Is it possible to detect neuronal activity directly with MRI?

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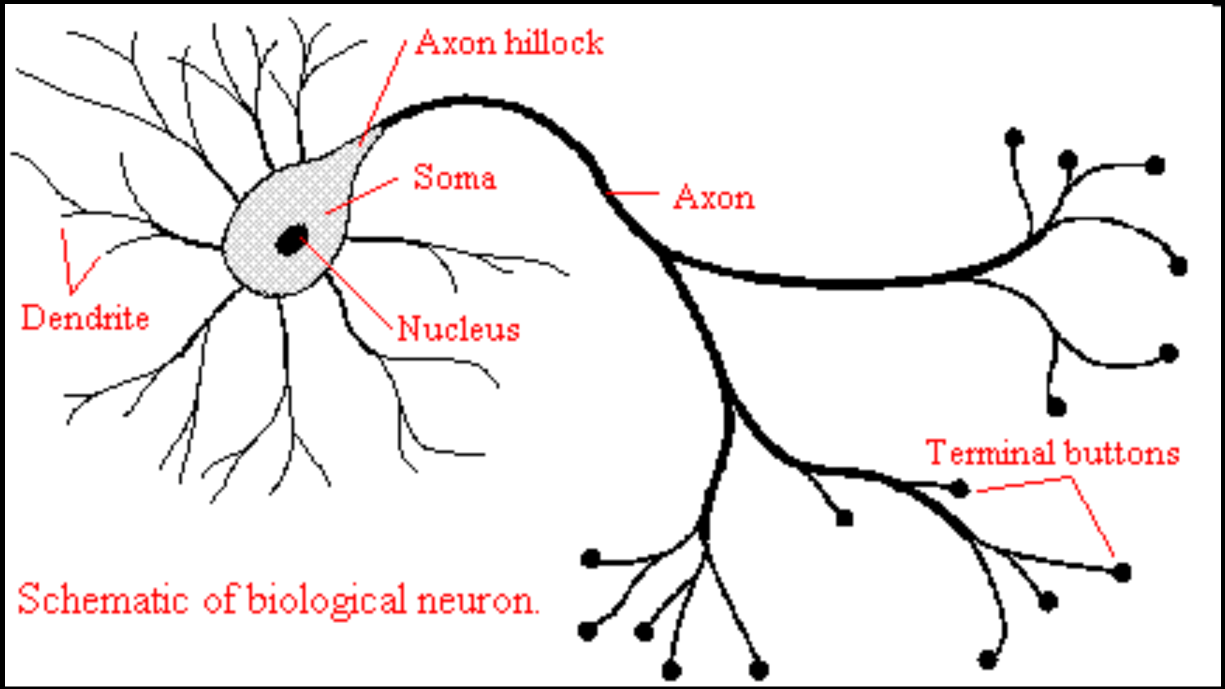
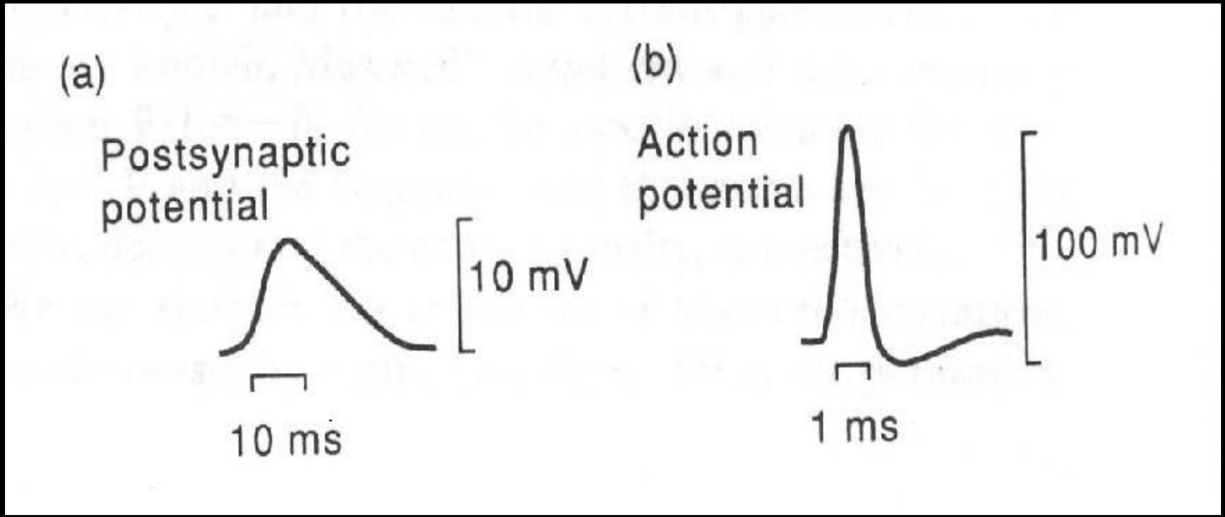
Laboratory of Functional and Molecular Imaging, NINDS, NIH

Dietmar Plenz

Unit of Neural Network Physiology, NIMH, NIH

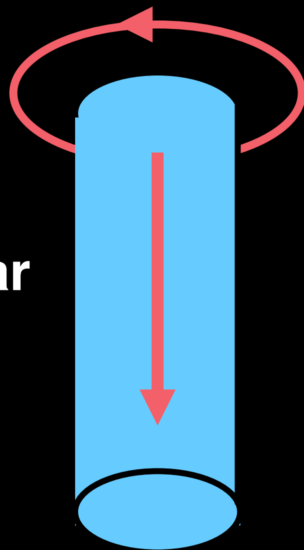
Neuronal Dynamics...



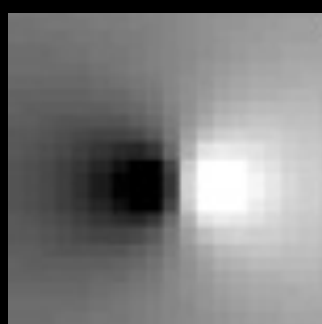


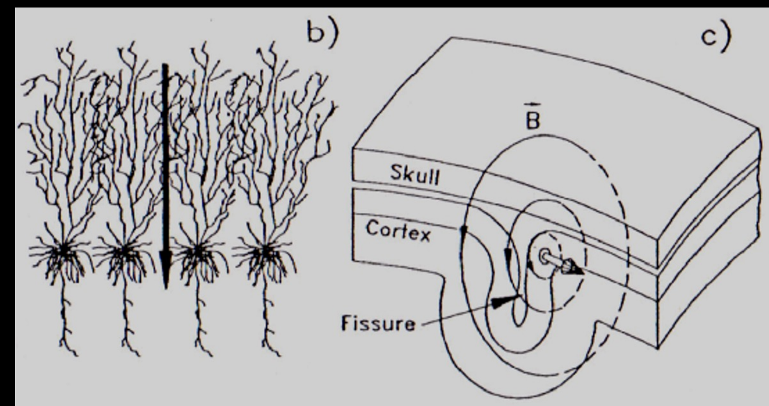
Magnetic Field

Intracellular Current



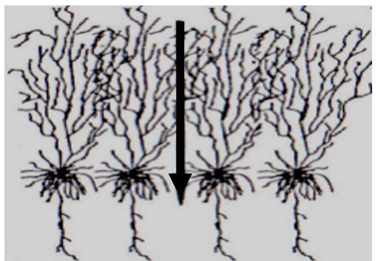
Surface Fields



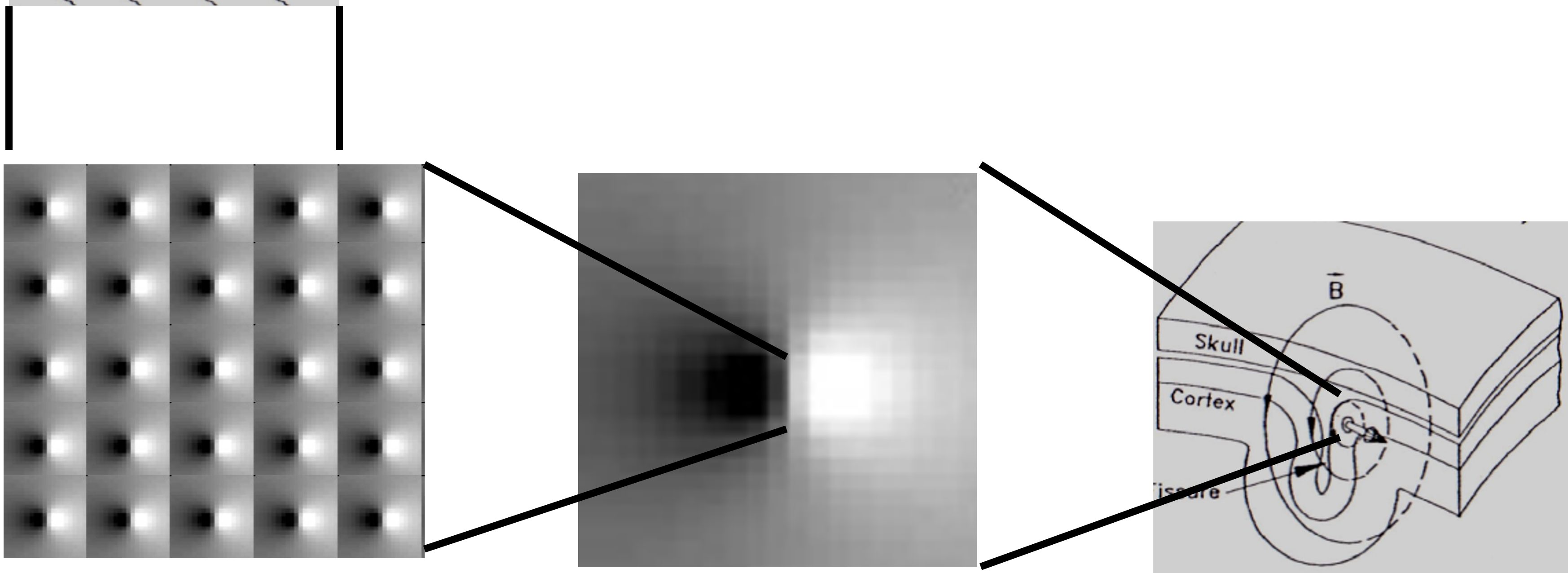


100 fT at on surface of skull

J.P. Wikswo Jr et al. *J Clin Neuronphy* 8(2): 170-188, 1991



Surface Field Distribution Across Spatial Scales



Adapted from: J.P. Wikswo Jr et al. ***J Clin Neurophy*** **8(2): 170-188, 1991**

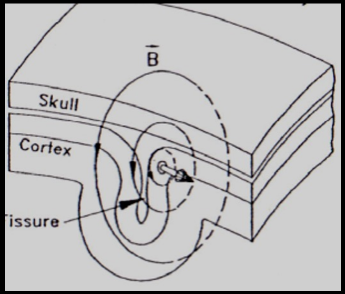
Magnetic field associated with single dendrite:

Single dendrite diameter = d, length = L, conductivity = σ. R=V/I, where $R=4L/(\pi d^2 \sigma)$.

$$B = \frac{\mu_0}{4\pi}\,\frac{Q}{r^2} = \frac{\mu_0 \quad d^2\,\sigma V}{16 \qquad r^2}$$

d = 4μm, $\sigma \approx 0.25\ \Omega^{-1}\ m^{-1}$, V = 10mV and r = 4cm (distance to MEG detector))

the resulting value measured at the MEG detector is: **B≈0.002 fT…**

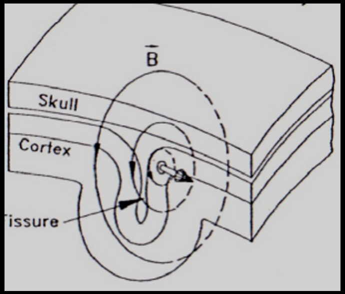


J. Bodurka, P. A. Bandettini. *Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes.* **Magn. Reson. Med. 47: 1052-1058, (2002).**

