Functional imaging based on blood oxygenation contrast

Quantitative and Functional Imaging

BME 4420/7450

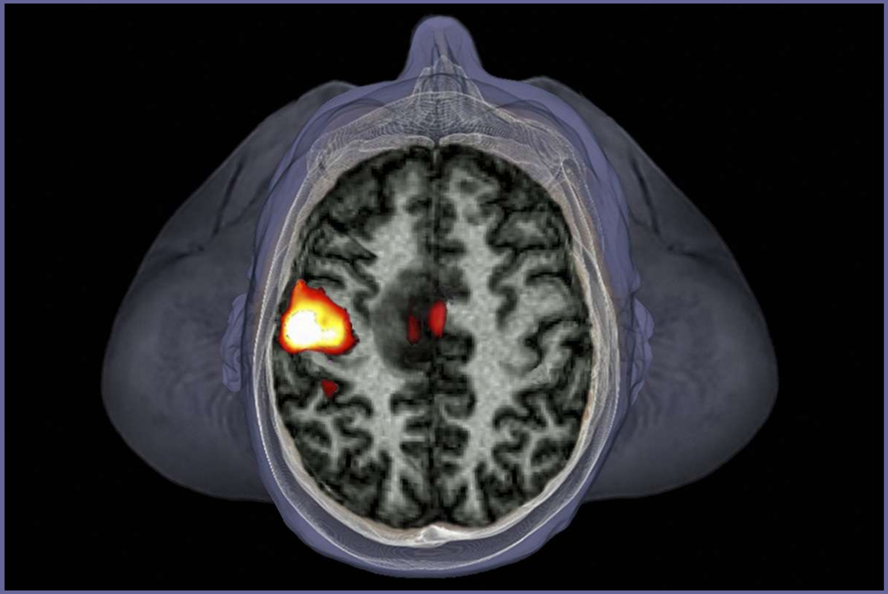
Fall 2022

Image-based measurements

- Tissue characteristics
- Volume and shape
- Motion
  - Random molecular diffusion
  - Microscopic flow (perfusion)
  - Macroscopic flow
- Metabolism
- Molecular imaging

Functional MRI (fMRI) Topics

- How blood oxygen
  - Reflects brain activity
  - Affects image contrast
- Data analysis
- Applications



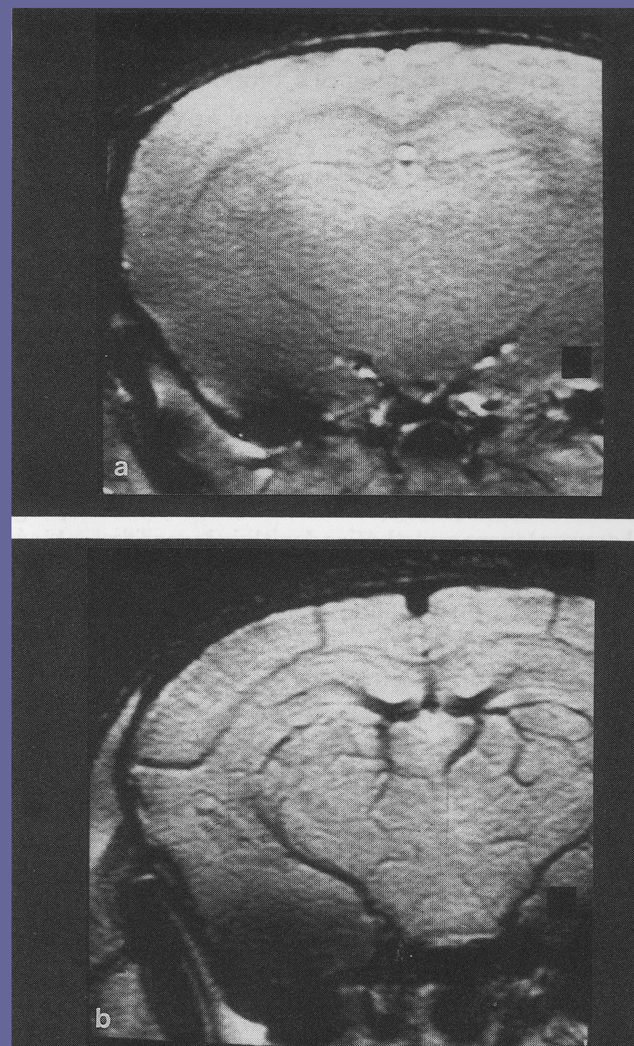
Zephyr/Science Photo Library

I. Blood Oxygenation Contrast

Effect of blood oxygenation on MR signal

100% Oxygen

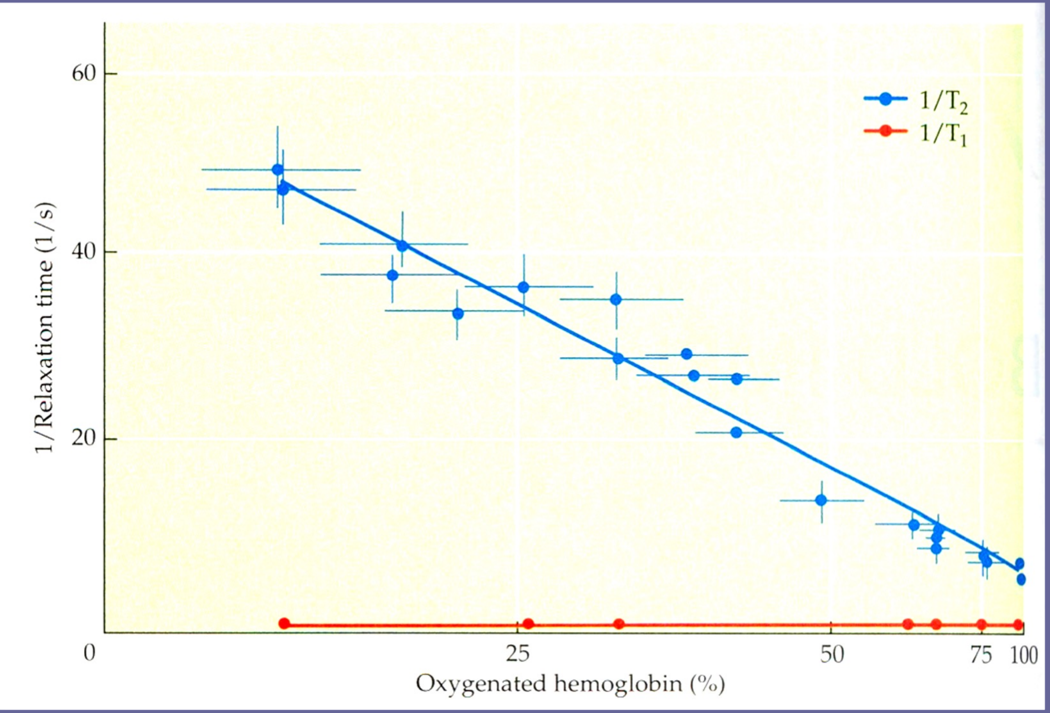
Air (20% Oxygen)



Ogawa et al, 1990

Relaxation rates of blood

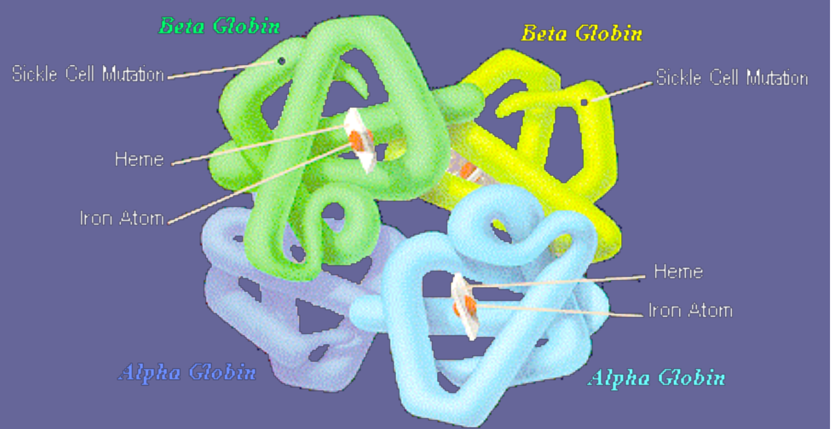
- As oxygenation increases
  - R2 relaxation rate decreases
  - T1 is constant



Huettel, 2004

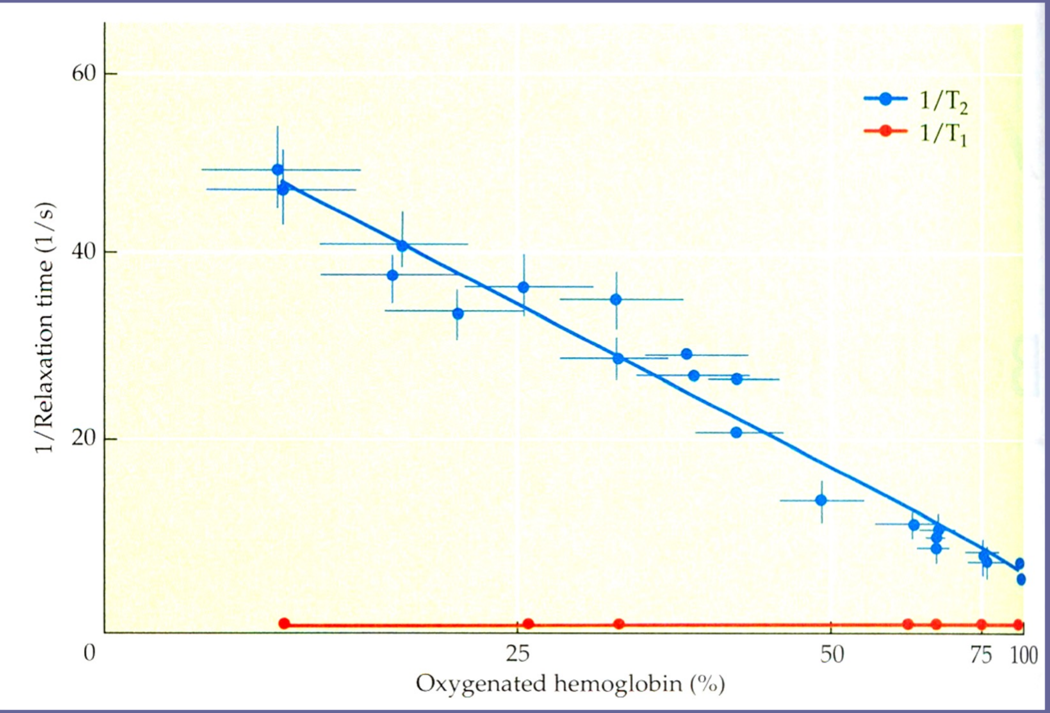
Hemoglobin

- Protein composed of 4 subunits
- Each subunit holds a heme group
- Heme contains one Fe atom
- O_2 binds to Fe
  - High affinity when $[O_2]$ is high
  - Lower affinity when $[O_2]$ is low
  - Hb carries O_2 from lungs to tissues
- Magnetic moment of Hb changes when oxygenated
- 97% of red blood cell (dry weight) is Hb



