Concurrent Multimodal Imaging

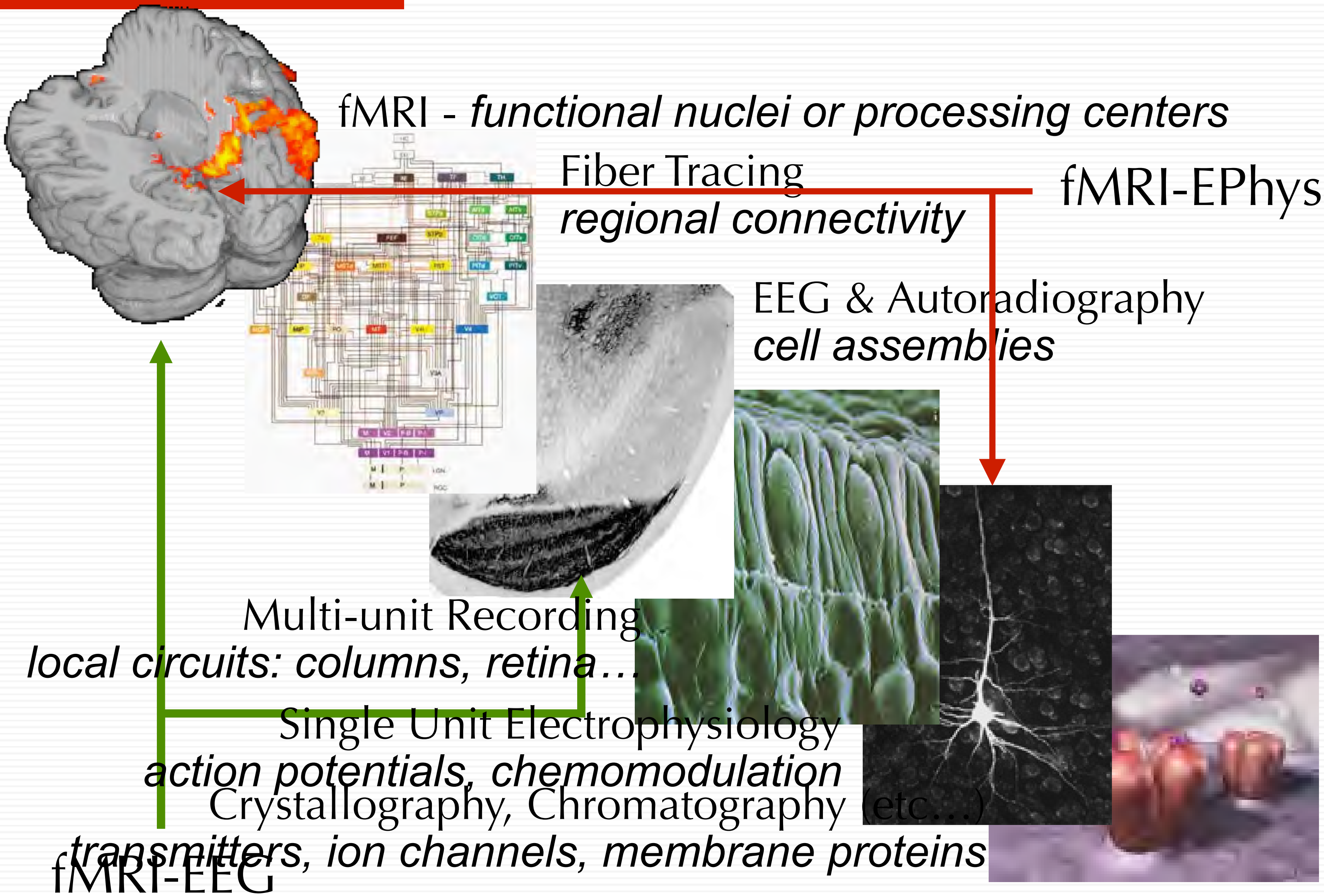
UCLA Medical Center

Center for Cognitive Neuroscience

Issues in Multimodal Imaging

- Why Bother? What can we hope to gain?
- General Issues for any multimodal experiment
  - Safety
  - Mutual Interference
  - Signal dependence or independence
  - Joint Analysis
- Some Results
  - PET-MRI
  - PET-CT
  - EEG-PET
  - Optical and E-Phys
  - MRI-EEG
  - MRI and Single Units
  - MRI and Spectroscopy
  - …

Levels of Understanding



fMRI - *functional nuclei or processing centers*

Fiber Tracing
regional connectivity

fMRI-EPhys

EEG & Autoradiography
cell assemblies

Multi-unit Recording
local circuits: columns, retina…

Single Unit Electrophysiology
action potentials, chemomodulation

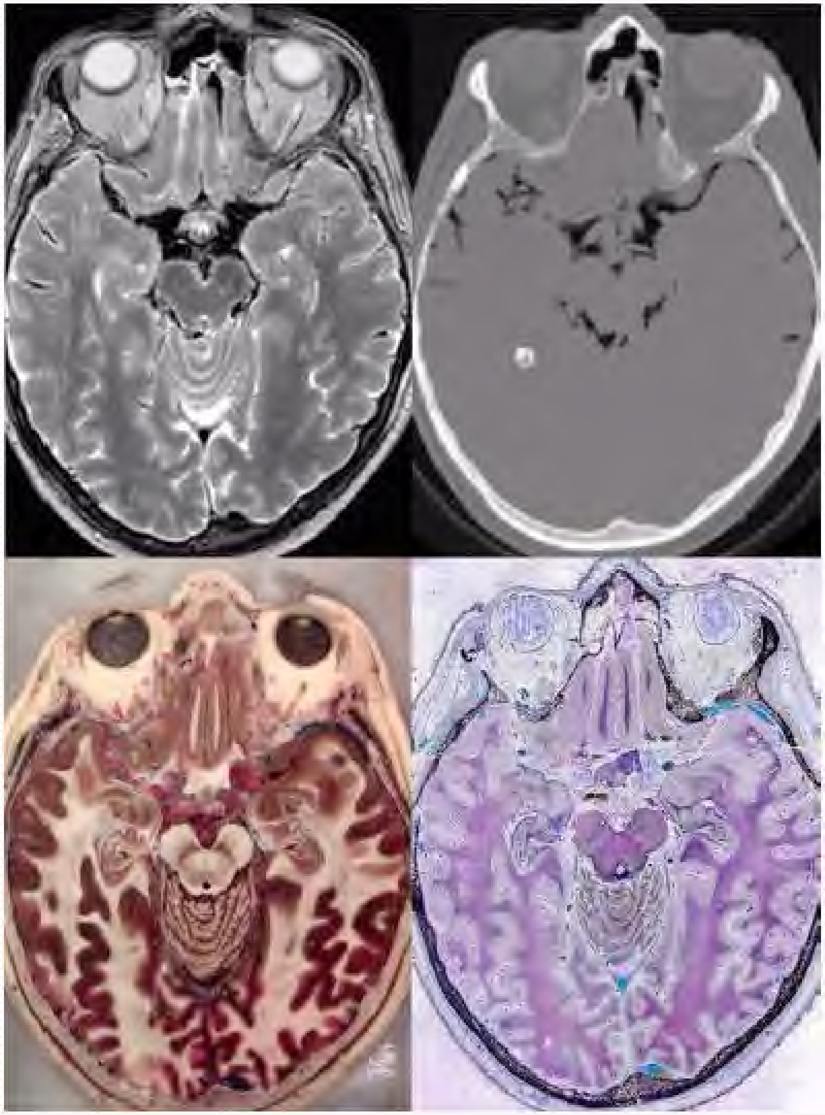
Crystallography, Chromatography (etc…)
transmitters, ion channels, membrane proteins

fMRI-EEG

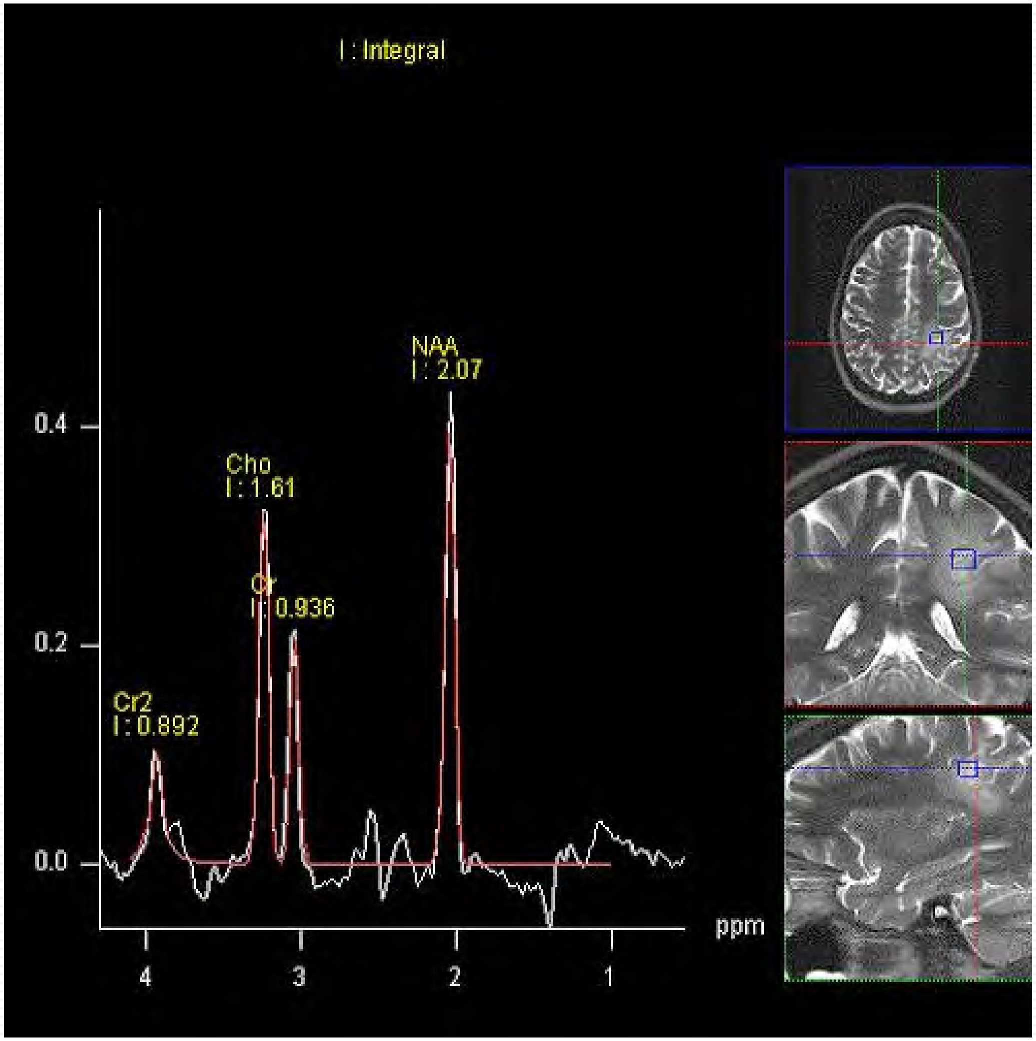
What is to be Gained?

- Many Experiments Can be Performed Separately!
  - *E.g.*, Sensory Processing is more or less time-invariant
- Reduced Study Time
- Spatiotemporal Resolution Sharing
- Registration
  - Shape distortions, poor alignment boundaries, soft tissues
- Transient or Uncontrolled Events
  - Interictal spikes, Response Errors
- Better Detection Power

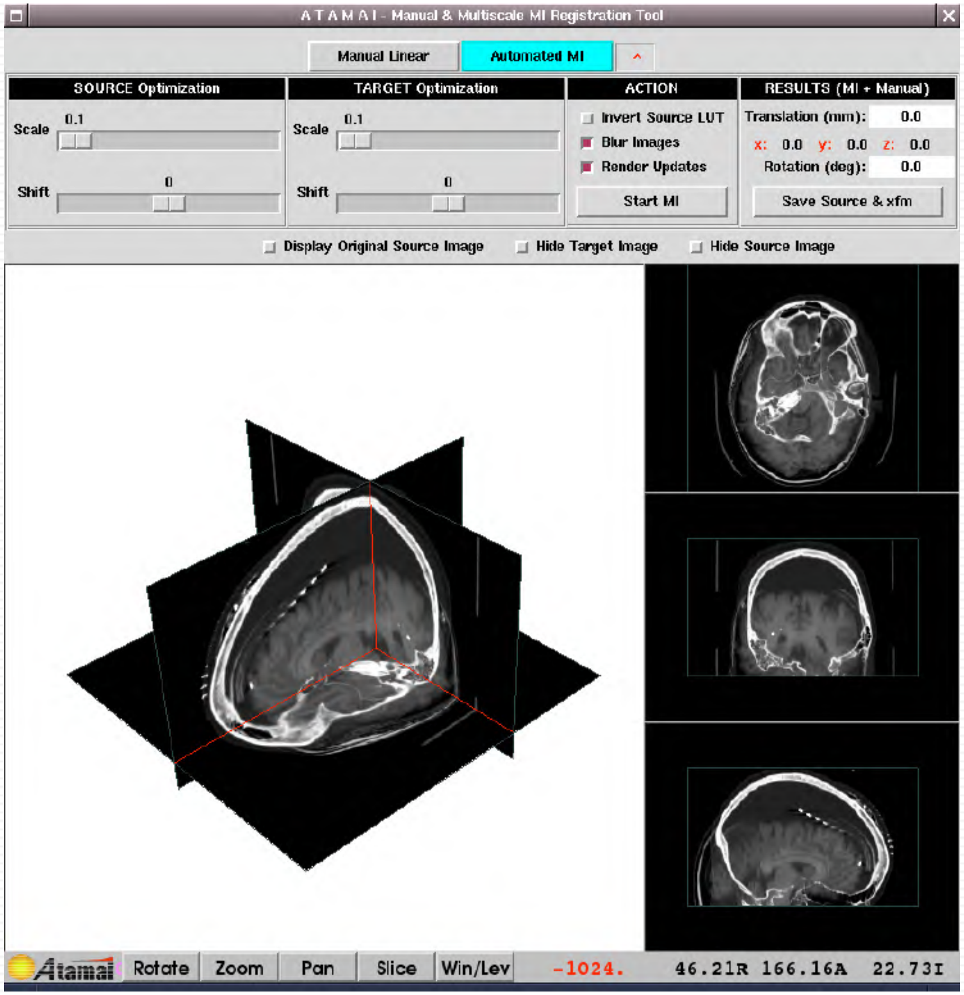
Visible Human



MR Spectroscopy



Intermodality Registration

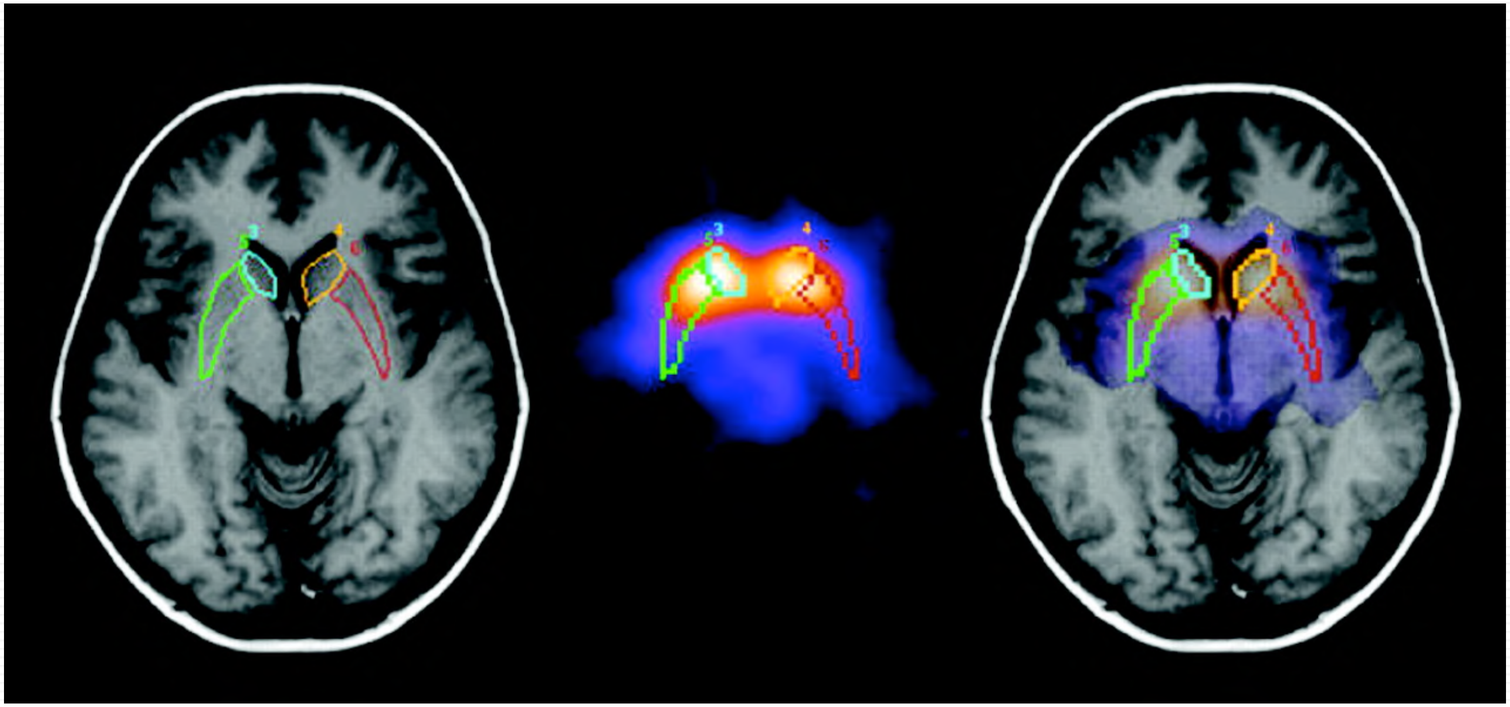


Automated Image Registration

Shape Distortions

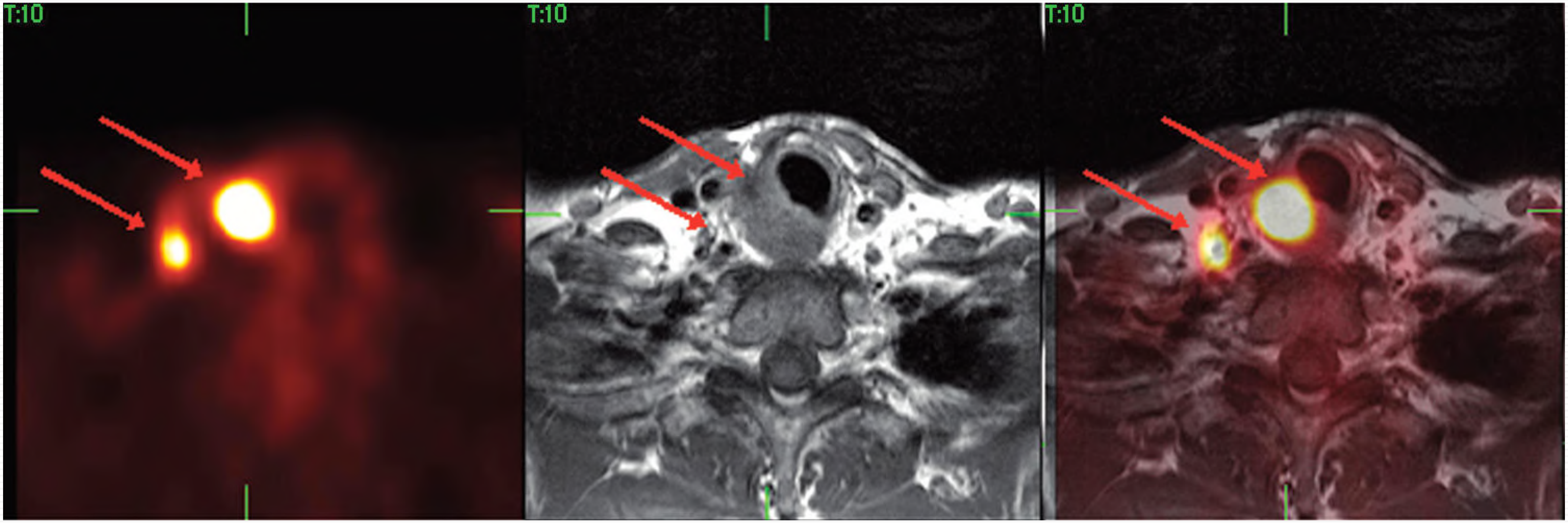
Recovery of Change in Brain Tissue due to Post Mortem Effects and Histologic Processing. Warping algorithms based on continuum-mechanical models can recover and compensate for patterns of tissue change which occur in post mortem histologic experiments. A brain section (left), gridded to produce tissue elements for biochemical assays. is reconfigured (middle) into its original position in the cryosection blockface (Mega *et al*., 1997; algorithm from Thompson and Toga, 1996, 1998). The complexity of the required deformation vector field in a small tissue region (magnified vector map, right) demonstrates that very flexible, high-dimensional transformations are essential (Thompson and Toga, 1996; Schormann *et al*., 1996). As well as measuring local patterns of mechanical tissue deformations, recovery of deformation fields allows projection of histologic and biochemical data back into the volumetric reference space of the cryosection image. In some cases, these data can also be projected, using additional warping algorithms, onto in vivo MRI and co-registered PET data from the same subject for digital correlation and analysis (Mega *et al*., 1997).

SPECT MRI by Image Fusion



Fusion of ^{123}I-ß-carbomethoxyiodophenyl tropane SPECT neuroreceptor images with MRI

PET MRI by Fusion



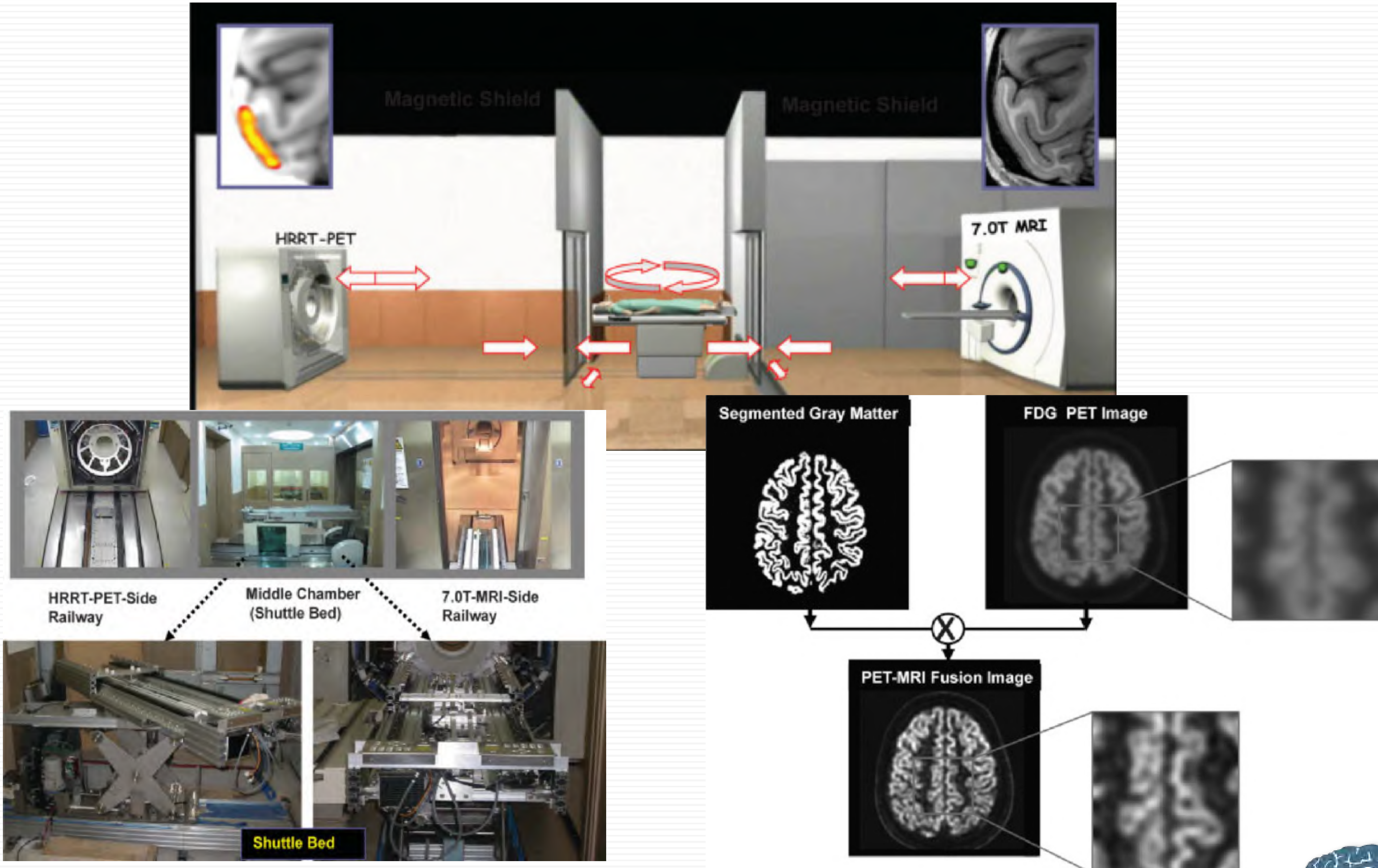
THYROID
Volume 18, Number 2, 2008

Utility of PET/Neck MRI Digital Fusion Images in the Management of Recurrent or Persistent Thyroid Cancer

Laura Seiboth,[1] Douglas Van Nostrand,[2] Leonard Wartofsky,[1] Yasser Ousman,[1] Jacqueline Jonklaas,[3] Calvin Butler,[2] Frank Atkins,[2] and Kenneth Burman[1]

NeuroImaging Training Program

PET MRI by Fusion



PET-MRI

PNAS

Simultane … omography
and magr

Ciprian Catana*†, Da … :hler§, Russell E. Jacobs‡,
and Simon R. Cherry‡

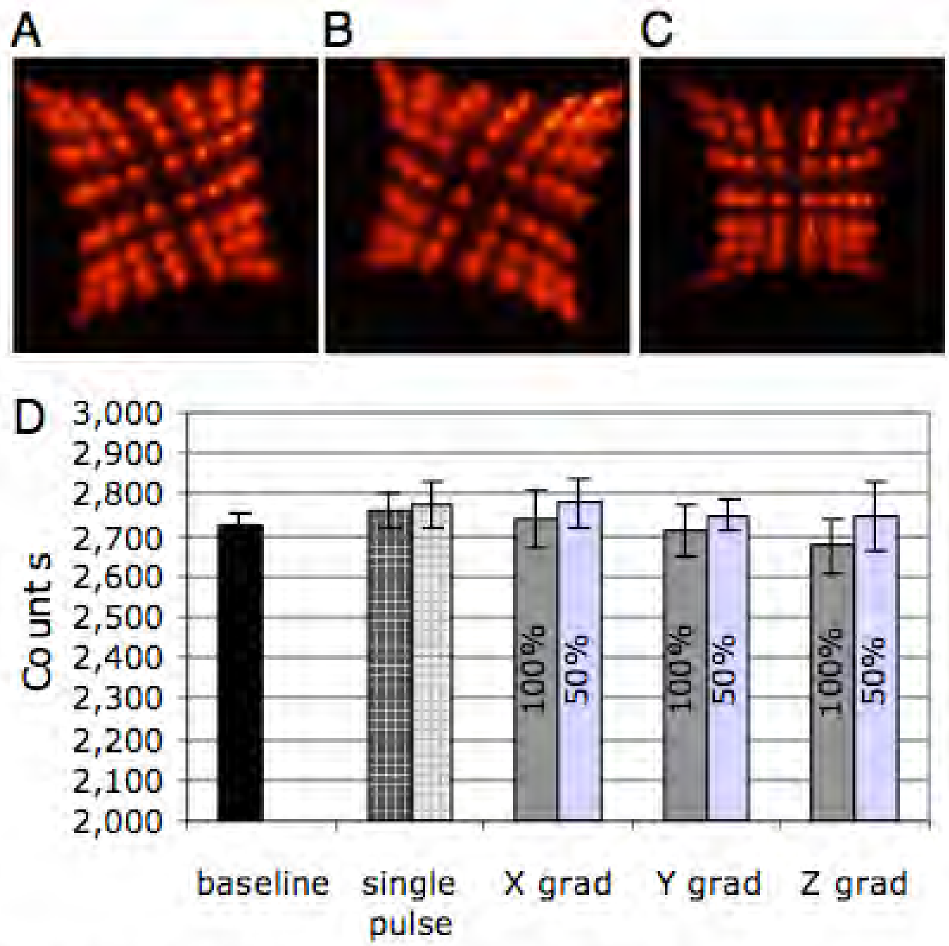
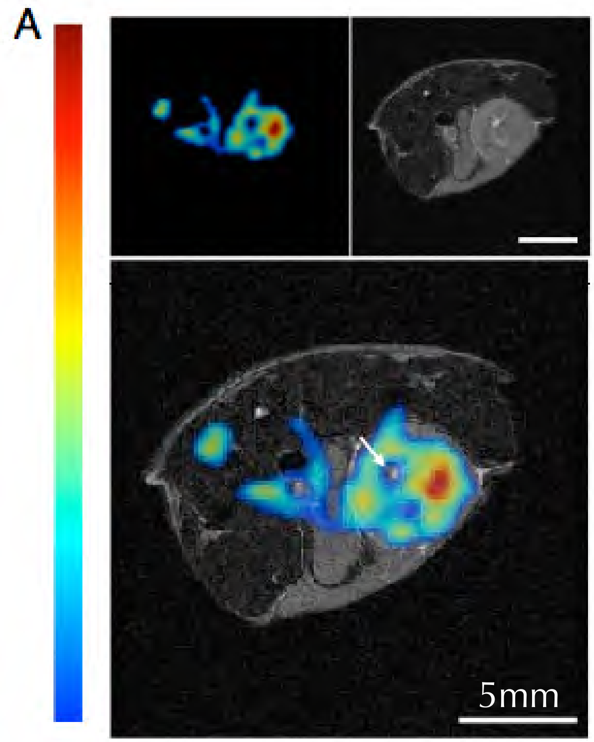
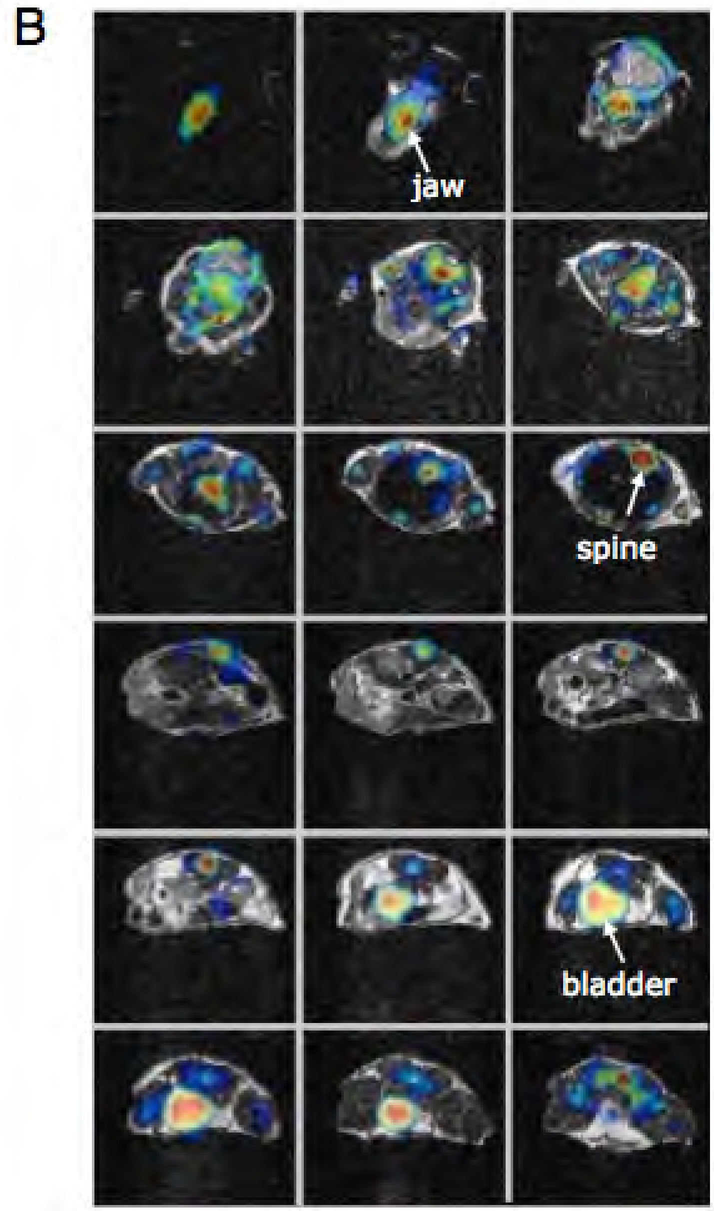


Fig. 1. MR scanner effect on PET system. (*A–C*) Detector histograms showing the anticlockwise (*A*) and clockwise (*B*) rotations of the crystal maps when compared with the data acquired outside of the magnet (*C*). (*D*) PET event rate measured under different conditions: (*i*) while applying only RF power (with 1,000 ms and 500 ms repetition times) and (*ii*) while switching the *x–z* gradients independently (at 100% and 50% power; 400 and 200 mT/m, respectively). Baseline represents the event rate recorded without running MR sequences.