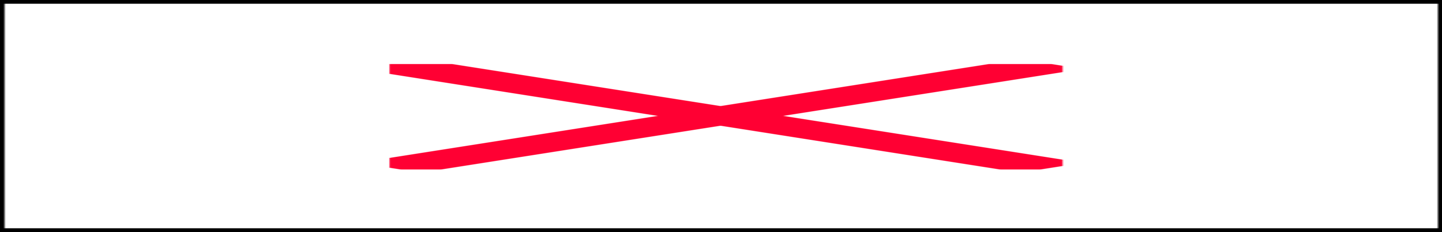
Magnetic field associated with

a bundle of dendrites

Because B_{MEG}=100fT is measured by MEG on the scalp



at least 50,000 neurons (0.002 fT x 50,000 = 100 fT), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel, 1 mm x 1 mm x 1 mm, a field of order:

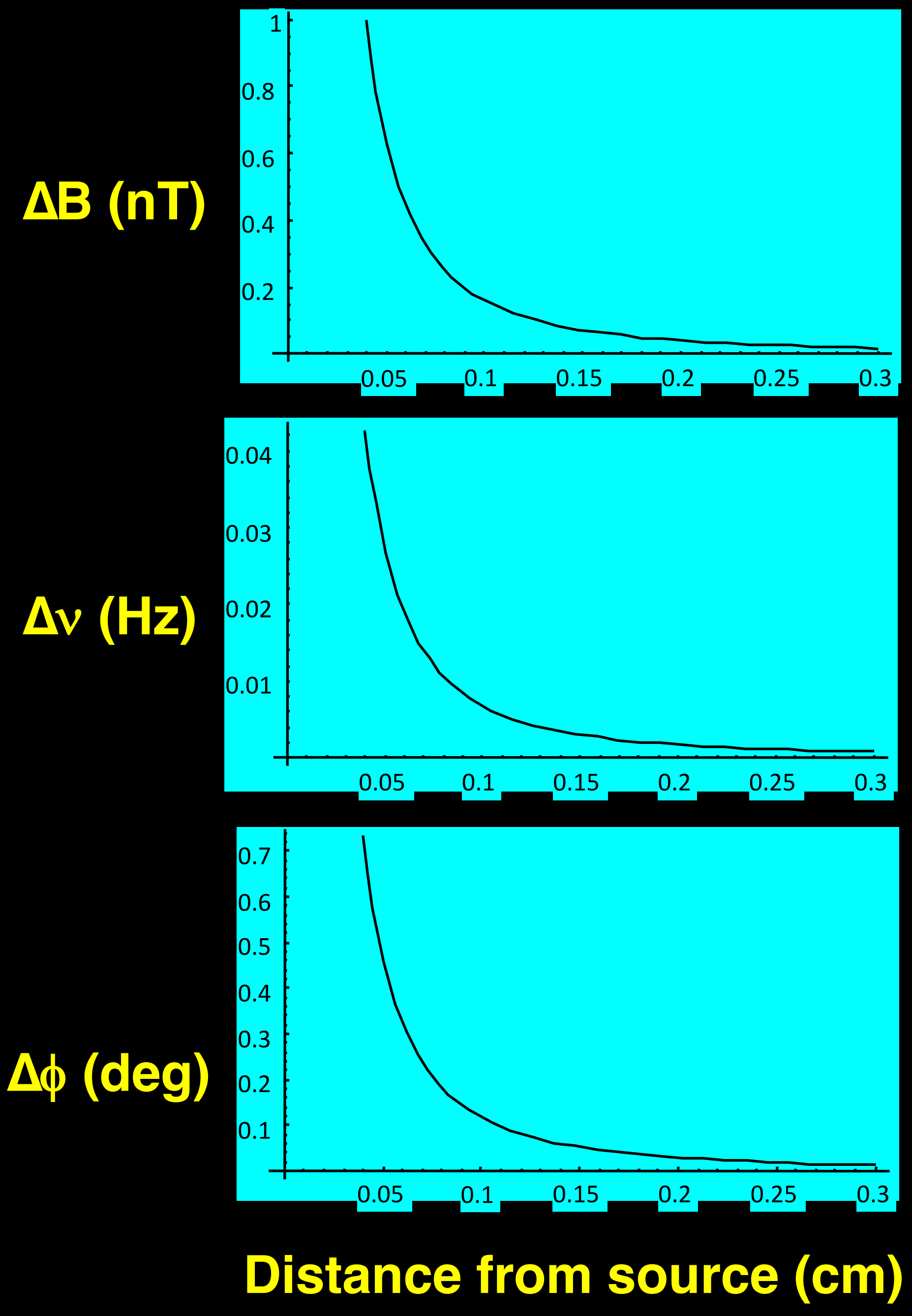


$B_{MRI} \approx$0.2nT

$$\Delta B = 100\text{fT} * (4\text{cm}/x)^2$$

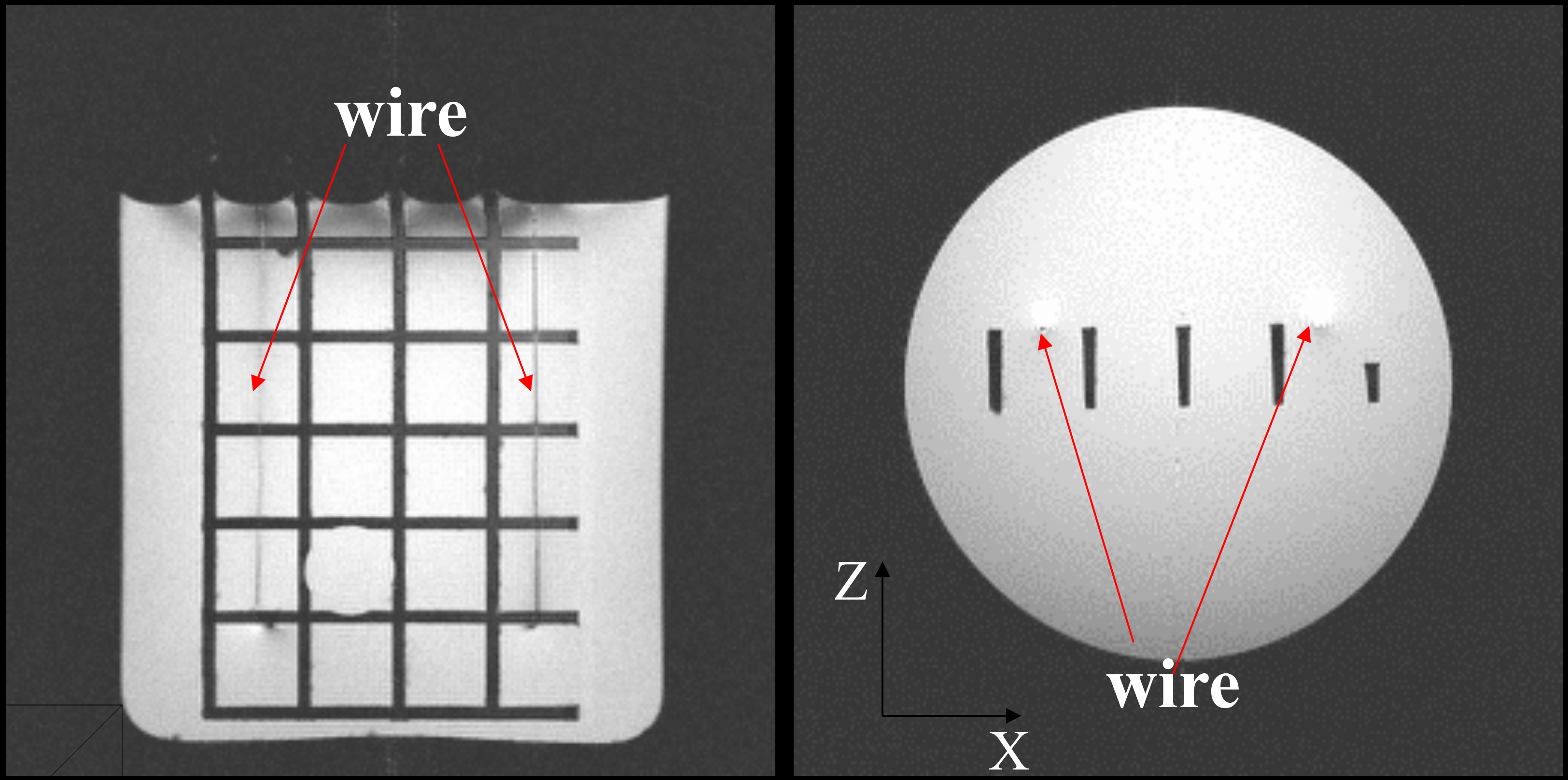
$$\Delta \nu = \gamma * \Delta B$$

$$\Delta\phi = \Delta \nu * TE * (\square\square\square/\pi)$$

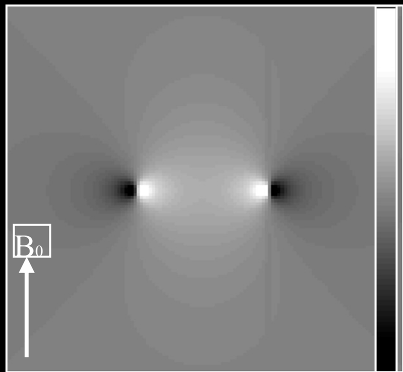


Is 0.2 nT detectable?