Relaxation rates of blood

- As oxygenation increases
  - R2 relaxation rate decreases
  - T1 is constant
- DeoxyHb makes B_z depend on position relative to red blood cell
- Motion of water around red cells causes random dephasing

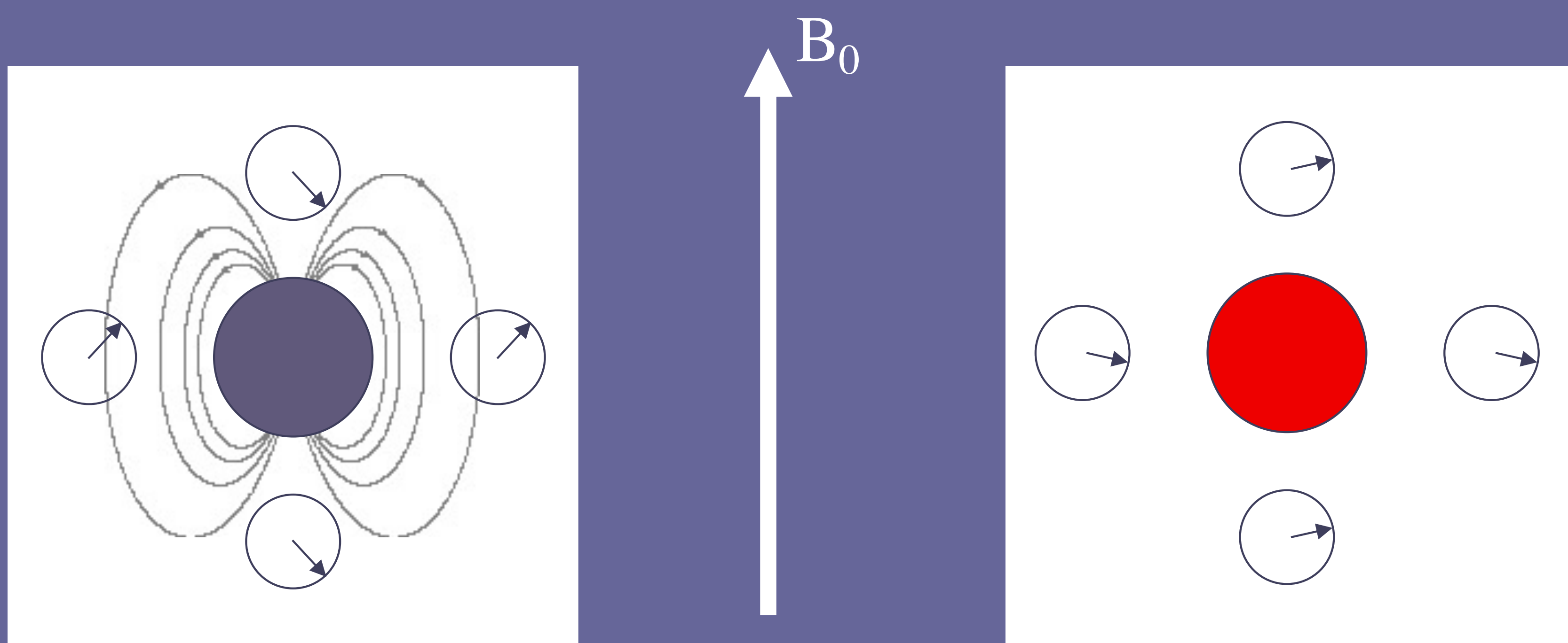


Huettel, 2004

Magnetic properties of blood

- DeoxyHb
  - Paramagnetic (unpaired Fe electrons)
  - Magnetized by applied field: $M=\chi B$
    - Magnetic susceptibility χ is due to electrons, not nucleus
  - $\chi(\text{deoxy blood}) - \chi(H_2O) \cong 10^{-7}$
- OxyHb
  - Not paramagnetic (no unpaired electrons)
  - $\chi(\text{oxy blood}) \cong \chi(H_2O)$

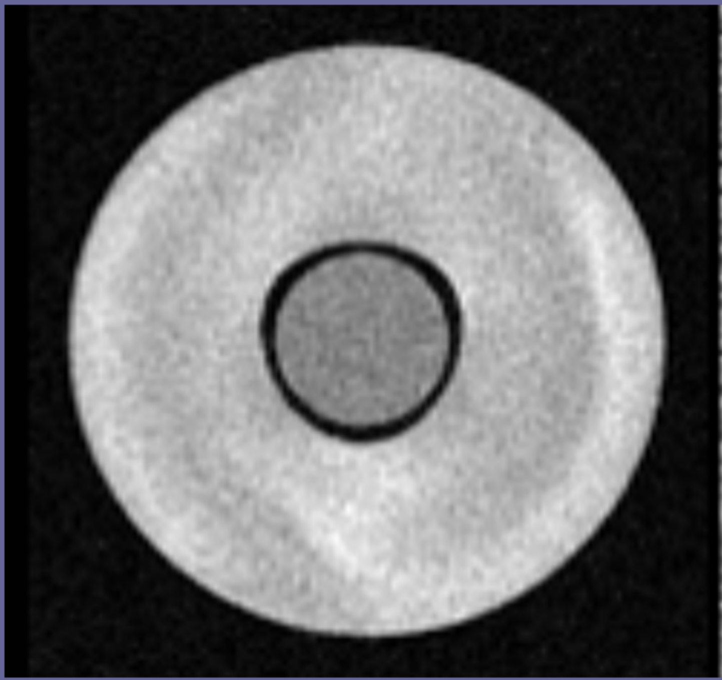
Relaxation of tissue water



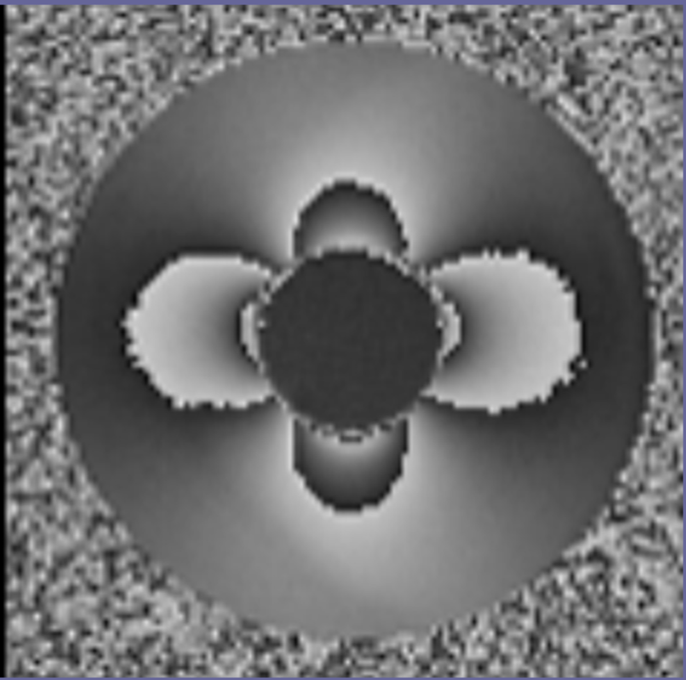
DeoxyHb

OxyHb

Deoxyhemoglobin content affects signal



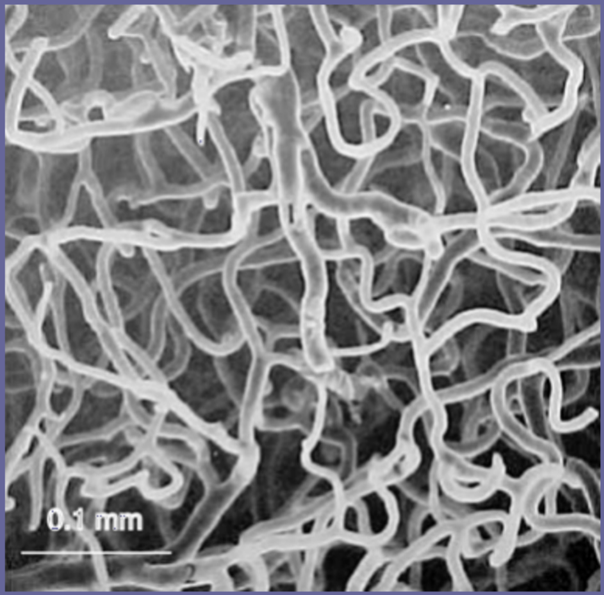
Idealized capillary in tissue



Magnetic field variations surrounding capillary

Water signal reflects both extravascular water and blood

- Extravascular signal
- Intravascular signal
  - Capillary blood
  - Venous blood
- Signal from one water pool or the other may be dominant



Capillary networks

Deoxygenated blood alters the magnetic field around capillaries and draining veins

Signal changes in brain

- Neurons need energy (glucose+O_2) to do work
- Cerebral blood flow (CBF) increases locally
  - Measure blood flow (perfusion) change
- Oxygen saturation increases locally
- Oxygen makes iron in Hb less magnetic
- Magnetic field around vessels becomes more uniform
  - Measure signal increase