PET MRI Results





Simultaneous PET, MRI

A. Mouse FDG Tumor imaging. *Top left*: PET. *Top* right: MRI

B. Fused PET and MR images of a mouse from head to bladder.

Projectiles

www.SimplyPhysics.com

Projectiles

NEVER TRY TO REMOVE OBJECTS ON YOUR OWN. CALL SERVICE or SENIOR CCN PERSONNEL.

www.SimplyPhysics.com

NeuroImaging Training Program

www.brainmapping.org

Center for Cognitive Neuroscience

Before you start

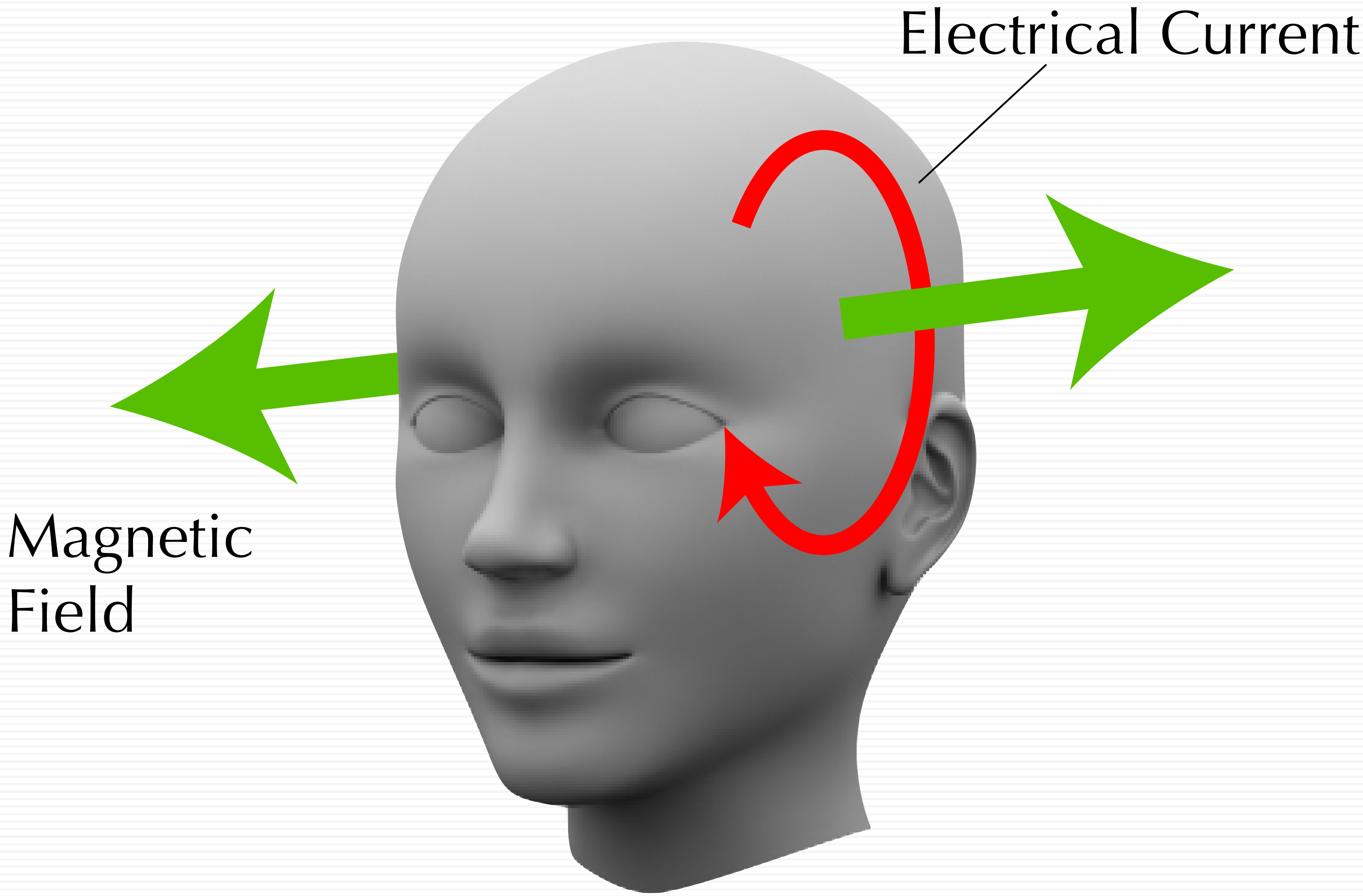
Projectiles account for 10% of reported safety incidents.

10% are from Implanted Devices

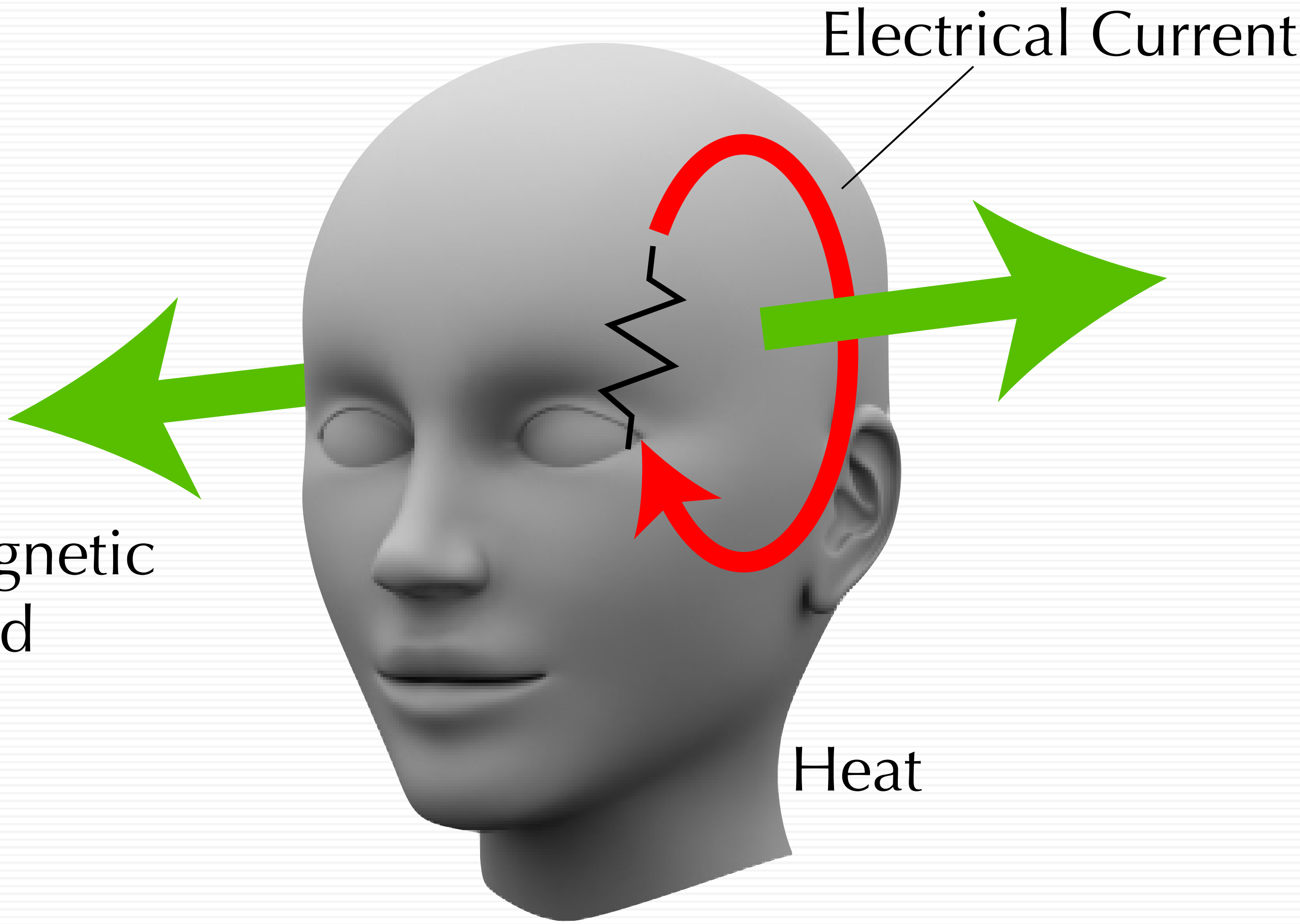
71% are burns!

M Mitka, "Safety improvements urged for MRI facilities." JAMA, 294: 2145. 2005

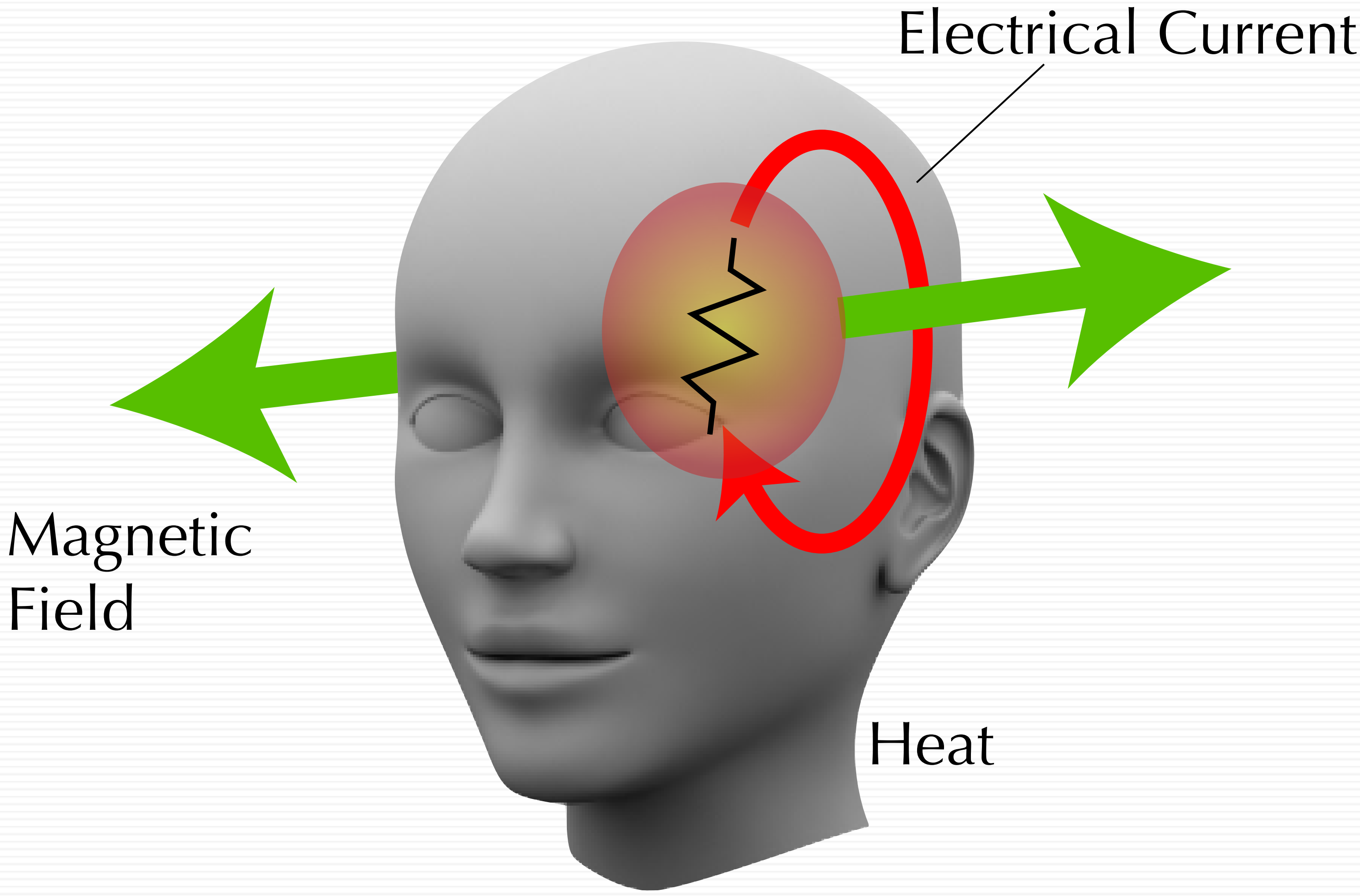
Induced Currents in the Body



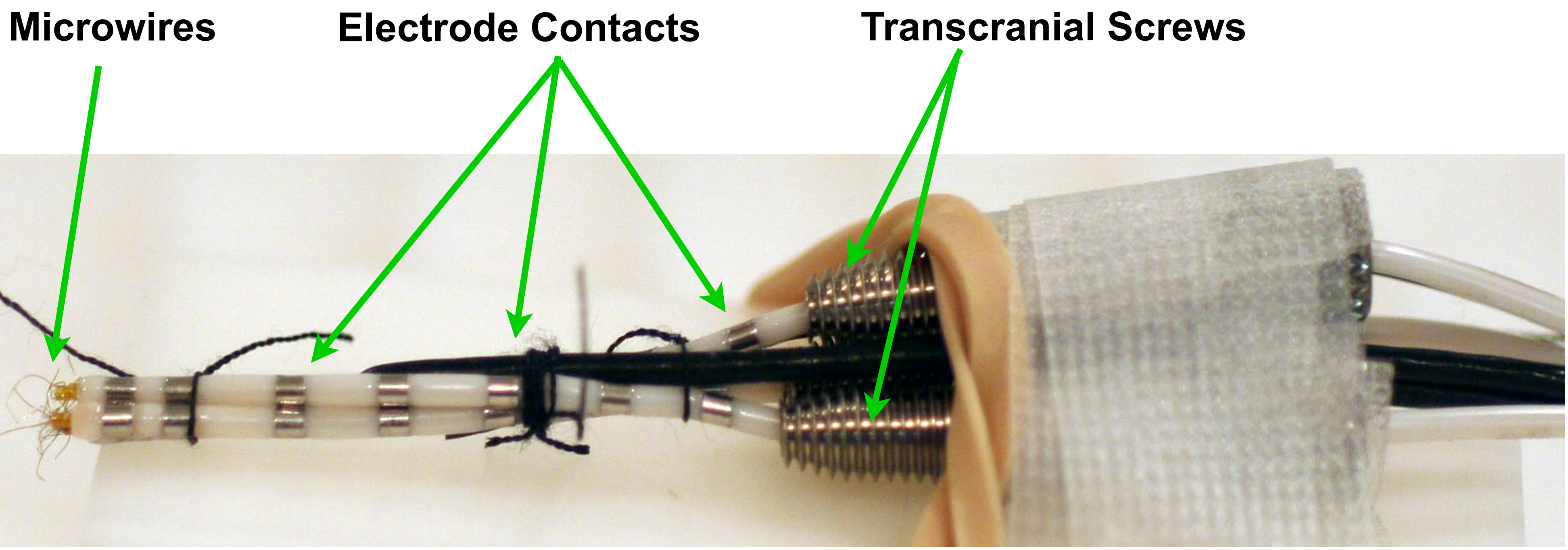
Specific Absorption Rate



Specific Absorption Rate



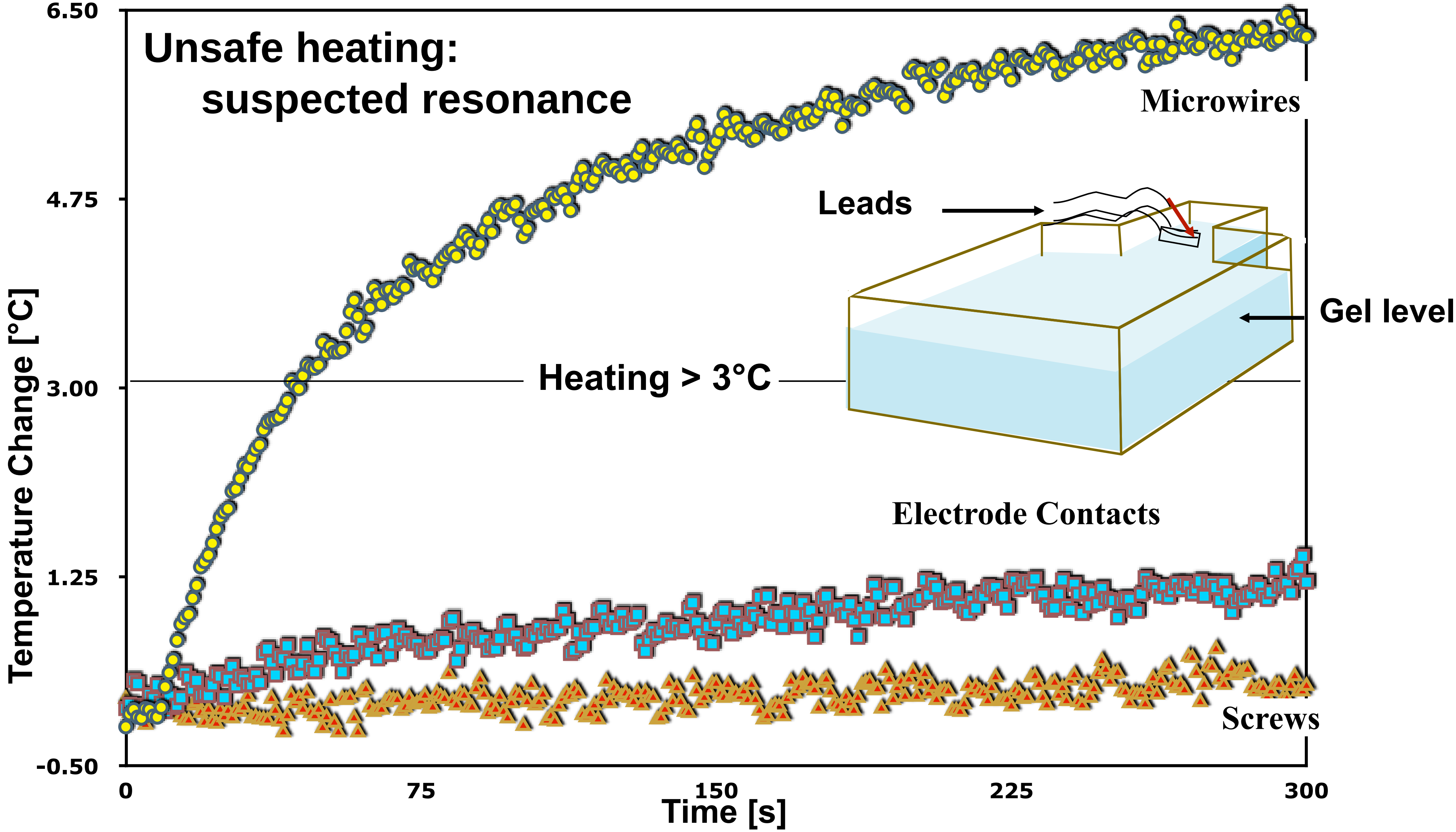
Heating - Experimental Set-up



- **In-vitro study: Semi-solid gel, head and torso phantom**
- **Fluoroptic thermometry system: MRI compatible**
- **High specific absorption rate (SAR) = 3.0 Watts/Kg**

Strick, *et al., Society for Neuroscience, 2007*

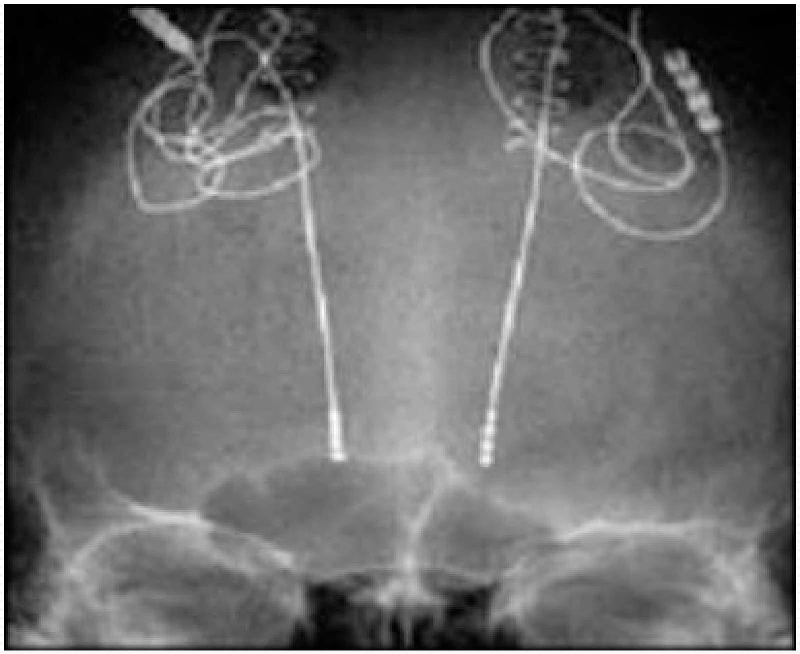
Safety Results

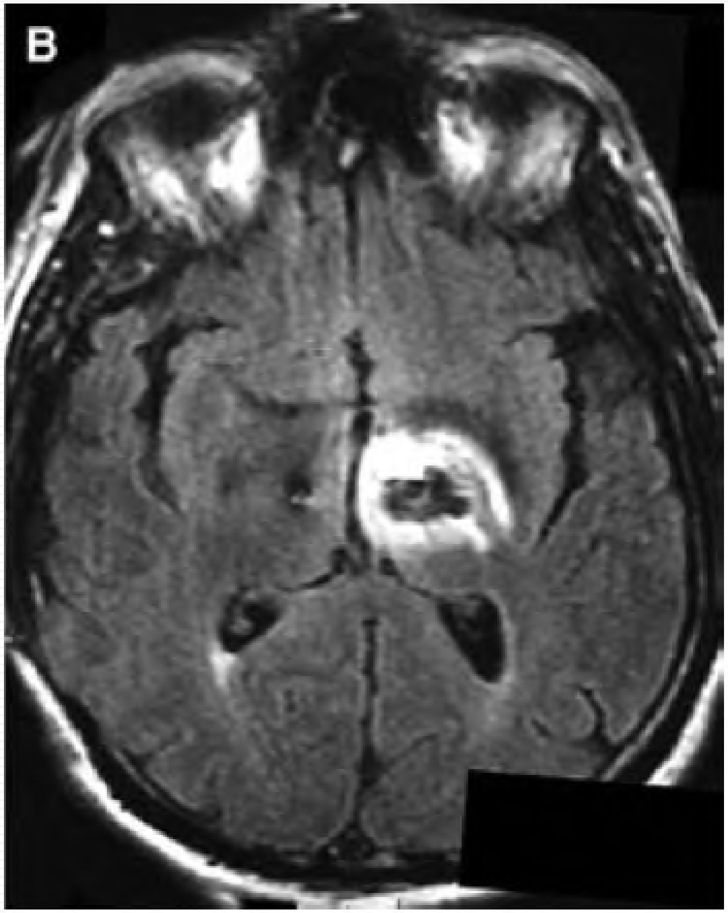


Strick, *et al., Society for Neuroscience, 2007*

UCLA

Deep Brain Stimulation (DBS) Electrodes





T2-weighted MRI scan of the brain showing edema around the left DBS electrode.

Safety Resources

http://www.semel.ucla.edu/staglin

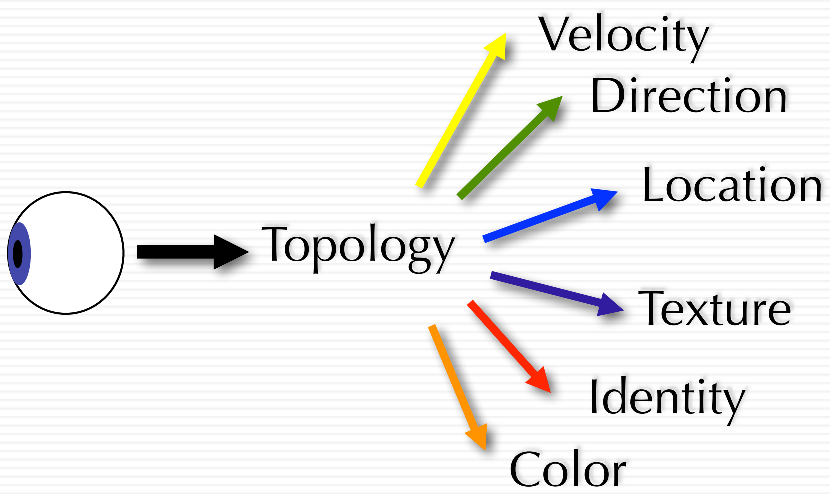
http://users.fmrib.ox.ac.uk/~peterj/safety_docs/index.html

Blobs are not the whole story

"…the classical concept of cerebral localization is of limited value, because of its static character and its failure to provide any answer to the question of how specialized parts of the cortex interact to produce the integration evident in thought or behavior. The problem here is one of the dynamic relations of the diverse parts of the cortex, whether they be cells or cortical fields."

--*Karl Lashley, 1931*

Distinct Visual Pathways



A Simple Question:

If fMRI is so slow, why not record electrical signals to correct the fMRI timing?

