

**MRI Tutorial for Neuroscience Boot Camp**  
*Melissa Saenz*  
**Figures and legends taken from**  
**“Introduction to Functional Magnetic Resonance Imaging” by Rick Buxton.**

## SECTION 1: MRI Basics

Magnetic resonance imaging (MRI) uses nuclear magnetic resonance (NMR) signals to create images of the brain. Hydrogen nuclei are the basis for the signal. Let's see why:

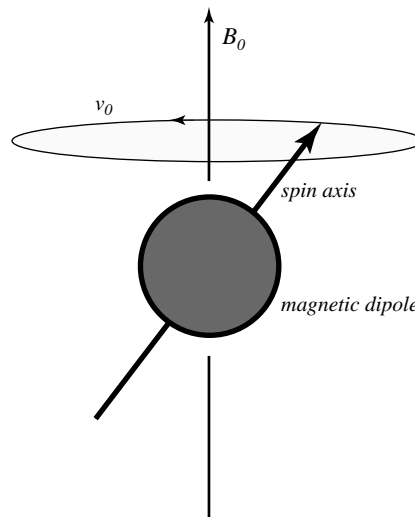
Hydrogen nuclei possess an intrinsic quantum property called *spin* that causes them to behave like small magnetic dipoles.

\*Elementary particles (electrons, protons and neutrons) have spin. In an atom, these particles combine in pairs of opposite spin. Only atomic nuclei with an odd number of protons plus neutrons (such as the hydrogen nucleus with a single proton) have a net spin. Hydrogen nuclei are the most abundant nuclei with spin in body tissue due to water.

In MRI, the brain is placed in strong magnetic field  $B$ . Hydrogen nuclei (like small magnets) align with the magnetic field producing their own net *longitudinal* magnetization (in the same direction as  $B$ ). This alignment, a relaxation towards the equilibrium state, occurs with a time constant  $T1$ . Full alignment is never reached and the nuclei precess around the axis of the field at a frequency ( $\nu$ ) proportional to the strength of the magnetic field. The precession frequency ( $\nu$ ), also called the Larmor frequency, is given by:

$$\nu = \gamma * B$$

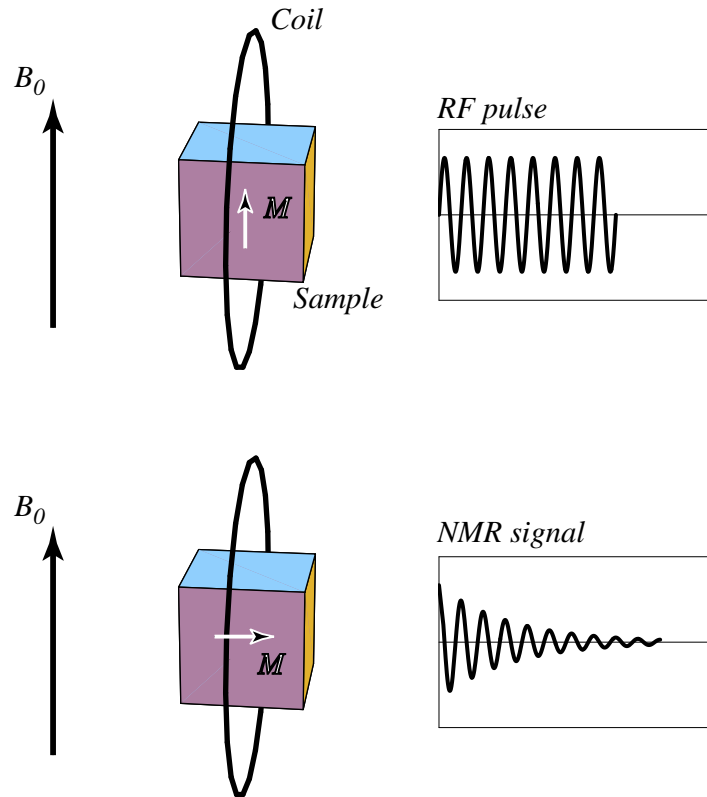
where  $\gamma$  is a constant (the gyromagnetic ratio equal to 42.6 Mz/T for the hydrogen nucleus).  $\nu = 128$  MHz in a 3 Tesla field.