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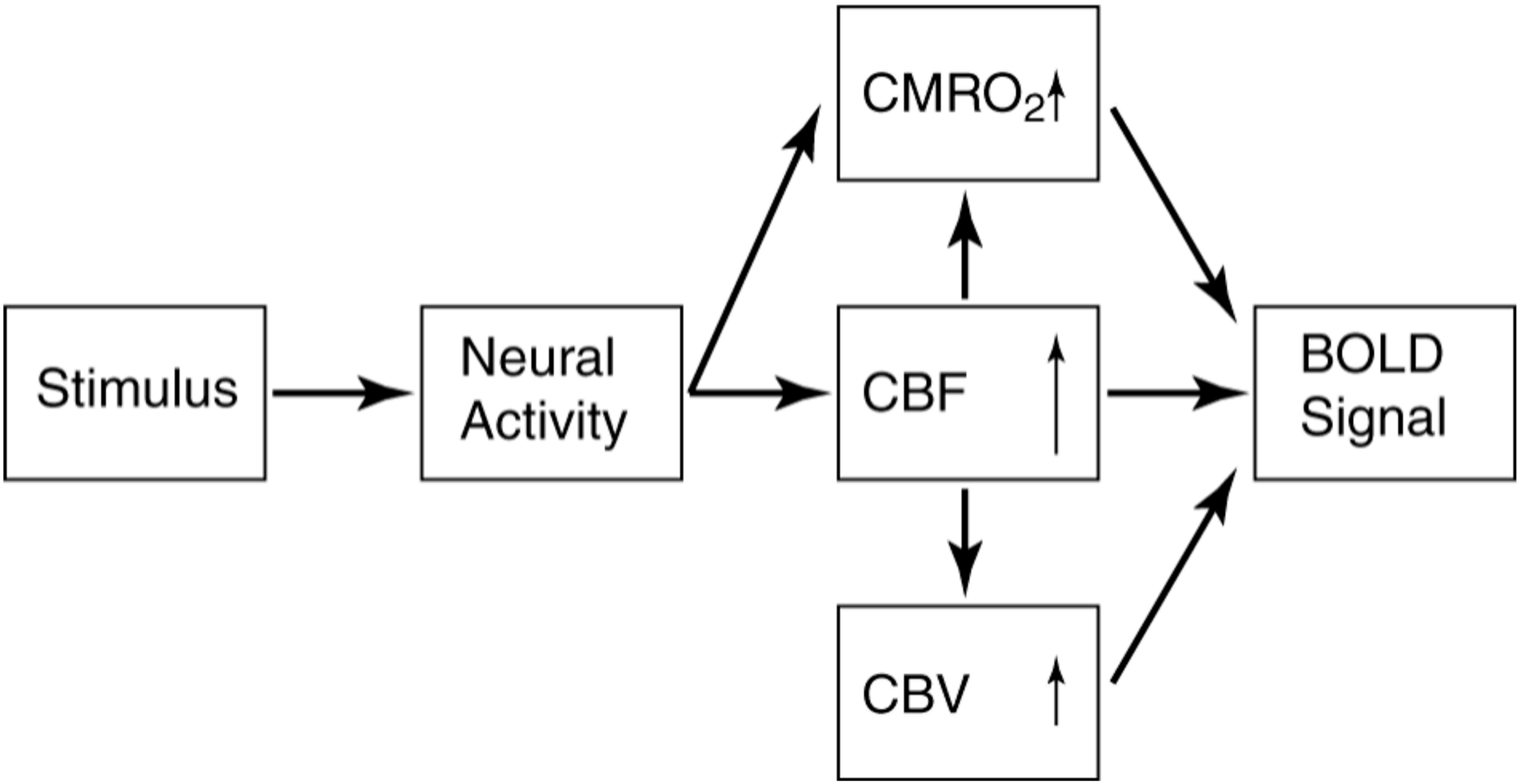
  - Measure signal increase
- DeoxyHb is the (endogenous) contrast agent

Physiological basis of the signal

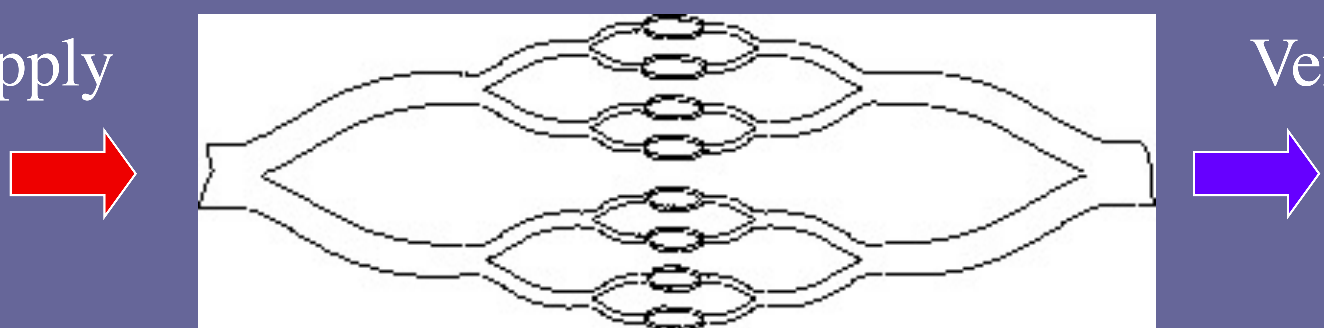
Cerebral Metabolic Rate of O2 consumption



Vascular response

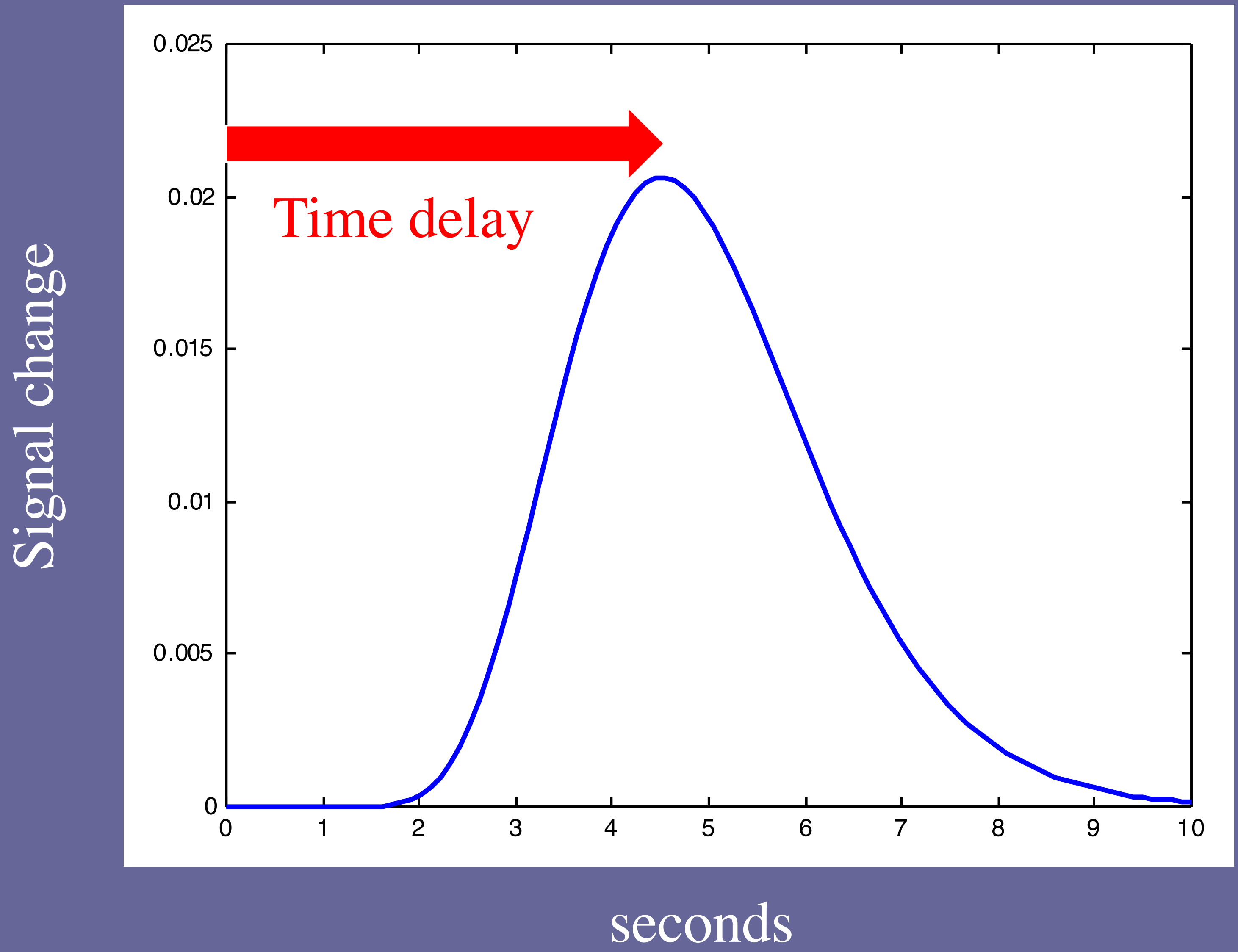
- Lags neuronal activity
- May not be specific to active region
  - Affects surrounding tissue as well
- May not scale linearly with activity

Arterial supply



Venous drain

Hemodynamic response function



Simple imaging experiment

- Acquire images when the brain is active (A)
- Acquire images when the brain is resting (baseline state, B)
- Find image intensity difference