Source Localization (Forward Model)

Signal at Sensor *j*

Lead Field

Location

Oriented Magnitude

$$\mathbf{x}_j(\mathbf{r}_i,\mathbf{q}_i,t) = \sum_{i=1}^{K} G(\mathbf{r}_i(t),\mathbf{p}_j)\bullet\mathbf{q}_i(t) + \varepsilon$$

Position of Sensor *j*

The Lead Field is interpreted as the signal detected by the given electrode from a Unit Dipole at the given location

Inverse Problem

Error model

$$\varepsilon(\mathbf{r},\mathbf{q}) = \sum_{i}^{K} \sum_{t=t_1}^{t_2} \sum_{j}^{M} (\mathbf{x}_j(t) - \hat{\mathbf{x}}_j(\mathbf{r}_i,\mathbf{q}_i,t))^2 + \lambda f(\mathbf{r},\mathbf{q})$$

$f(\mathbf{r},\mathbf{q}) > 0$ is used to regularize the solution

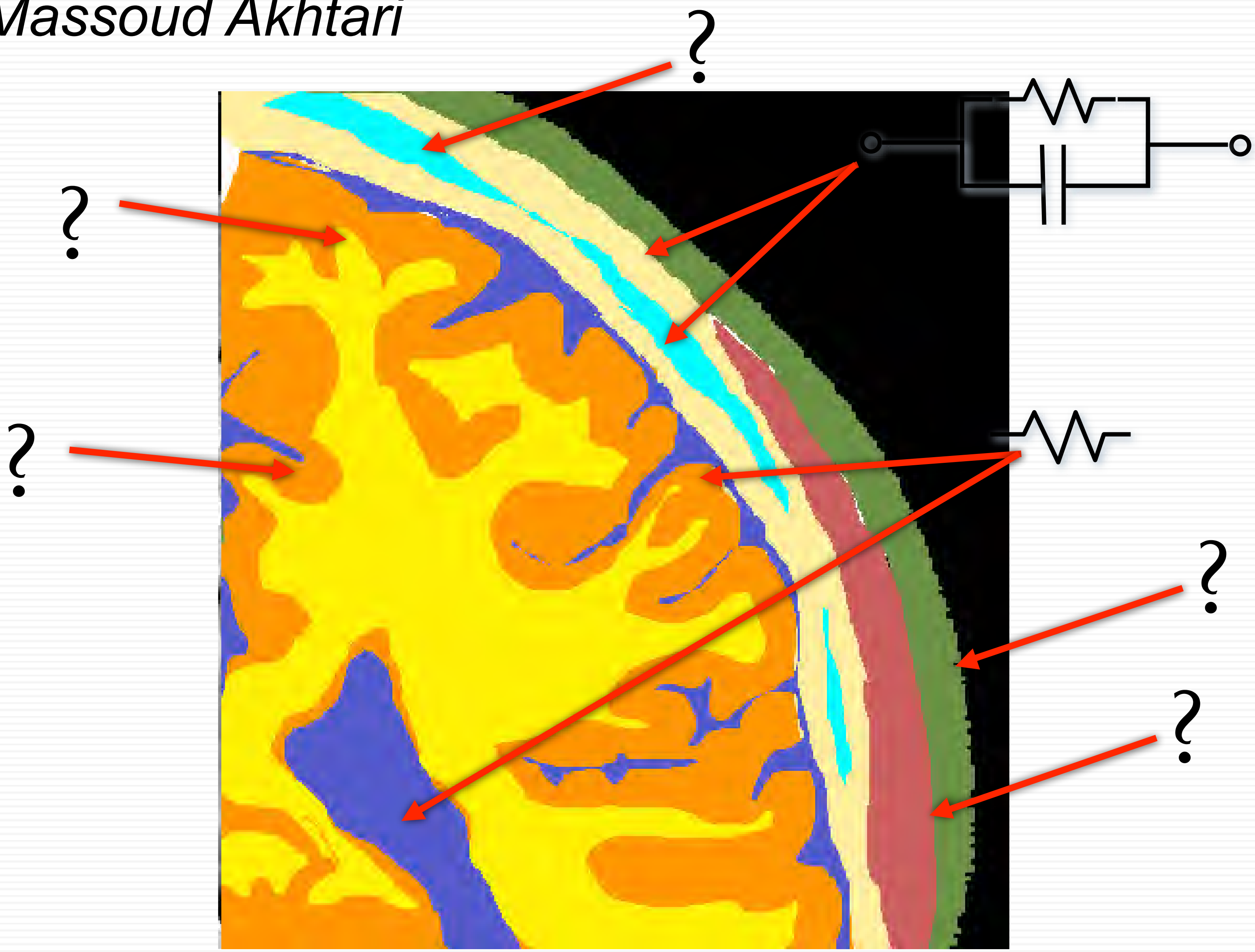
$\lambda > 0$ trades fit against regularization

General Limitations in EEG Localization

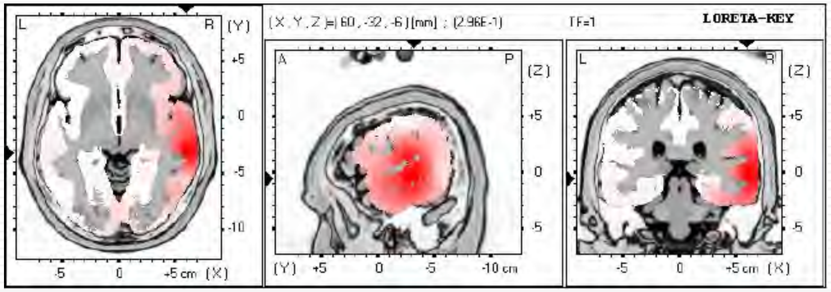
- Deeper Sources Show Weaker Signals
- Magnitude Depends on Dipole Orientation
- Magnitude Depends on Temporal Synchrony
- Magnitude Depends on Spatial Coherence
- Conductivity of Body Tissues (CSF, scalp) Blur the Scalp Potentials
- Accuracy is Limited by Knowledge of Electrode Locations Relative to Brain Structures

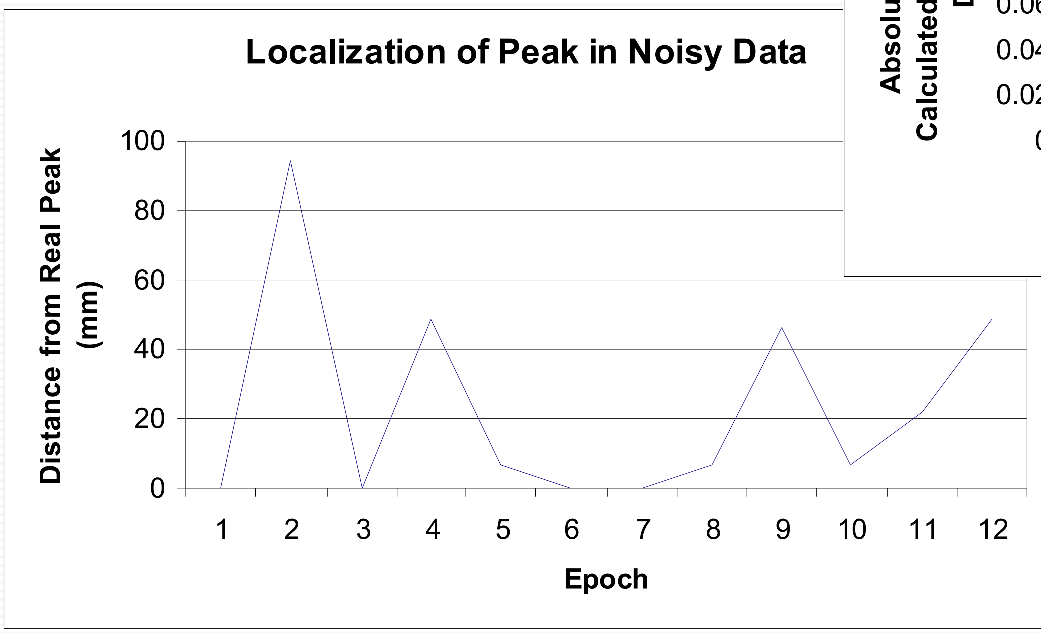
EEG Source Localization

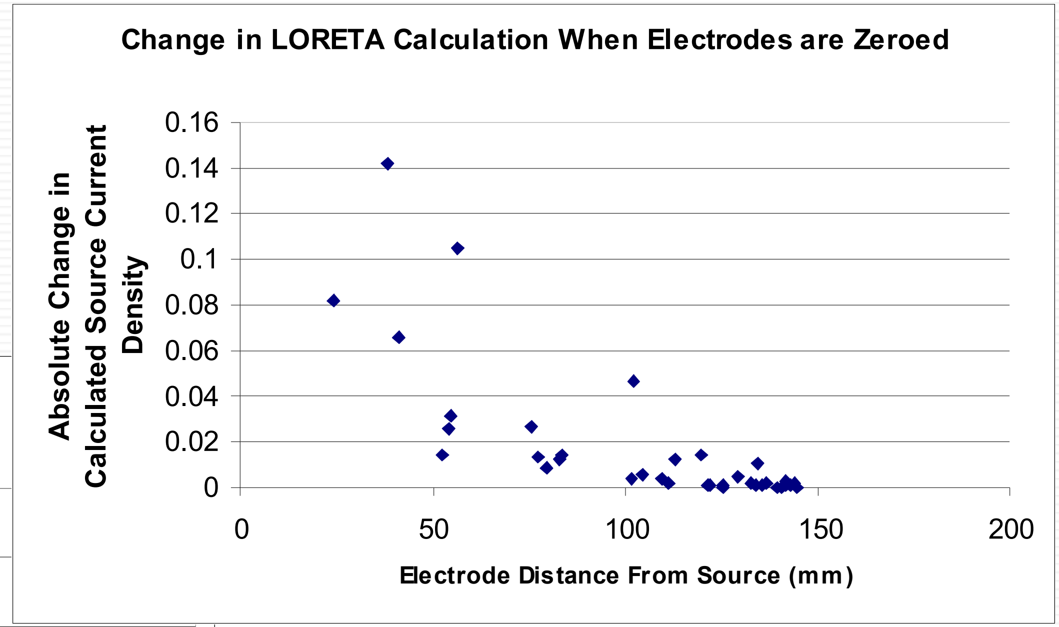
after Massoud Akhtari



Source Localization Stability (LORETA)



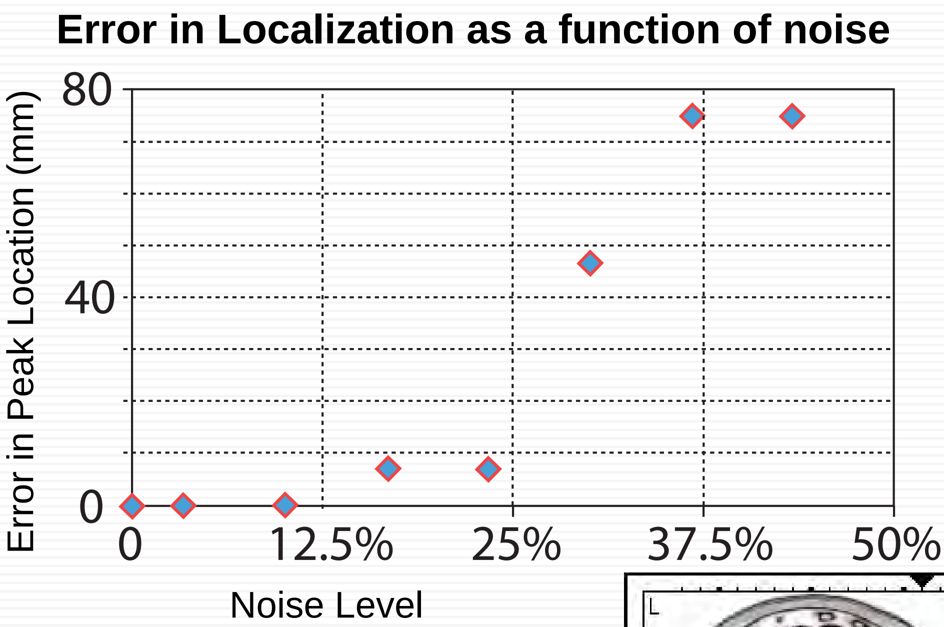


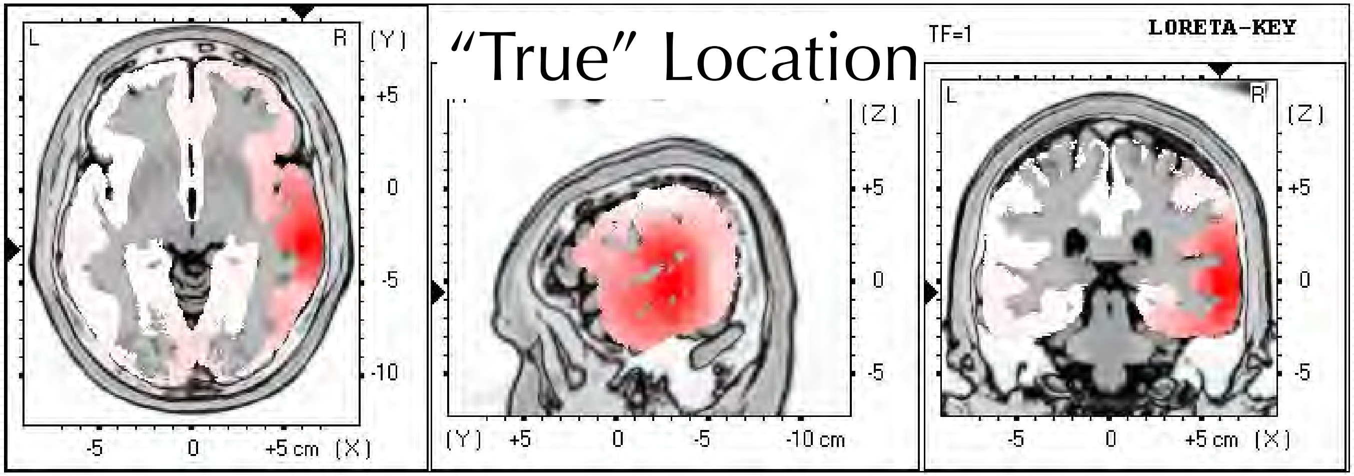


Nominal EEG Amplitude: 18

From Alex Korb (unpublished)

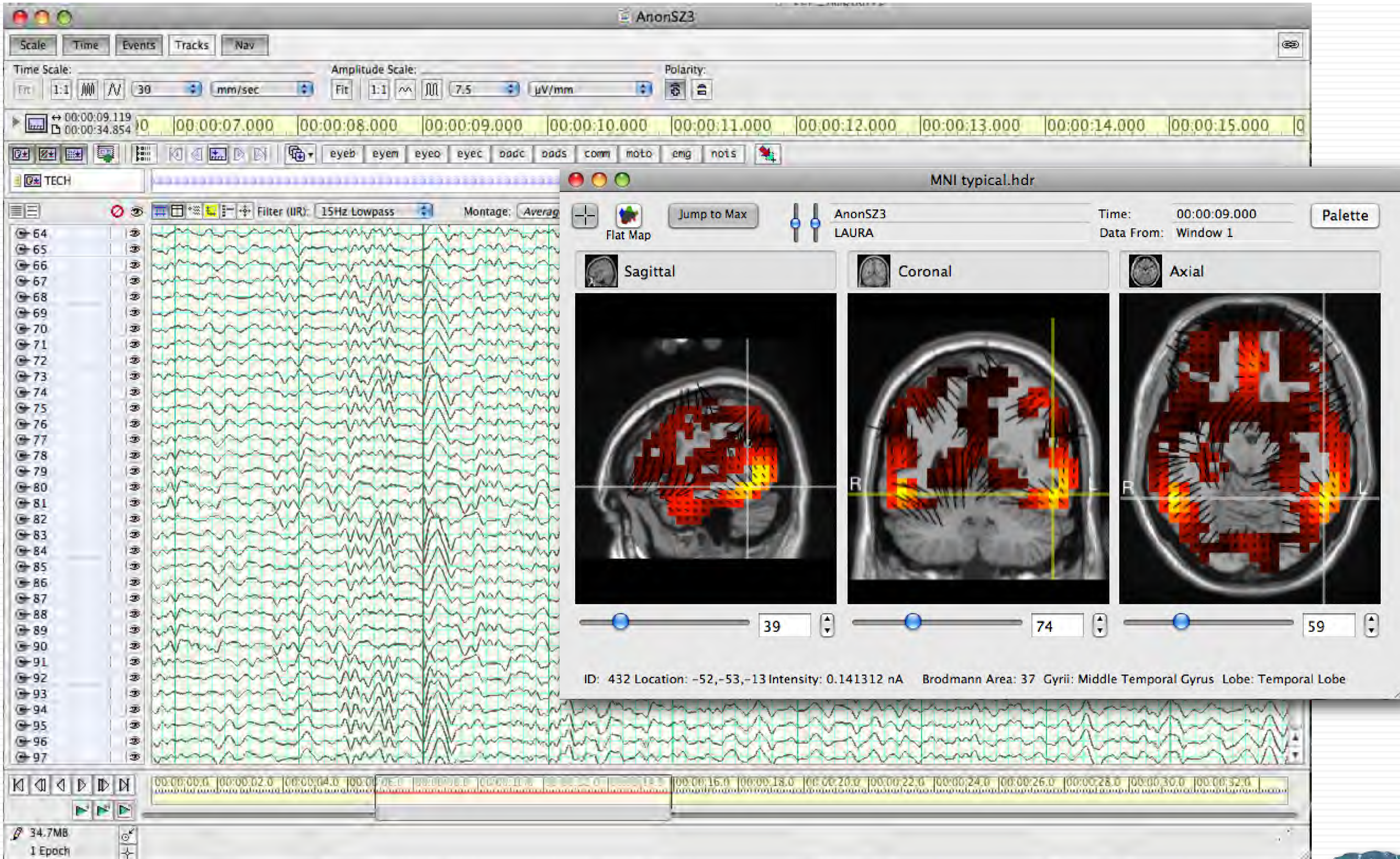
Source Localization Stability (LORETA)





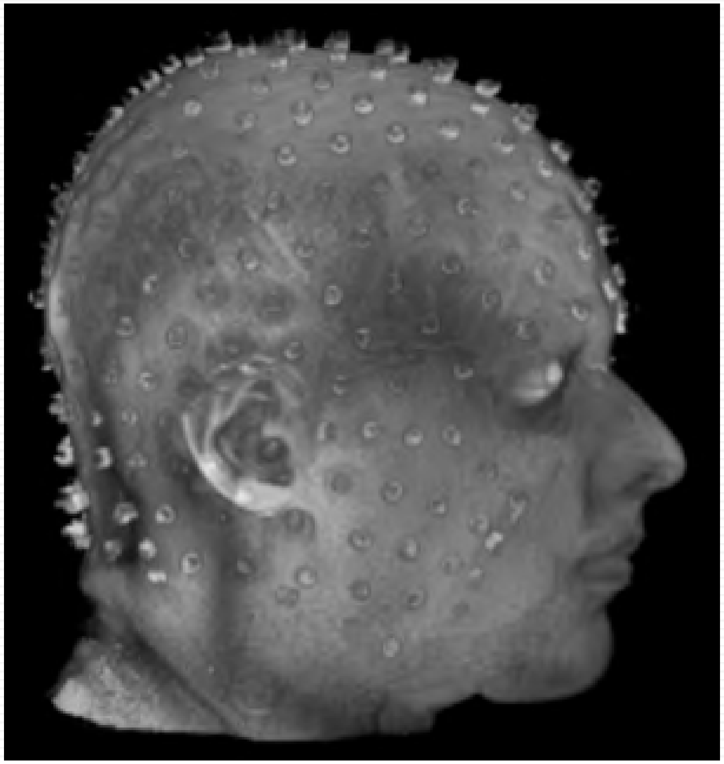
From Alex Korb (unpublished)

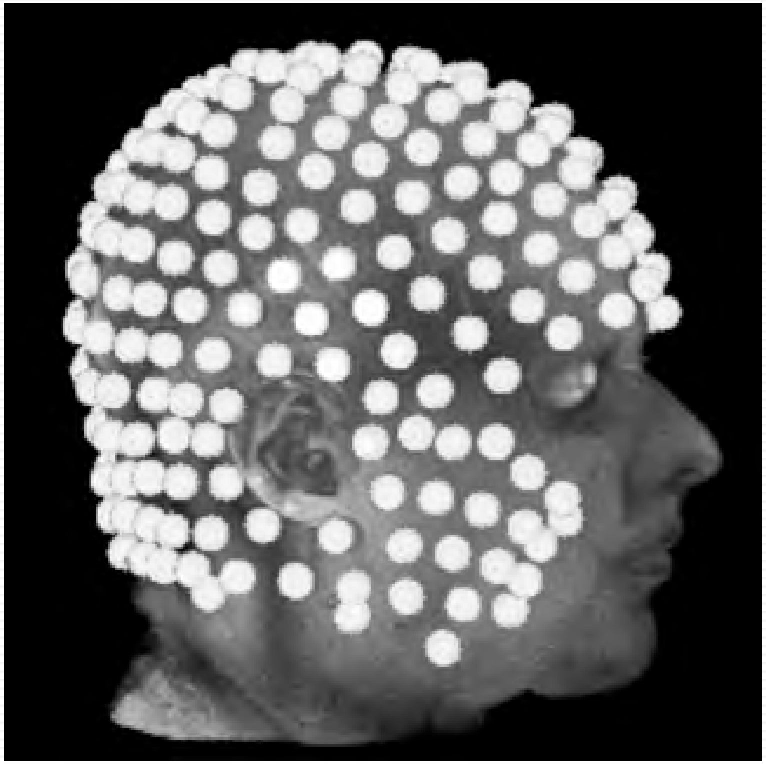
High Density EEG



Courtesy Electrical Geodesics, Inc.

Electrodes Can be Made Visible to MRI



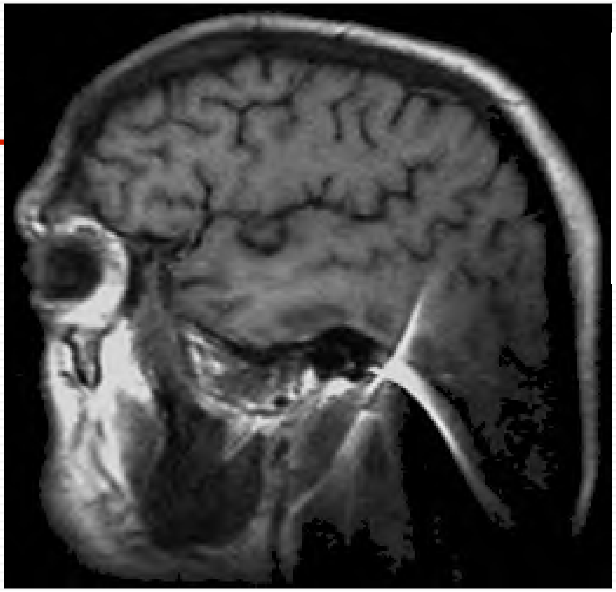


Cameron Rodriguez
Work in Progress

Combining EEG and MRI

- Project Goals
  - Unaltered MR Image Quality
  - Diagnostic Quality EEG During functional MRI:
  - Artifact Free
  - Dense Array of Channels
  - Tomographic Correlation of Scalp Electrical Activity
  - [Amplifiers Suitable for Single Units]
  - Subject Safety

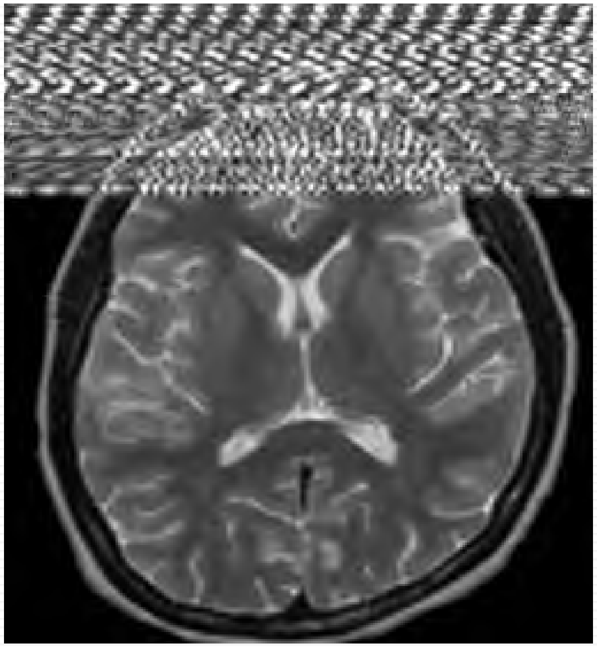
Artifacts - MRI



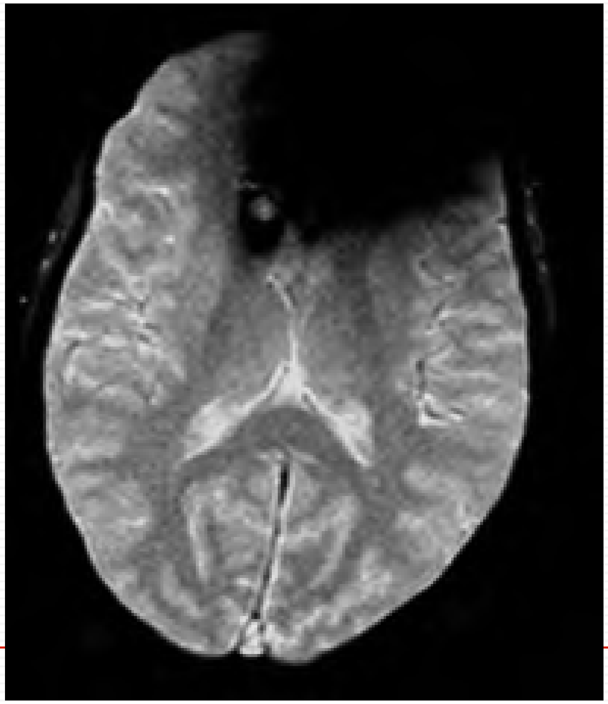
Magnetic Field Distortion

Non-magnetic material such as Silver

RF Noise



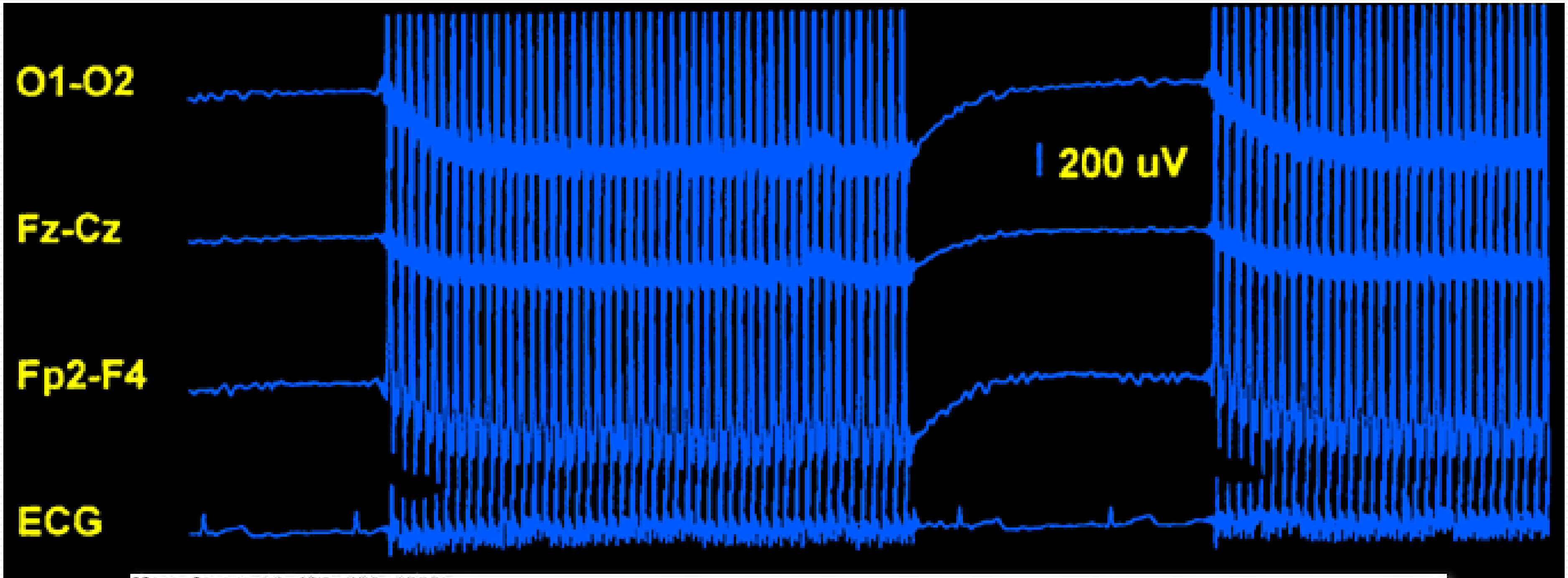
- *Properly-shielded Amplifiers*
- *Softened Logic Pulses*



Signal Losses

- *Careful Lead Dress*
- *Eliminate RF Loops*

EEG Amplifier Recovery



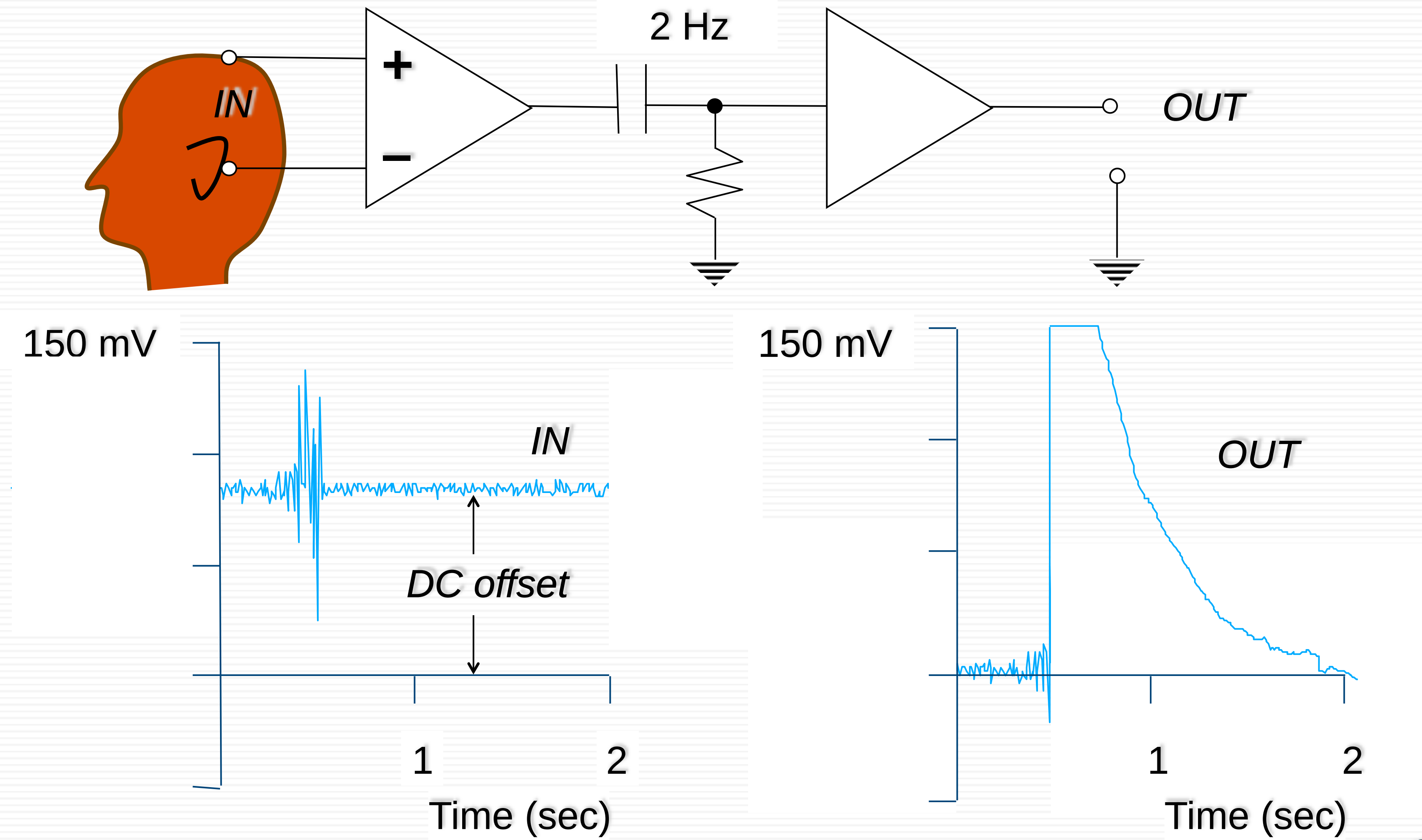
NeuroImage 12, 230–239 (2000)

A Method for Removing Imaging Artifact from Continuous EEG Recorded during Functional MRI

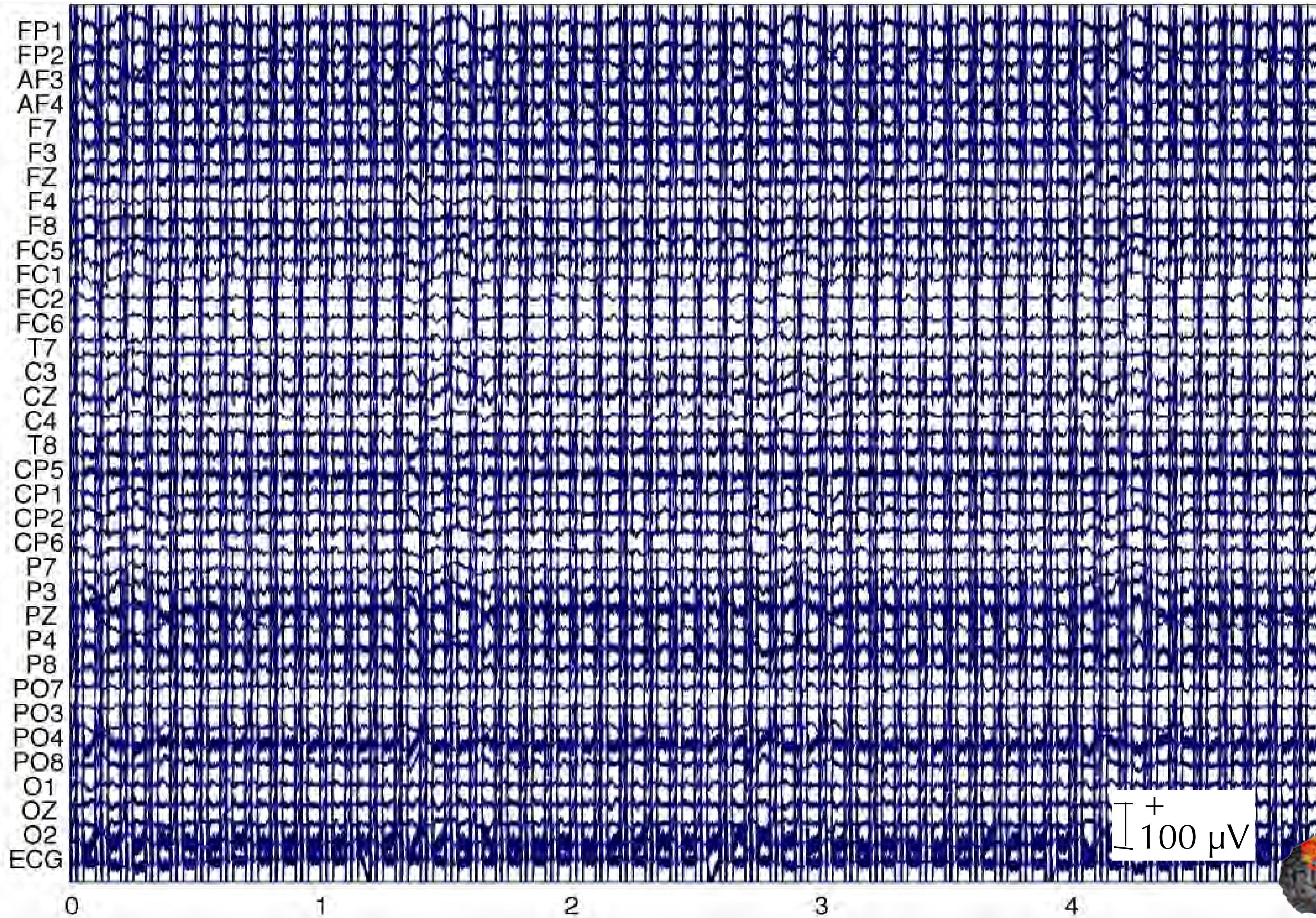
Philip J. Allen,* Oliver Josephs,† and Robert Turner†