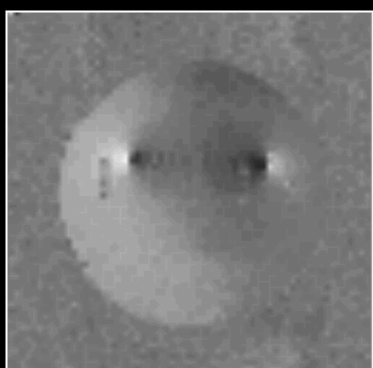
Current Phantom Experiment



calculated B_c || B_0



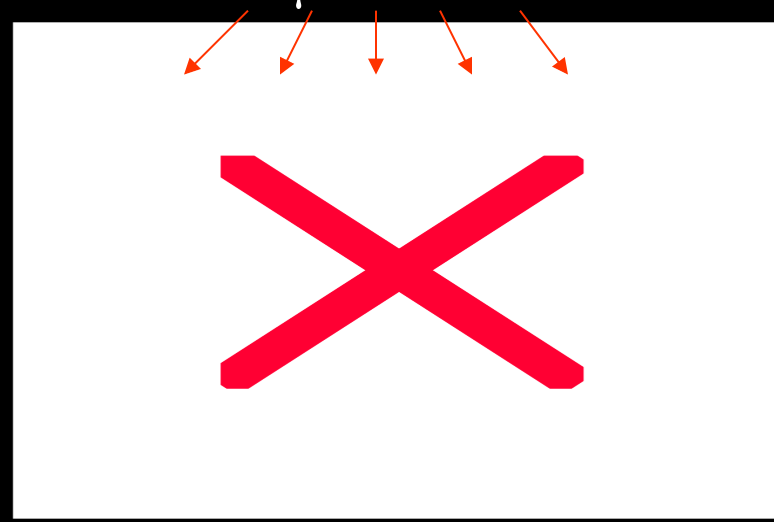
$\Delta\phi \cong 20^0$



Correlation image

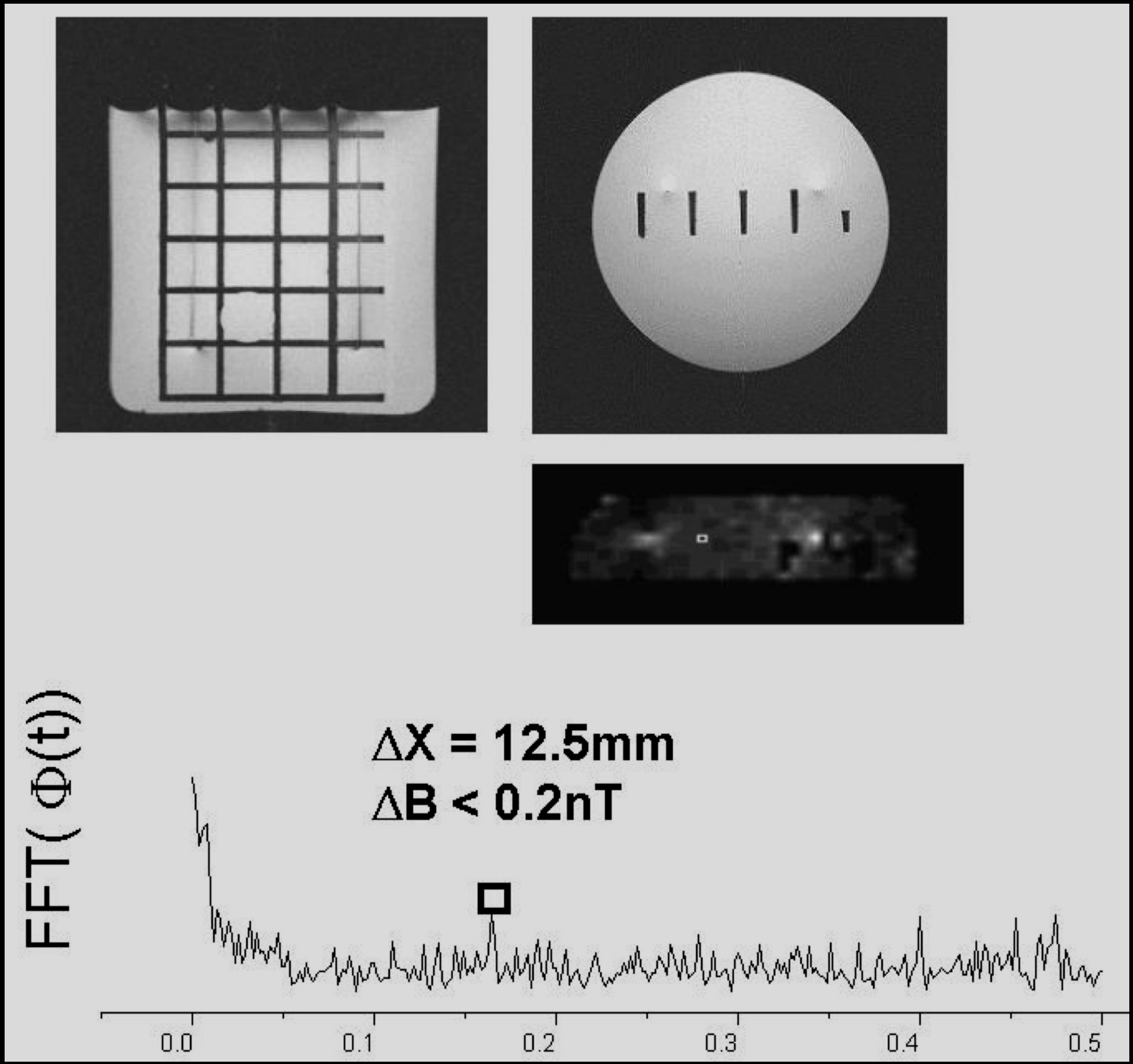
Measurement

70 μA current



Single shot GE EPI

J. Bodurka, P. A. Bandettini. Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes, Magn. Reson. Med. 47: 1052-1058, (2002).

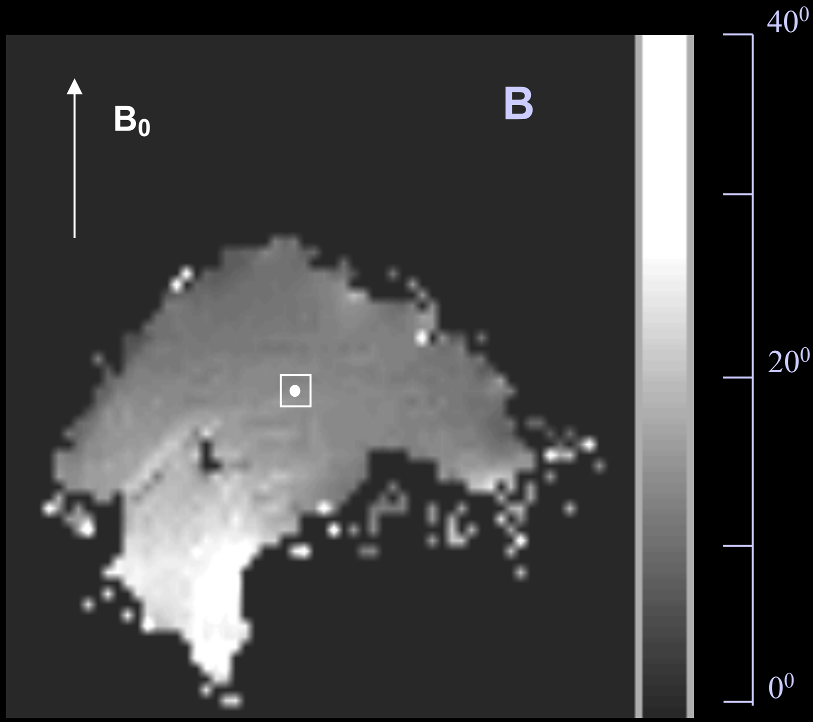


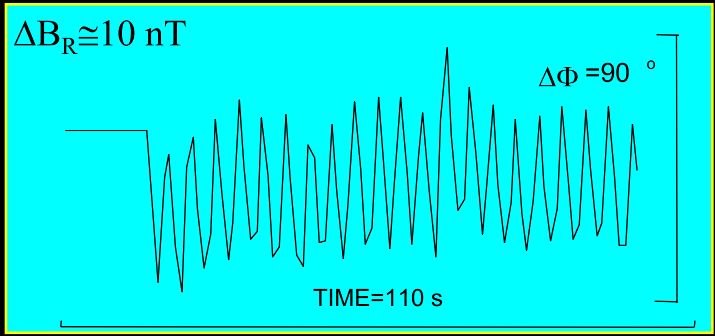
J. Bodurka, P. A. Bandettini. Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes, Magn. Reson. Med. 47: 1052-1058, (2002).

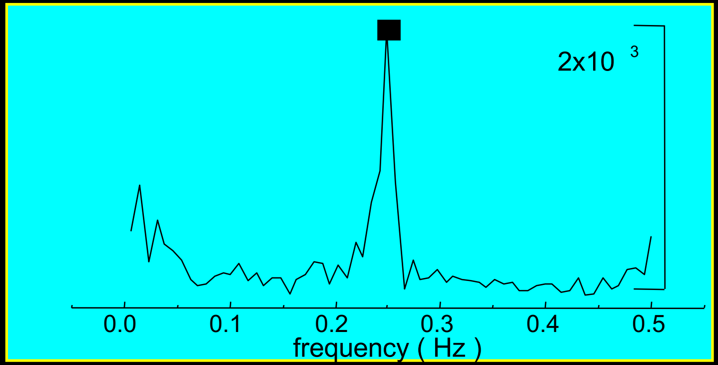
Main issues/obstacles:

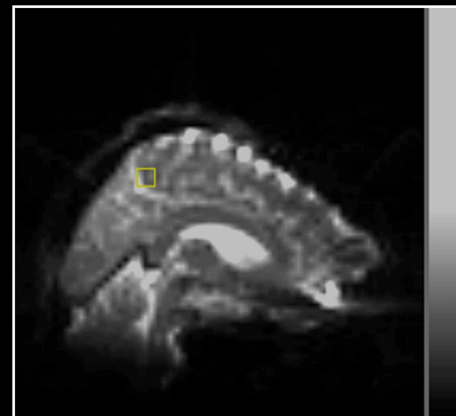
- The effect is small
- Artifactual changes (respiration, cardiac) are order of mag larger
- The effect itself depends on geometry (phase/magnitude)
- The timing of the effect is variable
- BOLD still ubiquitous…