$$\Delta I = \bar{I}_A - \bar{I}_B$$

Visual stimulation experiment

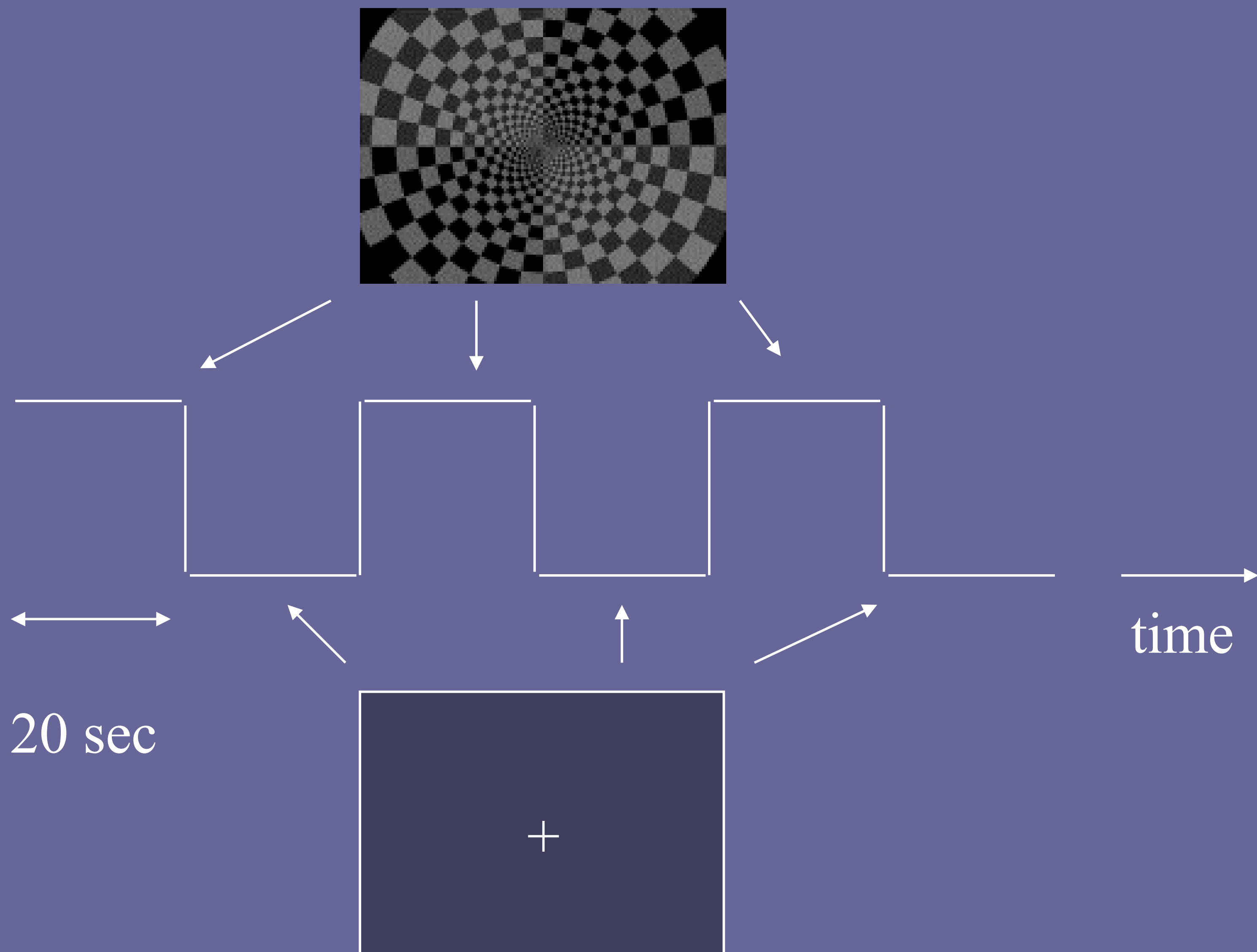
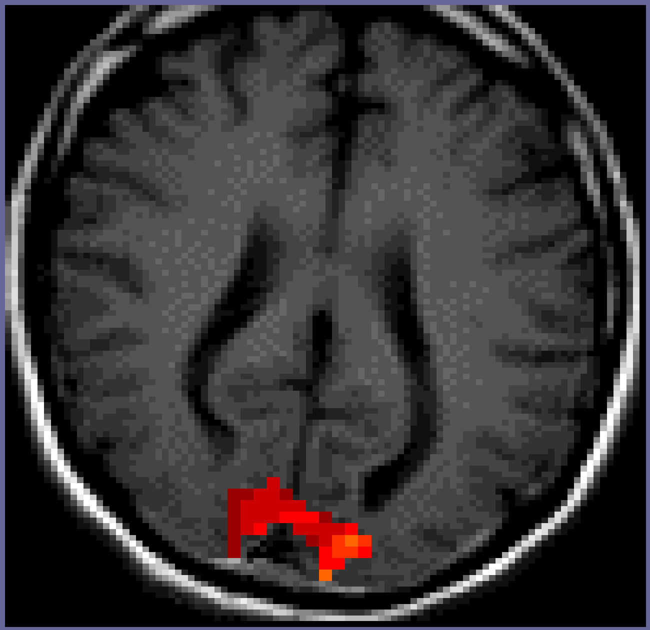