*Department of Clinical Neurophysiology, National Hospital for Neurology and Neurosurgery, University College London Hospitals, Queen Square, London WC1N 3BG, United Kingdom; and †The Wellcome Department of Cognitive Neurology, Institute of Neurology, University College London, Queen Square, London, United Kingdom

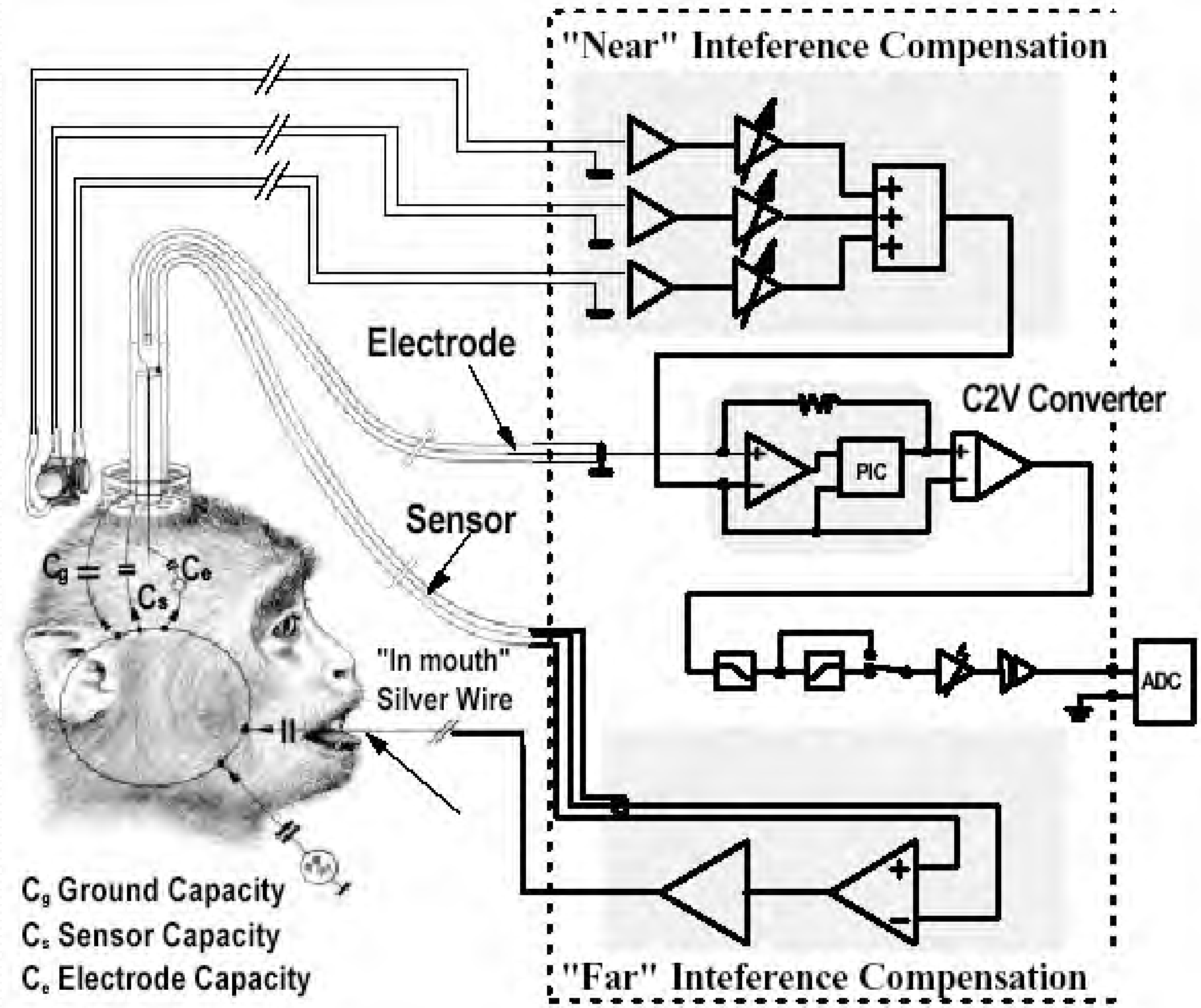
Receiver Saturation

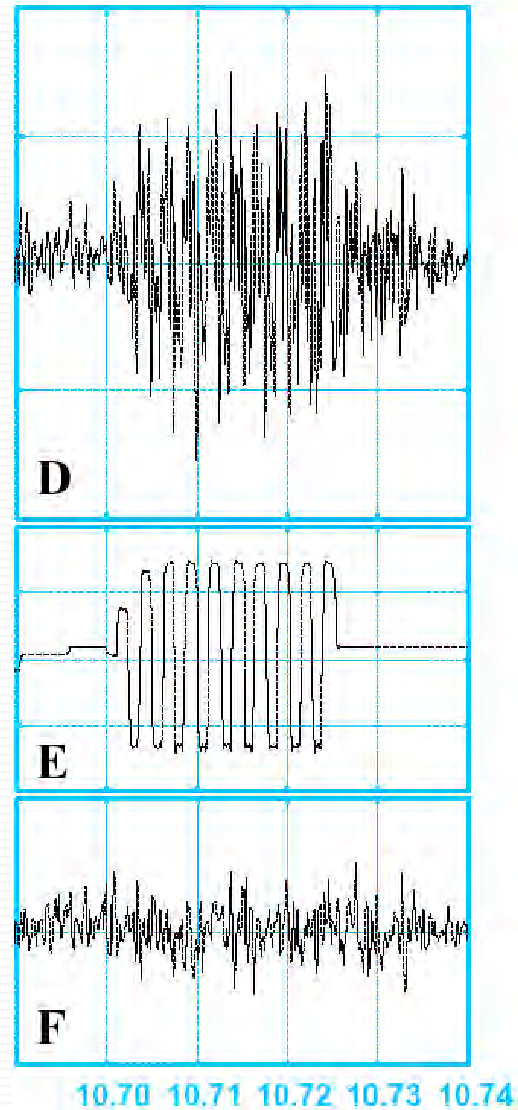


Artifacts During Scanning



Logothetis (recording method)





BOLD response reflects synaptic activity

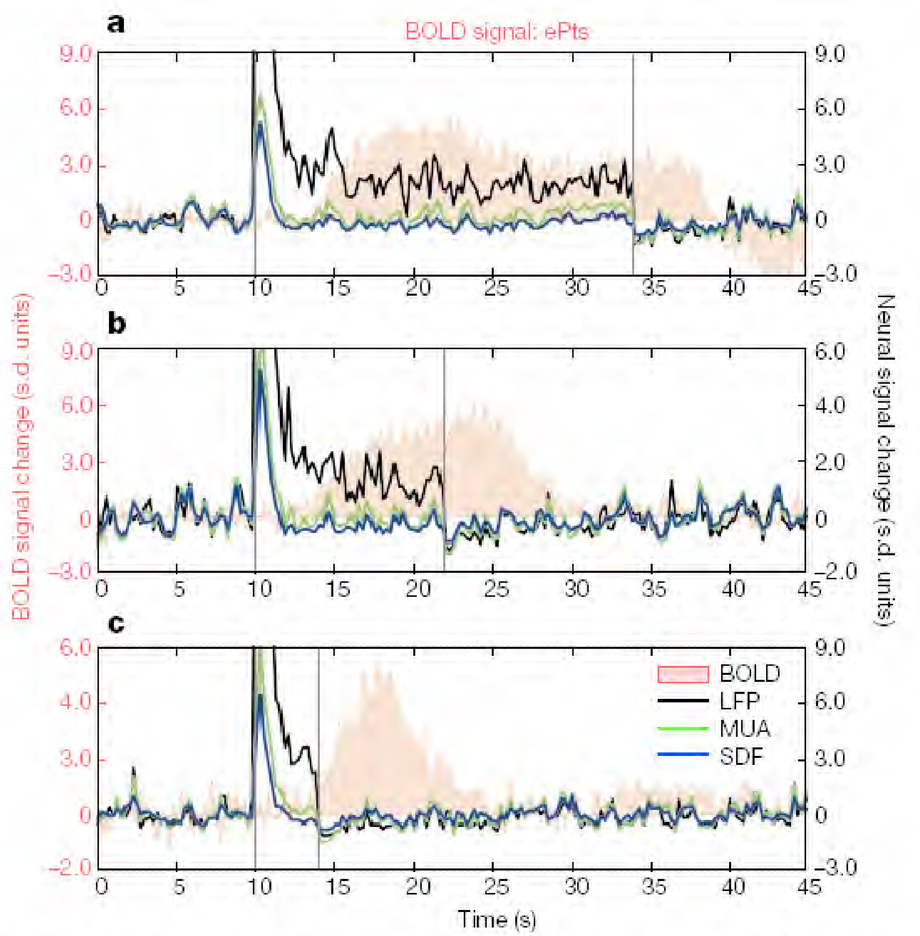


Figure 3 Simultaneous neural and haemodynamic recordings from a cortical site showing transient neural response. **a**–**c**, Responses to a pulse stimulus of 24, 12 and 4 s. Both single- and multi-unit responses adapt a couple of seconds after stimulus onset, with LFP remaining the only signal correlated with the BOLD response. SDF, spike-density function (see text); ePts, electrode ROI—positive time series.

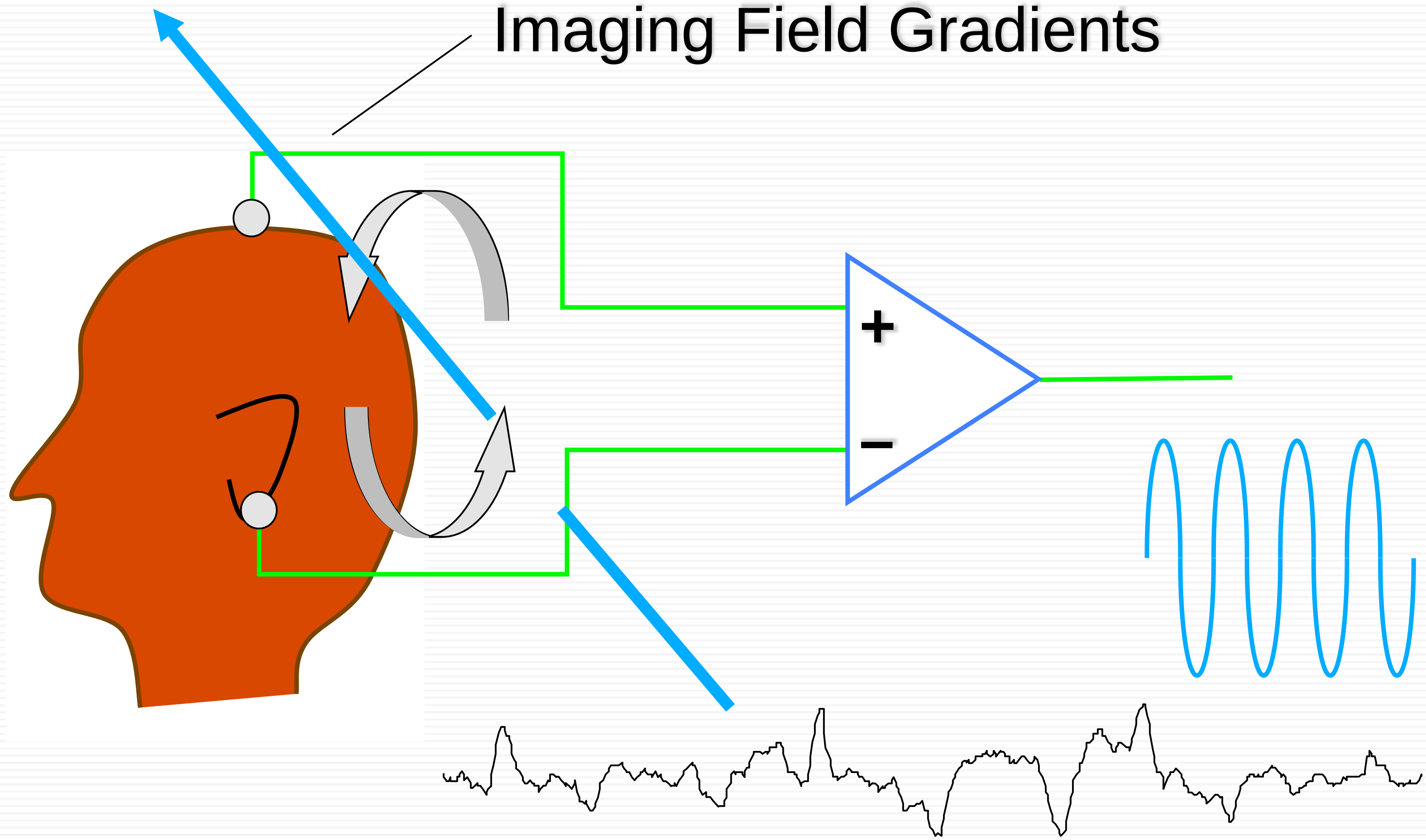
Local field potentials (LFP) reflect synaptic currents

Multi-unit activity (MUA) reflects spiking activity

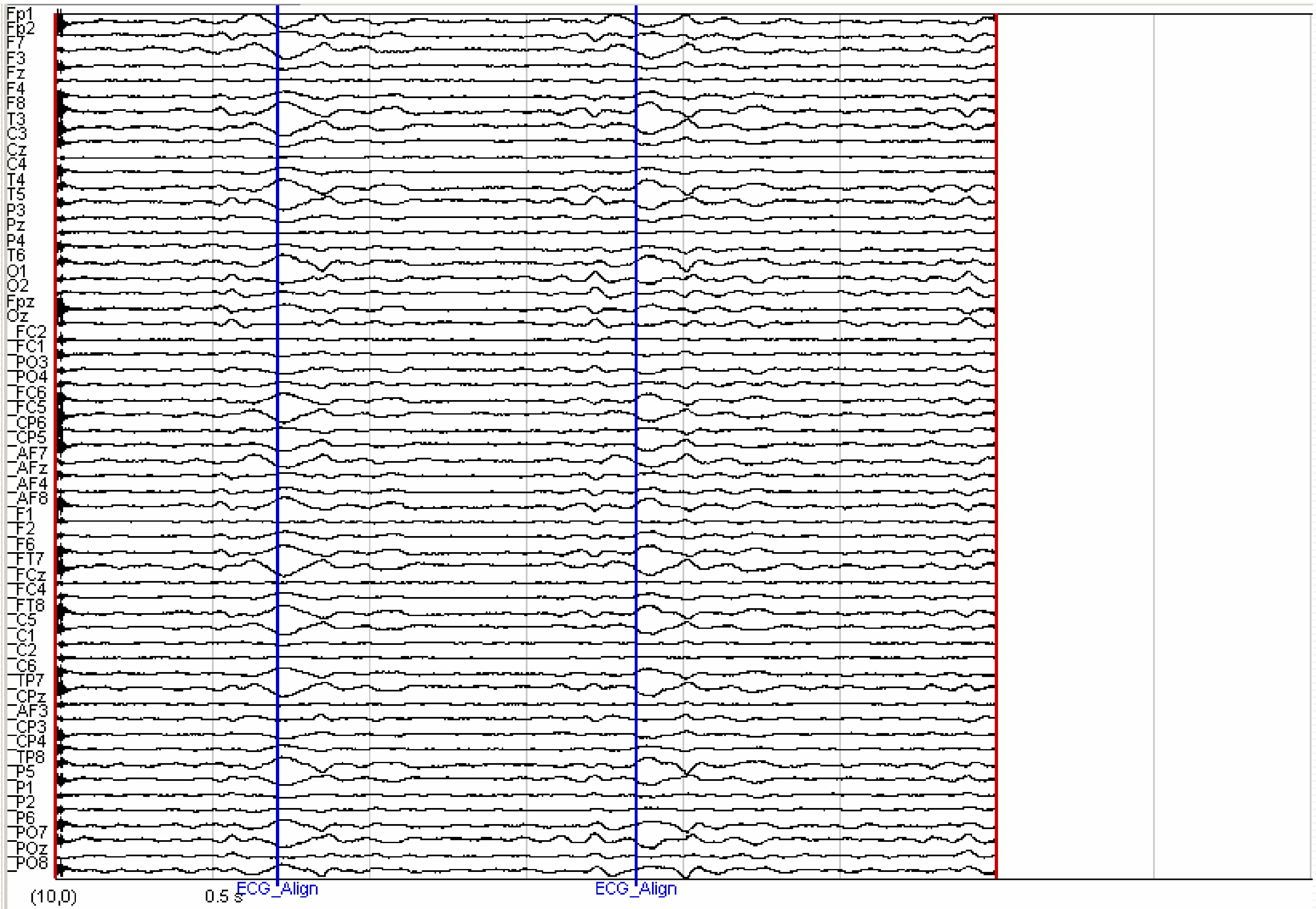
MUA attenuates quickly, while LFP shows an extended response that correlates better with the BOLD response

Logothetis, 2001

Inductive Pickup by EEG leads

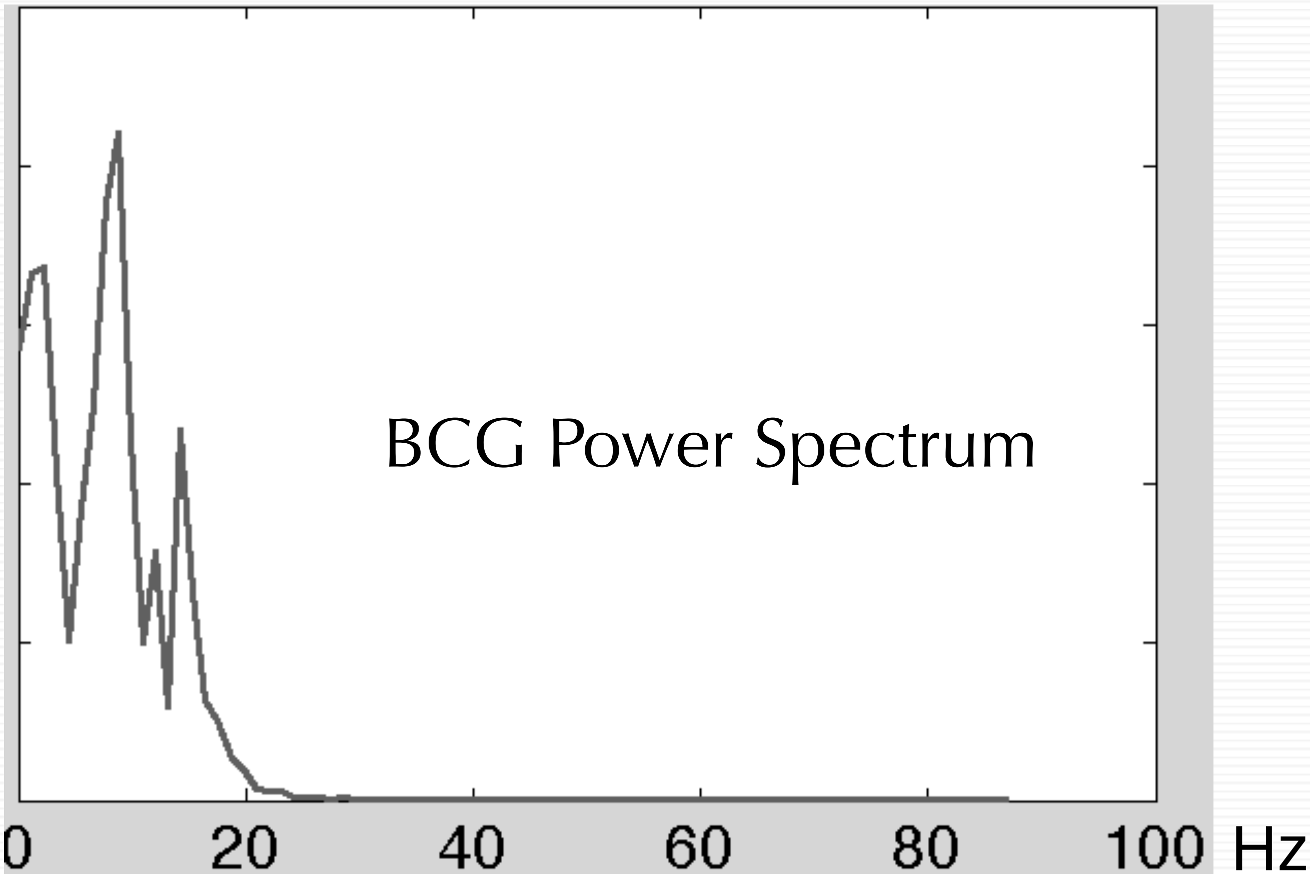


Ballistocardiogram

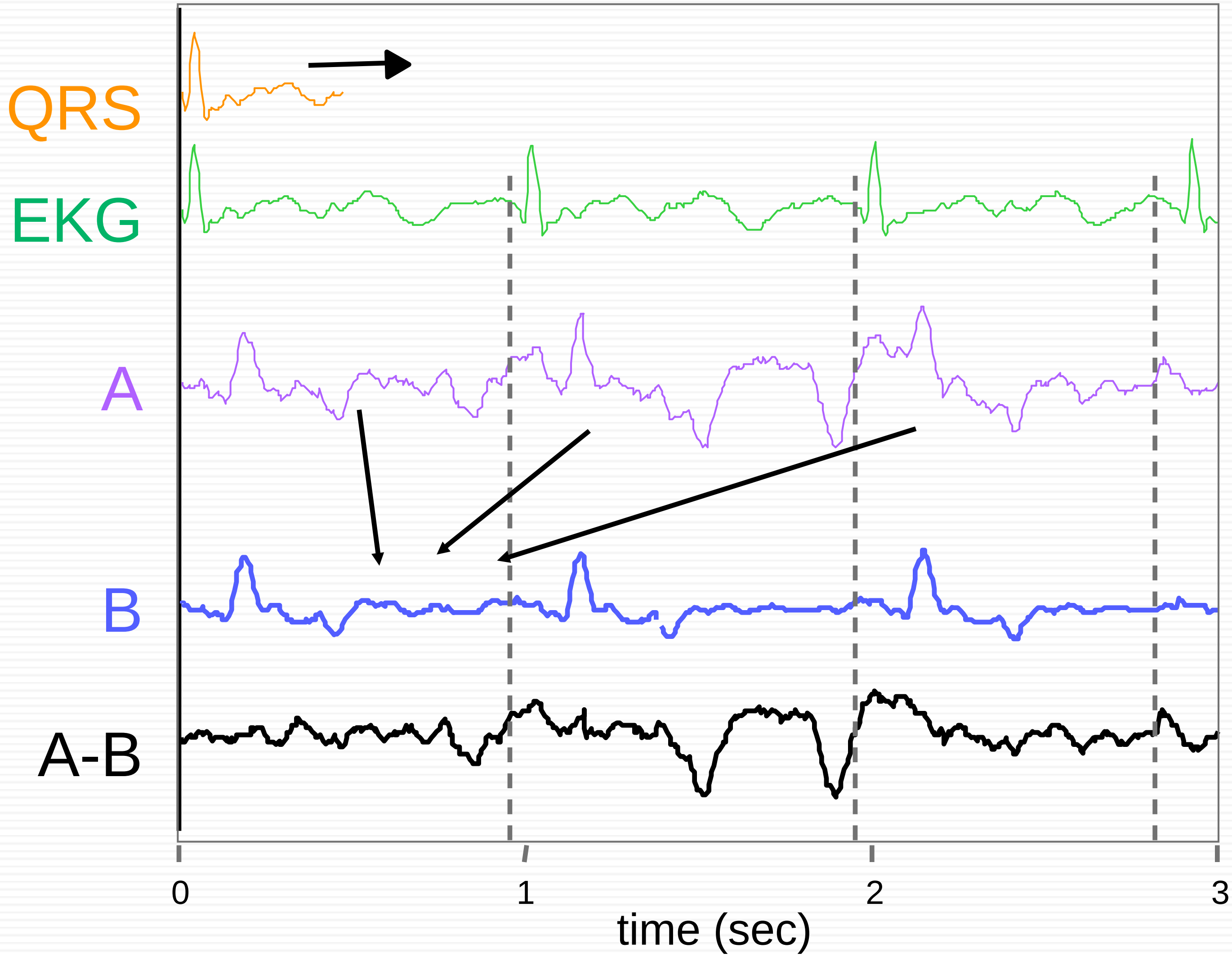


Jan de Munck

Can We Simply Filter?