Human Respiration



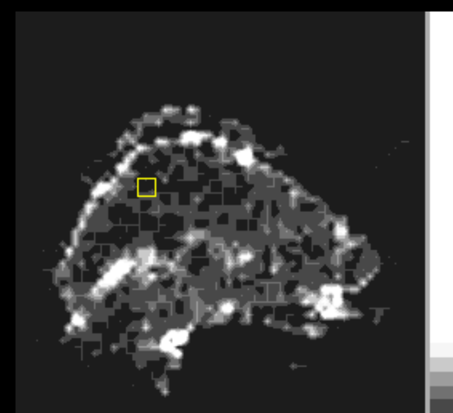




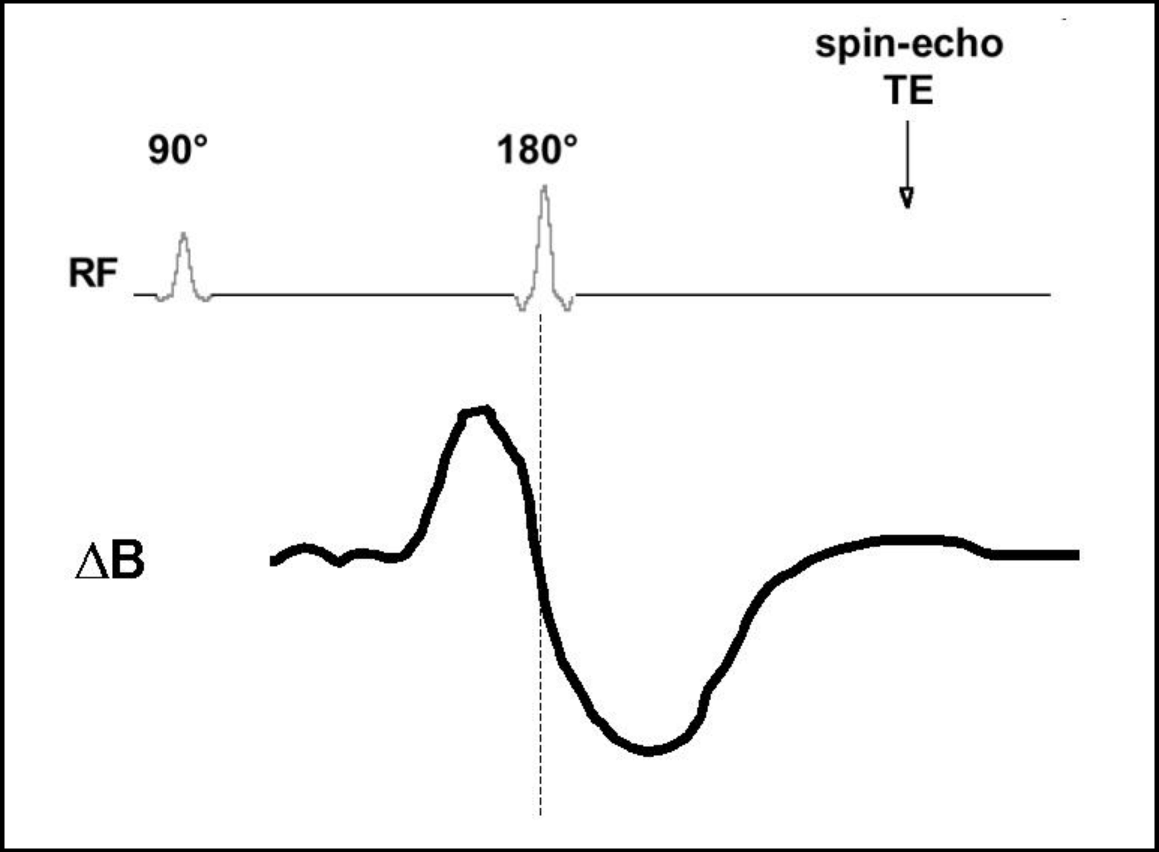


GE

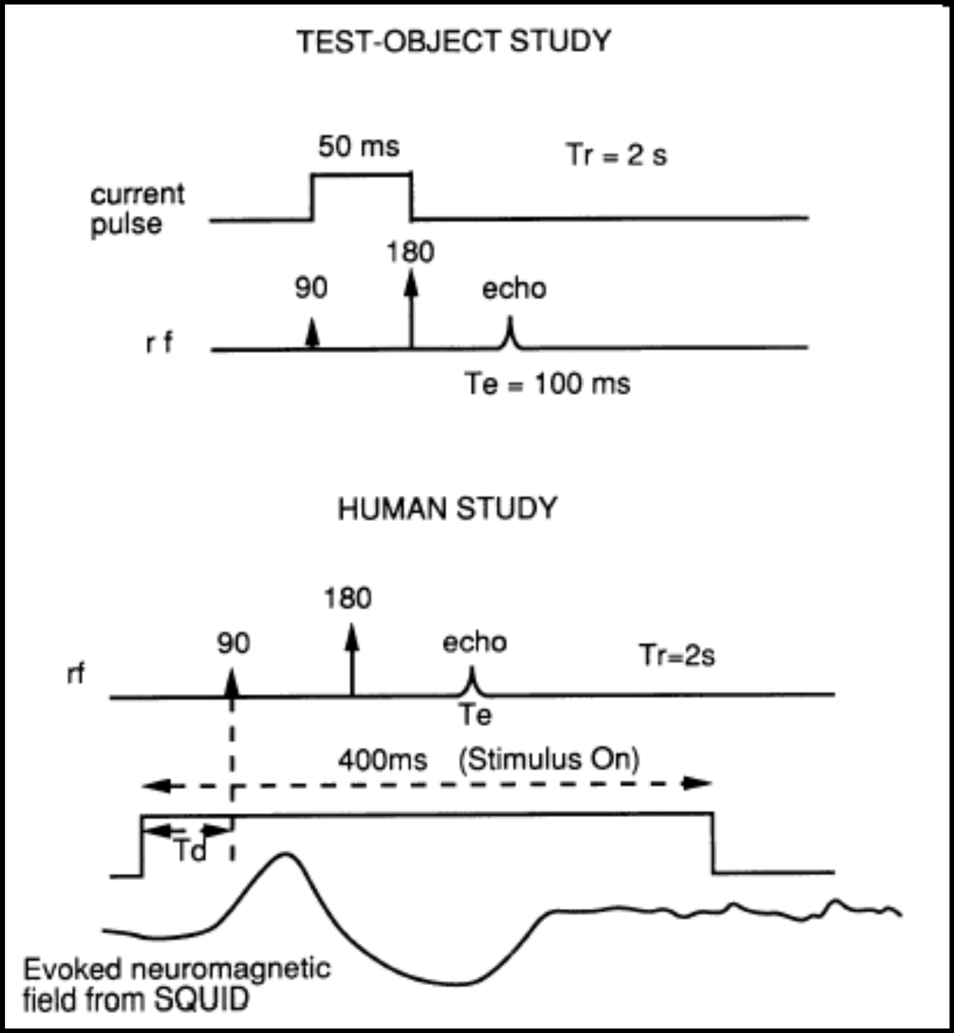
SE

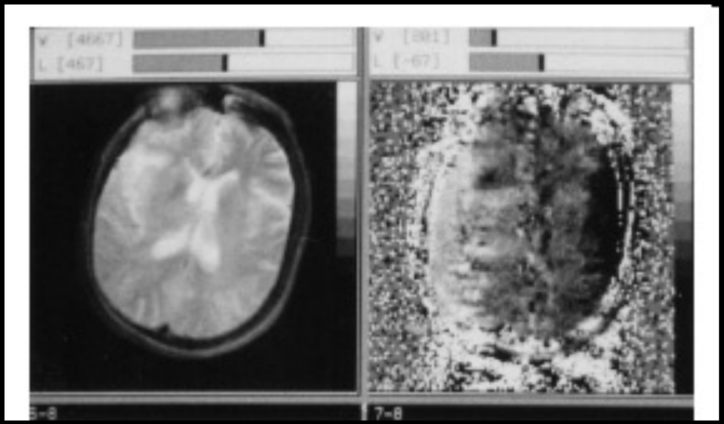


One strategy for removing low frequency changes…



The use of spin-echo to "tune" to transients..



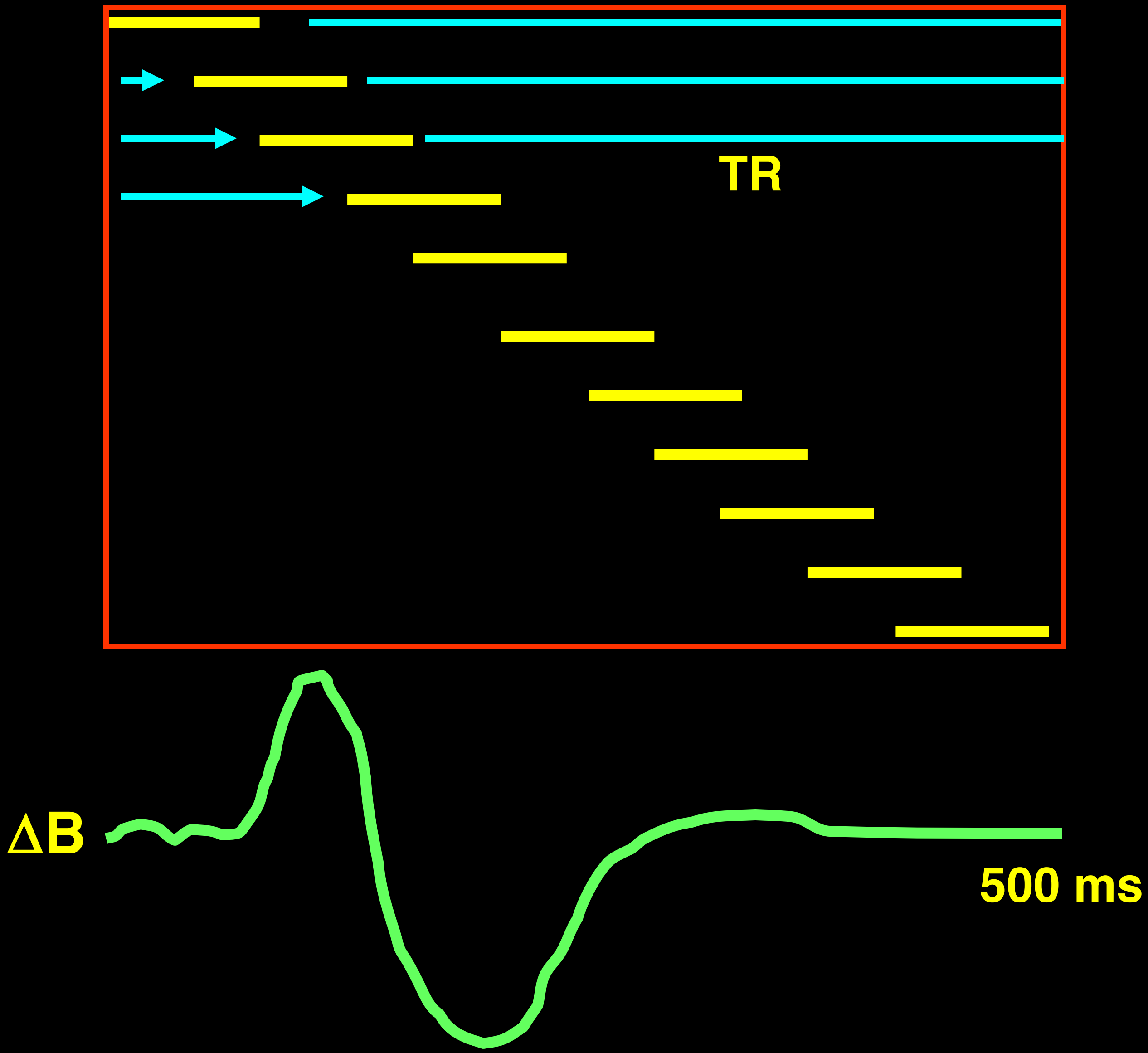


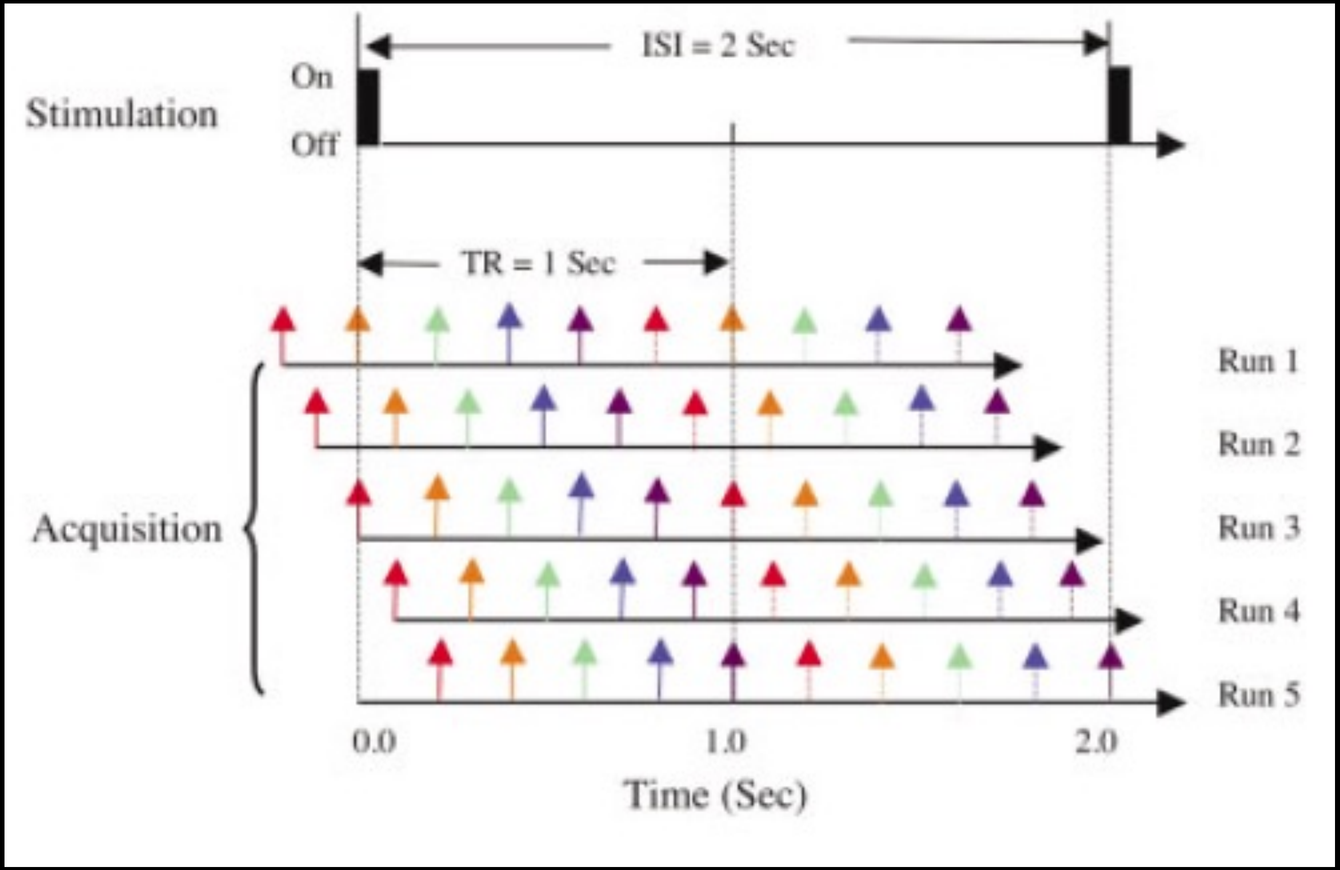
M. Singh, *Sensitivity of MR phase shift to detect evoked neuromagnetic fields inside the head.*

IEEE Transactions on Nuclear Science. 41: 349-351, (1994).