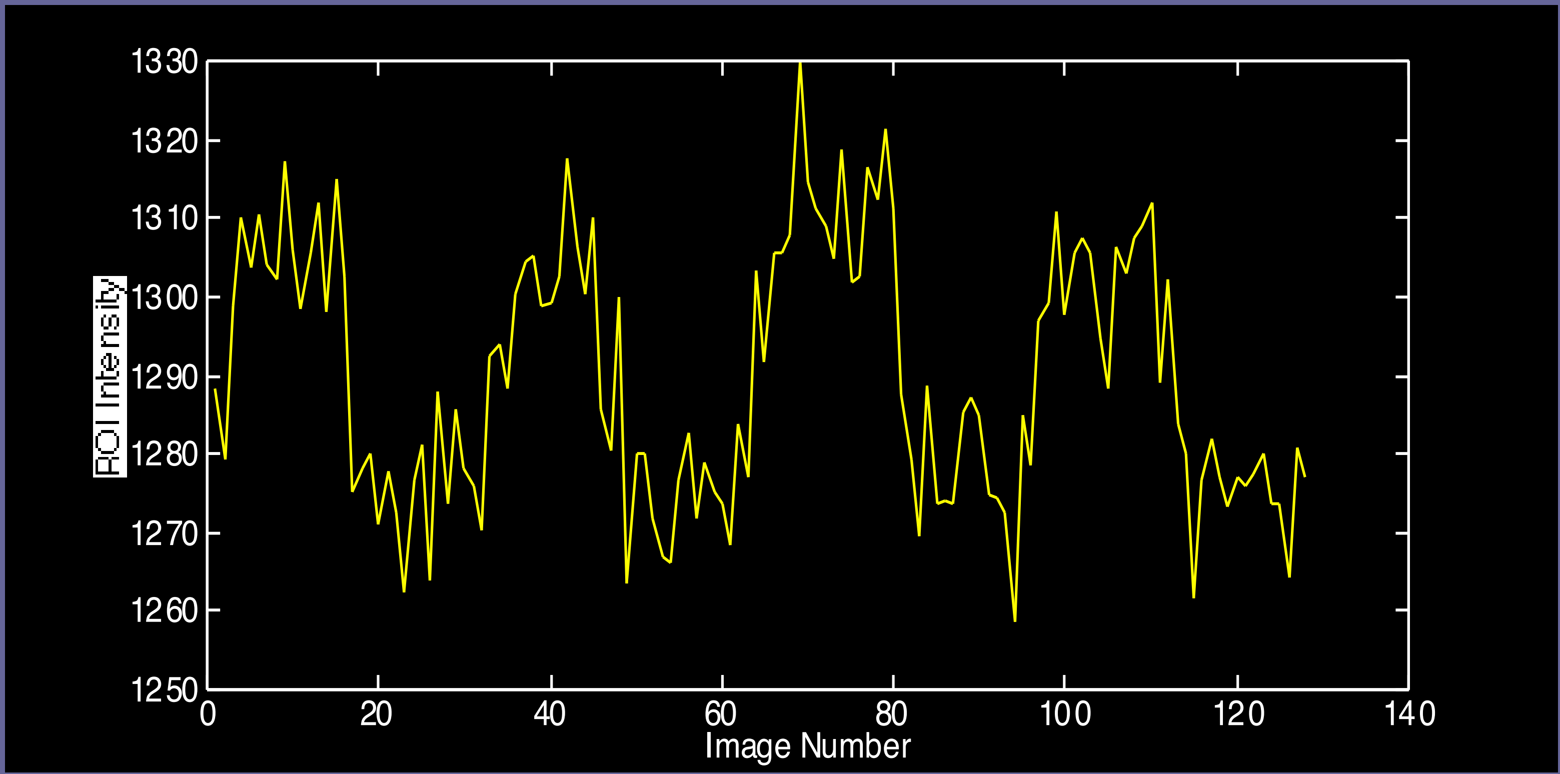
Image visual cortex

Map of signal difference



Pixels with significant signal change are shown in color

Signal time course



Reproducibility

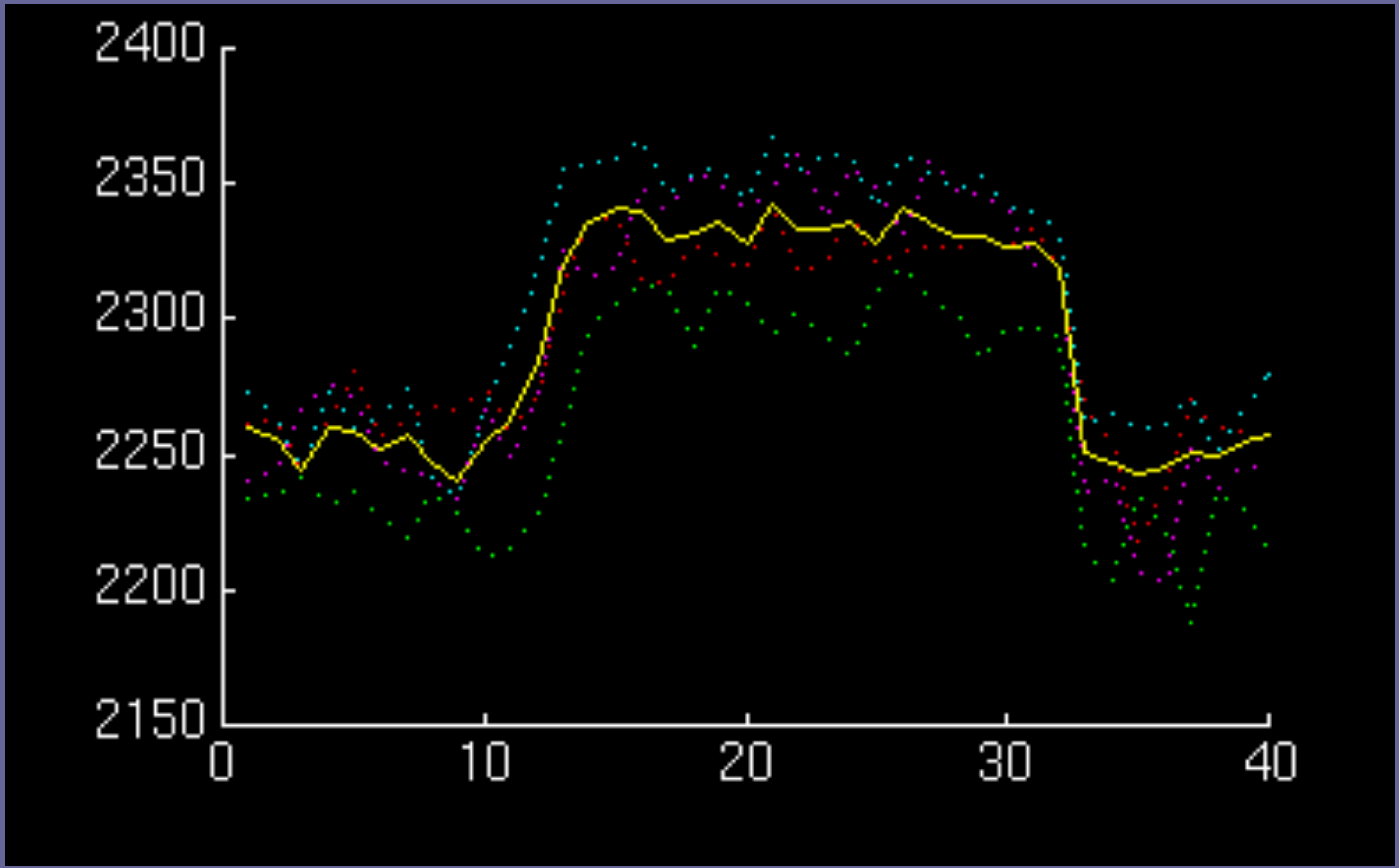


Image number

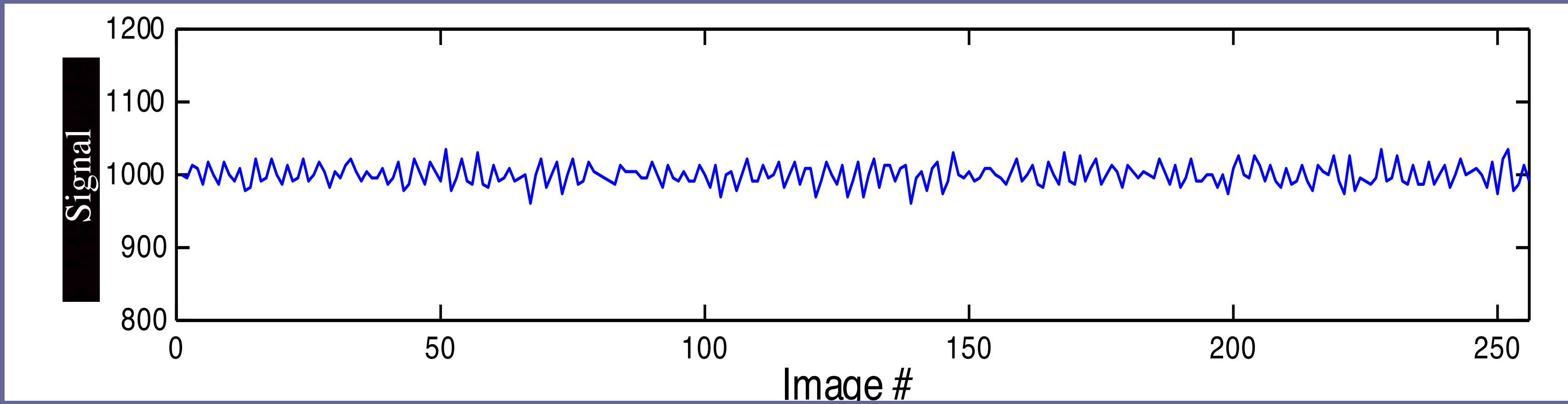
II. fMRI data analysis

The problem

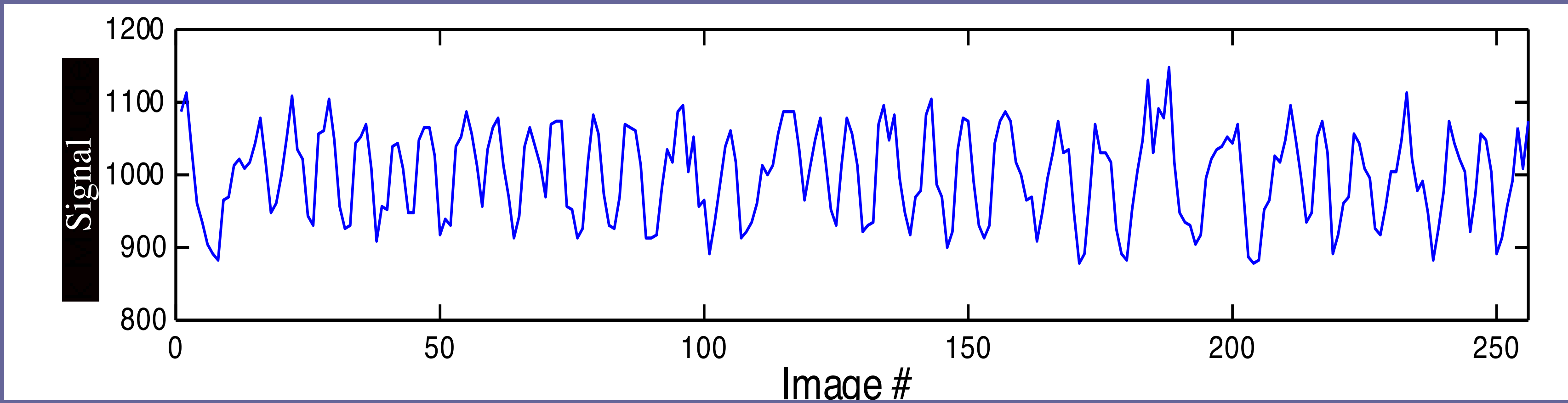
- Image intensity change is small
  - About 0.3% to 3%
- Contrast to noise ratio is ~0.6 to 6
- Many other sources of intensity variation on this level
  - Subject motion (especially at contrast boundaries)
  - Instrument drift
  - Electrical (Johnson) noise
  - Physiological changes not associated with brain activity ('physiological noise')
- Signal detection problem

In vivo noise >> object noise

Variation of integrated image intensity for 256 images

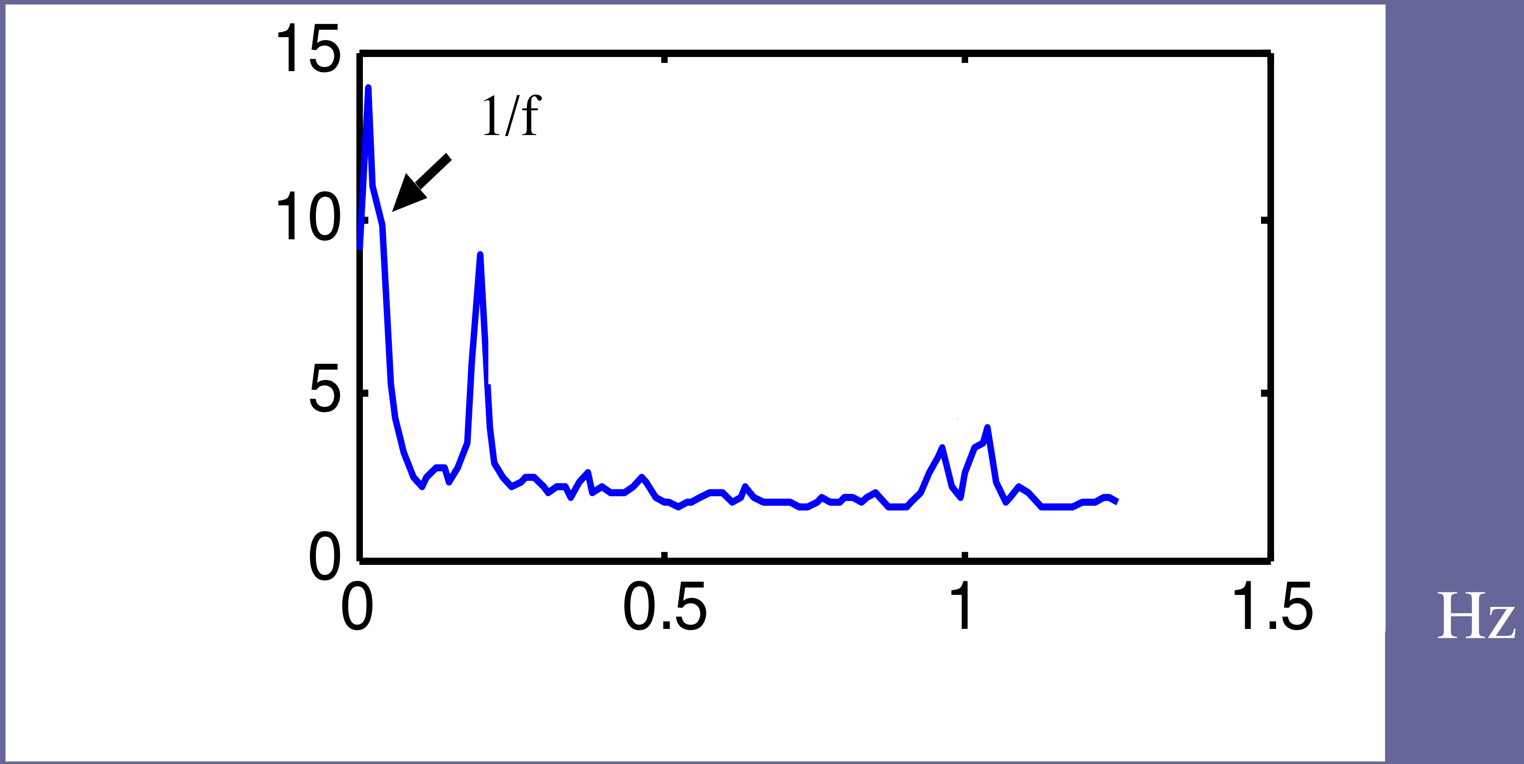


Water Phantom, Std = 1.5% Mean



Brain, Std = 6.1% Mean

Power Spectrum of Signal Variations from Whole Brain Slice



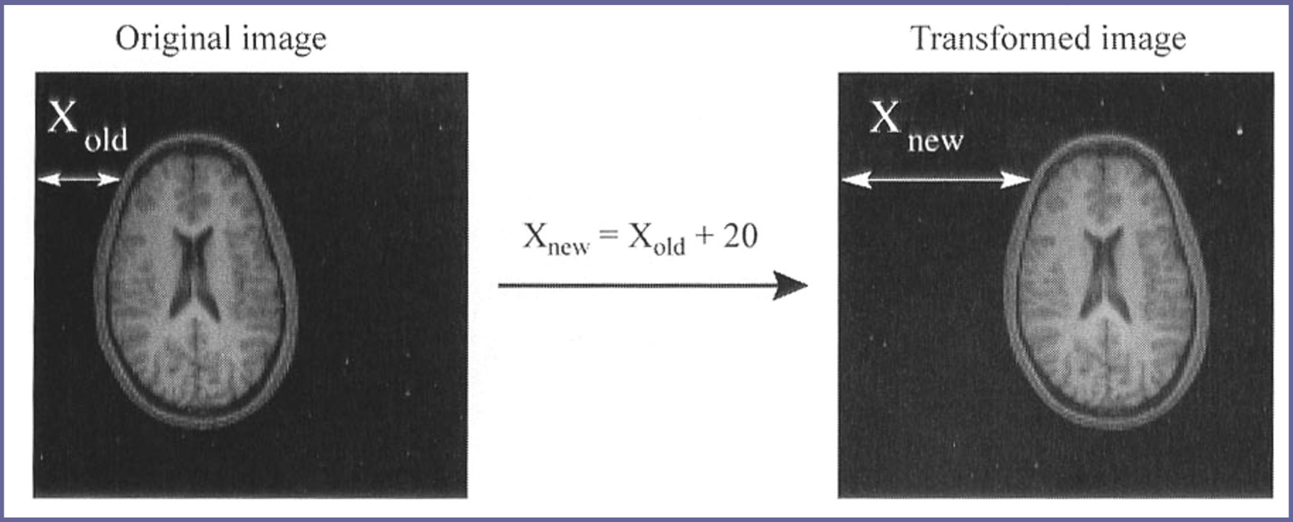
In-class exercise: what are the causes of two other spectral peaks?

