## Outline for Today

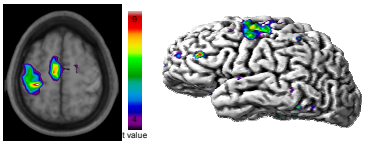
- Why use functional MRI (fMRI) to image brain function?
- Key concepts of fMRI
- History of fMRI

*Functional Magnetic Resonance Imaging, Huettel, Chapter 1*

Dr Sue Francis, Sir Peter Mansfield Magnetic Resonance Centre (SPMMRC)
email: susan.francis@nottingham.ac.uk

## Functional Neuroimaging

- **Functional neuroimaging** attempts to localize different mental processes to different parts of the brain to create a map of areas which are responsible for which processes.



## What is functional MRI (fMRI)?

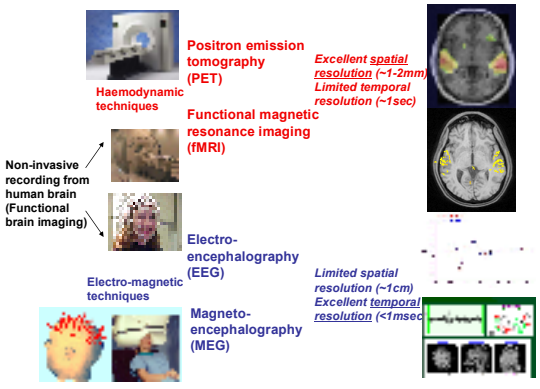
- A technique for measuring changes in brain activity over time using principles of **magnetic resonance**.

- Uses a strong magnetic field to create images. **Static magnetic field** in range 1.5 to 7 Tesla.
- The scanner uses a series of changing magnetic field gradients and oscillating electromagnetic fields, known as a **pulse sequence**.

## What is functional MRI (fMRI)?

- fMRI data is taken while the patient/subject is performing a specific task (i.e., linguistic, motor, sensory, attention) inside the magnet.
- Most fMRI studies use changes in **BOLD contrast**, although other measures exist.

## Studying brain function – imaging techniques




## Studying brain function – non-imaging techniques

- Lesion studies - historical, lesions often change over time and regions change their processing to compensate, difficult to find isolated damage.
- Temporary interruption of brain function possible using **transcranial magnetic stimulation (TMS).**
- Drug manipulation - allow investigation of large-scale brain systems.

# fMRI Key Concepts

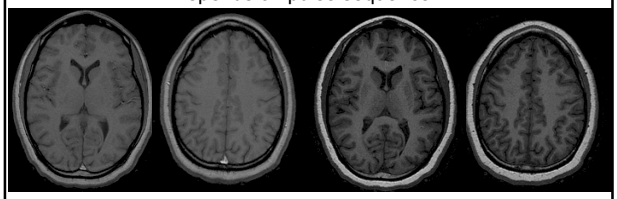
- Anatomical Contrast
- Functional Contrast
- Spatial Resolution
- Temporal Resolution
- Functional Resolution

# Anatomical Contrast

Definition: The ability to distinguish between two (or more) different properties of tissue.

• Contrast is often expressed with respect to the variation in contrast due to noise in terms of the **contrast-to-noise ratio**.

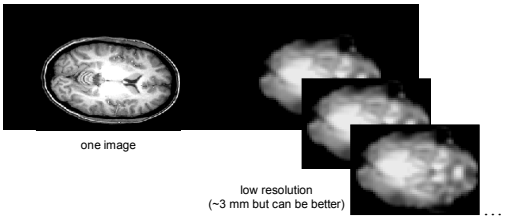
•Depends on pulse sequence



$T_1$ weighted – low contrast-to-noise ratio  $T_1$ weighted – high contrast-to-noise ratio

# Functional Contrast

**MRI vs. fMRI**



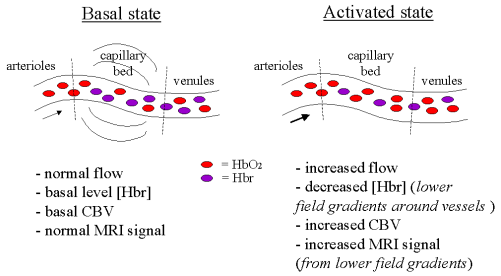

fMRI

Blood Oxygenation Level Dependent (BOLD) signal

indirect measure of neural activity

↑ neural activity ➔ ↑ blood oxygen ➔ ↑ fMRI signal

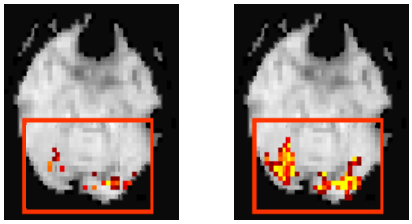
# Functional Contrast: BOLD Activation Physiology