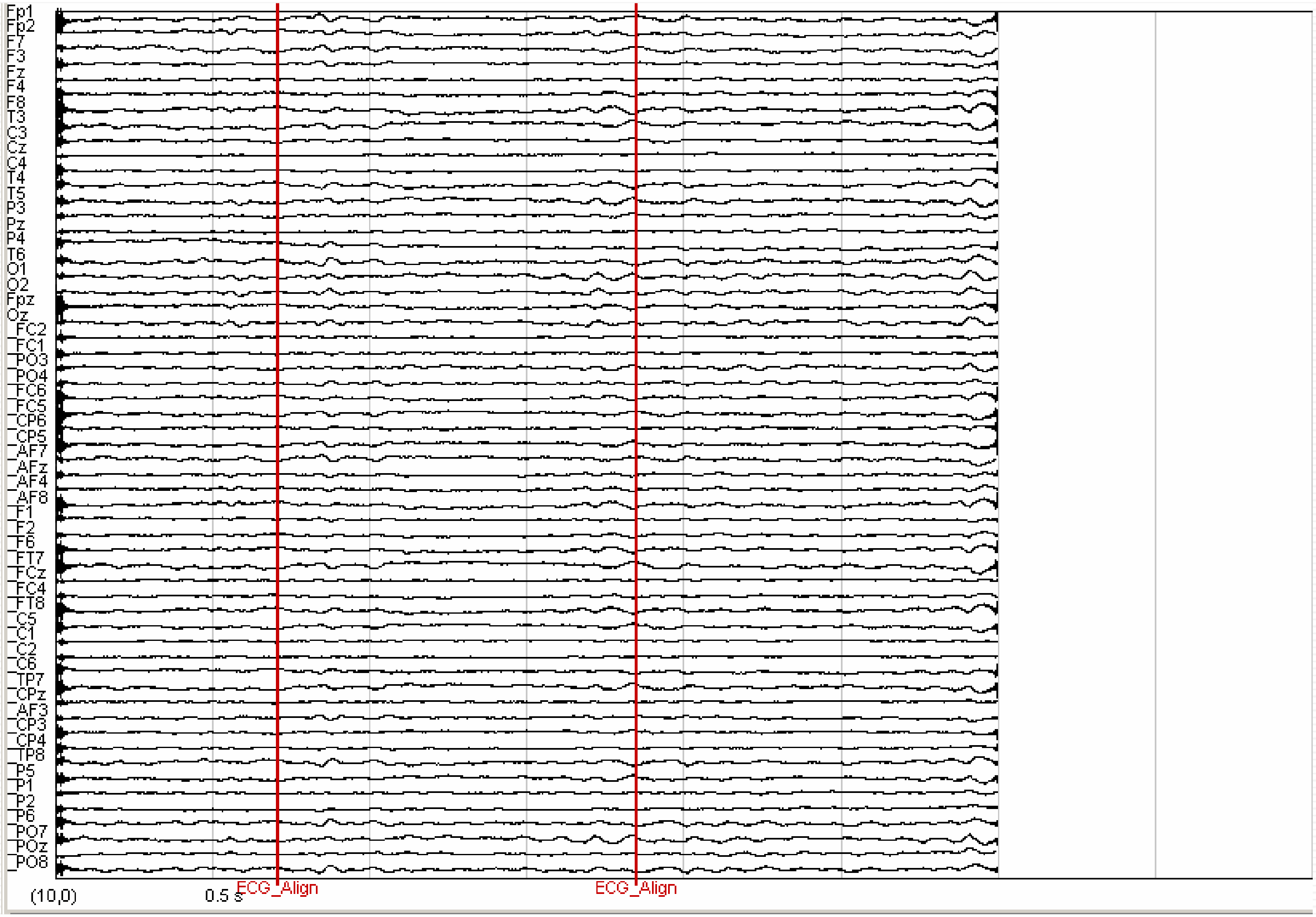


Ballistocardiogram Subtraction



Goldman, et al., Clinical Neurophysiology, 2000

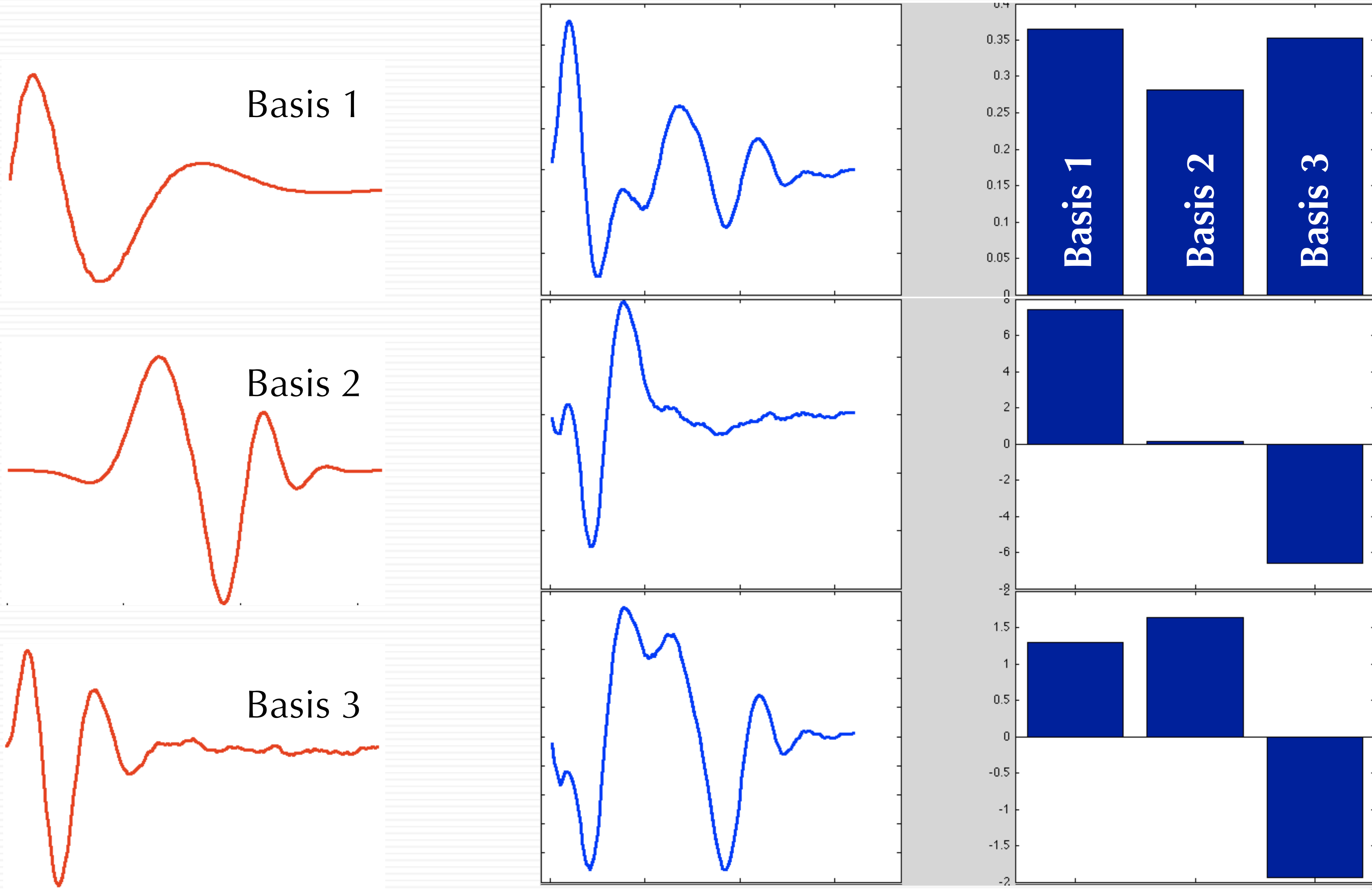
EEG after Ballistocardiogram Averaging



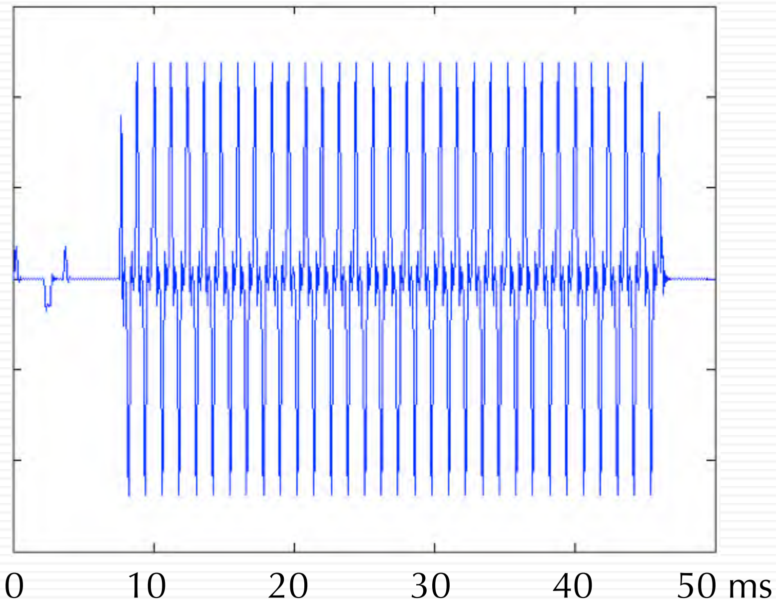
Jan de Munck

Optimal Basis Functions

- Model the BCG as the superposition of basis functions

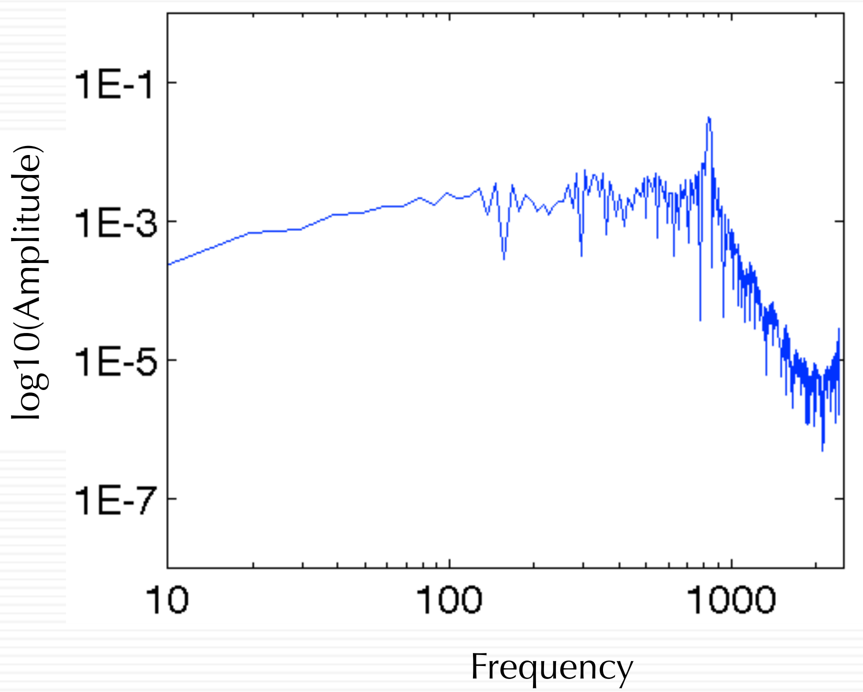


Spectral Suppression

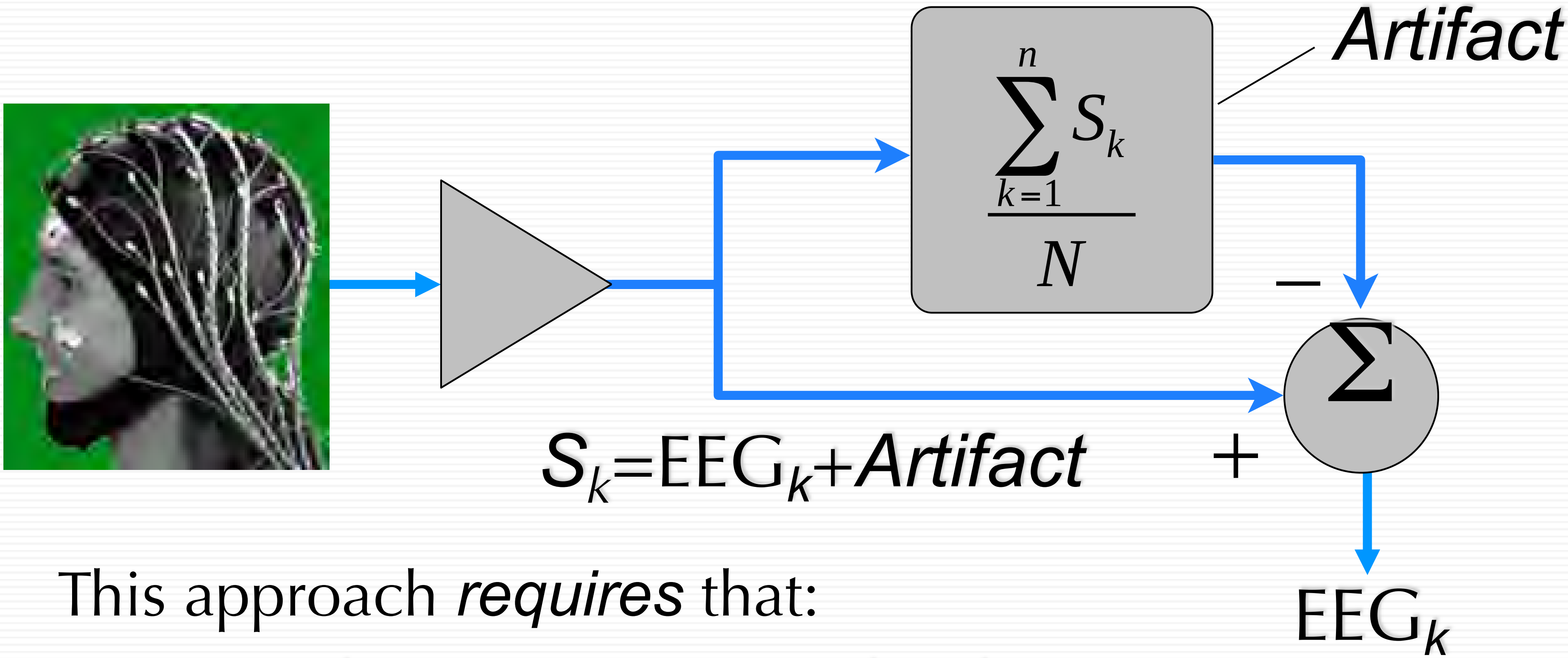


MR Artifact

Artifact Spectrum



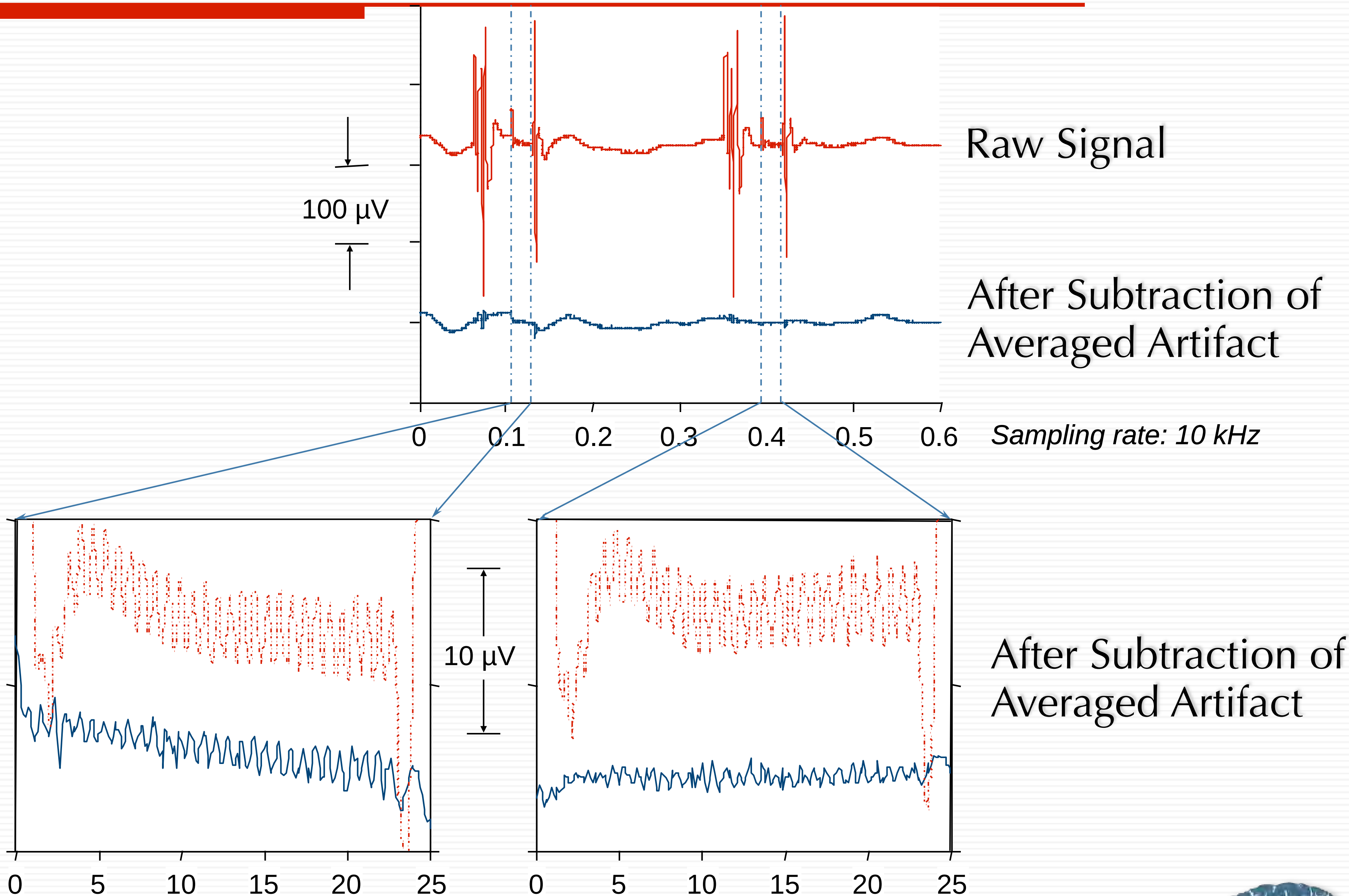
Approach to MR Artifact Removal



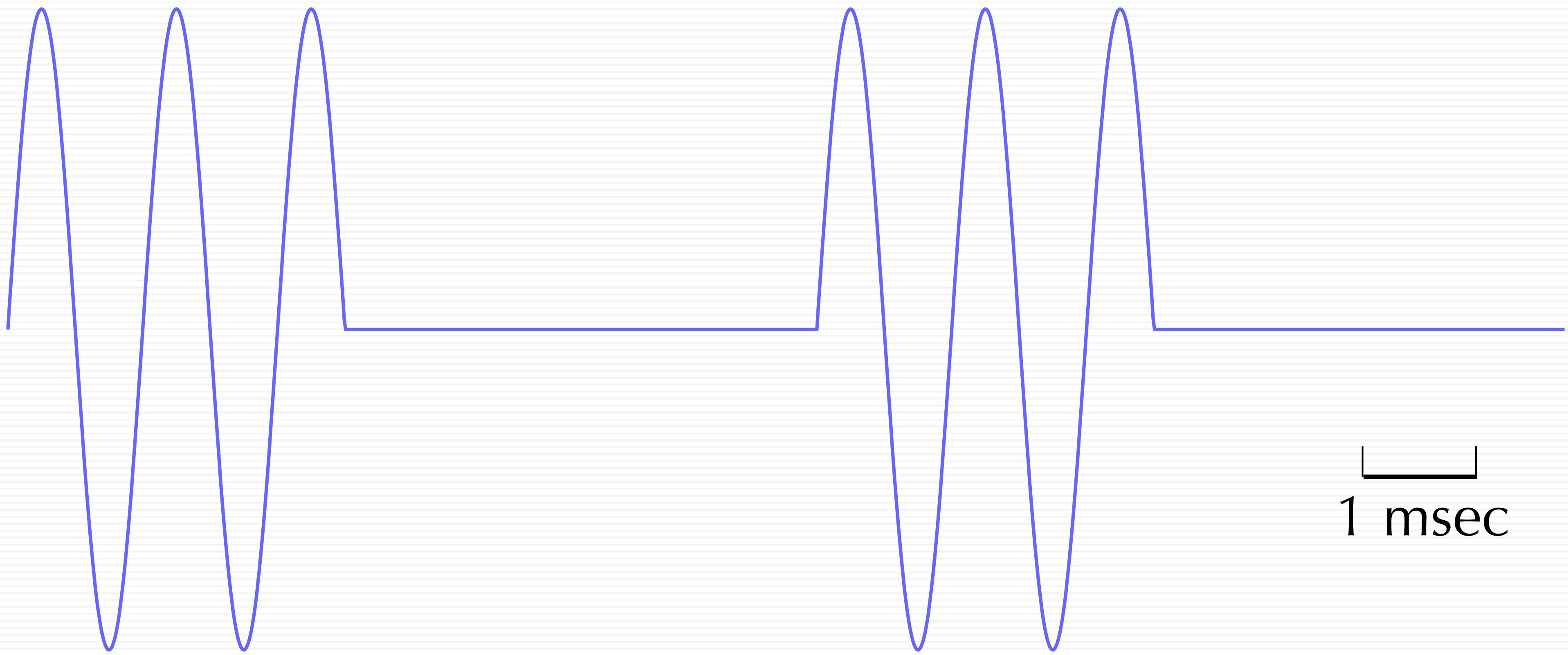
This approach ***requires*** that:

- EEG_k and *Artifact* are uncorrelated
- EEG_k and *Artifact* add linearly
- *Artifact* is identical at each time (k)

Fast Sampling is NOT enough

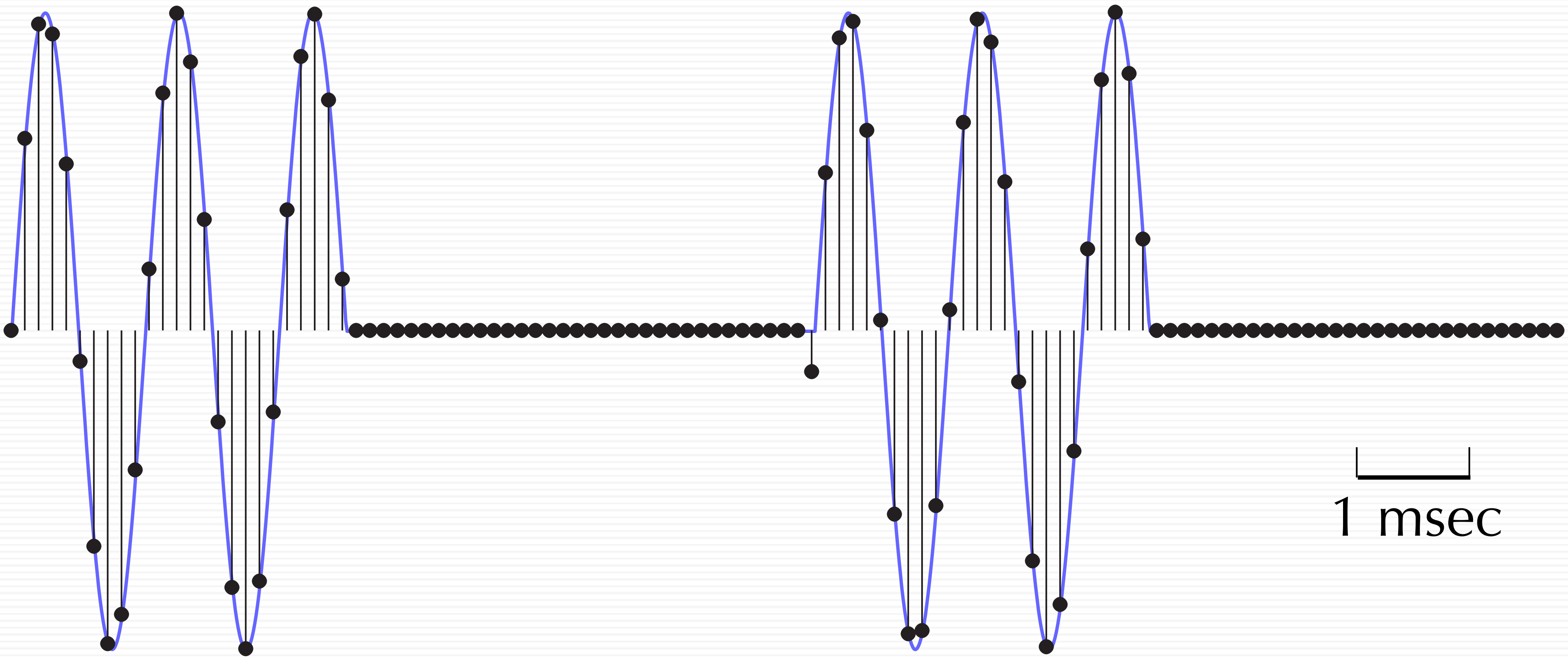


Sampling and Nyquist



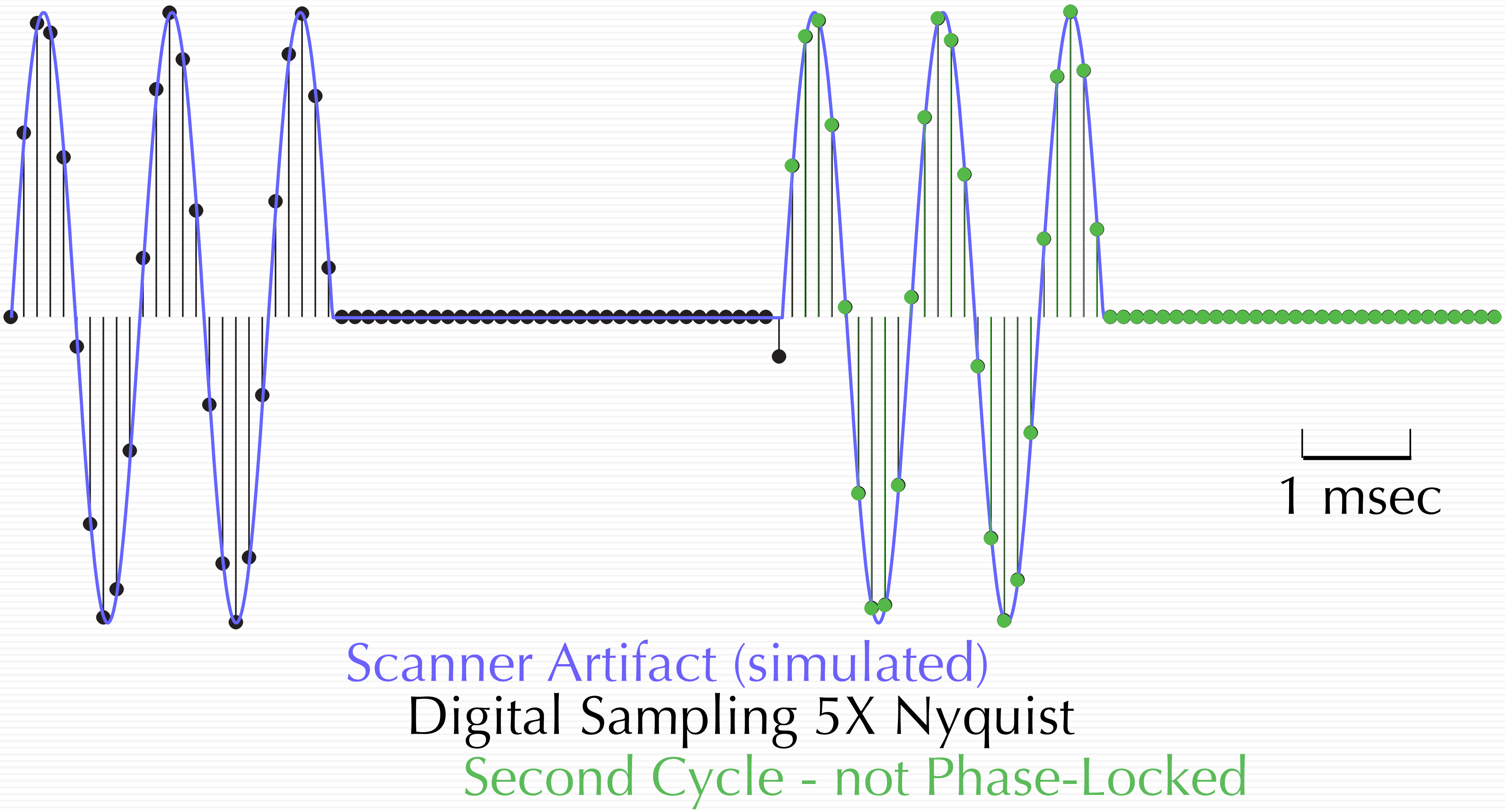
Scanner Artifact (simulated)

Sampling and Nyquist

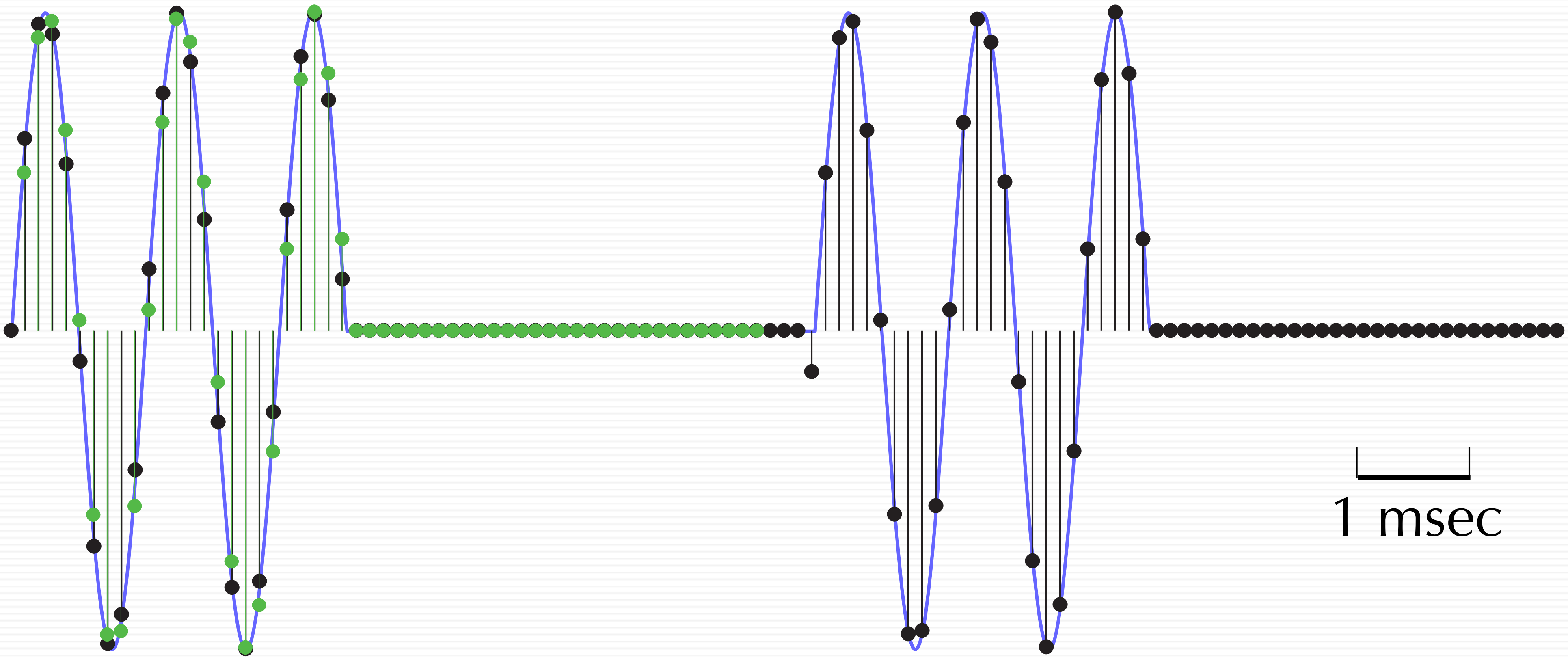


Scanner Artifact (simulated)
Digital Sampling >5X Nyquist

Sampling and Nyquist

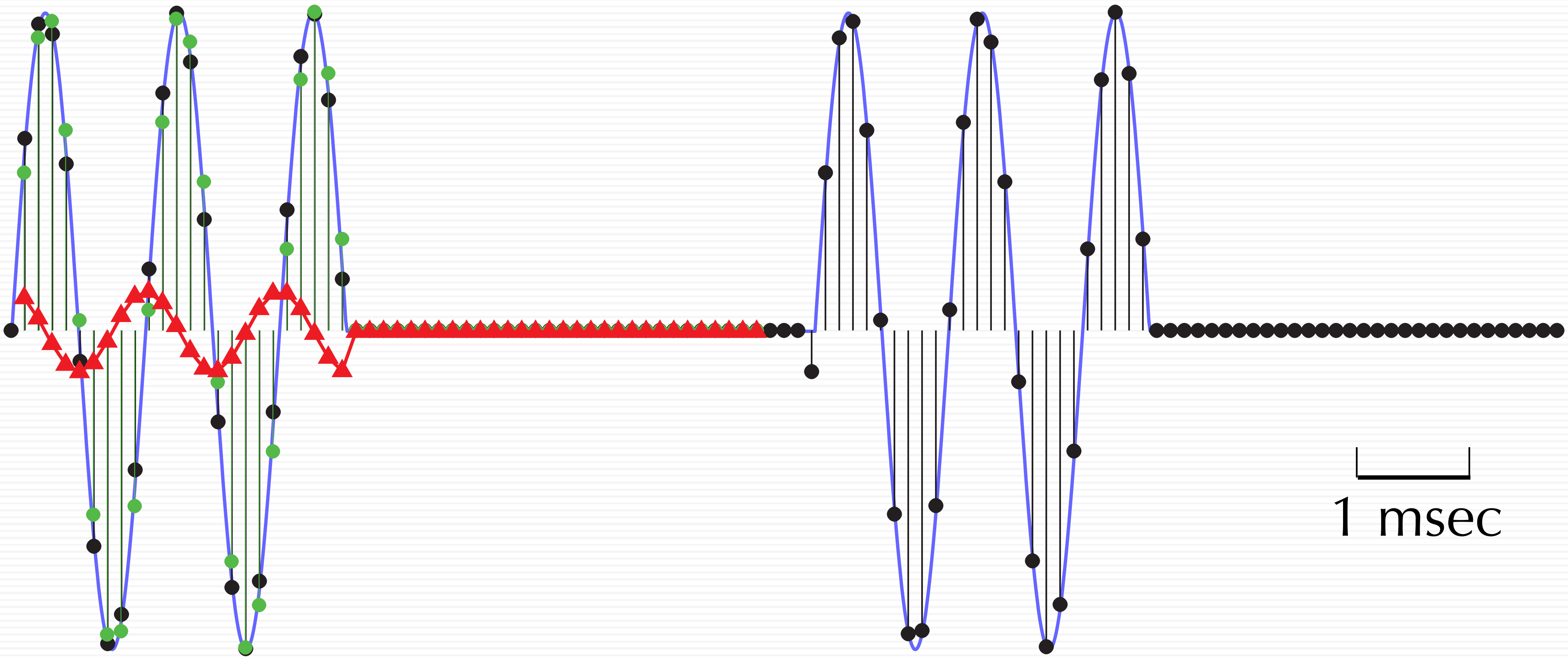


Sampling and Nyquist



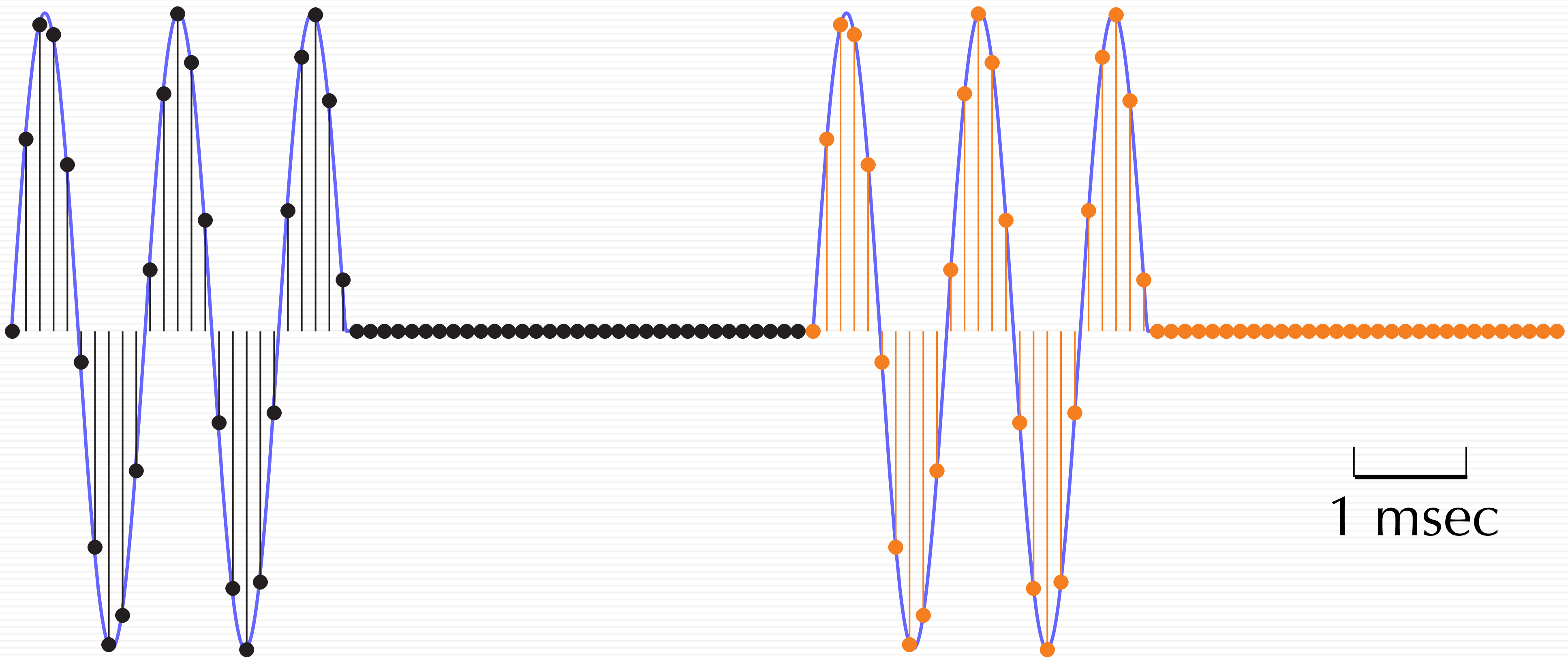
Scanner Artifact (simulated)
Digital Sampling 5X Nyquist
Second Cycle - not Phase-Locked