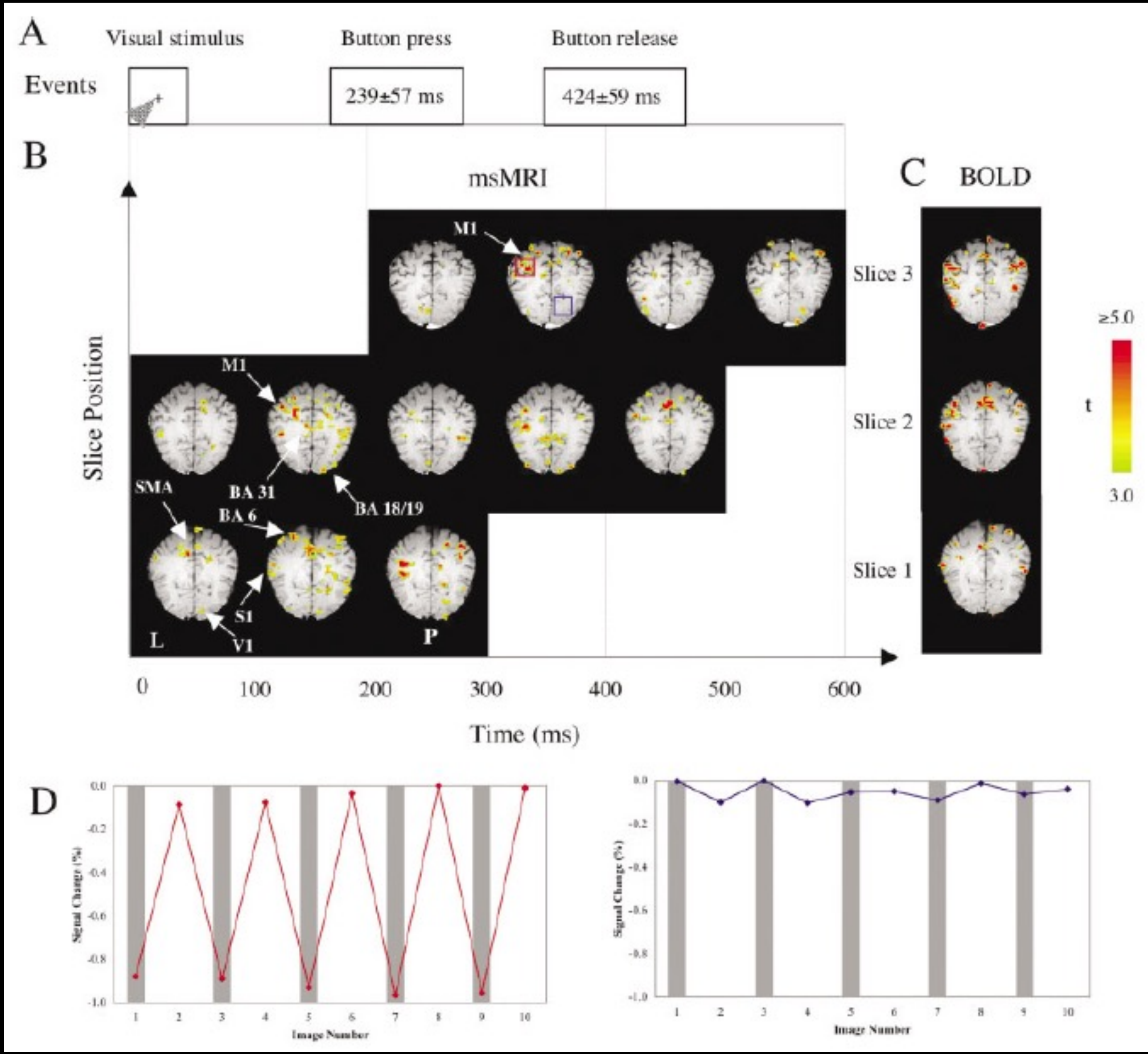
Strategies for Detection in Humans

- Time shifted sampling
- Under sampling

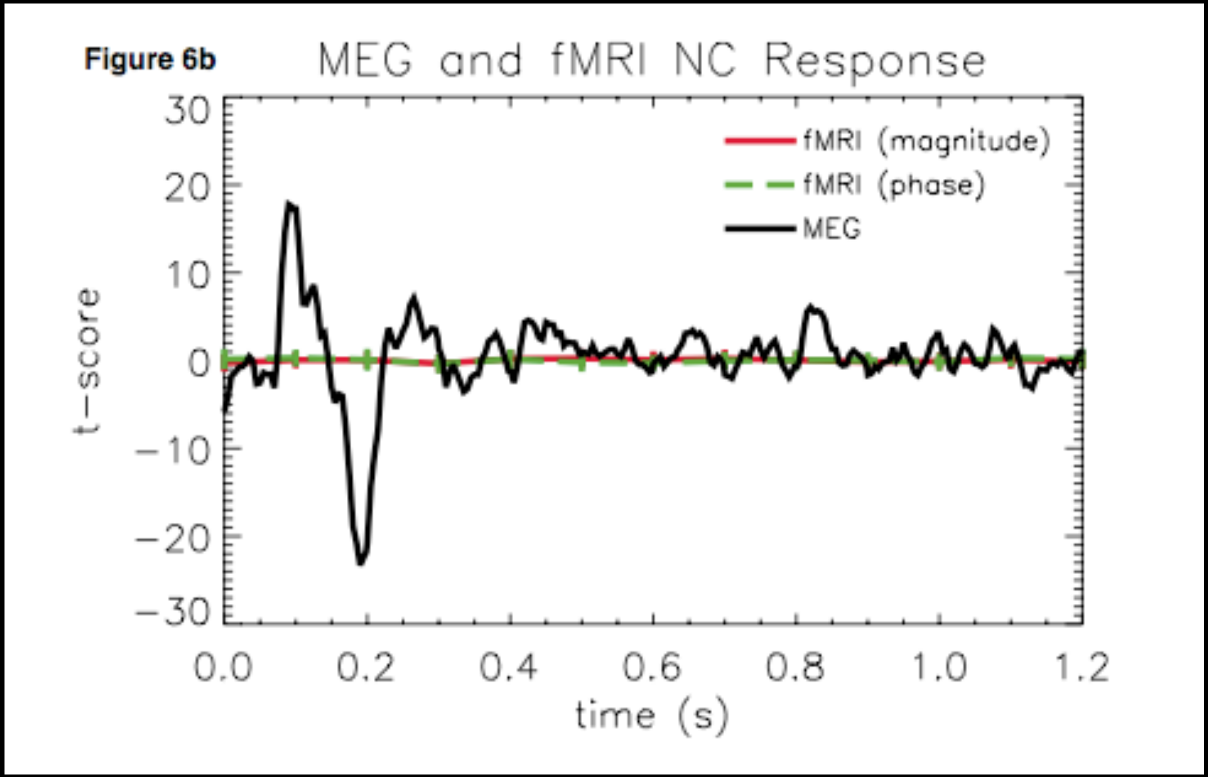

TR
ΔB
500 ms



J. Xiong, P. T. Fox, J.-H. Gao, *Direct MRI Mapping of neuronal activity.* **Human Brain Mapping, 20: 41-49, (2003)**



J. Xiong, P. T. Fox, J.-H. Gao, *Direct MRI Mapping of neuronal activity.* **Human Brain Mapping, 20: 41-49, (2003)**



R. Chu, J. A. de Zwart, P. van Gelderen, M. Fukunaga, P. Kellman, T. Hollroyd, J. Duyn. *Hunting for neuonal currents: absence of rapid MRI signal changes during visual evoked response.* **NeuroImage. 23: 1059-1067 (2004)**

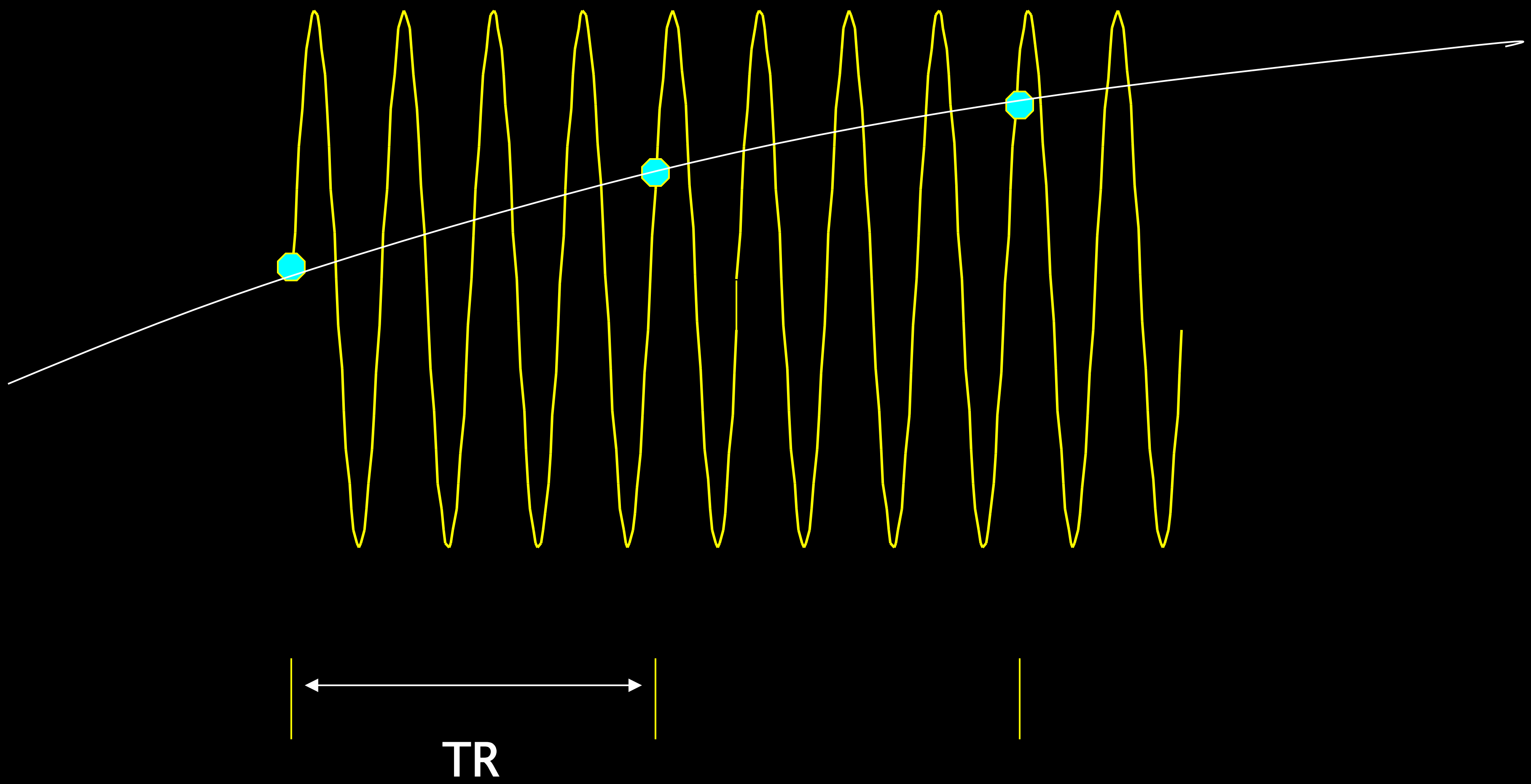
Undersampling...

8 Hz alternating checkerboard

8 Hz alternating checkerboard

Undersampling

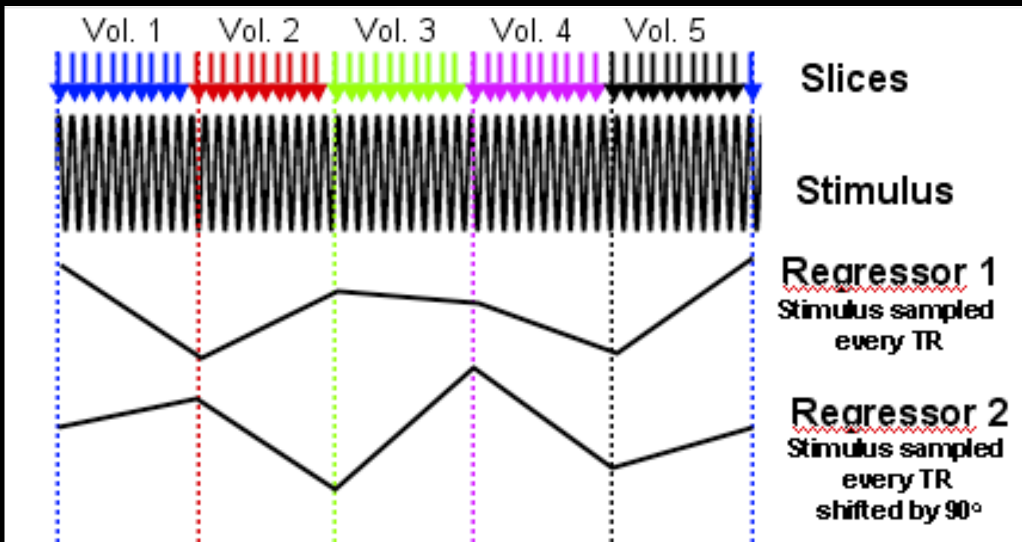
Alternating Checkerboard Frequency



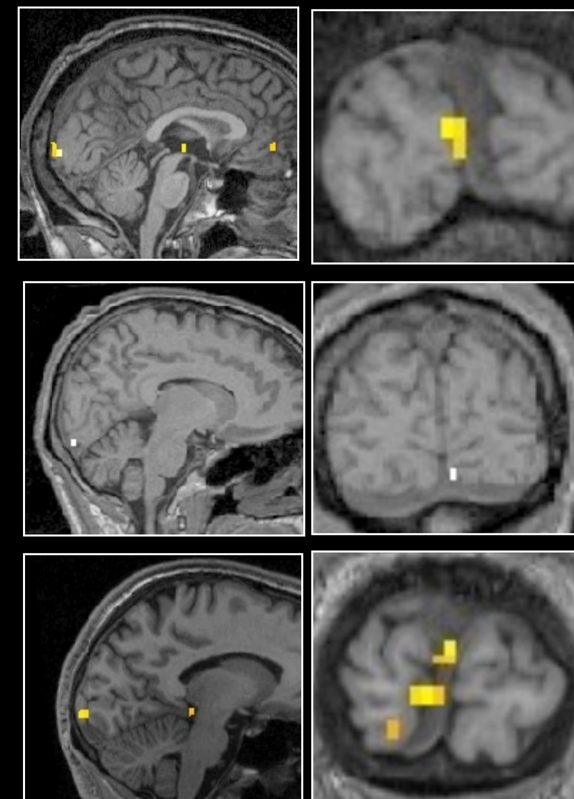
Comparison of phase and magnitude of the MR signal in measuring neuronal activity [for Petes' sake[1,2]]

