolar gradient -> suppress flowing spin in large vessels



28

Spatial limit - macrovasculature

- Reduce signal from large draining vein
  - Spin-echo
  - Bipolar gradient

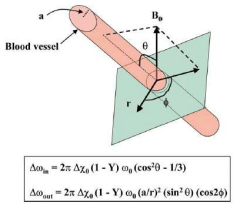


- de Zwart et al., NeuroImage 2005; 24: 667-677.

29

Blood vessel effect

- Susceptibility difference: $\Delta\chi(\fallingdotseq 0.27$ ppm at 37°C)
- Deoxy-Hb concentration: 1-Y
- Vessel size: a
- Vessel orientation: θ, ψ
- Distance: r



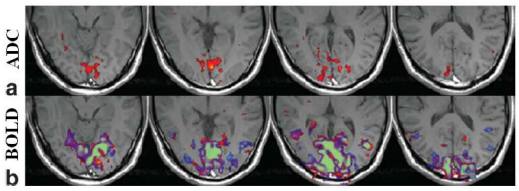
$$\Delta\omega_{in} = 2\pi\,\Delta\chi_0\,(1 - Y)\,\omega_0\,(\cos^2\theta - 1/3)$$

$$\Delta\omega_{ext} = 2\pi\,\Delta\chi_0\,(1 - Y)\,\omega_0\,(a/r)^2\,(\sin^2\theta)\,(\cos 2\phi)$$

- Kim et al., Methods 2003; 30: 28-41.

30

Biopolar gradient: human visual cortex

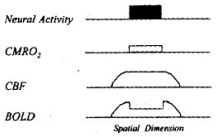


- Song, et al., MRM 2007 57: 417-422.

31

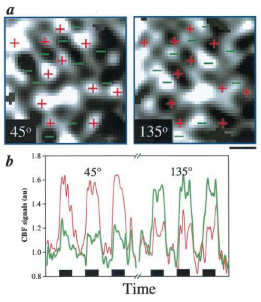
Spatial limit - hemodynamic

- Electrical activity
- Metabolic activity (closer)
  - Synaptic activity may increase in inactive neuron
- Hemodynamic activity (farther)
  - CBF
  - BOLD
    - Early negative response (closer)
    - Late positive response (farther)
- Assume $CMRO_2$ is exact
  - Largest signal is away



32

CBF: orientation columns in cat visual area



- Duong, et al., PNAS 2001; 98: 10904-10909.

33

Interpretation of fMRI signal

- fMRI signal is an index of ensemble of neural activity
  - presumably monotonic relation
- Neural source of BOLD signal is not clear
  - spiking activities vs. synaptic activity
  - excitatory vs. inhibitory
- Difficult to compare fMRI signals across cortical regions and subjects
  - BOLD signal depend on vascular structure and volume

34

Other issues

- **Normal physiology condition**
  - Age
    - inferior vascular response for aged people (CBF decrease)
    - neonate: deoxyHb increase
  - Disease
    - transient global ischemia: vascular response abolished
    - carotid stenosis: vascular response diminish
  - Drug
    - alter vascular response, cardiopulmonary function,…
- **Meaning of negative response**
  - Negative response -> decreased activity?
  - Inhibitory activity also increase glucose uptake

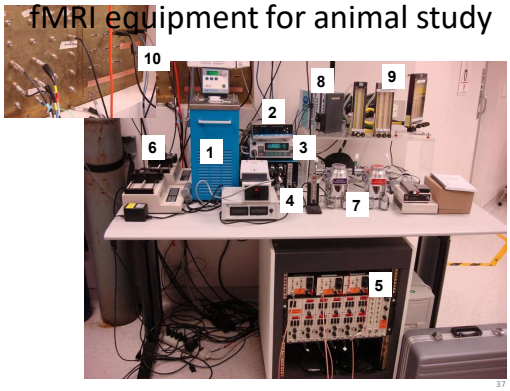
35

Challenge of quantification

- **Electrical activity**
  - Tiny perturbation in magnetic field: MRI phase
  - Ca^{2+} : manganese (Mn^{2+}) enhanced MRI
  - Glutamate, GABA : H^1-MRS
- **Metabolic activity**
  - Lactate : H^1-MRS
  - $CMRO_2$: combine CBF and BOLD
- **Hemodynamic activity**
  - Oxygenation: BOLD fMRI
  - CBF: Arterial Spin Labeling (ASL) MRI
  - CBV: contrast-injection / VASO