**Figure 1: Precession of a magnetic dipole in a magnetic field.** The magnetic field  $B_0$  exerts a torque on a nuclear magnetic dipole that would tend to make it align with  $B_0$ . However, because the nucleus also has angular momentum (*spin*), it instead precesses like a spinning top at an angle to the gravitational field. The precession frequency  $\nu_0$  is proportional to the magnetic field and is the resonant frequency of NMR.

Note: This page presents a classical physics description of a phenomenon that can only be accurately described by quantum physics. While we cannot really know how individual protons are behaving, this is an approximation of the net action of a lot of protons (useful for visualization!).

Next in MRI, a radio frequency pulse is transmitted to the sample at the resonant frequency. The precessing nuclei absorb that energy and re-emit a portion of it back at the same frequency. This is the detected signal. Here's what happens in more detail:



**Figure 2: The basic NMR experiment.** A sample is placed in a large magnetic field  $B_0$ , and hydrogen nuclei partially align with the field creating a net magnetization  $M$ . In the transmit part of the experiment an oscillating current in a nearby coil creates an oscillating radio frequency (RF) magnetic field in the sample which causes  $M$  to tip over and precess around  $B_0$ . In the receive part of the experiment, the precessing *transverse* magnetization creates a transient oscillating current (the NMR signal) in the coil.

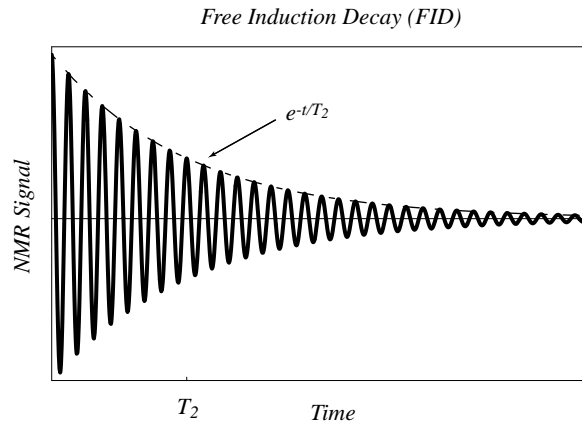
**In summary:**

- (1) Nuclei are placed in a magnetic field  $B$  and acquire a longitudinal magnetization that is orders of magnitude smaller than  $B$  and is not directly measurable.
- (2) A transmitted RF pulse (generated by an oscillating current in a coil) tips over the acquired longitudinal magnetization by 90 degrees into the transverse plane. The magnetization now precesses around  $B$  in the transverse plane.
- (3) Due to this precessing *transverse* magnetization, a detector located in the transverse plane will feel a small oscillating magnetic field. The changing magnetic field induces a current in the detector coil (electromagnetic induction) that can be measured.

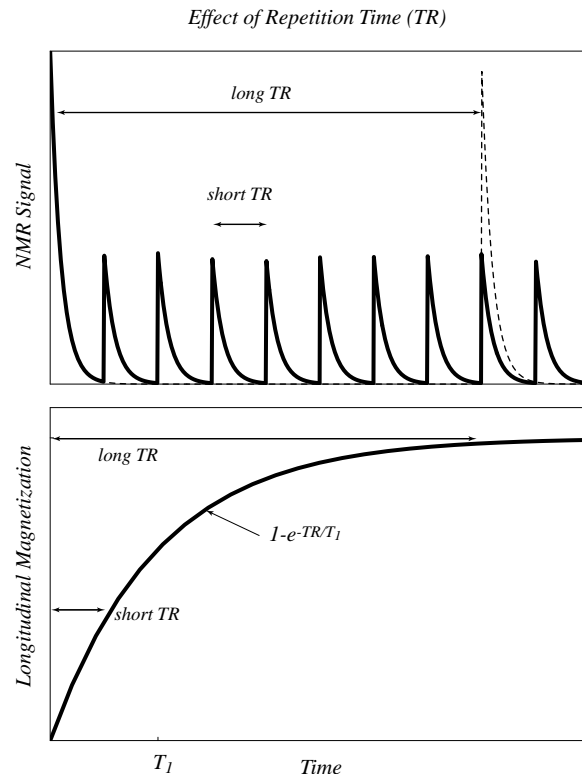
The resulting MR image will be an image of the transverse magnetization of hydrogen nuclei at the time when the signal is detected. The transverse magnetization is a transient phenomenon and we will see next how the strength of the signal depends critically on timing parameters during imaging.