James M. Kilner, Klaas E. Stephan, Oliver Josephs, Karl J. Friston

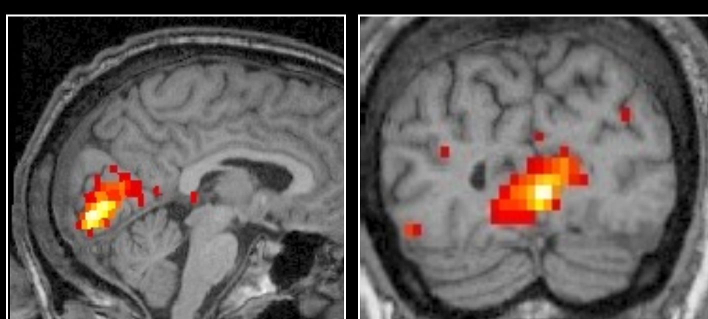
Wellcome Department of Imaging Neuroscience, 12 Queen Square, London



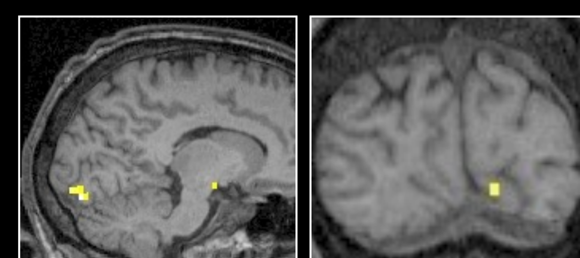
Phase



BOLD



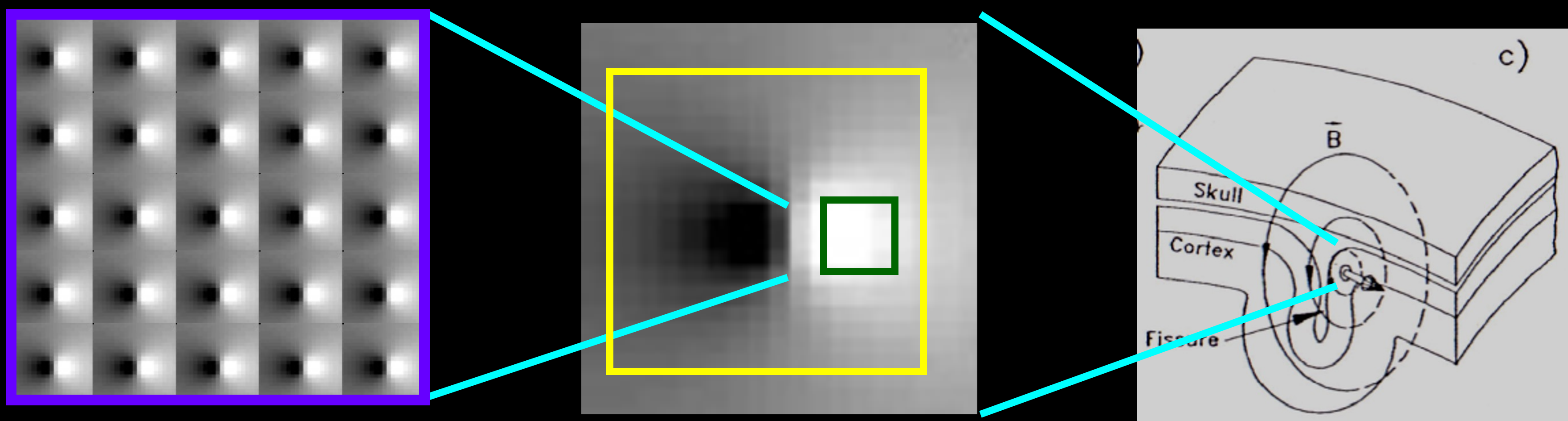
Mag

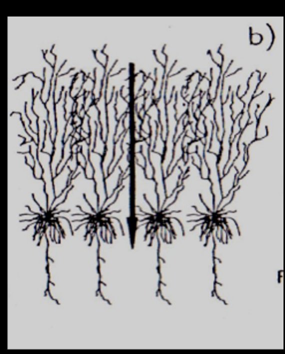


What should we be detecting?

Phase or Magnitude?

Phase vs. Magnitude





Δ phase

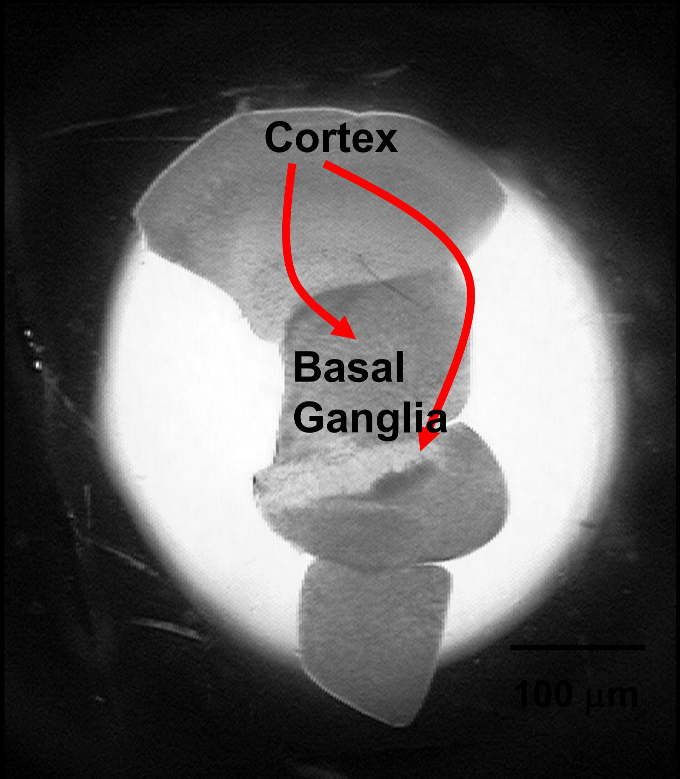
Δ magnitude, ?Δ phase (dep. on location)

Δ magnitude

In Vitro Studies

in vitro model

Organotypic (*no blood supply or hemoglobin traces*) sections of newborn-rat somato-sensory Cortex, or somato-sensory Cortex & Basal Ganglia



Plenz, D. et al. *Neurosci* 70(4): 861-924, 1996

- Size: in-plane:~1-2mm^2, thickness: 60-100µm
- Neuronal Population: 10,000-100,000

- Spontaneous synchronized activity < 2Hz
- Epileptiform activity
- Spontaneous beta freq. activity (20-30Hz)
- Network Activity Range: ~ 0.5-15µV

methods - setup

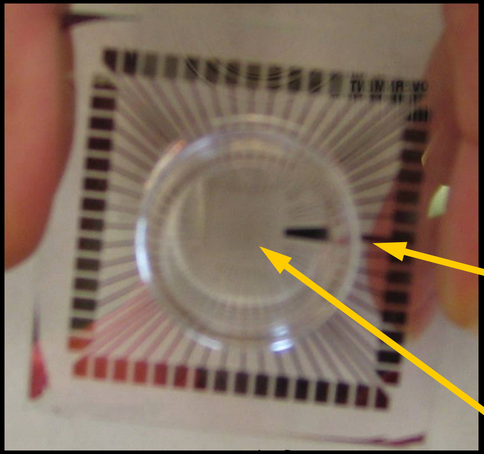
Culture Preparation

Multi-Electrode Arrays (MEA)

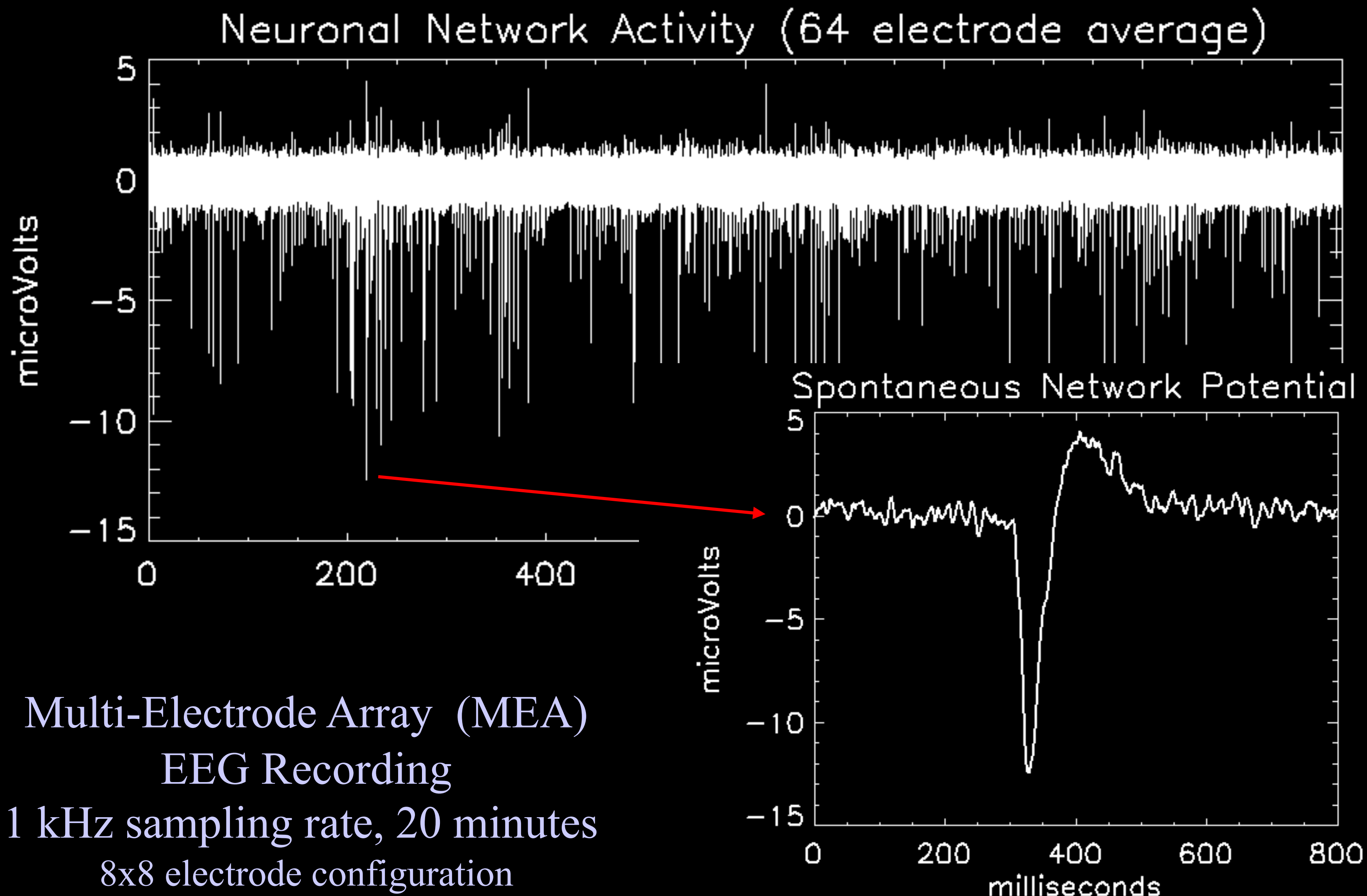
Multichannelsystems Germany 8x8 electrodes

0.8ml culture medium

Multi-Electrode Array



Multi-Electrode Array EEG recording



Multi-Electrode Array (MEA)
EEG Recording
1 kHz sampling rate, 20 minutes
8x8 electrode configuration

in vitro MR protocol

Imaging (3T)

• Spin-Echo EchoPlanar Imaging

SE EPI image

• voxel size: ~3x3x3 mm

• Sampling Rate :1 Hz (TR: 1sec)