- normal flow
- basal level [Hbr]
- basal CBV
- normal MRI signal

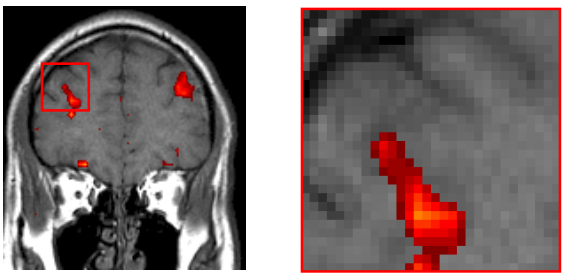
- increased flow
- decreased [Hbr] (*lower field gradients around vessels*)
- increased CBV
- increased MRI signal (*from lower field gradients*)

# Design Effects on Functional Contrast



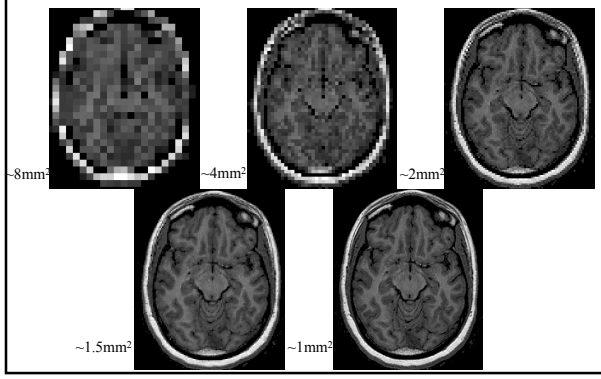
Contrast should really be considered as "contrast to noise": how effectively can we decide whether a given brain region has property X or property Y?

# **Spatial Resolution**: Voxels



**Voxel**: A small rectangular prism that is the basic sampling unit of fMRI. Typical functional voxel: (~ 25 mm)$^3$. Typical anatomical voxel: (1.5mm)$^3$.

## Spatial Resolution: Examples



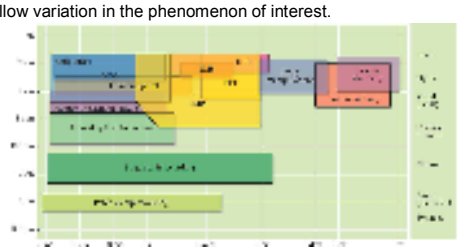

## Temporal Resolution

- Determining factors
  - Sampling rate, usually repetition time (TR)
  - Dependent variable, usually BOLD response
    - BOLD response is sluggish, taking 2-3 seconds to rise above baseline and 4-6 seconds to peak
  - Experimental design
- Importance depends upon research question
  - Type I: Detection
    - Temporal resolution is only indirectly important if your study investigates whether or not a given brain region is active.
  - Type II: Estimation
    - Temporal resolution is extremely important when attempting to understand the properties of an active region.

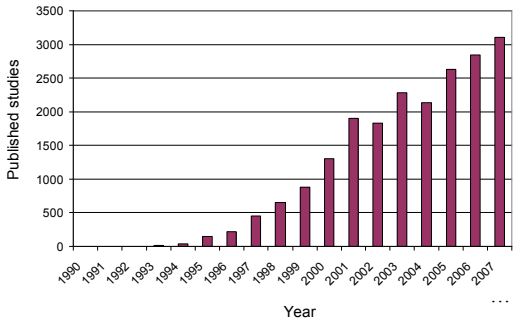
## Functional Resolution

-The ability to map measured physiological variation to underlying mental processes.

- Functional resolution is limited both by intrinsic properties of our brain and by our ability to manipulate the experimental design to allow variation in the phenomenon of interest.



## Growth of fMRI : Published Studies




## Why the Growth of fMRI?

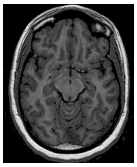
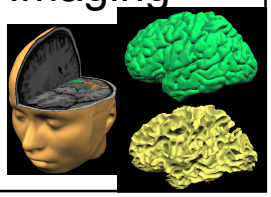
## Why the Growth of fMRI?