### Free Induction Decay (FID):

After the magnetization is tipped by the RF pulse, the transverse component (and thus the signal) decays with a time constant  $T_2$  and the longitudinal component regrows (towards equilibrium) with a time constant  $T_1$ . The signal decay, called free induction decay, is shown here.



**Figure 3: The free induction decay (FID).** After a  $90^\circ$  RF pulse tips the longitudinal magnetization into the transverse plane, a detector coil measures an oscillating signal which decays in amplitude with a time constant  $T_2$  in a perfectly homogeneous magnetic field. (In an inhomogeneous field the signal decays more quickly, with a time constant  $T_2^* < T_2$ .) The plot is not to scale; typically the signal will oscillate more than a million times during the interval  $T_2$ .



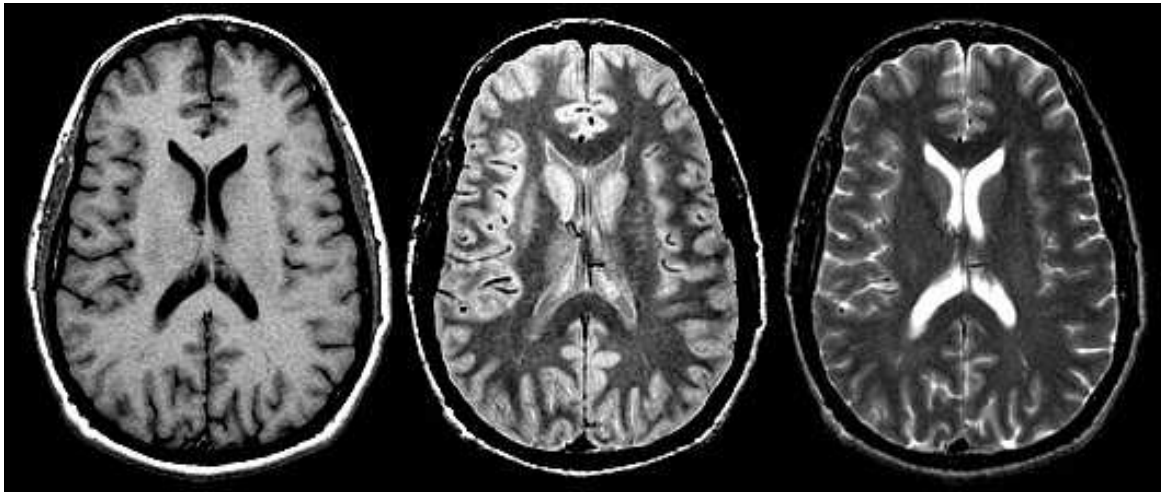
**Figure 4: Effect of repetition time (TR).** Repeated RF pulses generate repeated FID signals, but if the repetition time (TR) is short, each repeated signal will be weaker than the first (top). The magnitude of the signal with a  $90^\circ$  RF pulse is proportional to the magnitude of the longitudinal magnetization just prior to the RF pulse. After a  $90^\circ$  RF pulse the longitudinal magnetization recovers toward equilibrium with a relaxation time  $T_1$  (bottom). If this recovery is incomplete because  $TR < T_1$ , the next FID signal is reduced.

### Signal Contrast:

As shown in figure 4, in an MR imaging sequence successive RF pulses are transmitted and successive FID signals are measured. The strength of the signal measured depends critically on the imaging parameters **TE** (time between RF pulse and measurement) and **TR** (time between successive RF pulses).

The time constants  $T_2$  and  $T_1$  are on the order of one second but the actual rates depend on intrinsic properties of the tissue surrounding the nuclei. As a result, the strength of the signal will vary for different body tissues with different intrinsic  $T_2$  and  $T_1$  values (i.e. gray matter compared to white matter) creating the primary contrast in an MR image of the brain. The contrast can be manipulated by varying TR and TE:

### *Spin Echo Images*



*T<sub>1</sub>-weighted*  
(TR=600, TE=11)

*Density-weighted*  
(TR=3000, TE=17)

*T<sub>2</sub>-weighted*  
(TR=3800, TE=102)

**Figure 5: MR images of the same anatomical section showing a range of tissue contrasts. In the first image cerebrospinal fluid (CSF) is black, while in the last image CSF is bright. Contrast is manipulated by adjusting several parameters during image acquisition, such as the repetition time TR and the echo time TE (times given in milliseconds), which control the sensitivity of the signal to the local tissue relaxation times  $T_1$  and  $T_2$ , and the local proton density.**