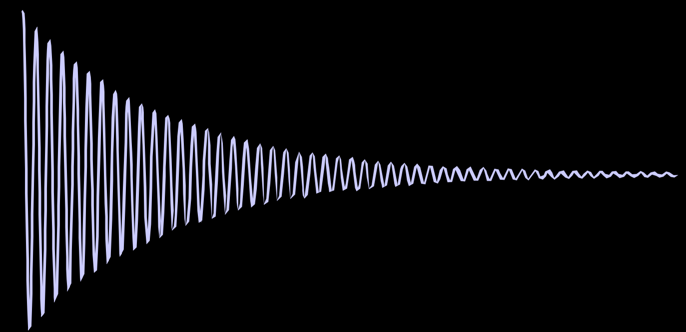
• TE: 60 ms

• Readout :44 ms

NMR (7T)

• free induction decay (FID) acquisition

FID



• slab size: ~2x10x1mm

• Sampling Rate :10 Hz (TR: 100ms)

• TE : 30 ms

• Readout : 41 ms

in vitro MR experiment design

Imaging (3T)

Six Experiments

two conditions per experiment

Active : 10 min (600 images) neuronal activity present

Inactive : 10 min (600 images) neuronal activity terminated via TTX administration

NMR (7T)

Six Experiments

two conditions per experiment

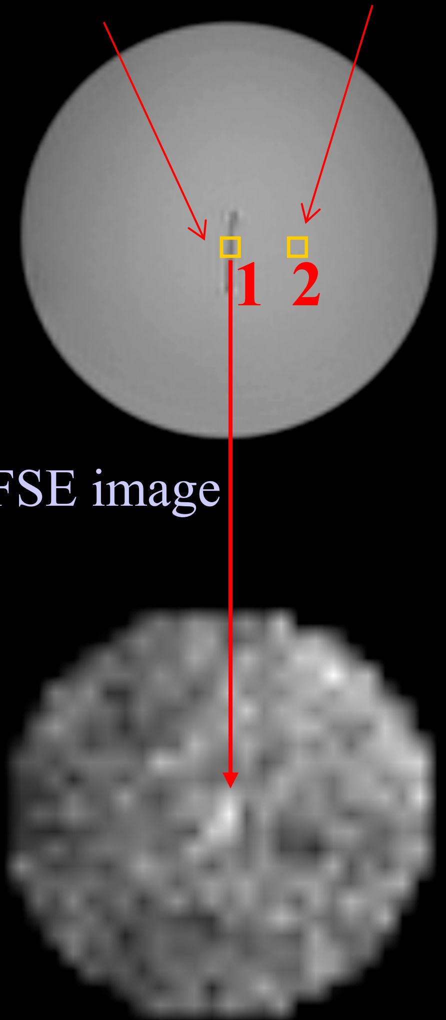
Active : ~17 min (10,000 images) neuronal activity present

Inactive : ~17 min (10,000 images) neuronal activity terminated via TTX administration

Pre- and Post- MR scan electrical recordings

3 Tesla data

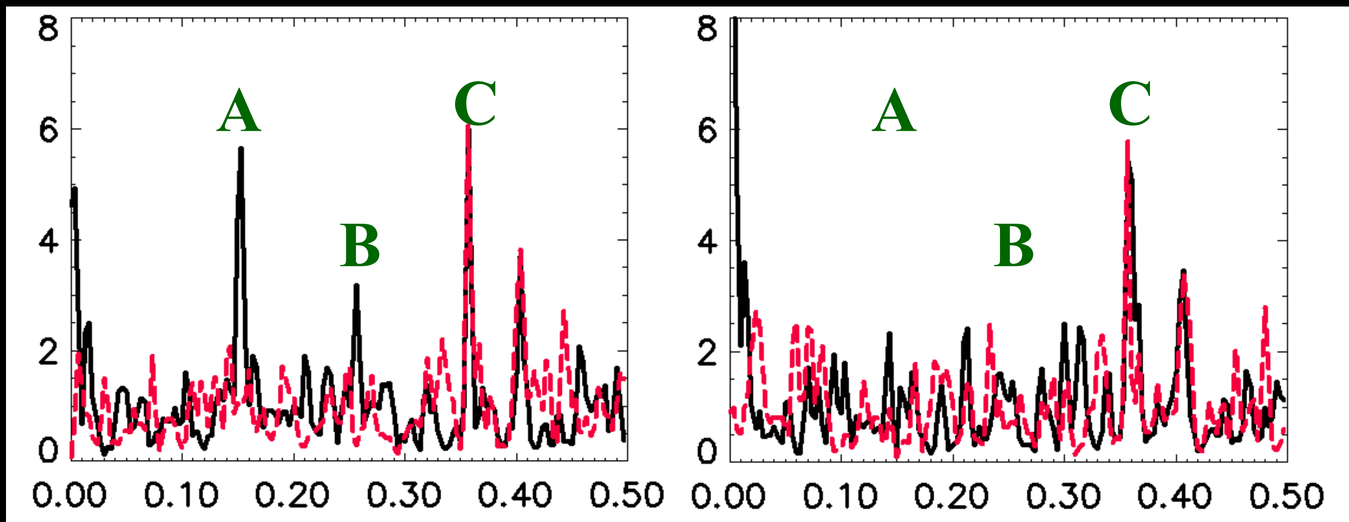
Culture ACSF



FSE image

0.15Hz map

1: <u>culture</u> *2: <u>ACSF</u>*



Hz Hz

Active condition: black line

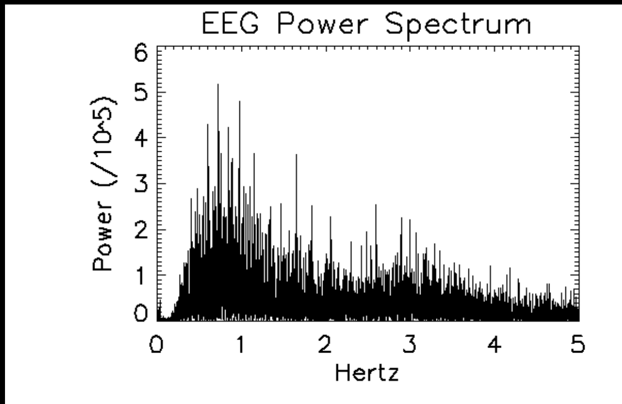
Inactive condition: red line

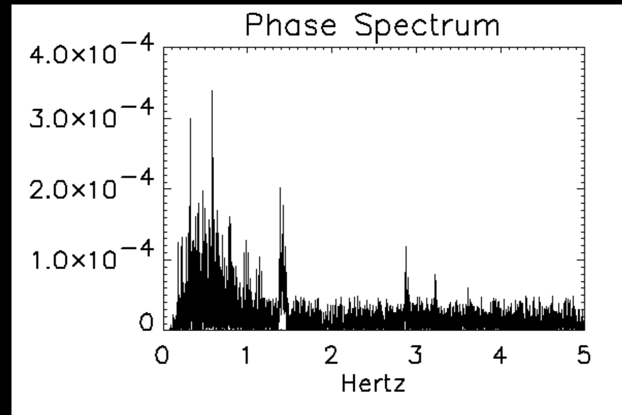
A: 0.15 Hz activity, on/off frequency

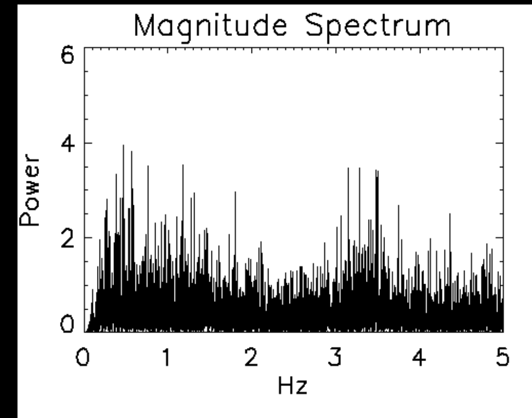
B: activity

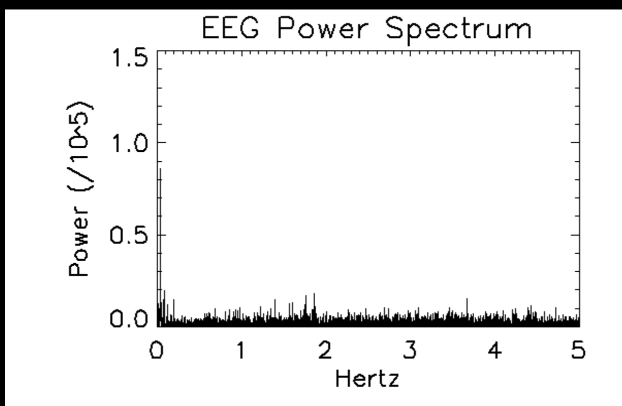
C: scanner noise (cooling-pump)

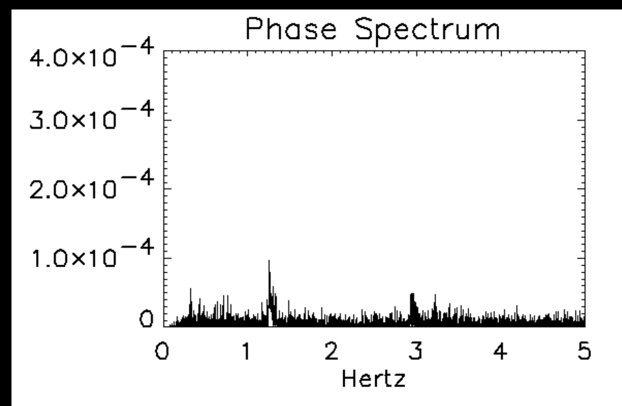
7 Tesla data

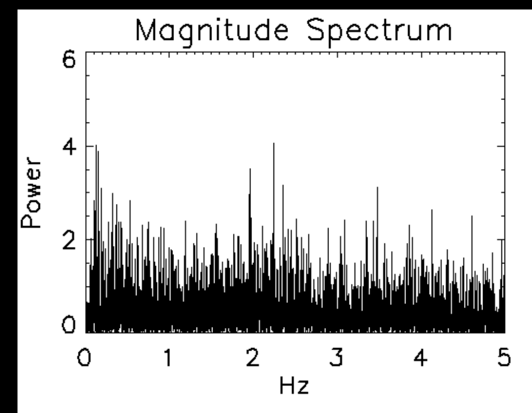












Power decrease between PRE & TTX EEG : ~ 81%

Decrease between PRE & TTX MR phase: ~ 70%

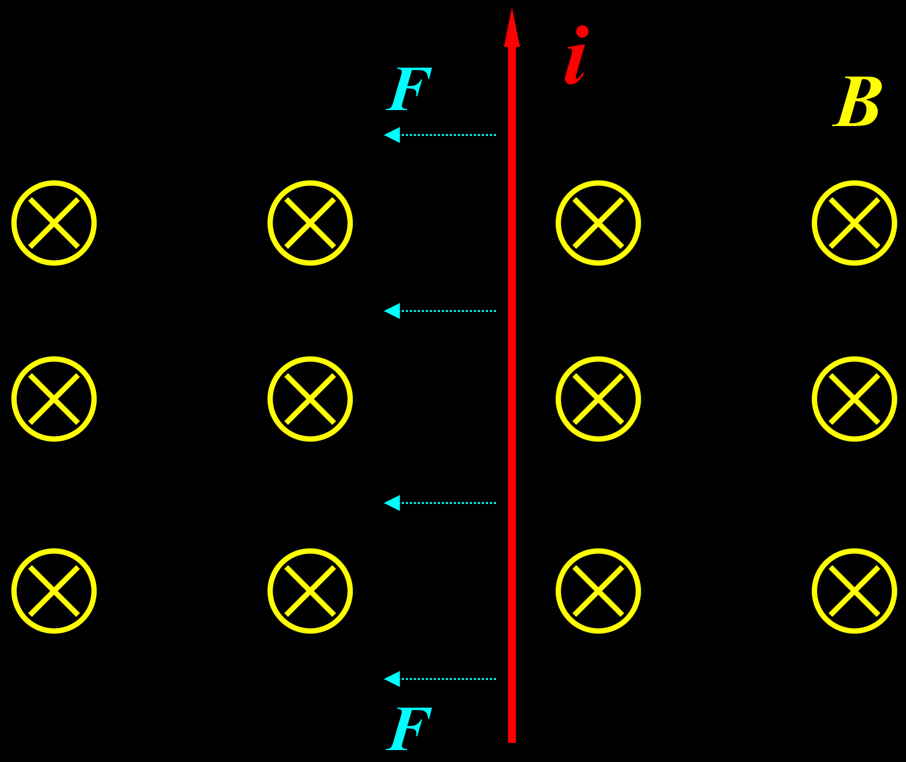
Decrease between PRE & TTX MR magnitude: ~ 8%