Sampling and Nyquist



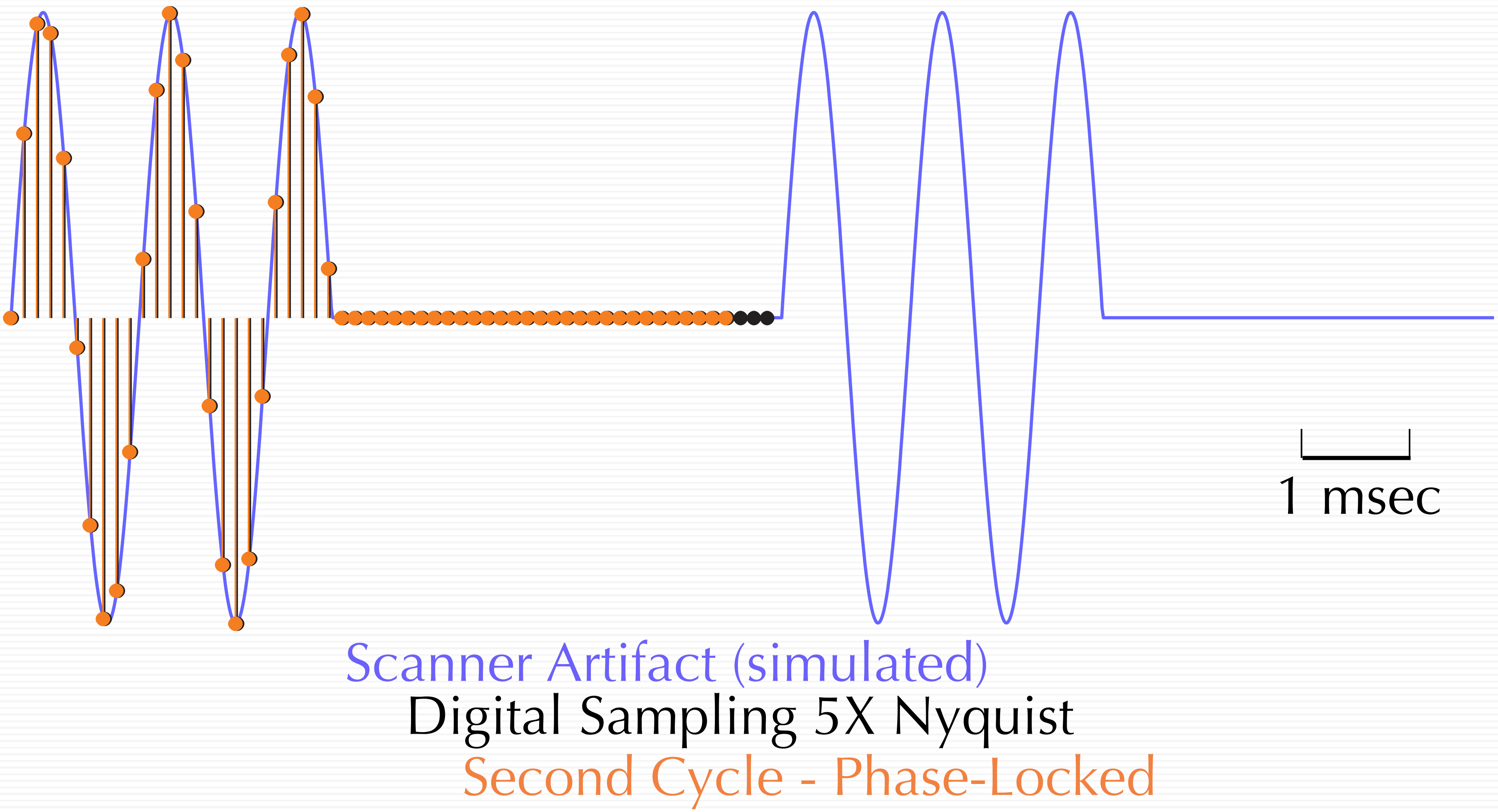
Scanner Artifact (simulated)
Digital Sampling 5X Nyquist
Second Cycle - not Phase-Locked
Error Difference Between Cycles

Synchronized Sampling

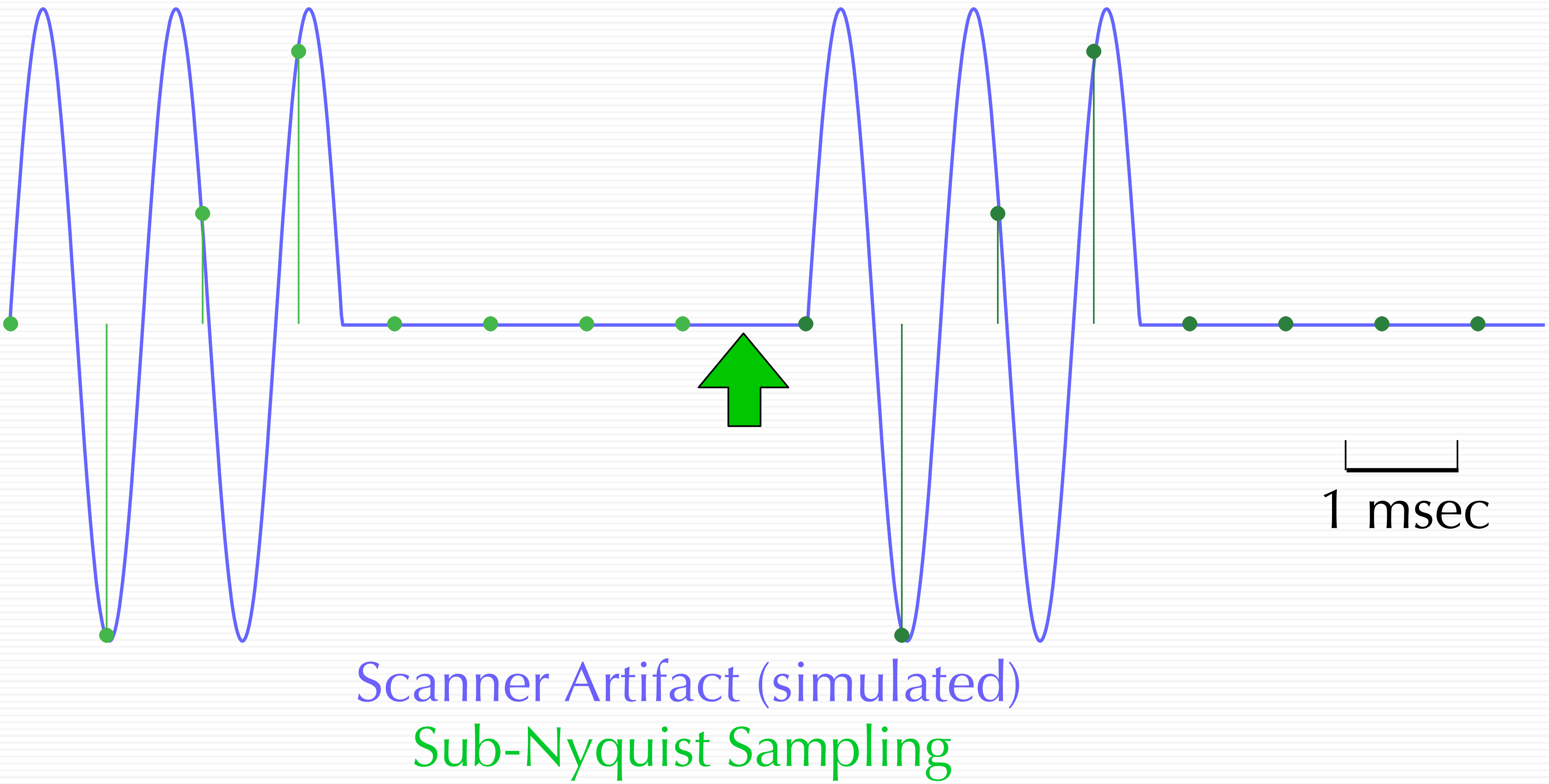


Scanner Artifact (simulated)
Digital Sampling 5X Nyquist
Second Cycle - Phase-Locked

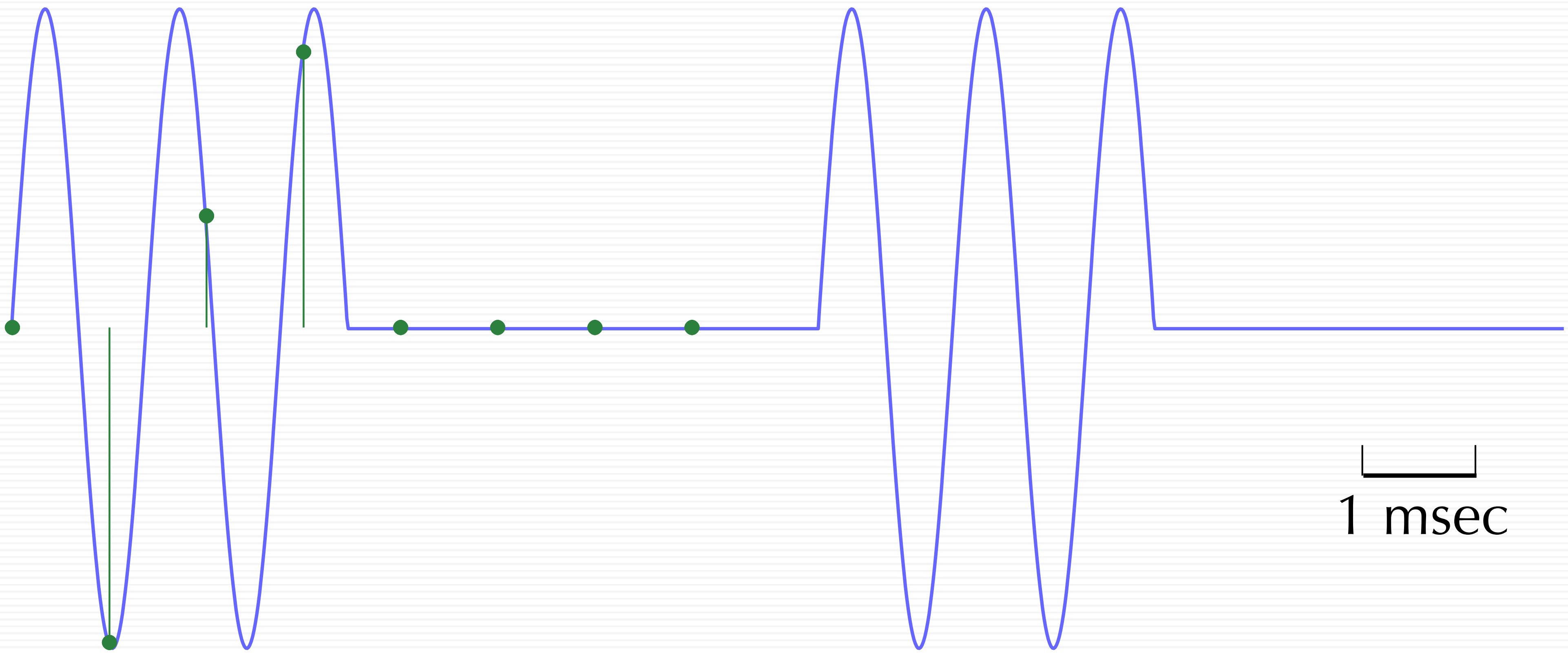
Synchronized Sampling



Synchronized Sampling



Synchronized Sampling

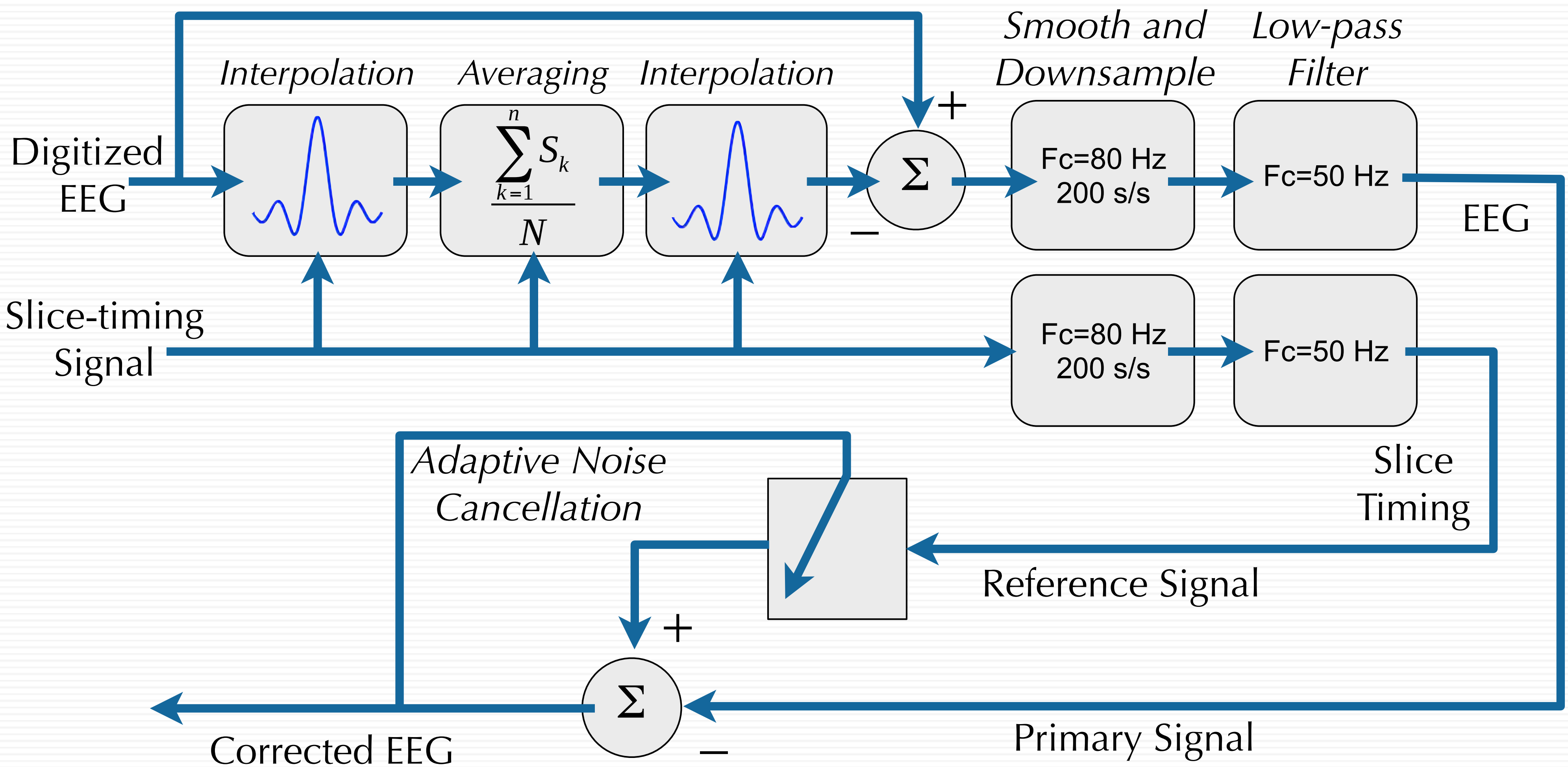


Scanner Artifact (simulated)

Sub-Nyquist Sampling

Error is Depends on ***Phase Accuracy*** - ***Independent*** of Sampling Rate

Allen Method



NeuroImage 12, 230–239 (2000)

A Method for Removing Imaging Artifact from Continuous EEG Recorded during Functional MRI

Philip J. Allen,* Oliver Josephs,† and Robert Turner†

Residual Errors

$$\varepsilon = \cos(2\pi ft) - \cos(2\pi ft - \varphi)$$
$$= \cos(2\pi ft)\cos(\varphi - 1) - \sin(2\pi ft)\sin\varphi$$

…where:

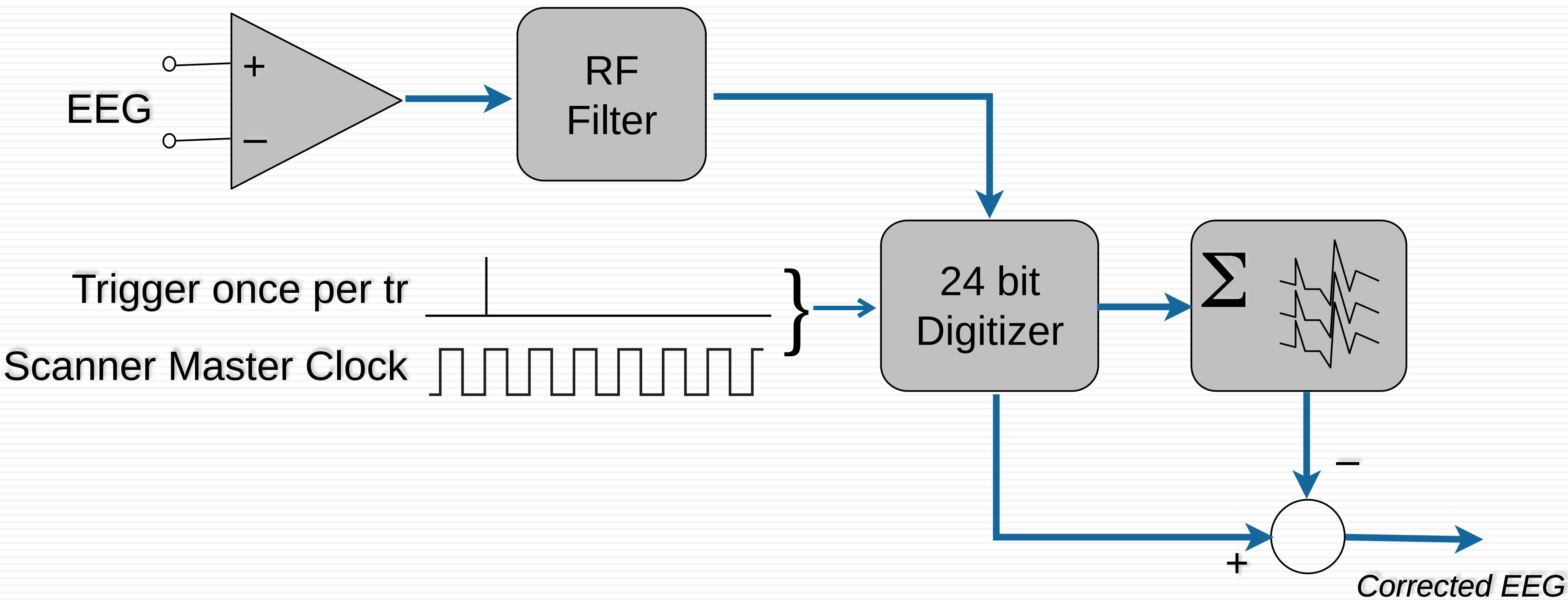
f is the frequency of the artifact

φ is the phase error, equal to $2\pi f_0/f_s$,

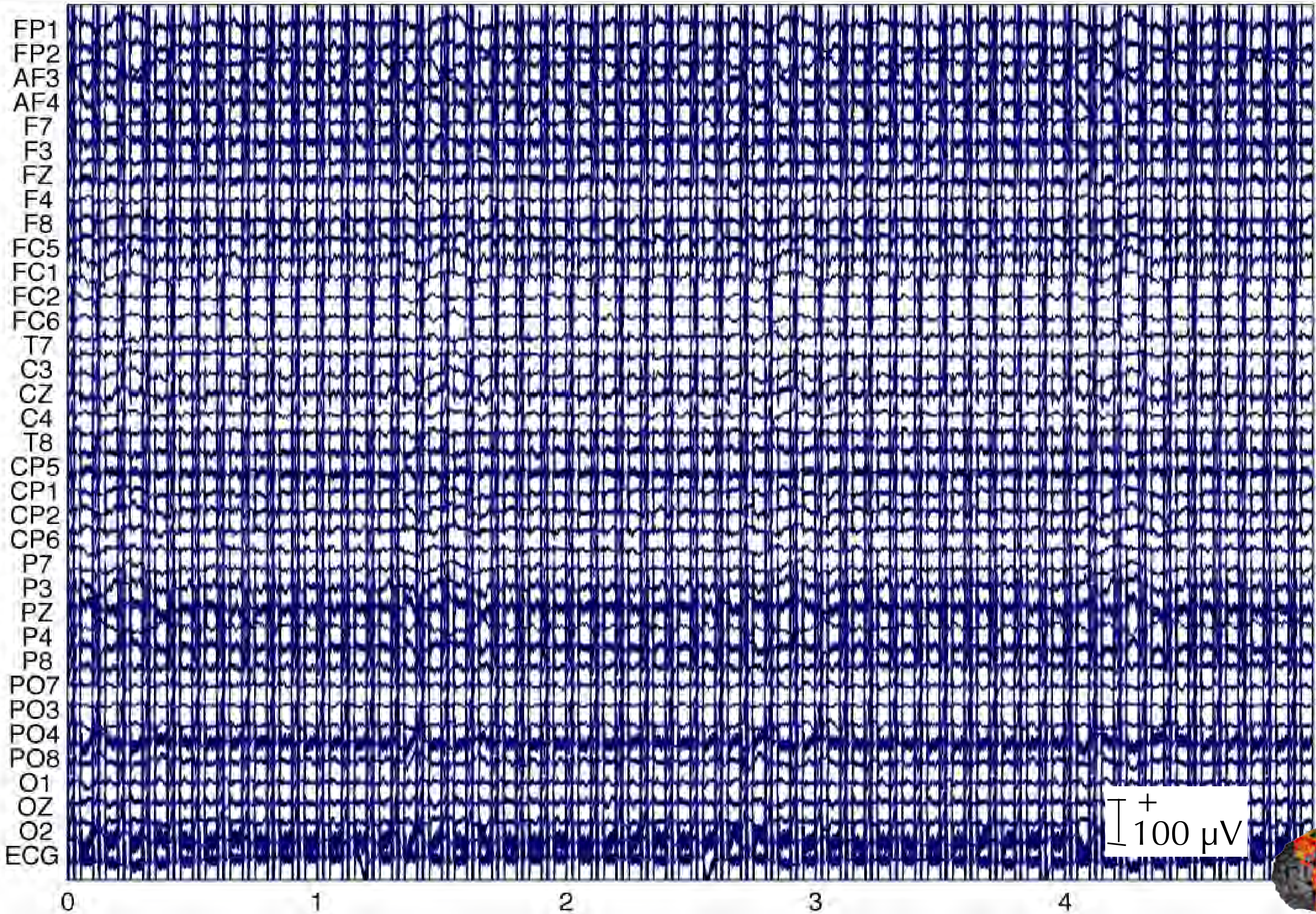
- f_0 is the EPI readout frequency and
- f_s is the sampling frequency.

At high sampling frequency (small φ) the error, ε, is linearly proportional to the sampling frequency

Synchronized Correction



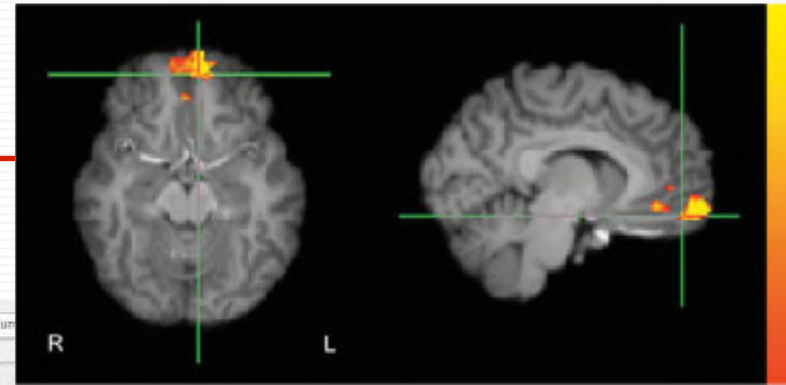
Artifacts During Scanning

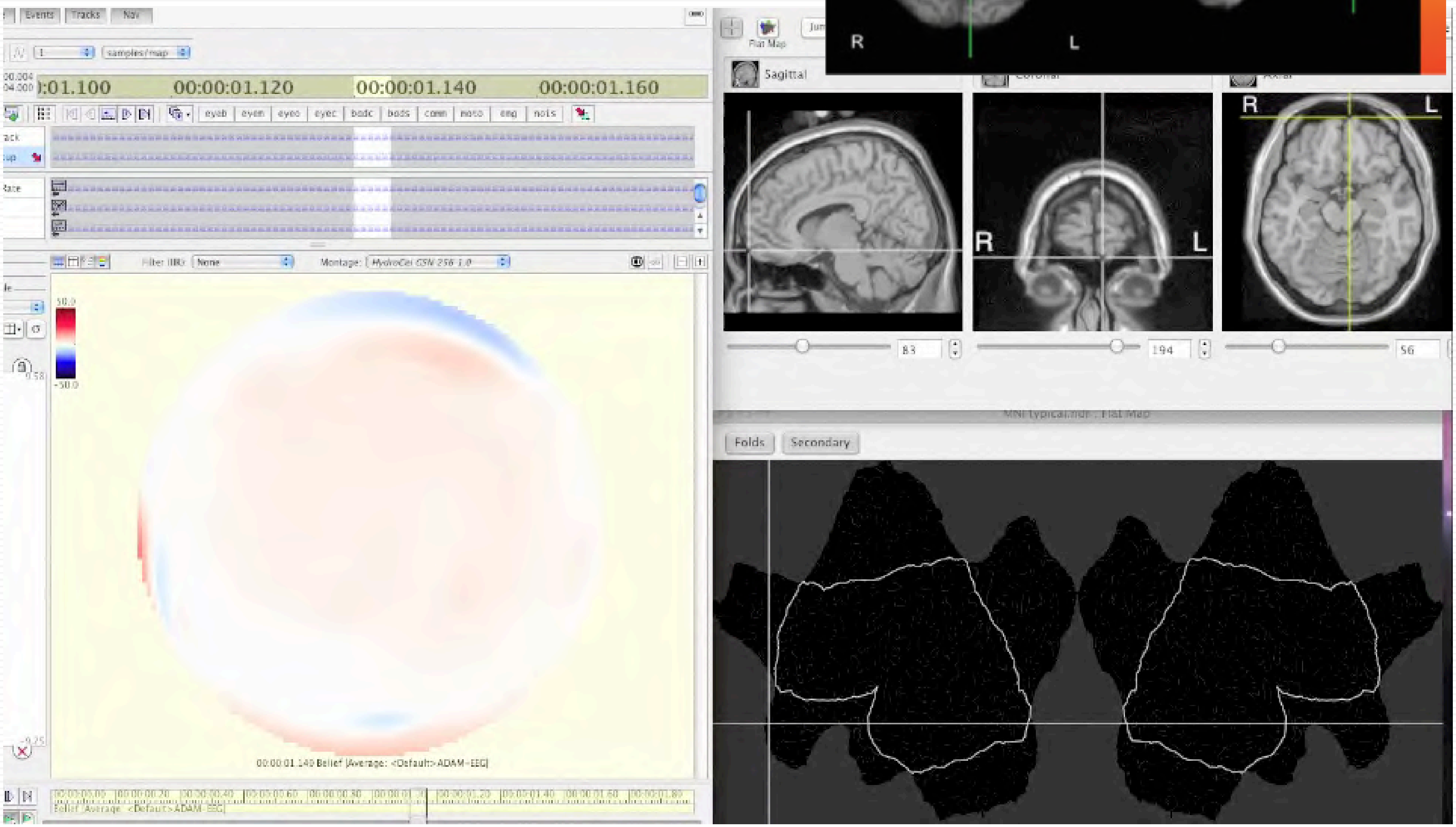


Simultaneous EEG & fMRI

Disclaimer: The author receives royalties on sales of the EGI instrument

Tomographic EEG Projection





Wei Li, Edward Lau
Pamela Douglas, Agatha Lenartowicz,

Example: Epilepsy

Affects 0.5-1% of population (e.g., 1.5 million Americans)

Source: Merck, AAFP & NINDS, others

Up to 50% cannot be treated with medication

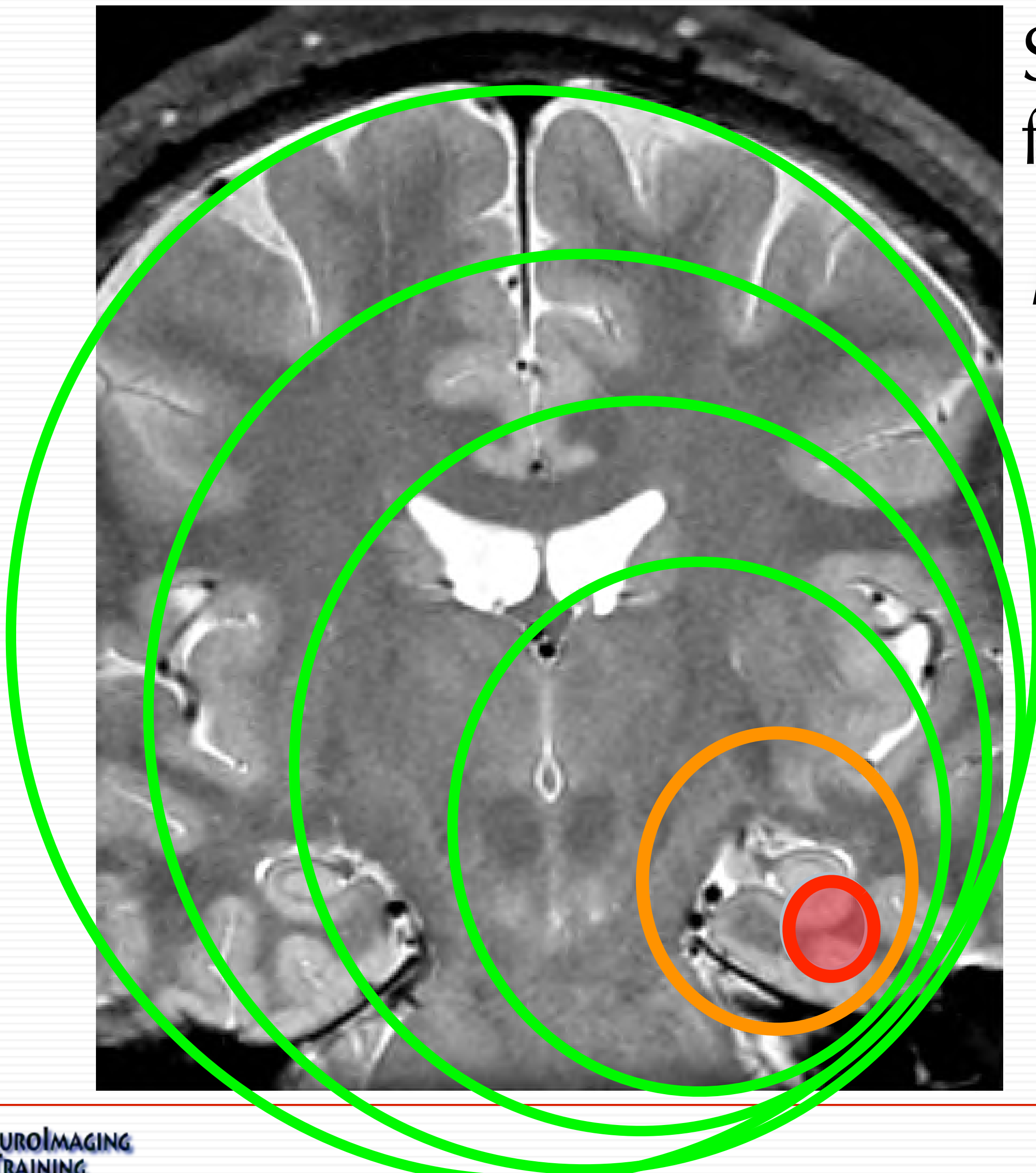
Source: AAFP, others

Surgical Treatment is probably the best first line treatment

Source: Wiebe, et al., NEJM, Engel (UCLA), others

Determination of Resectable Region is the Major Challenge!