- If TR is short, the longitudinal magnetization will not have a chance to fully regrow between pulses. The size of the next FID signal will be reduced (because there is less magnetization to tip) by an amount that depends on the  $T_1$  of each tissue (see Figure 4). If TE is also short, little  $T_2$  decay will have occurred before measurement. Thus, the contrast in the MR image will depend primarily on the intrinsic  $T_1$  values of the tissues. Such an image is said to be  $T_1$ -weighted.
- If TR is long, the longitudinal magnetization will fully regrow between pulses and  $T_1$  will provide no image contrast. If TE is long enough for some (but not all)  $T_2$  decay to occur then the signal strength will depend on the intrinsic  $T_2$  values of the tissues. The resulting image is said to be  $T_2$ -weighted.
- If TR is long, so that the magnetization fully regrows between pulses, and TR is short, so that little  $T_2$  decay occurs before measurement, then the signal will depend little on the  $T_1$  and  $T_2$  values of the tissue. Rather it will depend absolute strength of the acquired magnetization in each tissue (which depends primarily on proton density). The resulting image is said to be density weighted.

**\*Note that we have not yet discussed how the signal is localized to make an image. See Section 3.**

## SECTION 2: fMRI basics (BOLD Imaging)

The basic idea behind *functional* MRI is simple: we measure a series of MR images (like a movie) and look for small changes in MR signal intensity over time caused by changes in brain activity.

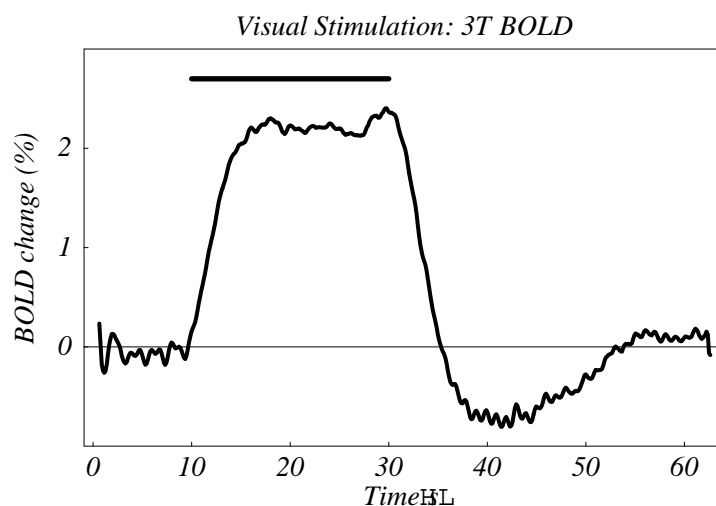
This change in the MR signal depends on two factors:

- First, brain activity is accompanied by a local increase in blood flow that supplies oxygen at a rate faster than its consumption. As a result of the oversupply, brain activity leads to an increase in the local concentration of oxygenated hemoglobin compared to deoxygenated hemoglobin in venous blood.
- Second, deoxygenated hemoglobin is paramagnetic and attenuates the MR signal more quickly than oxygenated hemoglobin. (because it generates local field inhomogeneities) As a result, the increase in the ratio of oxygenated to deoxygenated hemoglobin leads to a local increase in the MR signal (the image becomes brighter).

This change in signal intensity is called the blood oxygenation level dependent (BOLD) effect. BOLD imaging is non-invasive because it depends on an internal contrast agent (blood oxygenation).

This is a young technology! In 1990, Ogawa et al. first demonstrated that blood oxygenation had a measurable effect on MR signals in the rat. Then in 1992, Kwong et al. showed that brain activation led to local increases in the BOLD signal in human subjects. With the right pulse sequences and adjustments, *functional* imaging could now be performed using the standard MRI scanners possessed by many medical centers.

### *The BOLD Signal*



**Figure 6.** Example BOLD response in the visual cortex measured at 3T. Subjects wore goggles that flashed a grid of red lights at 8 Hz. The stimulus (indicated by a horizontal bar) lasted for 20 sec, followed by 40 sec of darkness. The data shows the average response of 32 cycles of stimulus/rest for 3 subjects. Characteristic features of the BOLD response are a delay of a few seconds after the start of the stimulus, a ramp of about 6 sec up to a plateau, and a post-stimulus undershoot before the signal returns to baseline.