Preprocessing the data

- Goal: to eliminate as much of the uninteresting signal variation as possible
- Model (and eliminate) causes of signal variation
  - Head motion (translation and rotation)
  - Respiration-related changes
  - Instrument drift (linear or low-frequency baseline drift)

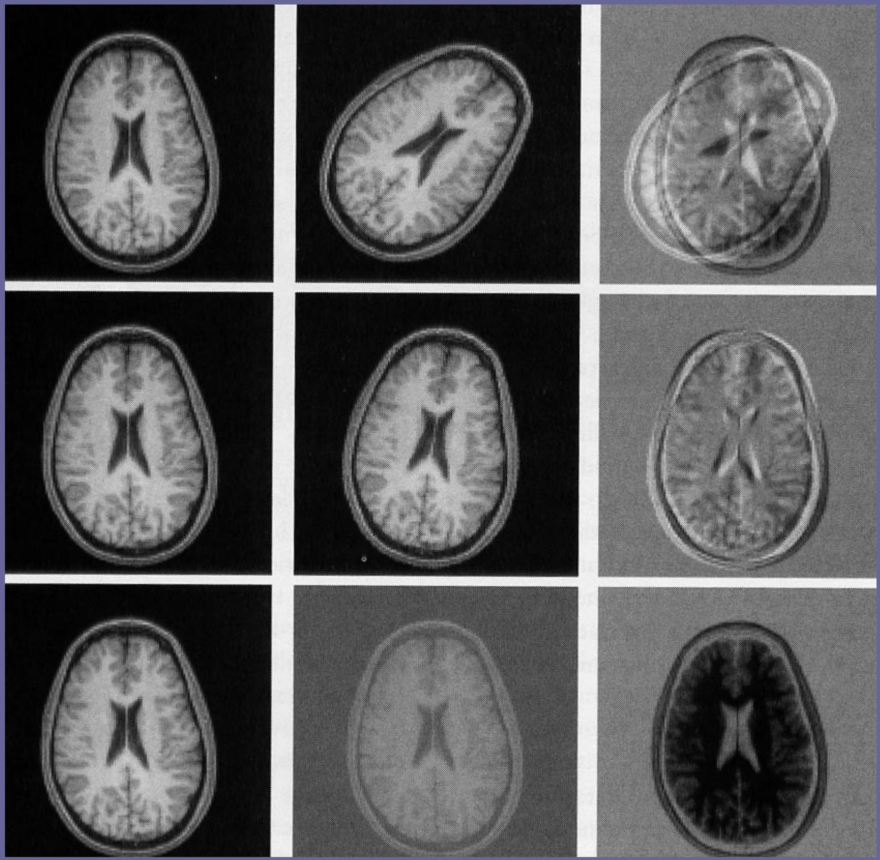
Correcting for motion

- Estimate translation and rotation of head relative to first image volume
- Register (align) images to remove motion

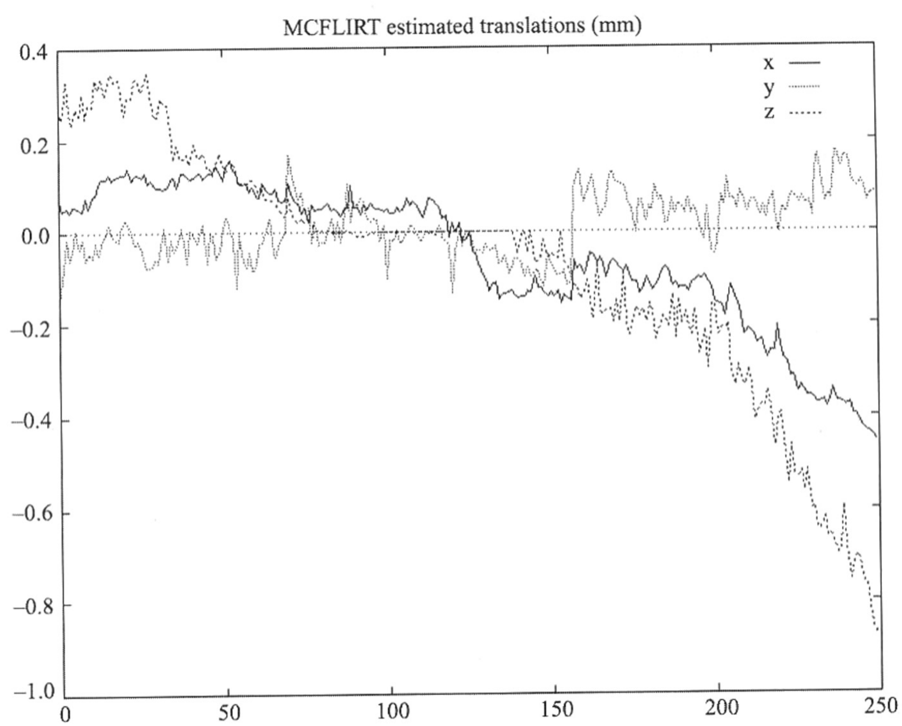


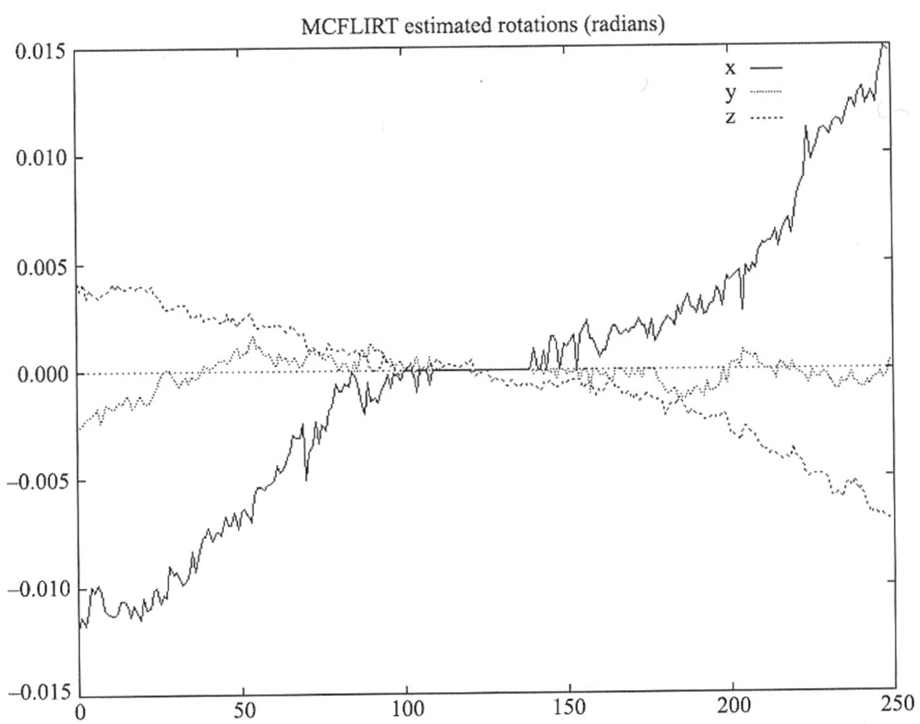
Estimating global image differences

- Find transformations that make images most similar
  - Rotation
  - Translation
  - Intensity scaling



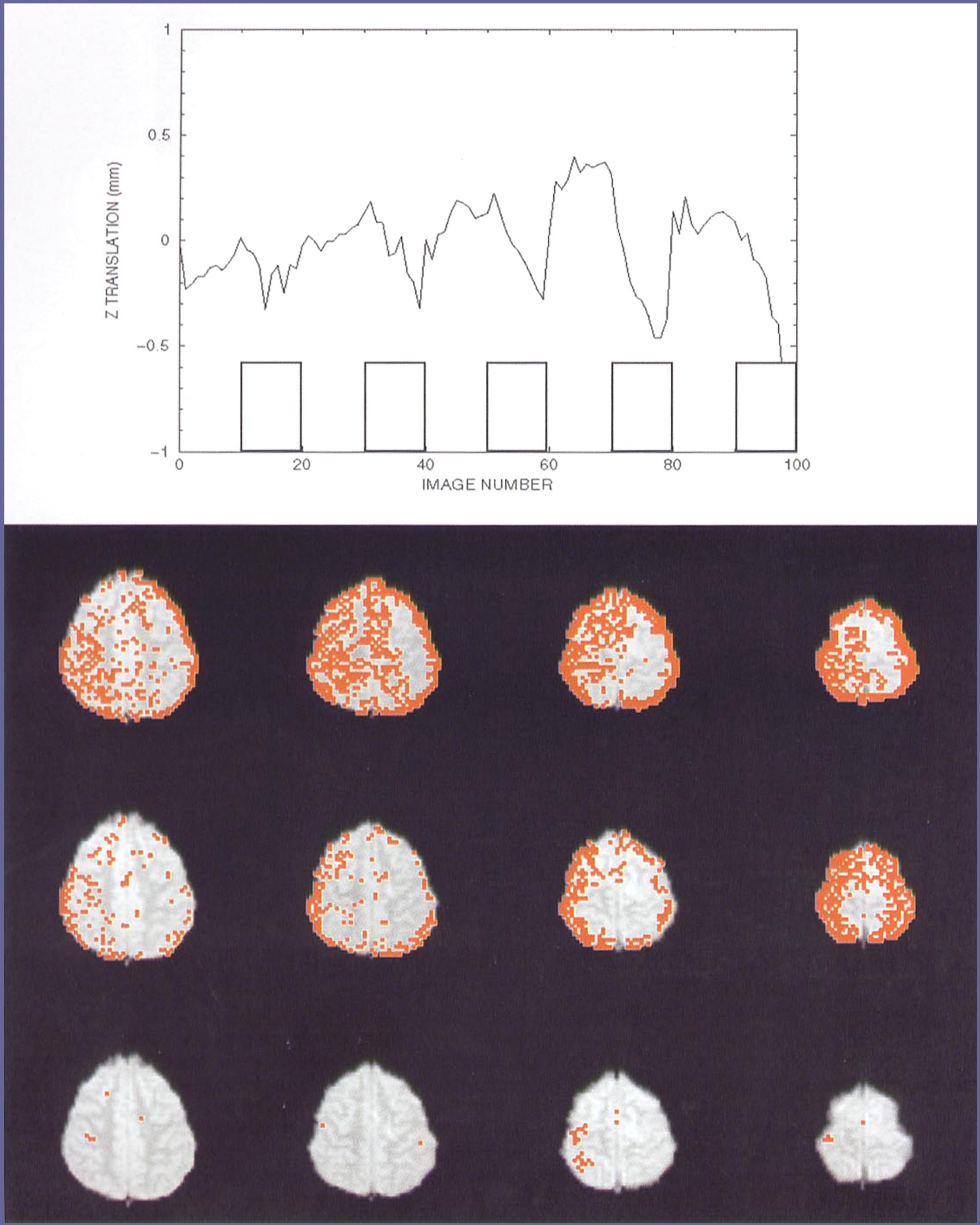
Estimation of motion





Translations (mm)