- Powerful
  - Improved ability to understand basic brain mapping to a task and cognition
  - Better spatial and temporal resolution than positron emission tomography (PET)
  - Allows new forms of analysis:
    - Event-related: sorting trials by accuracy, response time, type of condition
    - Rapid stimulus presentation
- High benefit/risk ratio
  - Non-invasive (no contrast agents)
  - Repeated studies (multisession, longitudinal)
- Accessible
  - No isotopes required



# History of (f)Magnetic Resonance Imaging



# Timeline of MR Imaging

1924 - Pauli suggests that nuclear particles may have **angular momentum (spin).**

1937 – Rabi measures magnetic moment of nucleus. Coins "**magnetic resonance**".

1944 – Rabi wins Nobel prize in Physics.

1946 – Purcell shows that matter absorbs energy at a **resonant frequency**.

1946 – Bloch demonstrates that **nuclear precession can be measured in detector coils**.

1952 – Purcell and Bloch share Nobel prize in Physics.

1959 – Singer measures blood flow using NMR (in mice).

1972 – Damadian patents idea for large NMR scanner to detect malignant tissue.

1973 – Lauterbur publishes method for **generating images using NMR gradients**.

1973 – Mansfield **independently publishes gradient approach to MR**.

1975 – Ernst develops 2D-Fourier transform for MR.

1977 – Mansfield proposes EPI – a rapid image acquisition method. for MR.

1985 – Insurance reimbursements for MRI exams begin.

MRI scanners become clinically prevalent.

1990 – Ogawa and colleagues create **functional images using endogenous, blood-oxygenation contrast**.

NMR becomes MRI

1920 1930 1940 1950 1960 1970 1980 1990 2000

# Discovery of Nuclear Magnetic Resonance Absorption (1946)


Felix Bloch


Edward Purcell

- Bloch and Purcell independently discovered how to measure **nuclear moment** in bulk matter (1946)
  - Determined relaxation times.
- They showed that energy applied at a resonant frequency was absorbed by matter, and the re-emission could be measured in detector coils
- They shared the 1952 Nobel Prize in Physics

# Timeline of MR Imaging

1924 - Pauli suggests that nuclear particles may have **angular momentum (spin).**

1937 – Rabi measures magnetic moment of nucleus. Coins "**magnetic resonance**".

1944 – Rabi wins Nobel prize in Physics.

1946 – Purcell shows that matter absorbs energy at a **resonant frequency**.

1946 – Bloch demonstrates that **nuclear precession can be measured in detector coils**.

1952 – Purcell and Bloch share Nobel prize in Physics.

1959 – Singer measures blood flow using NMR (in mice).

1972 – Damadian patents idea for large NMR scanner to detect malignant tissue.

1973 – Lauterbur independently publishes method for **generating images using NMR gradients**.

1973 – Mansfield **publishes gradient approach to MR**.

1975 – Ernst develops 2D-Fourier transform for MR.

1977 – Mansfield proposes EPI – a rapid image acquisition method. for MR.

1985 – Insurance reimbursements for MRI exams begin.

MRI scanners become clinically prevalent.

1990 – Ogawa and colleagues create **functional images using endogenous, blood-oxygenation contrast**.

NMR becomes MRI

1920 1930 1940 1950 1960 1970 1980 1990 2000

# Early Uses of NMR

- Most early NMR was used for chemical analysis
  - No medical applications
- 1971 – Damadian publishes and patents idea for using NMR to distinguish healthy and malignant tissues
  - "Tumor detection by nuclear magnetic resonance", *Science*
  - Proposes using differences in relaxation times
  - No image formation method proposed
- 1973 – Mansfield (1973) describes gradient approach to produce NMR images
  - Lauterbur (1973) independently describes projection method for creating NMR images

# The First ~~ZMR~~ NMR Image

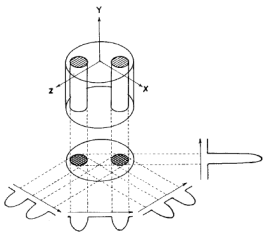
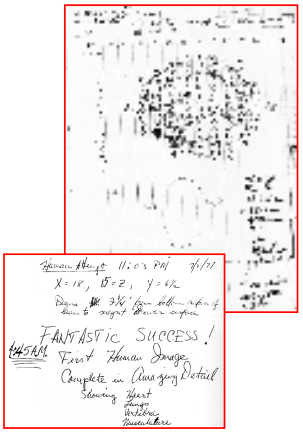


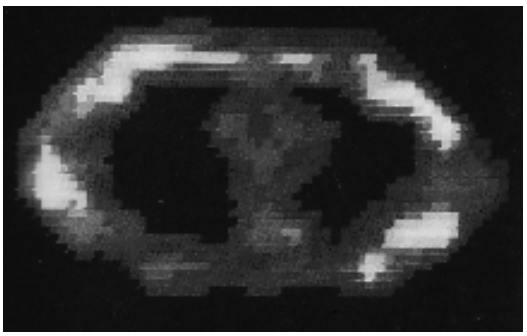

Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.

Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

Lauterbur, P.C. (1973). Image formation by induced local interaction: Examples employing nuclear magnetic resonance. *Nature*, 242, 190-191.

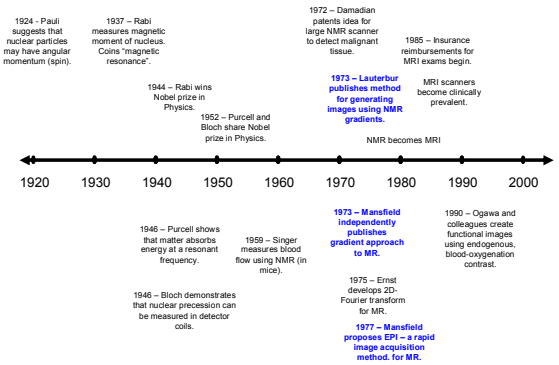
## Early Human MR Images (Damadian)

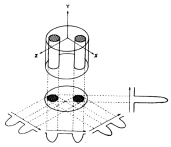
Mink5 Image – Damadian (1977)

## Timeline of MR Imaging




## Discovery of Magnetic Resonance Imaging

2003 Nobel Prize: **"for their discoveries concerning magnetic resonance imaging"**



Paul Lauterbur, Nature, 1973

Sir Peter Mansfield – development of fast imaging technique

Imaging of water proton

Heuttel
Chapter 1

## History of fMRI

Heuttel
Chapter 1

•1990 - Ogawa observes BOLD effect with $T_2$*: blood vessels became more visible as blood oxygen decreased.
*Ogawa S, Lee TM, Kay AR, Tank DW. "Brain magnetic resonance imaging with contrast dependent on blood oxygenation" Proc Natl Acad Sci U S A. 1990 Dec;87(24):9868-72.*

•1991 - Belliveau observes first functional images using a contrast agent.
*Belliveau, et al., "Functional mapping of the human visual cortex by magnetic resonance imaging", Science, Vol 254, 716-719, 1991*

•1992 - Ogawa & Kwong publish first functional images using BOLD signal.
*S. Ogawa, et al., PNAS USA, 89:5951-5955 (1992)*
*K. K. Kwong, et al., PNAS USA, 89:5675-5679 (1992),*

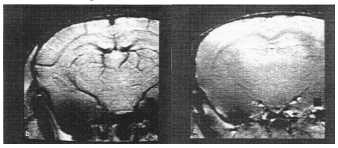
## Blood Oxygenation Level-dependent Contrast

Ogawa et al. MRM, 1990

- Oxyhemoglobin is diamagnetic (like biological tissue).

- Deoxyhemoglobin (dHb) is paramagnetic
  increase transverse relaxation rate ($R_2$) of water protons
  induce susceptibility effect around dHb

Breathing air  Breathing 100% $O_2$

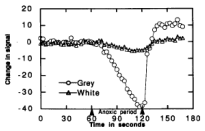


Mouse brain images at 360 MHz

## Dynamic BOLD MR Measurements in Cats

**Turner R, Le Bihan D, Moonen CT, Despres D, Frank J "Echo-planar time course MRI of cat brain oxygenation changes"** Magn Reson Med. 1991 Nov;22(1):159-66

Abstract: When deoxygenated, blood behaves as an effective susceptibility contrast agent. Changes in brain oxygenation can be monitored using gradient-echo echo-planar imaging. With this technique, difference images also demonstrate that blood oxygenation is increased during periods of recovery from respiratory challenge.




## First Human BOLD fMRI Studies

Ogawa S, Tank DW, Menon R, Ellermann JM, Kim SG, Merkle H, Ugurbil K. "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging", Proc Natl Acad Sci U S A. 1992 Jul 1;89(13):5951-5.

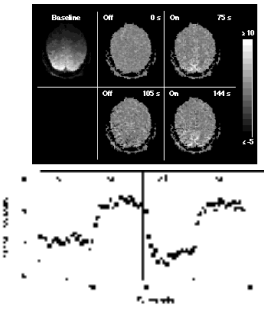
Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, Kennedy DN, Hoppel BE, Cohen MS, Turner R, et al. "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation", Proc Natl Acad Sci U S A. **1992** Jun 15;89(12):5675-9.