**\* Note that hemodynamics are slow and limit the temporal resolution of fMRI.**

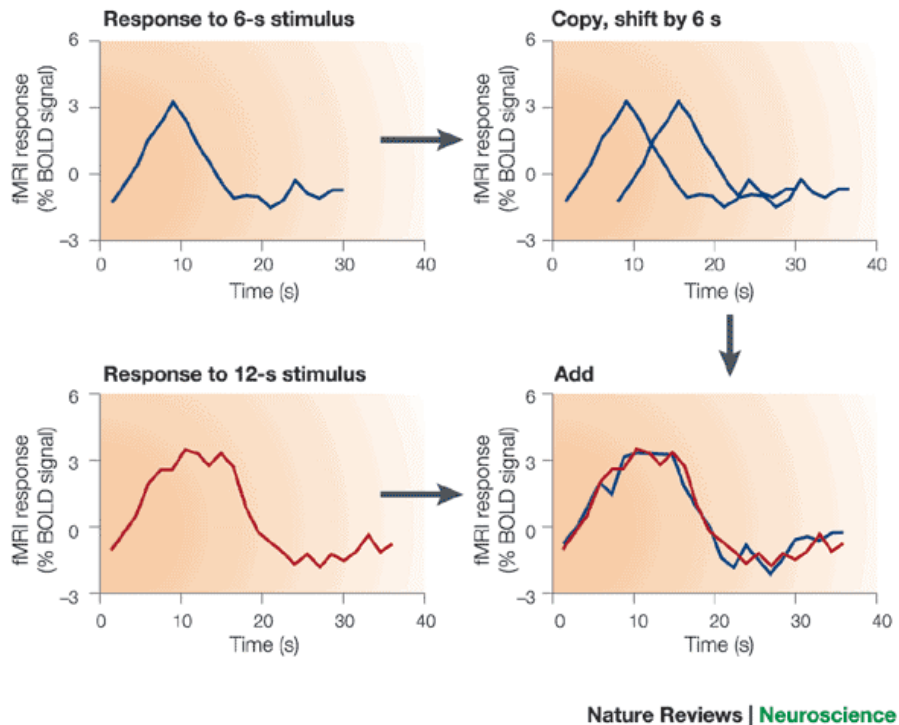
#### **Refs:**

Ogawa et al. (1990) *Man. Reson. Med.* 14, 68-78.

Kwong et al. (1992) *Proc. Natl. Acad. Sci. USA.* 89, 5675-9.

## Many Questions Remain!

How does the BOLD response quantitatively relate to neural activity? Ultimately, the goal is to understand the complex relationships between neuronal activity, metabolism, and blood flow. For now, the accumulating evidence suggests that the BOLD response is roughly a linear function of neuronal activity (at least to a first approximation). For example, in a test of linearity, Boynton et al. showed that the BOLD response (in visual cortex to visual stimulation) sums roughly linearly with stimulus duration.



**Figure 7. Temporal summation of fMRI responses.** Left: measured functional magnetic resonance imaging (fMRI) responses from the visual cortex for 6- and 12-s stimulus presentations. Right: the procedure for measuring temporal summation, by comparing the responses to the two different stimulus durations. BOLD, blood oxygen level dependent (this figure from Heeger review, ref below).