Red and Green Spikes



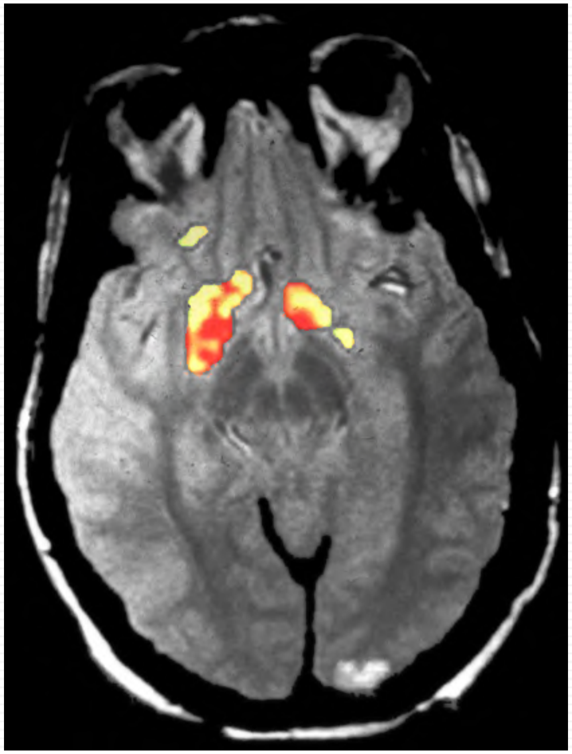
Seizure Activity Spreads from an Irritative Zone

Hypotheses:

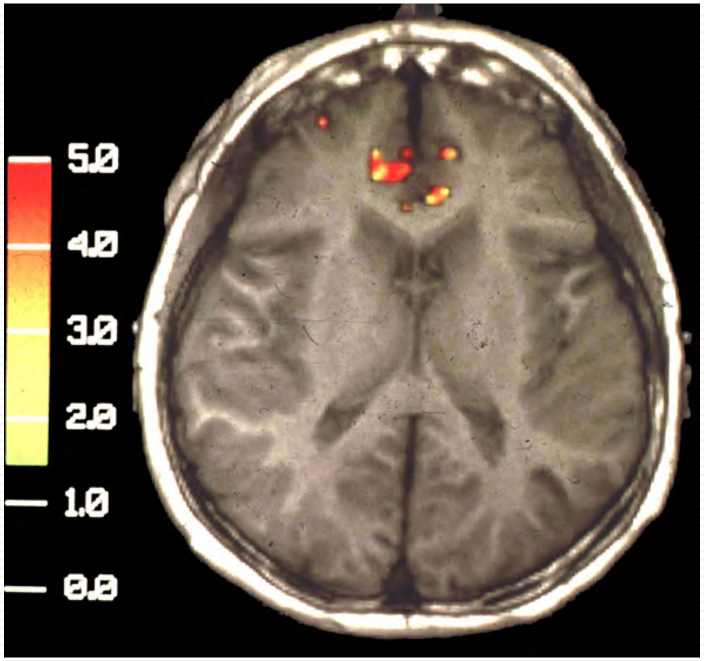
- Initial Event is Energetically Costly
- Spreading Depolarization is Not

Functional MRI may be timed by Epileptiform Spikes

Spike-Triggered fMRI



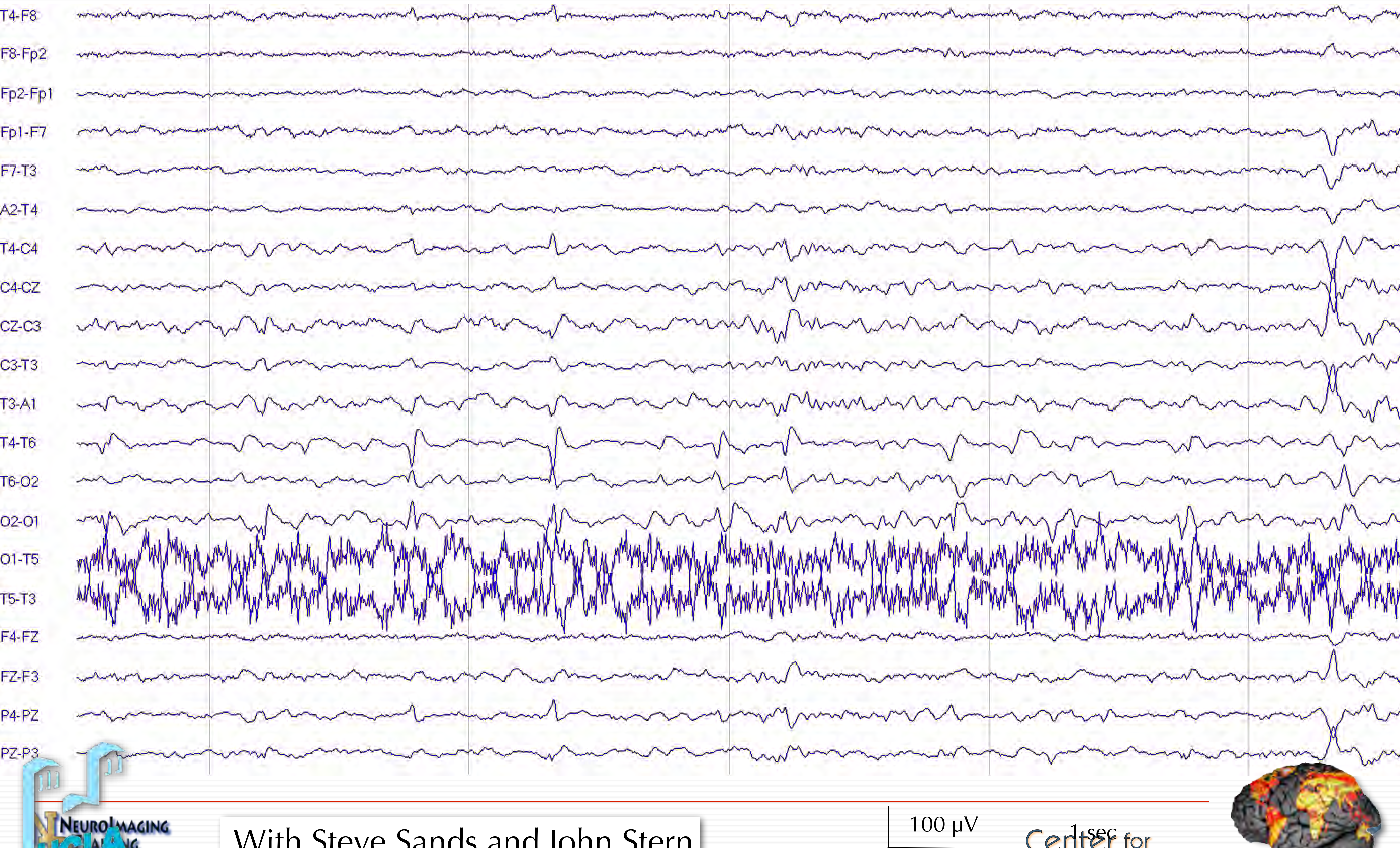
- Complex partial seizures, rare generalization
- EEG: generalized interictal discharges, some with left temporal onset
- MRI: normal



- Complex partial seizures, occasional generalization
- EEG: multifocal and generalized interictal discharges
- MRI: symmetric subependymal heterotopias

Warach, et al. (1996)

Interictal Discharge

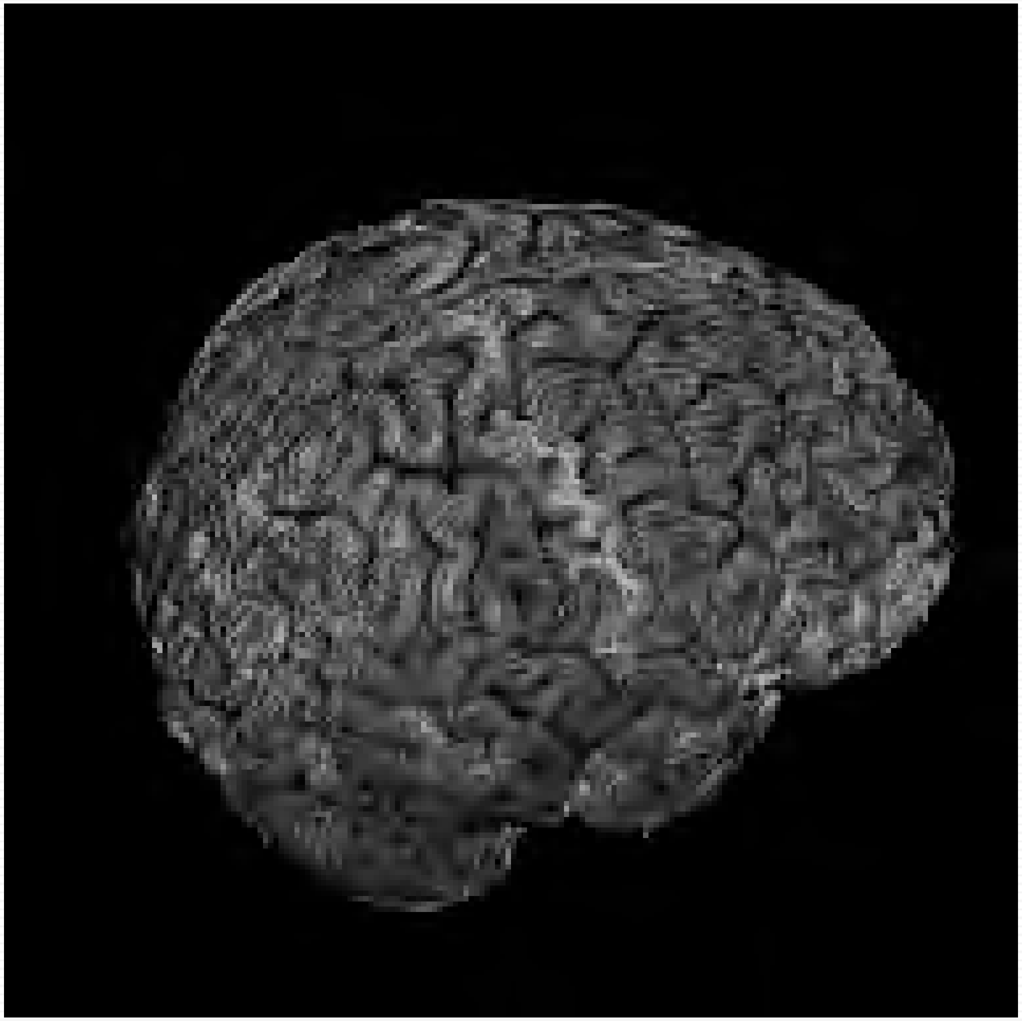


With Steve Sands and John Stern

www.brainmapping.org

Center for Cognitive Neuroscience

IED Time Course



with
John Stern
Alex Korb
Manjar Tripathi
Massoud Akhtari

State Measurements

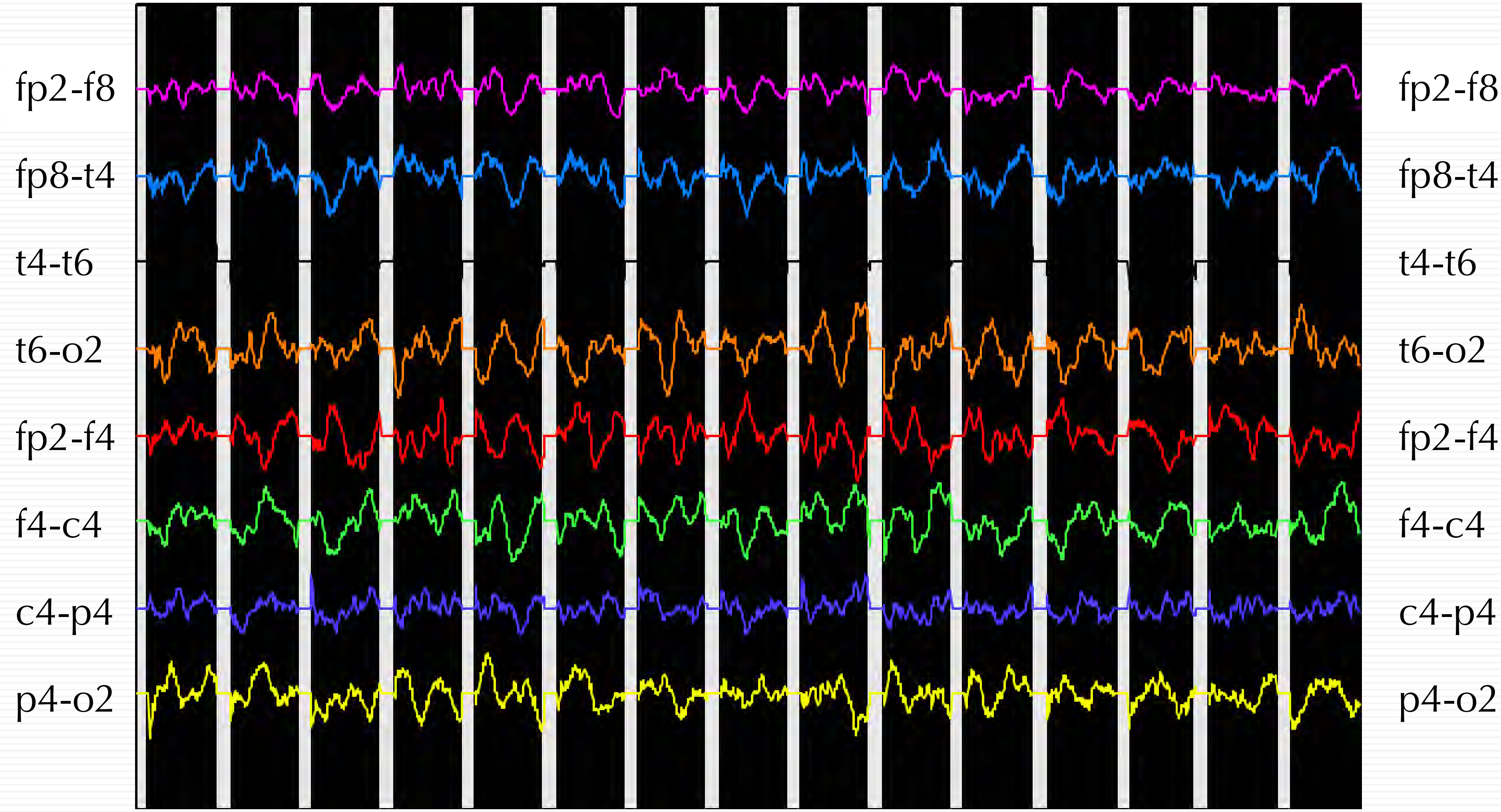
EEG may be the best available measure of state:

- √ Sleep
- √ Attentiveness
- √ Arousal
- √ Responsiveness

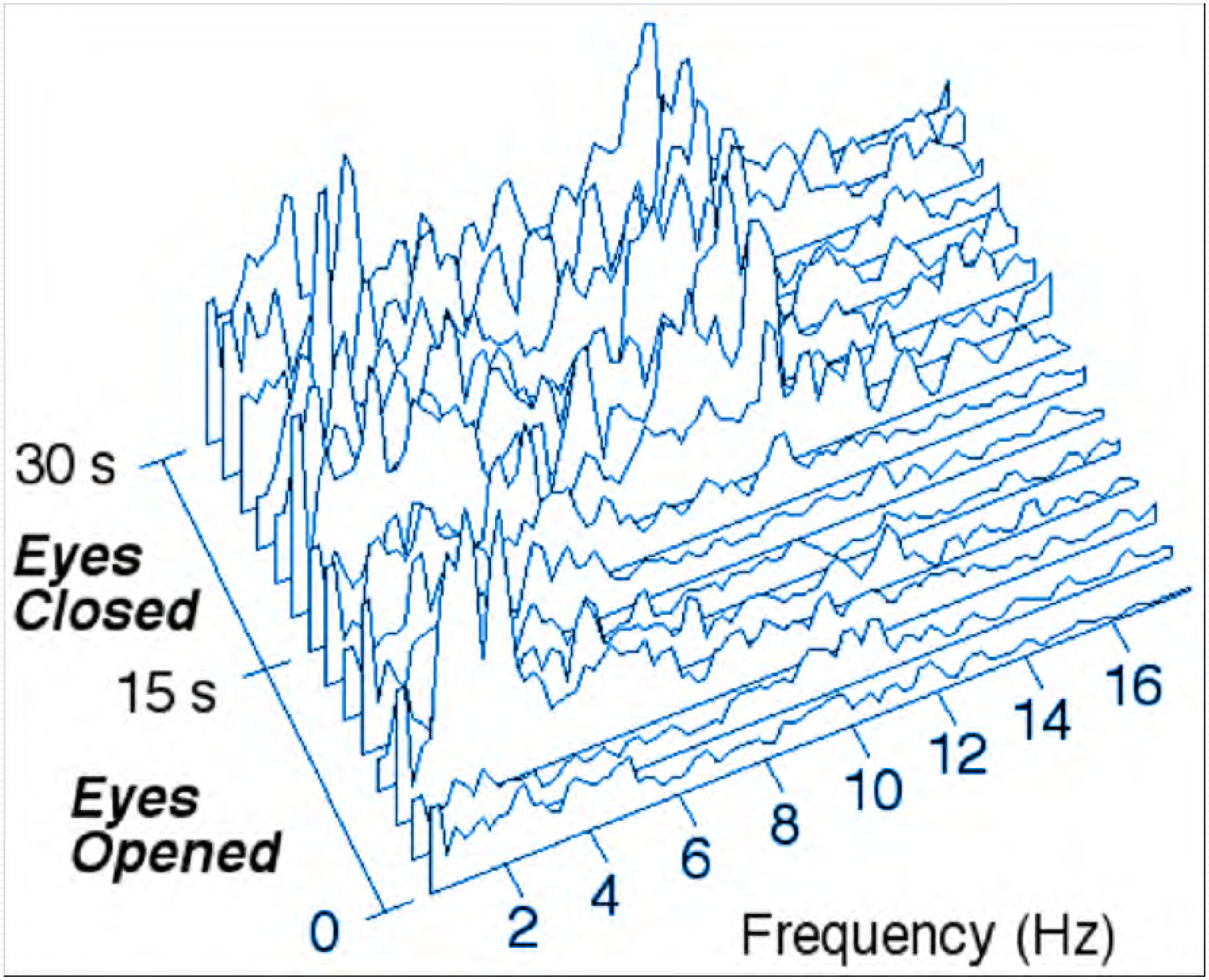
NeuroImaging Training Program

Center for Cognitive Neuroscience

EEG during Sleep (corrected)