Rotations (radians)



Z translation vs. time

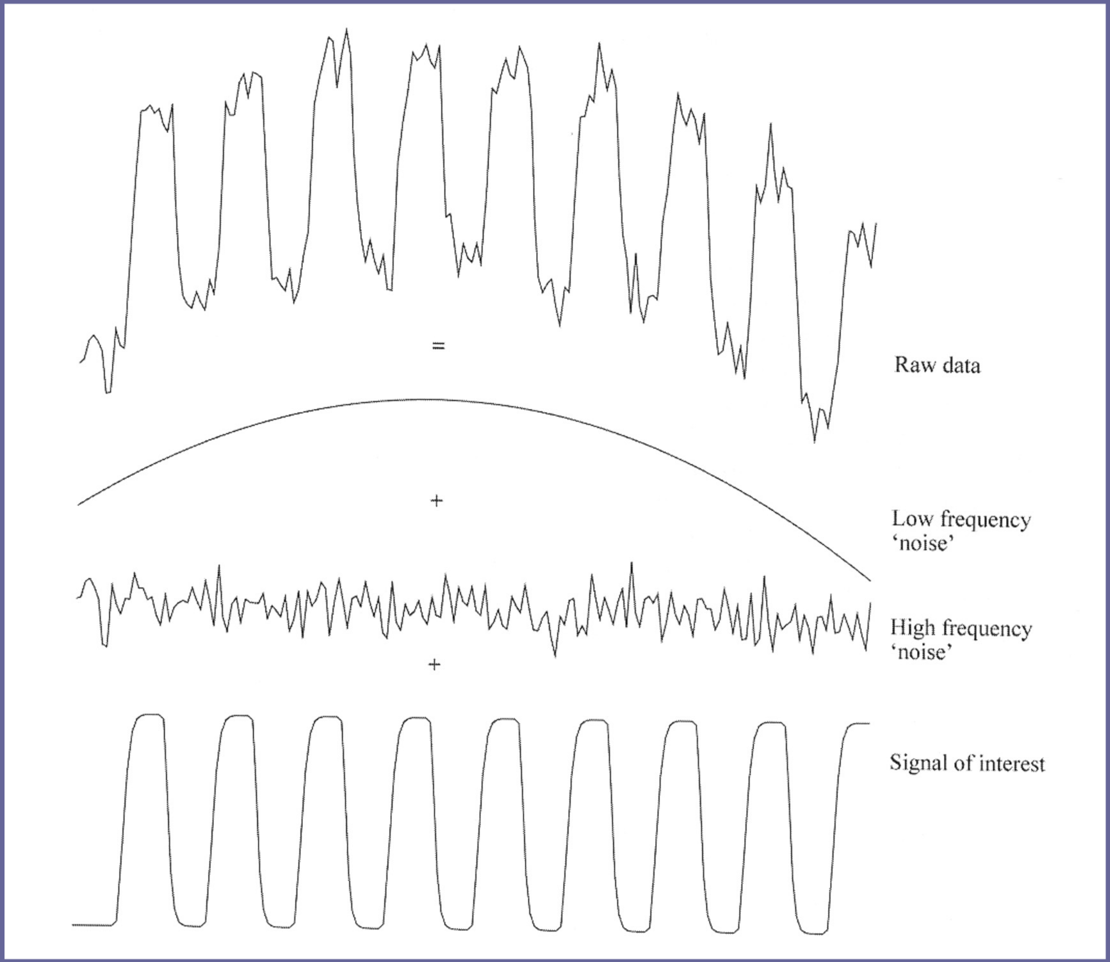
No correction

Registered images

Registered and detrended

Apply frequency filter to the signal

- High pass filter can remove baseline ‘roll’
- Avoid changing signal at frequency of desired signal

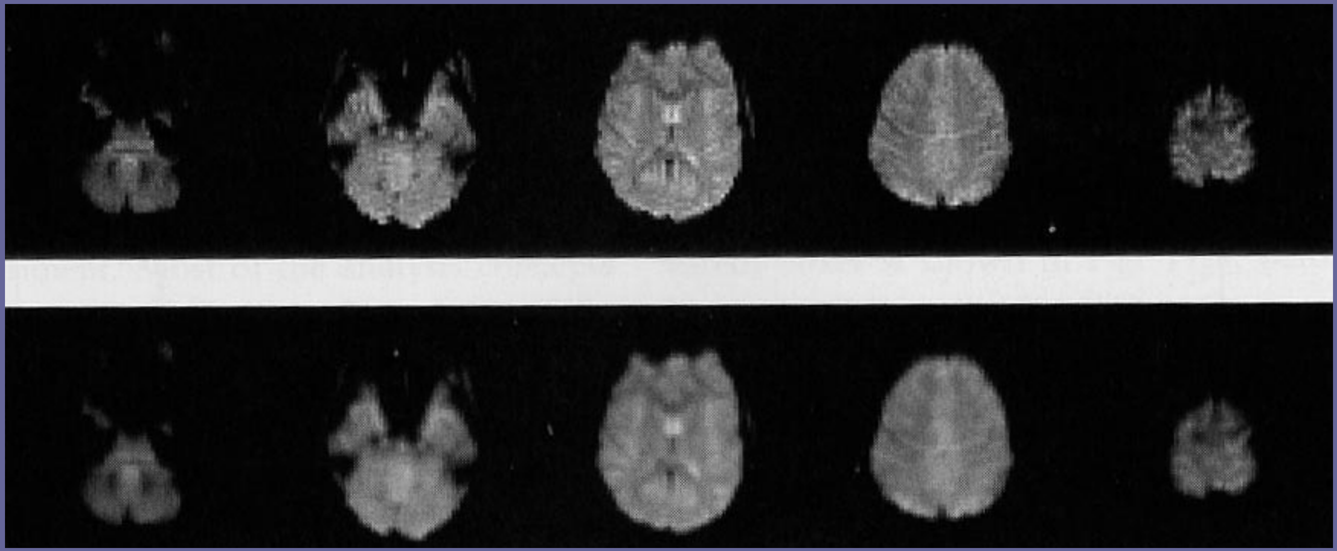


Reducing high spatial frequency noise

- Reduce noise by local averaging
- Smooth by convolution
  - What effect does this have on resolution?
  - What should width of convolution kernel be?

Before smoothing

After smoothing



Measuring the activation signal

- Create a function, Y(t), that has the expected time dependence of the activation signal
- Find the image intensity in a voxel as a function of time
- How well does the measured signal variation follow the function Y(t)?
- Repeat for all voxels
- Display results as a statistical map

Statistical mapping

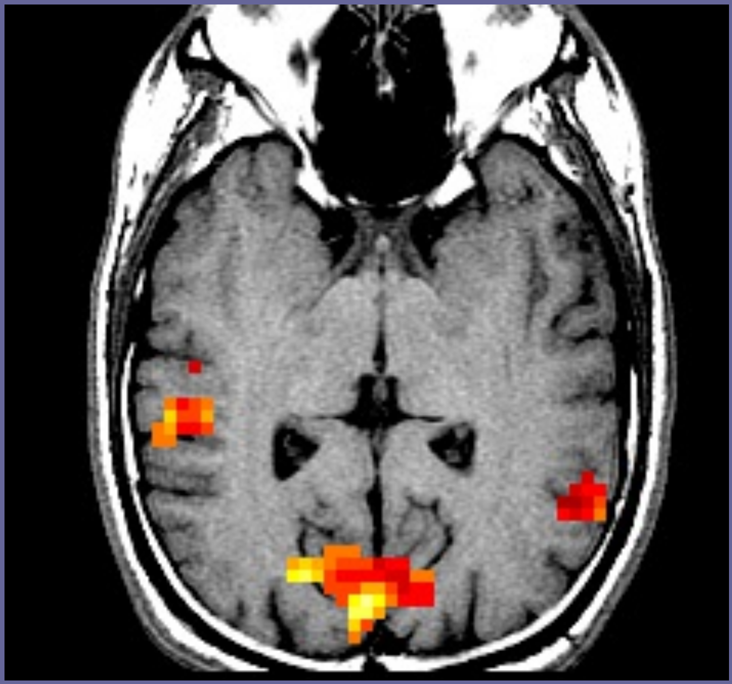
- Why not just map the signal difference (stimulation - baseline)?