Bandettini PA, Wong EC, Hinks RS, Tikofsky RS, Hyde JS, "Time course EPI of human brain function during task activation", Magn Reson Med. **1992** Jun;25(2):390-7

## First Human fMRI Studies


JW Belliveau, DN Kennedy Jr, RC McKinstry, BR Buchbinder, RM Weisskoff, MS Cohen, JM Vevea, TJ Brady, and BR Rosen, "**Functional mapping of the human visual cortex by magnetic resonance imaging", *Science***, Vol 254, Issue 5032, 716-719, **1991**

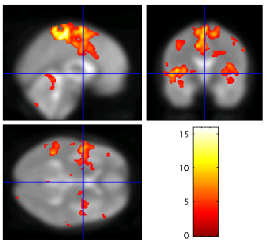
## First Human fMRI Studies




*Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, Kennedy DN, Hoppel BE, Cohen MS, Turner R, et al. "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation", Proc Natl Acad Sci U S A. 1992 Jun 15;89(12):5675-9.*

## fMRI: Examples

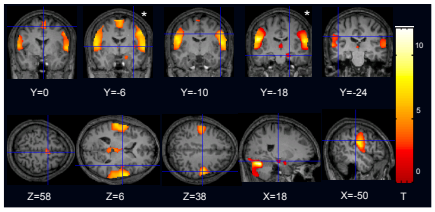
***Mapping areas involved in motor tasks***



3 Tesla

## fMRI: Examples

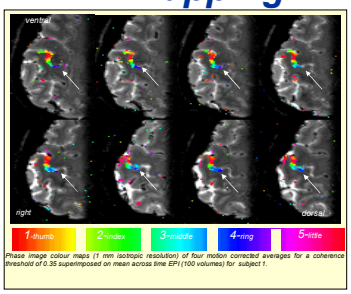
***Mapping taste areas***




3 Tesla

## fMRI: Examples

### *High resolution Somatotopic mapping*



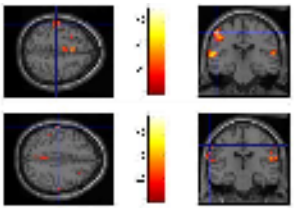

7 Tesla

## fMRI: Examples

### *Somatosensory areas - schizophrenia*

Healthy subjects

Schizophrenic patient

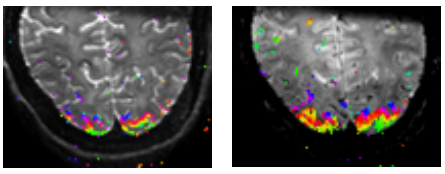


3 Tesla

## fMRI: Examples

### *Retinotopic mapping*

*spin echo* *gradient echo*




7 Tesla

*c > 0.4*

## Mechanism of BOLD Functional MRI

?

Brain activity ↑

Oxygen consumption ↑ | Cerebral blood flow ↑↑

Oxyhemoglobin ↑
Deoxyhemoglobin ↓

Magnetic susceptibility ↓

T2* ↑

MRI signal intesity ↑

## Methods based on Magnetic Resonance Imaging

| | | |
|---|---|---|
| 30 Sep | Basic MR physics and BOLD physics I | Dr Sue Francis/ Prof Penny Gowland SPMMRC |
| 07 Oct | Basic MR physics and BOLD physics II | Dr Sue Francis/ Prof Penny Gowland SPMMRC |
| 14 Oct | Basic MR physics and BOLD physics III | Dr Sue Francis/ Prof Penny Gowland SPMMRC |
| 21 Oct | BOLD physiology | Prof Dorothee Auer, Academic Radiology |
| 28 Oct | Functional MRI I | Dr Denis Schluppeck, School of Psychology |
| 04 Nov | Functional MRI II | Dr Denis Schluppeck, School of Psychology |
| 11 Nov | Functional MRI III | Dr Denis Schluppeck, School of Psychology |
| 18 Nov | Functional MRI IV | Dr Denis Schluppeck, School of Psychology |
| 25 Nov | Basic MR morphometry | Dr Mirjam Schubert, Academic Radiology |
| 02 Dec | Advanced MR morphometry | Dr Alain Pitiot, Brain and Body Centre Prof Tomas Paus, Brain and Body Centre |
| 09 Dec | Diffusion tensor imaging | Prof Dorothee Auer, Academic Radiology |