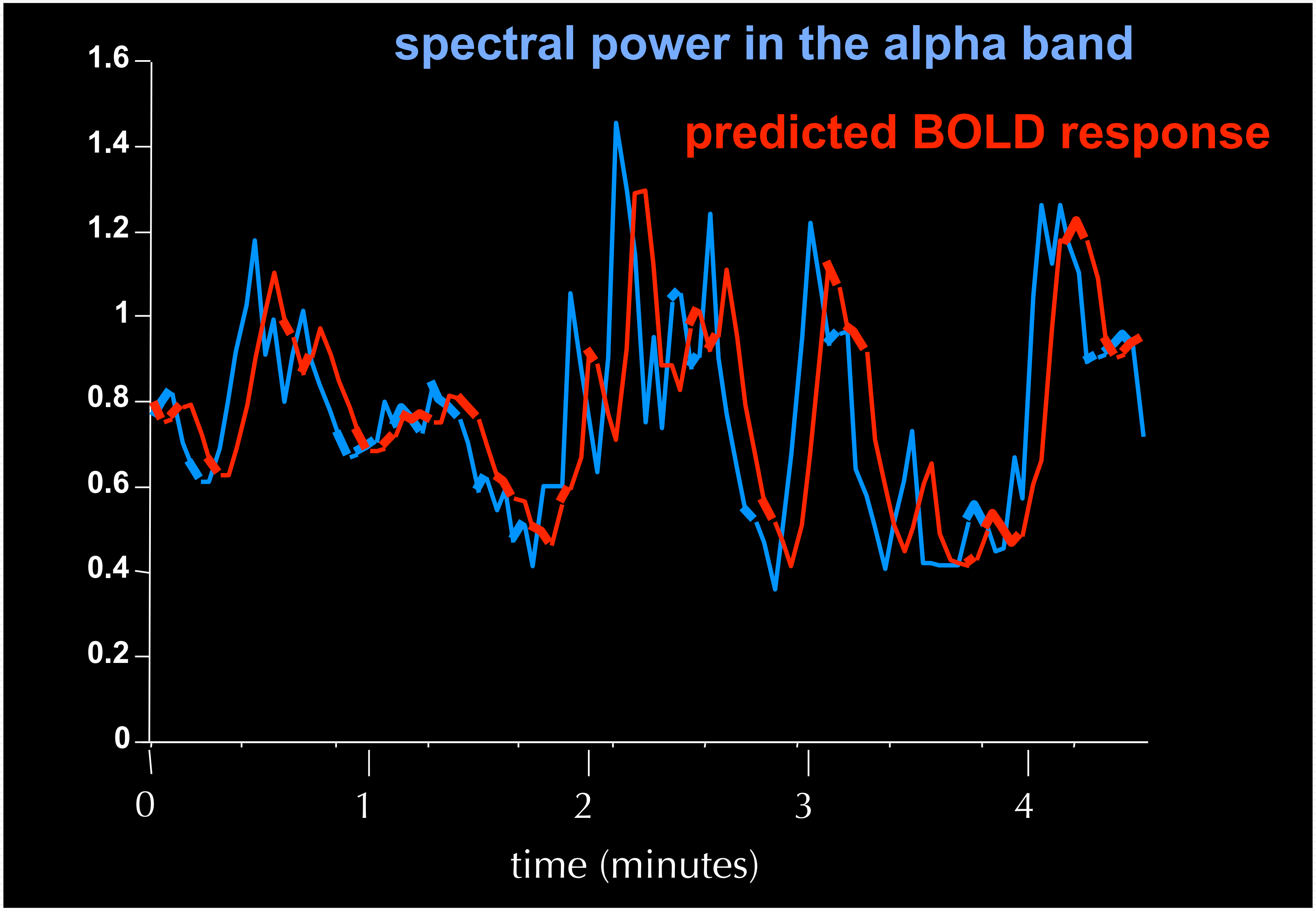


EEG Spectral Content

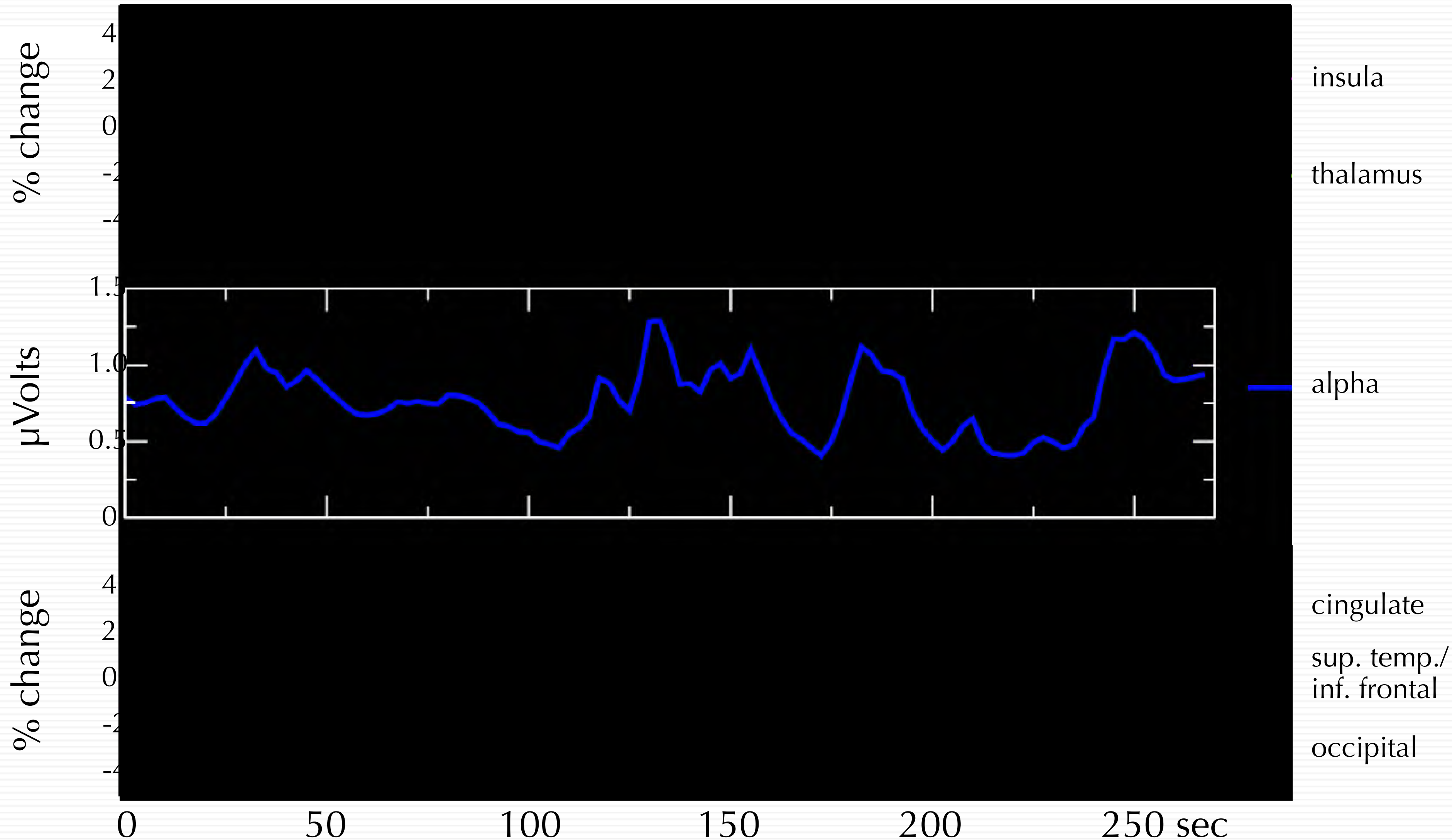


Goldman, et al., Clinical Neurophysiology, 2000

Alpha Mapping

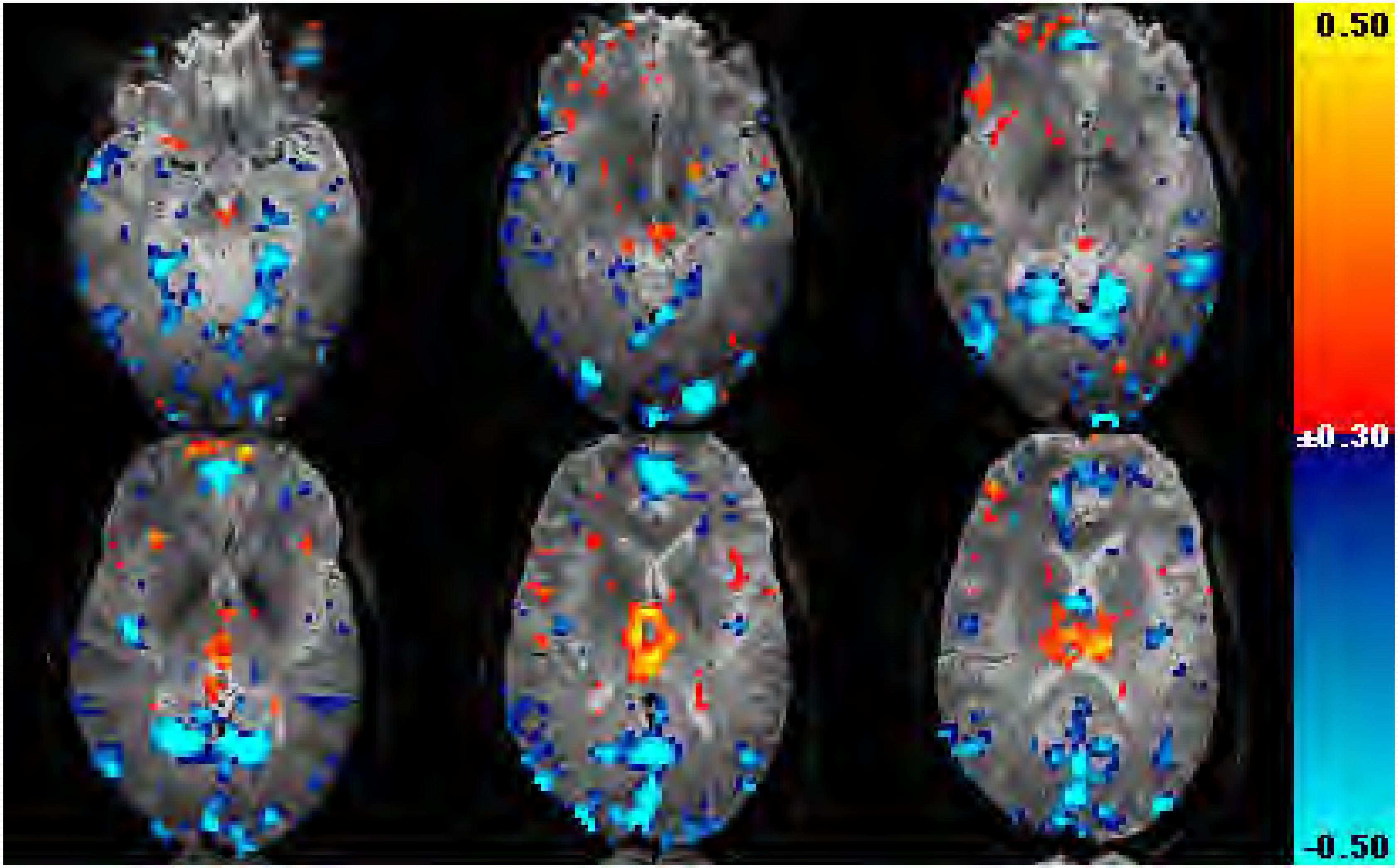


Alpha Rhythm and BOLD



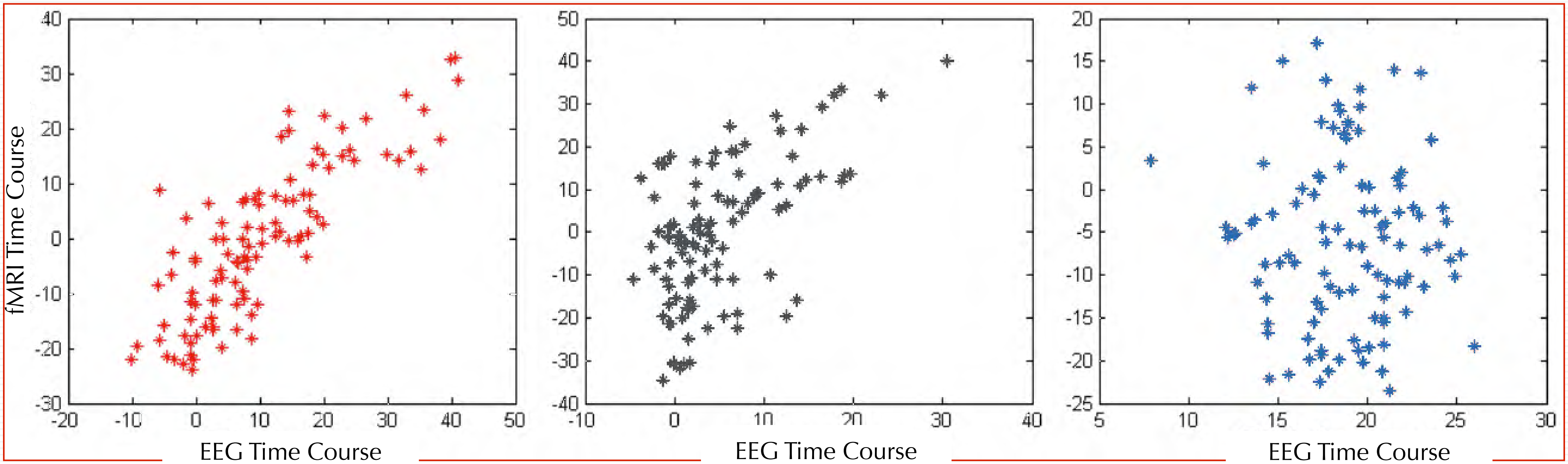
Goldman (2002) NeuroReport 13(18):2487

Alpha Tomograms



Goldman (2002) NeuroReport 13(18):2487

Correlation of EEG and fMRI data



Alpha
$r^2 = 0.83$
$p < 0.05$

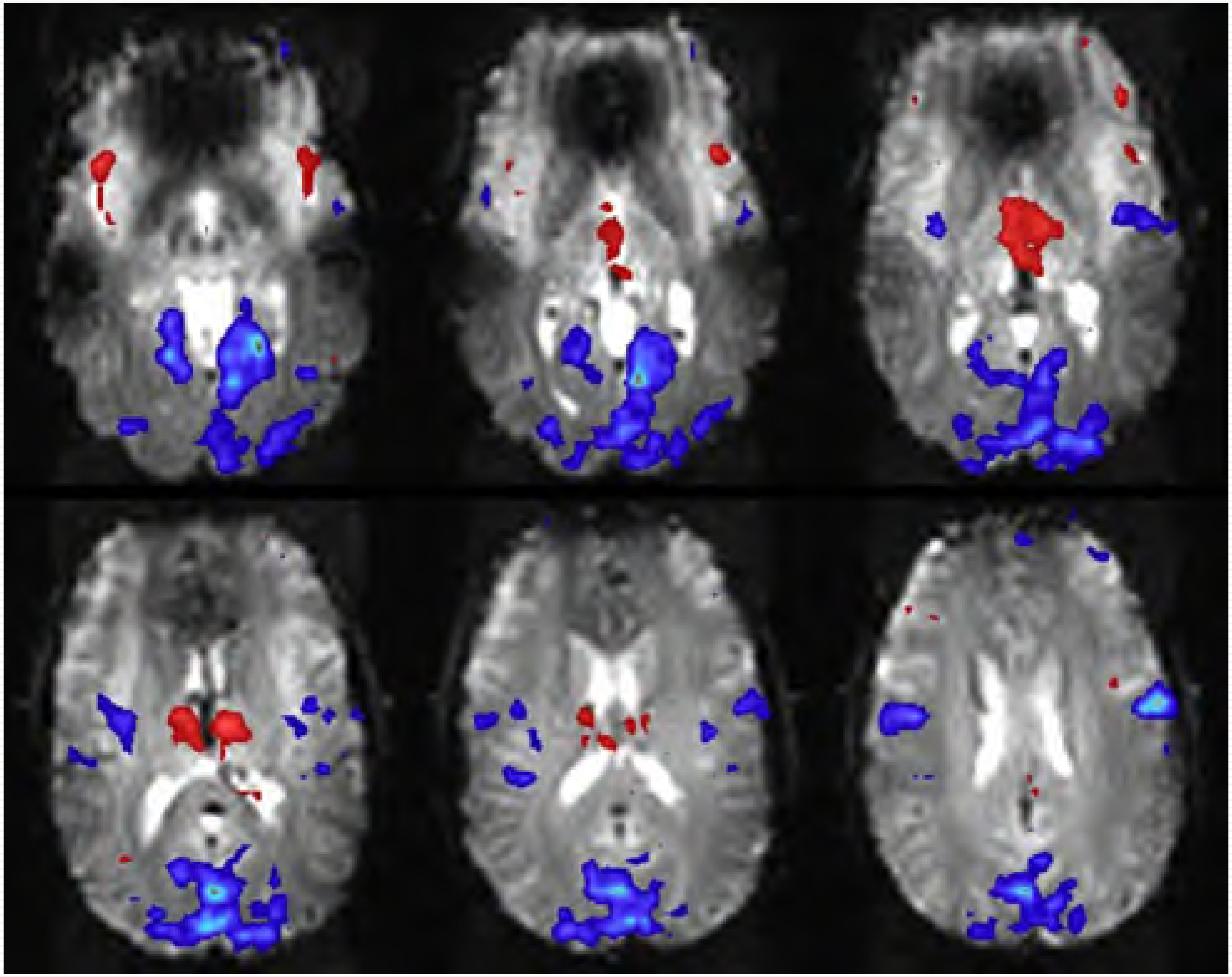
Theta
$r^2 = 0.56$
$p \approx 0.07$

Gamma
$r^2 = -0.03$
p = n.s.

E. Martinez-Montes, et al., NeuroImage 22:1023-34, 2004

JackKnife pseudo t-image

L

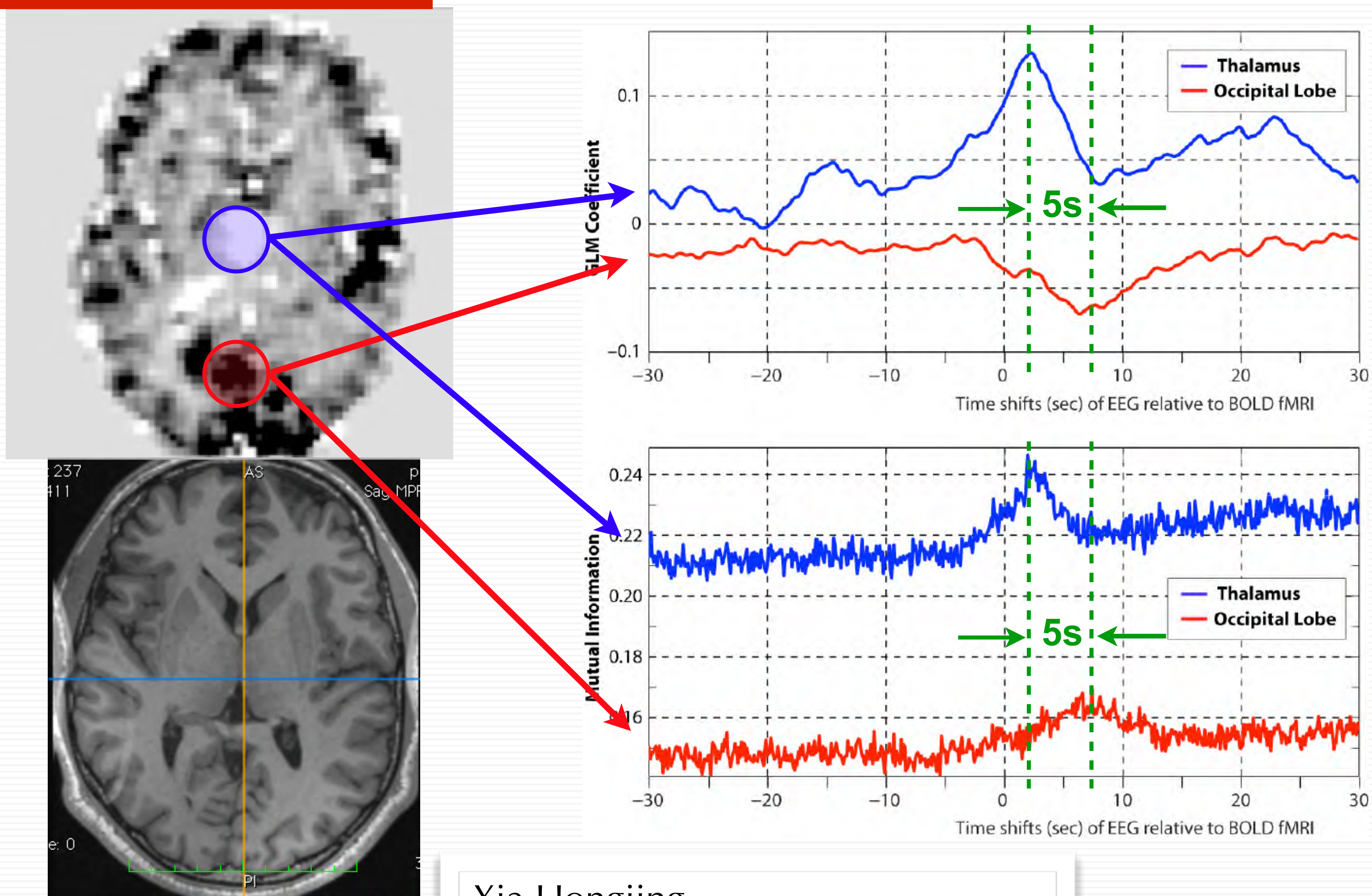


R

Alpha

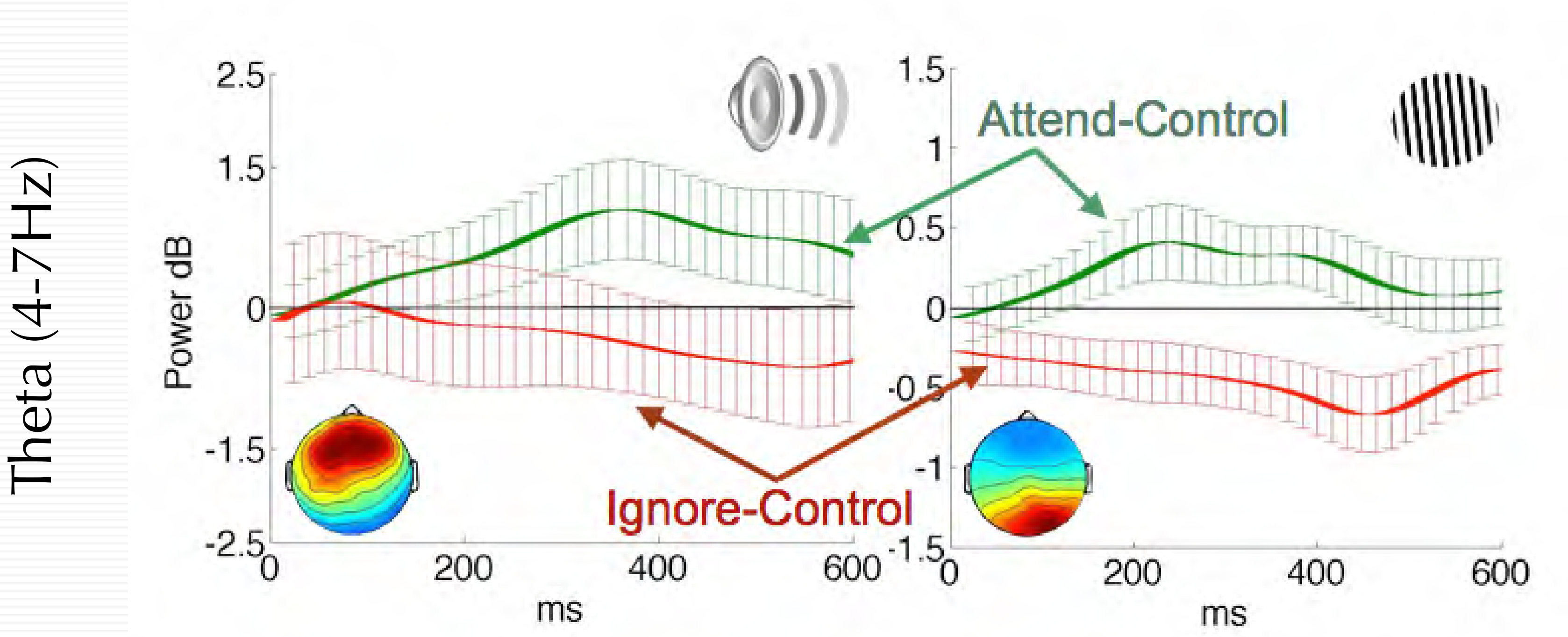
E. Martinez-Montes, et al., NeuroImage 22:1023-34, 2004

EEG-fMRI Coupling - A Variety of Mechanisms?



Xia Hongjing
Organization for Human Brain Mapping 2012

States of Attention

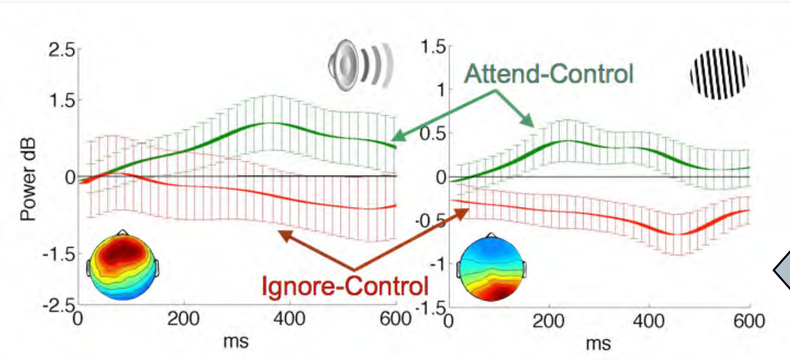


- attention comprises enhancement of attended signals and suppression of ignored signals
- spatio-temporally distinct EEG signatures can be calculated for attended and ignored signals in both auditory and visual modalities
- these can be tracked across trials to assess focus and distractibility

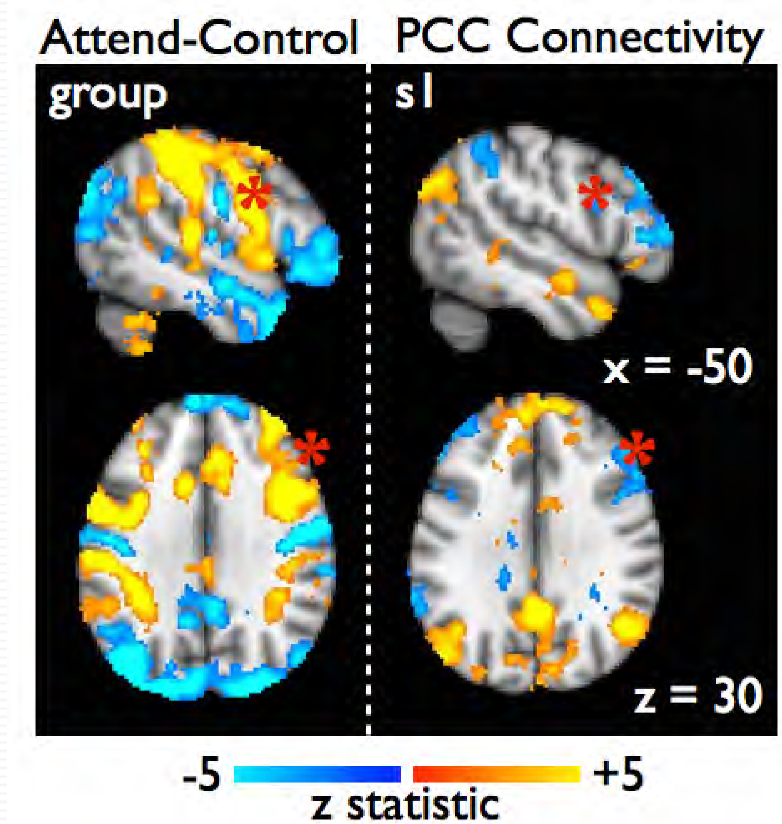
Agatha Lenartowicz
Work in Progress

States of Attention

- How are the EEG traces of attending and ignoring affected by activity in critical neural networks such as fronto-parietal (FPN) & default mode (DMN), and their interactions?



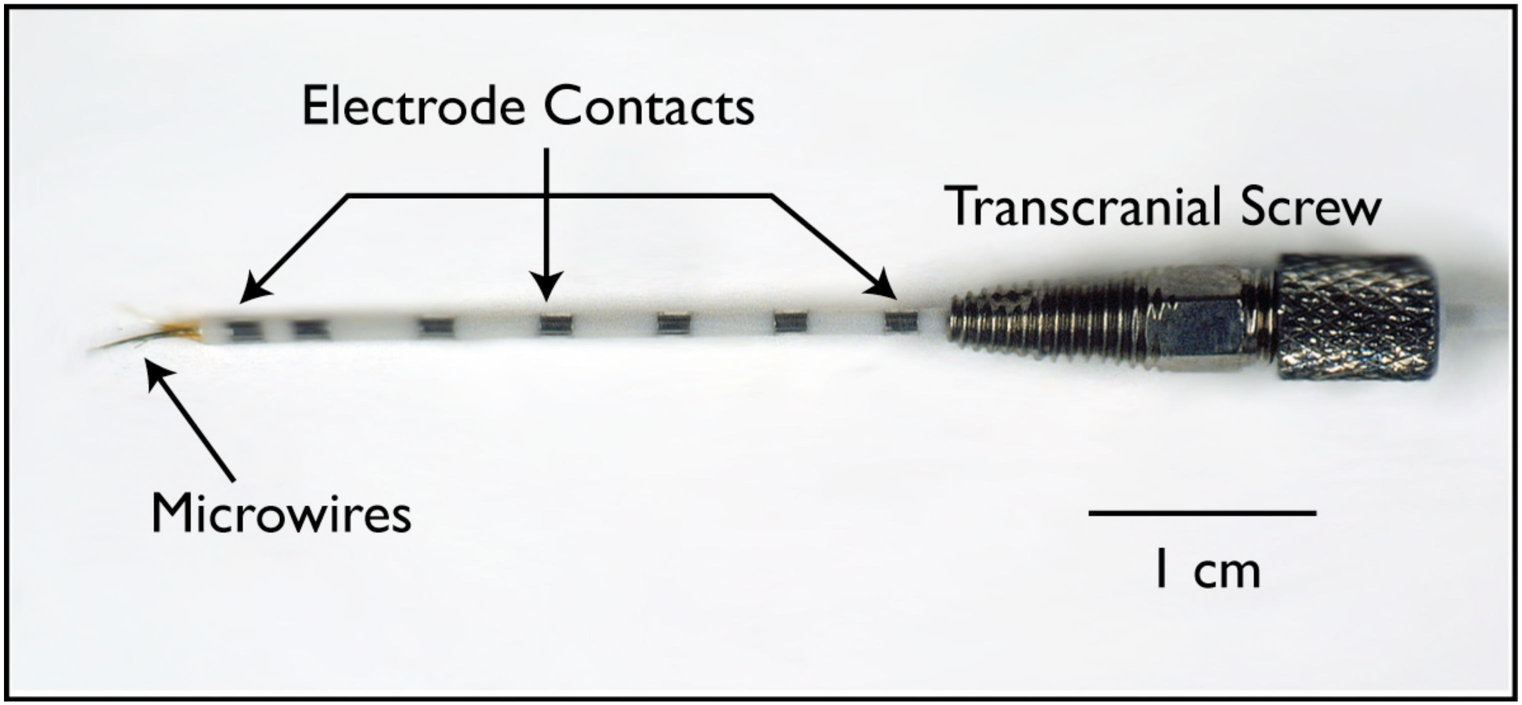
?



- Answering this question will allow us to neurally dissociate attention states - such as fatigue, distractibility and mind-wandering.

Agatha Lenartowicz
Work in Progress

Application



- **Temporal-Lobe Epilepsy Depth Electrode and Microwire Array**

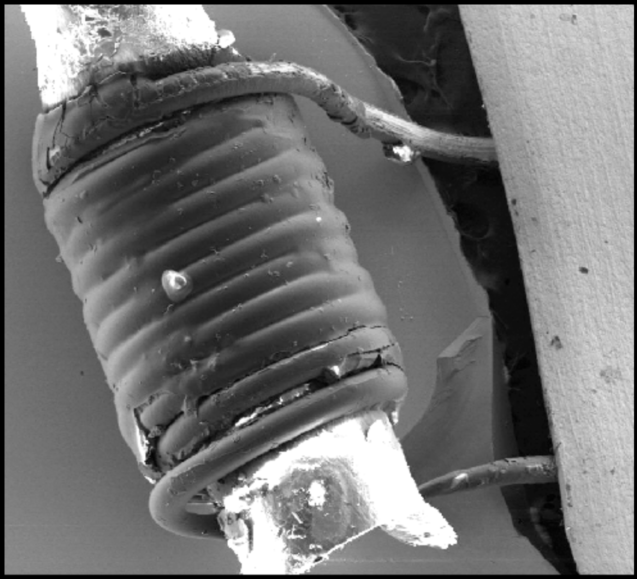
Strick, *et al., Society for Neuroscience, 2007*

UCLA

Objectives

- **Design pick-up coil to integrate with depth electrode**
  - **Potential:**
    - **Microscopic imaging**
    - **Small-volume spectroscopy**
      - **1 mL→1/1000 mL**
- **Investigate depth electrodes**
  - **Established heating experiments**
  - **Rare resonant-frequency characterization**

1-mm coil diameter



200 µm

Strick, *et al.*, *Society for Neuroscience, 2007*

UCLA

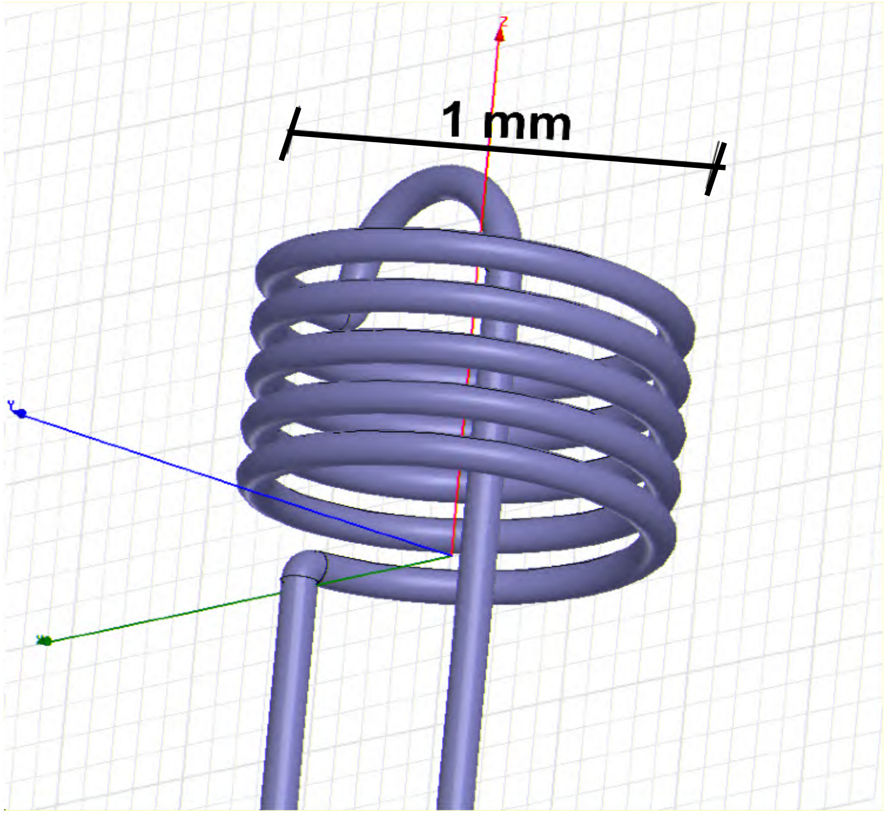
Novel Implantable Design

- **Small diameter < 2 mm**
- **Prioritize homogeneity magnetic flux density**
- **Orthogonal to static magnetic field**
- $f_{coil} > 3 \cdot f_{operating}$
- **Maximize**

$$Q = \frac{(2 \cdot \pi \cdot f_{operating}) \cdot L}{R}$$

f = frequency, L = inductance,

R = resistance



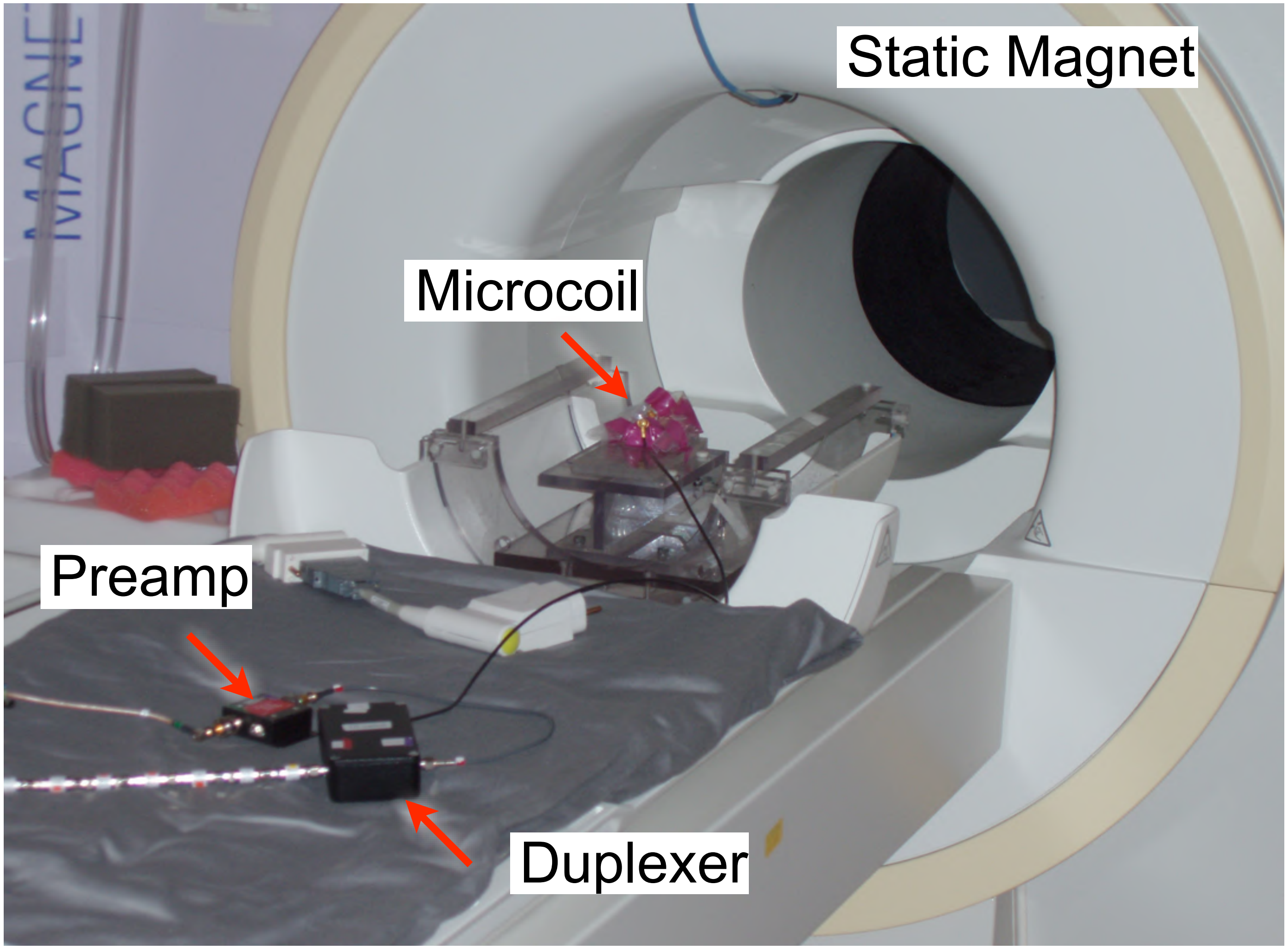
Transform NMR microcoil into implantable design

NOVEL: INTRACRANIAL MRI MICROCOIL

Strick, *et al.*, *Society for Neuroscience, 2007*

UCLA

Imaging Set-up



Lewis Center for Neuroimaging, University of Oregon

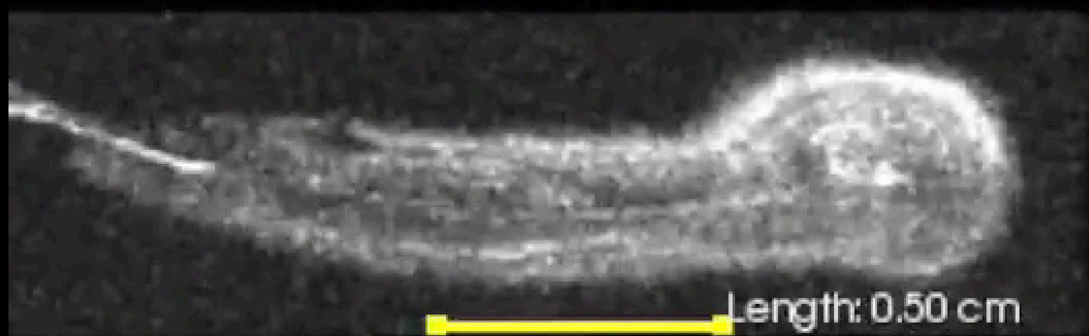
Strick, *et al., Society for Neuroscience, 2007*

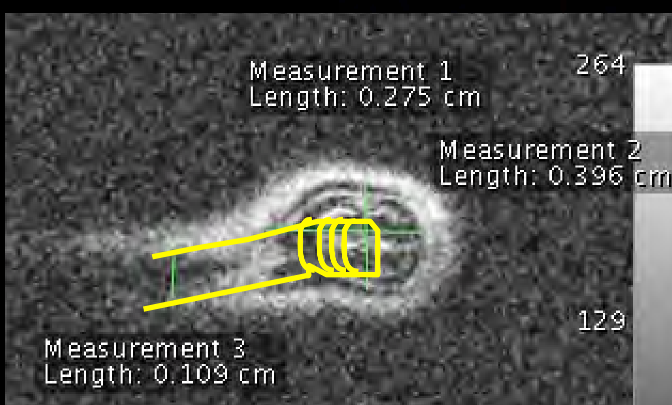
UCLA

Experimental Results

3-Tesla Magnetom Allegra (Siemens, Erglangen, Germany)
Butcher-grade *Ovis aries*

Turbo Spin Echo, TR/TE 4000/22 ms, slice 0.4 mm, FOV 26 × 25 mm, 256 × 256





Strick, *et al., Society for Neuroscience, 2007*

UCLA

Experimental Results

Gradient Echo,TR/TE 123/48 ms, FOV 22 × 14 mm, 640 × 1024,
slice thickness 0.14 mm, NEX 4

3-Tesla Magnetom Allegra (Siemens, Erglangen, Germany)
Butcher-grade *Ovis aries*

Strick, *et al., Society for Neuroscience, 2007*

UCLA