36

fMRI equipment for animal study



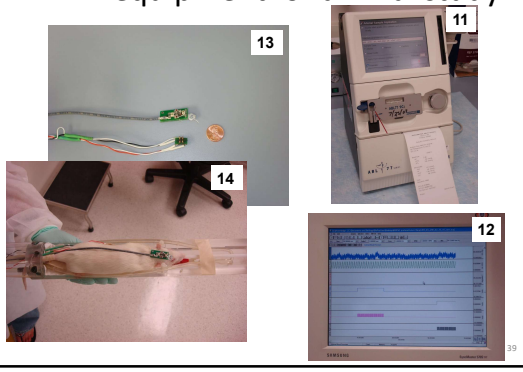
37

fMRI equipment for animal study

- 1. Water bath
- 2. Temperature controller
  - temperature probe and monitor
- 3. $ETCO_2$ monitor
  - for monitor respiration
- 4. Ventilator
  - provide constant air flow
- 5. Electrical stimulator (4 channels)
- 6. Syringe pump
  - provide constant IV injection of anesthesia
- 7. Anesthesia
- 8. Amplifier / gating system
- 9. Air mixer
- 10. Filter panel

38

fMRI equipment for animal study



39

fMRI equipment for animal study

- 11. Blood gas analyzer
  - analyze blood pH, pO_2, and pCO_2
  - maintain the same BOLD condition
- 12. Physiological monitoring, gating software
  - record arterial blood pressure, rectal temperature, $ETCO_2$, EPI trigger
  - output trigger pulse to stimulator and/or MRI
- 13. Coil, electrode
- 14. Rat holder positioning stand (in MRI)
  - with ear bar and bite bar

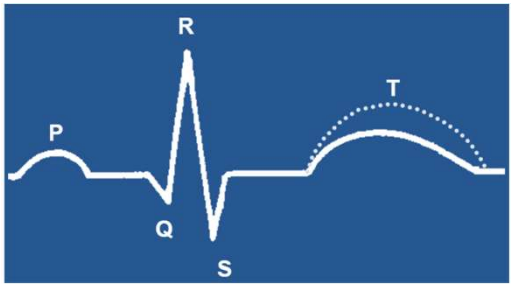
40

Bioeffects of Main Field

- Enhanced T-wave in ECG
- Magnetohydrodynamic effect
- Blood is electrically conductive
- Electrical induction from moving conductor in magnetic field
- Detected by ECG surface electrodes

41

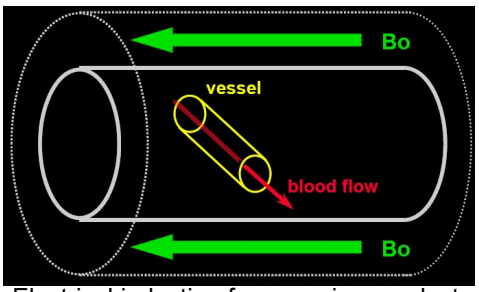
Enhanced T-wave in Electrocardiogram



- A known effect from MRI main field

42

Magnetohydrodynamic Effect



- Electrical induction from moving conductor

43

RF Bioeffects

- Local temperature increases with too much RF
- FDA: specific absorption rate (SAR) limits (2004):
  - Mean < 3.0 W/Kg in head
  - Mean < 4.0 W/Kg whole-body
  - Mean < 8.0 W/Kg body (軀幹)
  - Mean < 12 W/Kg locally (四肢)
- Automatic detection by MRI system (body weight)
- Related to protocol, e.g. fast spin echo

44

Heating Effects from RF

- Temperature raise induced by RF
  - ~1°C
  - Head < 38°C, body < 39°C, limbs < 40°C
- Homeostasis for maintaining body temperature in human
- Blood flow carries away the heat