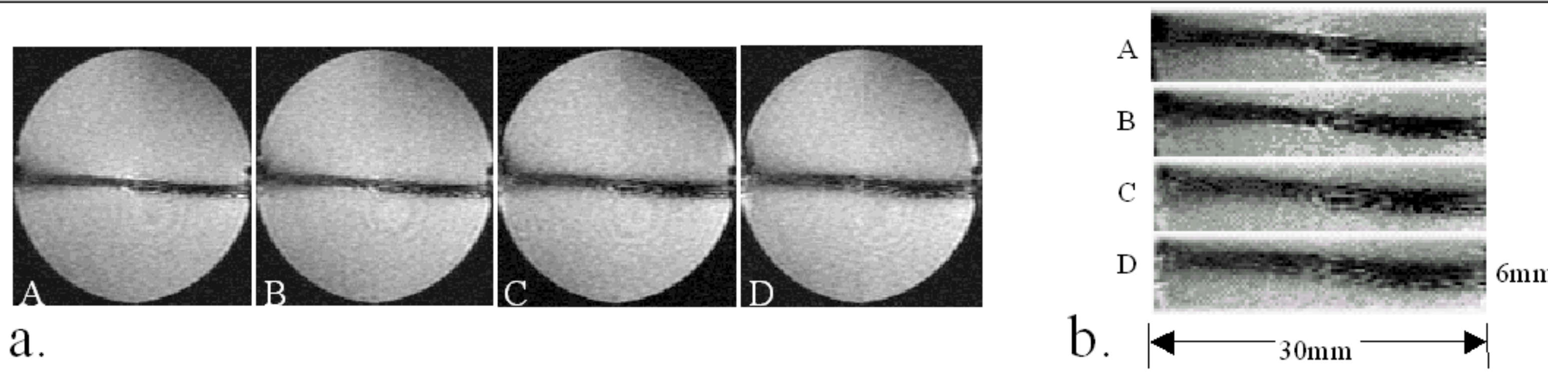
Other Methods??

The principle and application of the Lorentz Effect Imaging

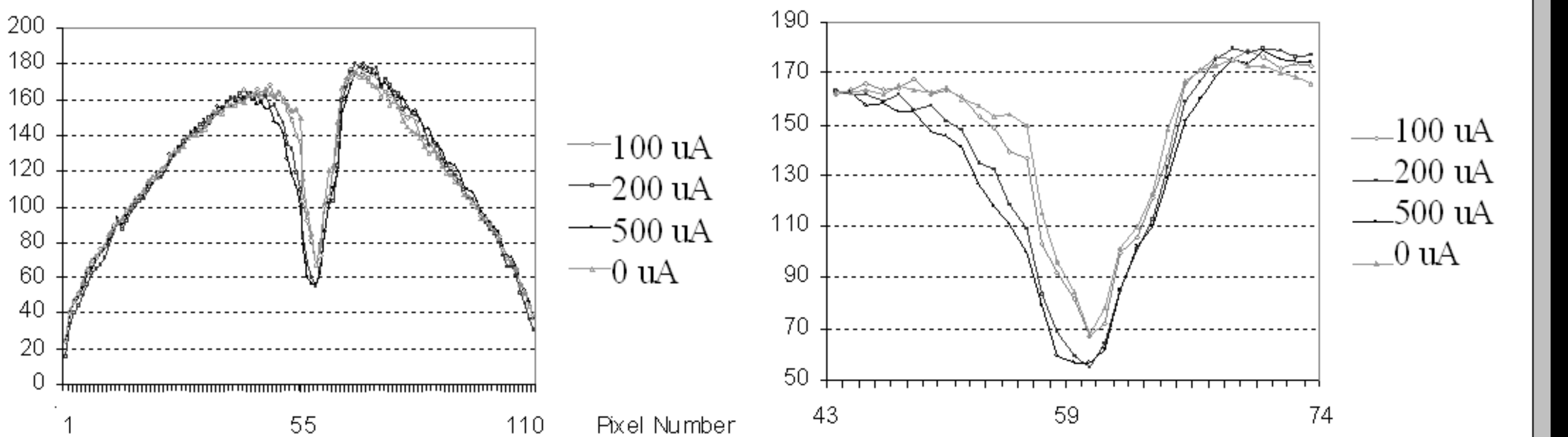
Song et al ISMRM 2000, p. 54

Lorentz Force



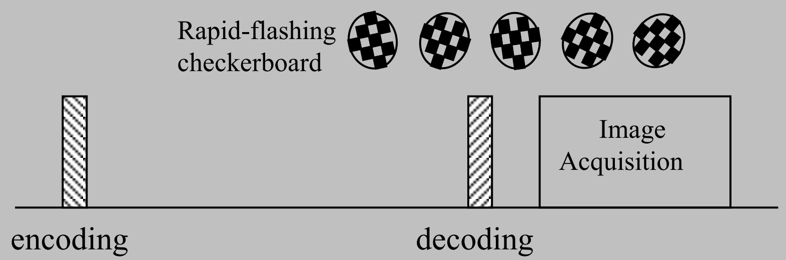


(a) LEI images at different current levels: A) 0 μA, B) 100 μA, C) 200 μA and D) 500 μA.,
(b) Magnified center portions of the corresponding images.

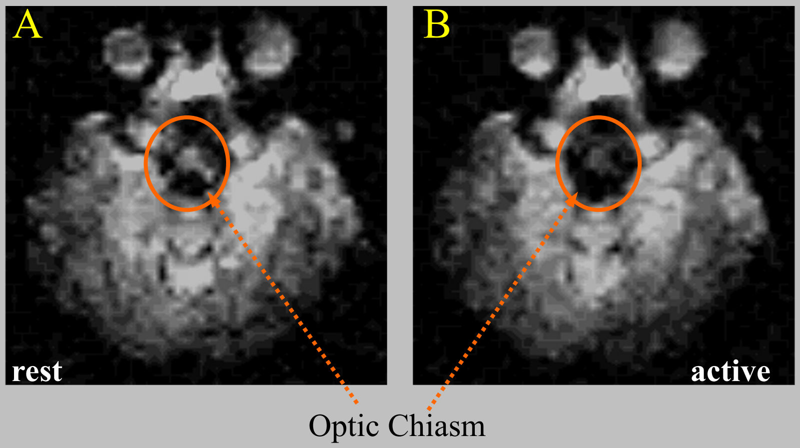


Signal intensity profiles along the vertical axis of the images, the gradual widening of the central dip reflects stronger Lorentz effects from 0 uA to 500 uA, and the direction of the widening effect towards anterior part of the phantom indicates the direction of the Lorentz force.

Preliminary Experiment on the Optical Nerve



Schematic illustration of the data acquisition.



EPI images without visual stimuli (A) and with visual stimuli (B).

Caution…

- Need to rule out BOLD or other mechanisms

Despair…

- Noise 1% is larger than effect 0.1%.
- MR sampling rate is slow and transient.
- Neuronal activation timing is variable and unspecified.
- Models describing spatial distribution of ΔB across spatial scales are crude…could be off by up to an order of magnitude.

Hope…

- We are understanding more about precise effects of stimuli.
- "Transient-tuned" pulse sequences (spin-echo, multi-echo)
- Sensitivity and/or resolution improvements
- Lower field strengths? (effect not B_o dependent)
- Simultaneous electrophysiology.
- Again..models describing spatial distribution of ΔB across spatial scales are crude…could be off by up to an order of magnitude (cancellation at specific spatial and temporal scales..)

related papers

M. L. Joy, G. C. Scott, R. M, Henkelman, *In vivo detection of applied electric currents by magnetic resonance imaging.* **Magn Reson Imaging 7: 89-94, (1989).**

G. C. Scott, M. L. Joy, R. L. Armstrong, R. M. Henkelman, *RF current density imaging homogeneous media.* **Magn. Reson. Med. 28: 186-201, (1992).8**

M. Singh, *Sensitivity of MR phase shift to detect evoked neuromagnetic fields inside the head.* **IEEE Transactions on Nuclear Science. 41: 349-351, (1994).**

J. Bodurka, P. A. Bandettini. *Current induced magnetic resonance phase imaging.* **Journal of Magnetic Resonance, 137: 265-271, (1999).**

H. Kamei, J, Iramina, K. Yoshikawa, S. Ueno, *Neuronal current distribution imaging using MR.* **IEEE Trans. On Magnetics, 35: 4109-4111, (1999)**

J. Bodurka, P. A. Bandettini. *Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes.* **Magn. Reson. Med. 47: 1052-1058, (2002).**

...

...related Papers, continued

D. Konn, P. Gowland, R. Bowtell, *MRI detection of weak magnetic fields due to an extended current dipole in a conducting sphere: a model for direct detection of neuronal currents in the brain.* **Magn. Reson. Med. 50: 40-49, (2003).**

J. Xiong, P. T. Fox, J.-H. Gao, *Direct MRI Mapping of neuronal activity.* **Human Brain Mapping, 20: 41-49, (2003)**

R. Chu, J. A. de Zwart, P. van Gelderen, M. Fukunaga, P. Kellman, T. Hollroyd, J. Duyn. *Hunting for neuonal currents: absence of rapid MRI signal changes during visual evoked response.* **NeuroImage. 23: 1059-1067 (2004)**

A. D. Liston, A. Salek-Haddadi, S. J. Kiebel, K. Hamandi, R. Turner, L. Lemieux, ***The MR detection of neuronal depolarization during 3-Hz spike-and-wave comnplexs in generalized epilepsy.*** **Mag. Res. Imag. 22: 1441-1444 (2004).**

D. Konn, S. Leach, P. Gowland, R. Bowtell, *Initial attempts at directly detecting alpha wave activity in the brain using MRI.* **Mag. Res. Imag. 22 1413-1424 (2004)**

T. S. Park, S. Y. Lee, J. H. Park, S. Y. Lee, *Effect of nerve cell currents on MRI images in snail ganglia.* **Neuroreport, 15: 2783-2786, (2004)**

Neuronal Current Abstracts at ISMRM 2005

Monday Oral 12:48 #33. Direct Detection of Axon Firing in the Optic Nerve and Visual Cortex Using MRI
Li Sze Chow1, Greg G. Cook1, Elspeth H. Whitby1, Martyn Paley1
1University of Sheffield, Sheffield, South Yorkshire, UK

Monday Oral 16:30 #116. Direct MR Detection of Neuronal Electrical Activity in Vitro at 7T
Natalia Petridou1, Afonso C. Silva1, Dietmar Plenz1, Jerzy Bodurka1, Peter A. Bandettini1
1National Institutes of Health, Bethesda, Maryland, USA

Monday Poster #1411. Magnetic Field Effect of Neuronal Currents on MRI: A Snail Ganglia Study
Tae Seok Park1, Sang Yeon Lee1, Ji Ho Park1, Soo Yeol Lee1
1Kyung Hee University, Yongin, Kyungki, Republic of Korea

Monday 17:54 #123. Neurogenic Inhomogeneity Localization for Detection of Activity (NILDA)
Gaby S. Pell1, David F. Abbott1,2, Graeme D. Jackson1,2, Steven W. Fleming1, James W. Prichard3
1Brain Research Institute, Melbourne, Victoria, Australia; 2University of Melbourne, Melbourne, Victoria, Australia; 3Yale University, West Tisbury, Massachusetts, USA

Tuesday Poster #1416. EEG Recordings and Spin-Echo Magnetic Resonance Imaging of Visual Evoked Responses
Marta Bianciardi1, Francesco Di Russo, 1,2, Teresa Aprile1,3, Bruno Maraviglia3,4, Gisela E. Hagberg1
1Santa Lucia Foundation, Rome, Italy; 2University Institute of Motor Science, Rome, Italy; 3University of Rome La Sapienza, Rome, Italy; 4Enrico Fermi Center, Rome, Italy

Wednesday Poster #1425. MRI of Neural Currents: Numerical Study
Krastan B. Blagoev1, Bogdan Mihaila1, Ludmil B. Alexandrov1, Bryan J. Travis1, Istvan Ulbert2, Eric Halgren2, Van J. Wedeen2
1Los Alamos National Laboratory, Los Alamos, New Mexico, USA; 2Massachusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts, USA