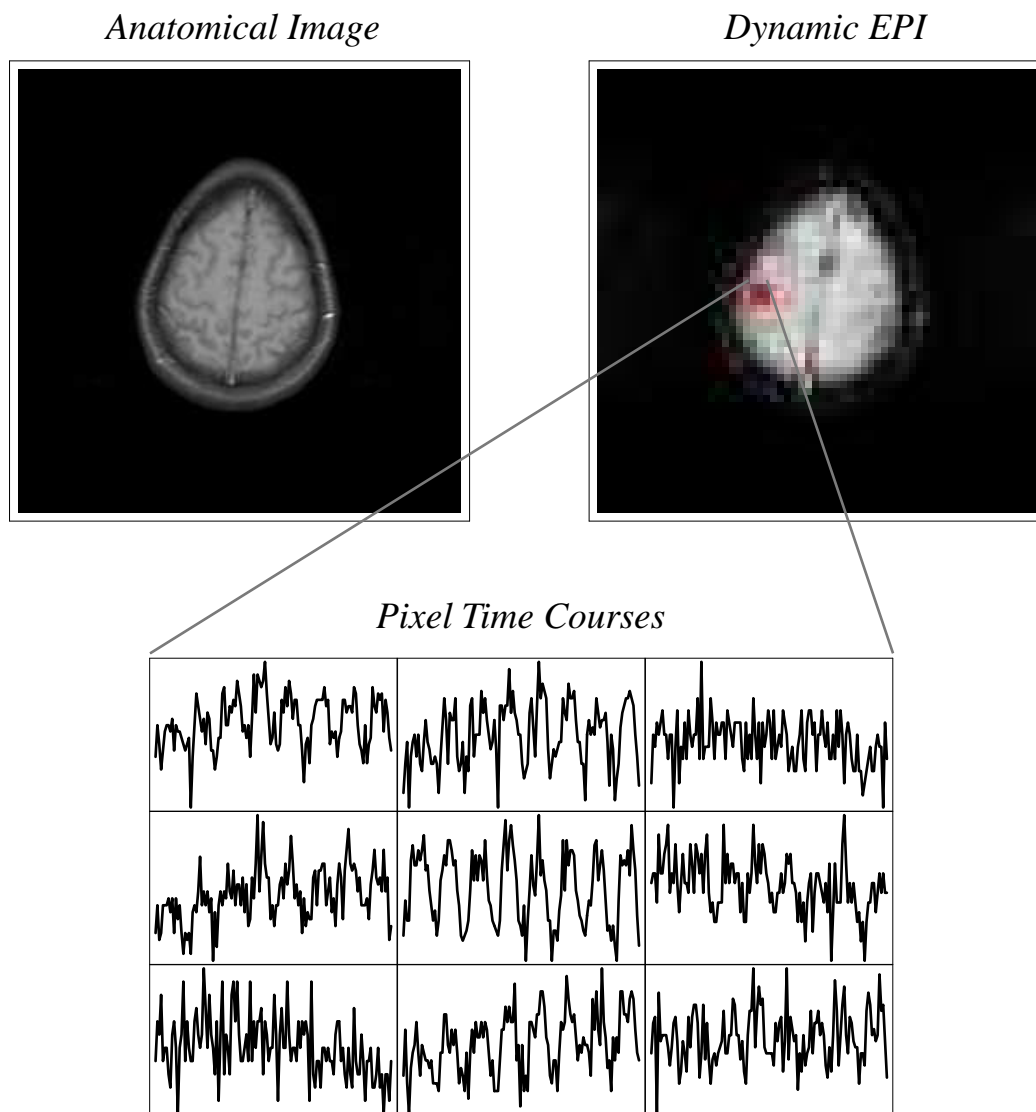
However, other factors besides the spike rate of neurons may contribute to the BOLD response including subthreshold activity, neuronal inhibition, and changes in firing patterns that may not affect the spike rate (see Heeger for review). A promising approach towards understanding the BOLD response is to compare electrophysiological and fMRI data recorded from the same animal. Logothetis at the Max Plank Institute in Germany is leading the way by developing methods for simultaneous recordings and high resolution imaging in the monkey.

### Refs:

- Boynton, G. M., S. A. Engel, et al. (1996). "Linear systems analysis of functional magnetic resonance imaging in human V1." *J Neurosci* **16**(13): 4207-21.
- Heeger, D. J. and D. Ress (2002). "What does fMRI tell us about neuronal activity?" *Nat Rev Neurosci* **3**(2): 142-51.
- Logothetis, N. K., J. Pauls, et al. (2001). "Neurophysiological investigation of the basis of the fMRI signal." *Nature* **412**(6843): 150-7.

**Preview** of the type of data you will see this week in the visual and auditory areas of cortex:

## *Blood Oxygenation Level Dependent (BOLD) Data*



**Figure 8: Blood Oxygenation Level Dependent (BOLD) signal changes.** On the left is a high resolution anatomical image (256x256 matrix) cutting through the central sulci and the hand motor and sensory areas. On the right is one image from a series of 128 low resolution dynamic images (64x64 matrix) collected every 2 sec with echo planar imaging (EPI). The signal time courses from a 3x3 block of pixels is shown at the bottom. During the data acquisition the subject performed 8 cycles of a bilateral finger tapping task, with one cycle consisting of 16 sec of tapping followed by 16 sec of rest. Several pixels show clear patterns of signal variation that correlate with the task. (Data courtesy of L. Frank)