45

Gradient Bioeffects

- Magnetophosphene
- Rapid B_0 change on conductive human body
- Electric induction due to fast dB/dt
- Flash-like vision when optic nerves fire action potential

46

Magnetophosphene

- Smaller effects near MRI isocenter
- Peripheral nerve stimulation
- Response gone after scan stops
- Optic nerves unharmed
- Present in EPI scan only

47

Protection for MRI Safety

- What kind of protection do we need if MRI is so safe?
- No worry under normal operation
- Abnormal operation can be extremely dangerous

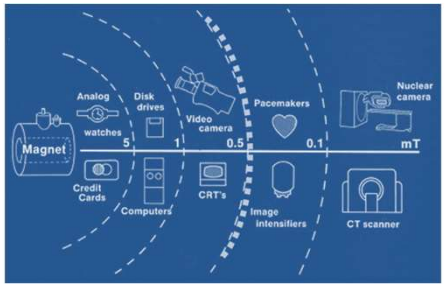
48

The Strong MRI Magnet

- Earth field: 0.5 Gauss
- Toy magnets: ~ 50 Gauss
- MRI magnet: 15,000~117,000 Gauss

49

Magnetic Effect to Electronic Devices



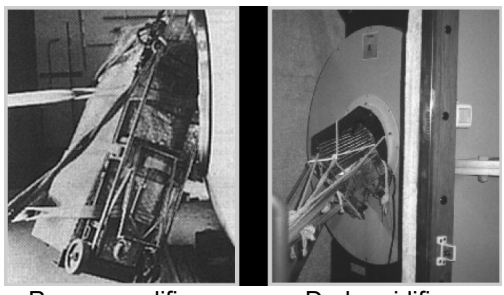
50

Danger of Strong B_0

- Huge attractive force for appliance
  - Nail scissors, tweezers
  - Wrench, screwdriver, hammer
  - Computer, chair, oscilloscope

51

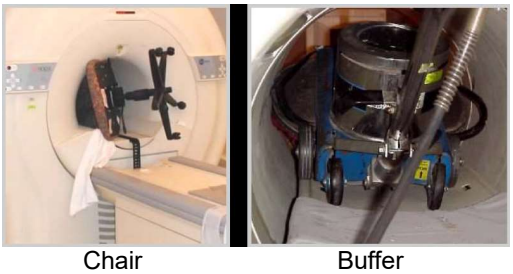
Danger of Ferromagnetic Object in MRI



Power amplifier De-humidifier

52

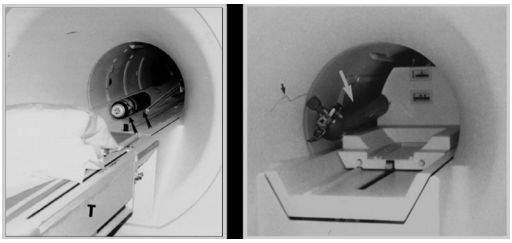
Danger of Ferromagnetic Object in MRI



Chair Buffer

53

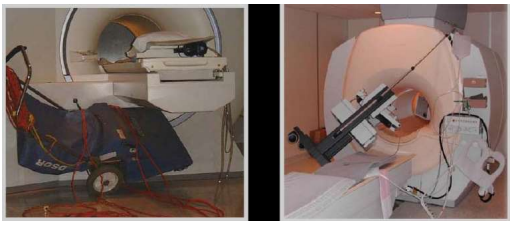
Danger of Ferromagnetic Object in MRI



Nitrous oxide tank Oxygen cylinder

54

Danger of Ferromagnetic Object in MRI



Vacuum cleaner i.v. injector

55

Other "Bad" Things

- Metal or magnetic stuff
  - Implants
    - Surgical clips
    - Cochlear implants
    - Injection pump
    - Prosthesis
  - Carry-on
    - Dental work
    - Leather belt
    - Make-up (eye shadow)
    - Hair pin
- Discomfort or image distortions

56

Some Known "Bad Things"

57

Superfunction or Susceptibility Artifact

58

Safety information

- http://www.mrisafety.com/safety_info.asp

59

Thank you for your attention

May the force be with you