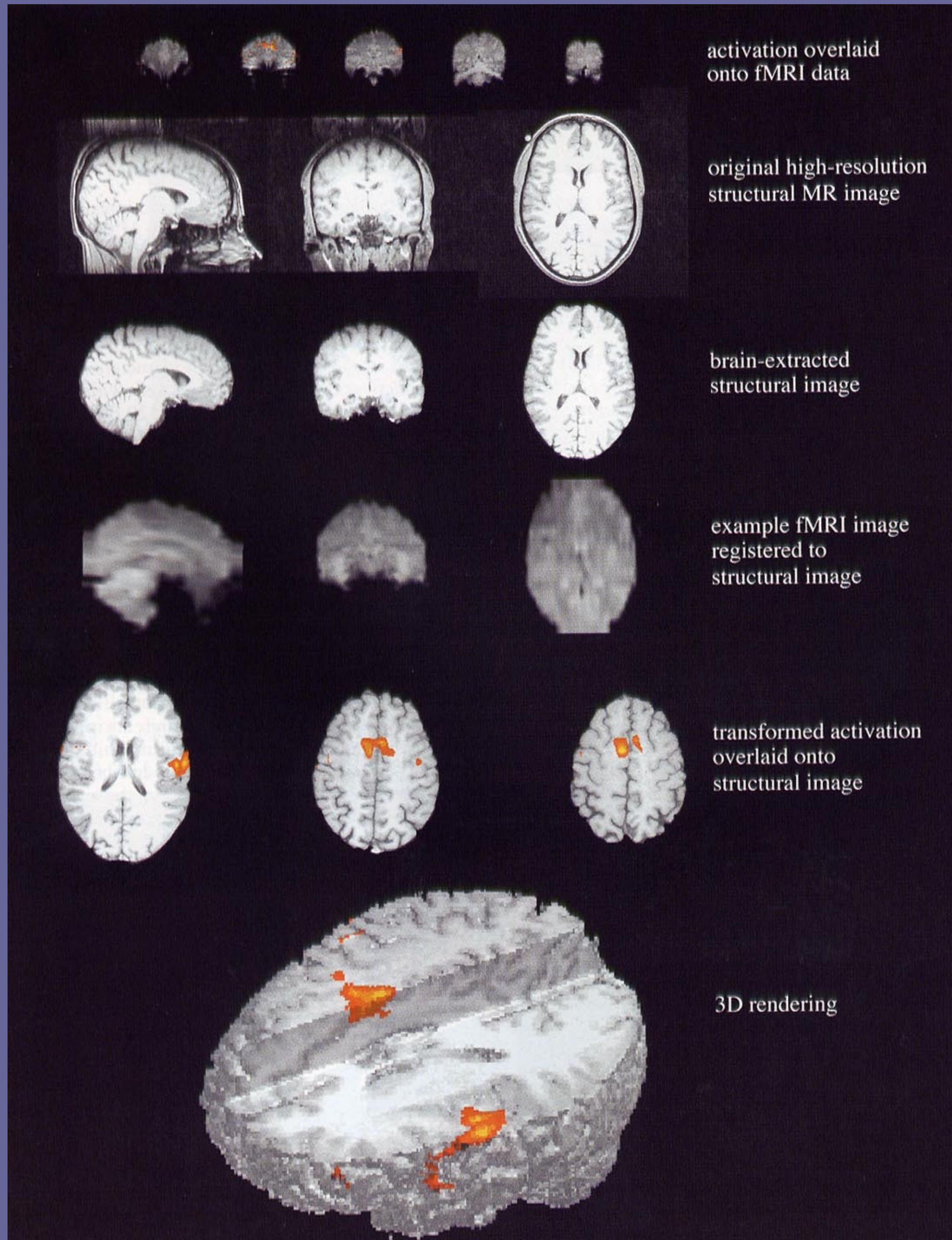
Statistical mapping

- Why not just map the signal difference (stimulation - baseline)?
- Noise contributes to signal difference
  - Some voxels are noisier than others
- No way to distinguish signal differences due to noise from brain activity
- Use statistical measures of the size of the signal difference relative to the noise
  - Correlation coefficient
  - Student's t-statistic

Activation map display

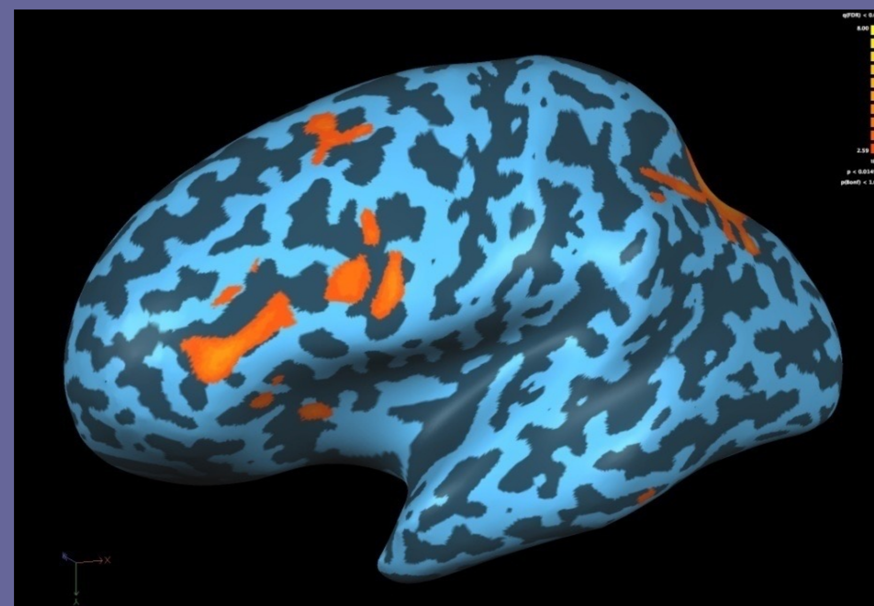
- Threshold the statistical map at some level of significance
- Display map (in color) overlaid on anatomical image or 3D volume




activation overlaid onto fMRI data
original high-resolution structural MR image
brain-extracted structural image
example fMRI image registered to structural image
transformed activation overlaid onto structural image
3D rendering

Rendering activation of curved surface of the brain

- Rendered on an inflated brain surface
  - Neuronal activity during an approximation task
- Differences between subjects
  - Location?
  - Amplitude?
  - What factors lead to cognitive differences?



15
37
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40 50 60

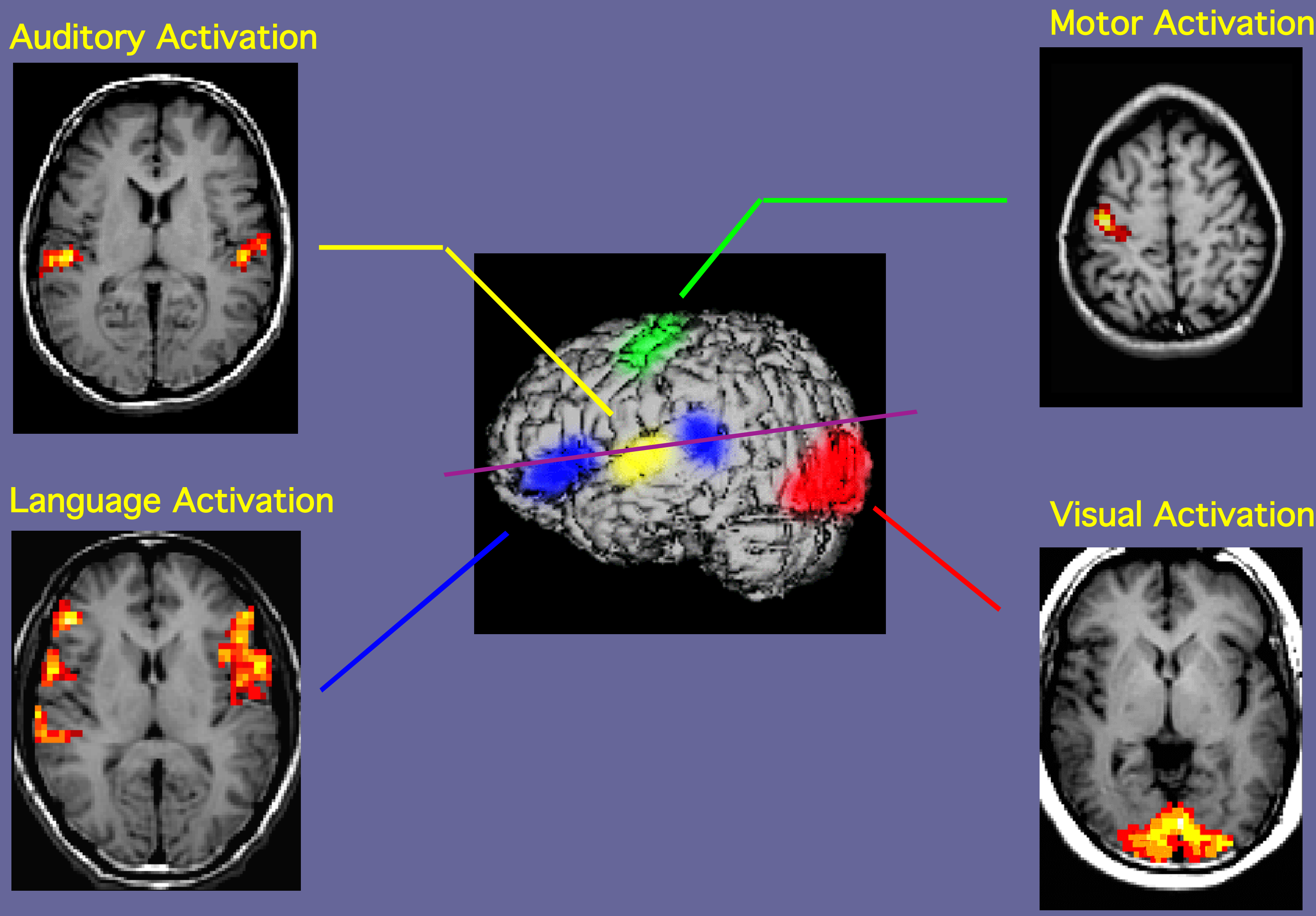
Summary of data processing steps

- Preprocessing can remove spurious signal variation
- Statistical tests are used to judge the significance of signal changes
- Activation maps can be displayed in 2D, 3D, or inflated brain maps

What brain functions can be mapped?

- Sensory systems
  - Visual
  - Auditory
  - Tactile
  - Olfactory
  - Gustatory
- Active tasks
  - Motor
  - Cognitive
  - Pharmacology

- Mapping basic sensory/motor and language areas of the brain is useful, e.g. in neurosurgery



Summary

- Deoxygenated Hb is an endogenous contrast agent
- Can be used to map brain activity
- CNR of fMRI is low
  - Signal processing is important
  - Statistical mapping
- Applications
  - Clinical (e.g., neurosurgical planning)
  - Neuroscience (e.g., cognition and learning)

Sources

- R.B. Buxton, Introduction to Functional Magnetic Resonance Imaging: Principles and Techniques (Cambridge, 2002).
- SA Huettel, AW Song, G McCarthy, *Functional Magnetic Resonance Imaging* (Sinauer, 2004).
- P. Jezzard, P.M. Matthews, S.M. Smith, Functional MRI: an Introduction to Methods (Oxford, 2001).