Concurrent Multimodal Imaging
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

MRI

CT

Photograph

Stained Slice
MR Spectroscopy
Intermodality 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

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 Burman¹
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.
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
NEVER TRY TO REMOVE OBJECTS ON YOUR OWN. CALL SERVICE or SENIOR CCN PERSONNEL.

www.SimplyPhysics.com
Before you start

Projectiles account for 10% of reported safety incidents.

10% are from Implanted Devices

71% are burns!

Induced Currents in the Body

Magnetic Field

Electrical Current

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Specific Absorption Rate

- Electrical Current
- Magnetic Field
- Heat
Specific Absorption Rate

- Electrical Current
- Magnetic Field
- Heat
In-vitro study: Semi-solid gel, head and torso phantom

Fluoroptic thermometry system: MRI compatible

High specific absorption rate (SAR) = 3.0 Watts/Kg

Unsafe heating: suspected resonance

Heating > 3°C

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
“…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

- Topology
- Velocity
- Direction
- Location
- Texture
- Identity
- Color
A Simple Question:

If fMRI is so slow, why not record electrical signals to correct the fMRI timing?
Source Localization (Forward Model)

$$x_j(r_i, q_i, t) = \sum_{i=1}^{K} G(r_i(t), p_j) \cdot q_i(t) + \varepsilon$$

Signal at Sensor $j$  Lead Field  Oriented Magnitude

Location  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

\[
\varepsilon(r, q) = \sum_{i}^{K} \sum_{t=t_{1}}^{t_{2}} \sum_{j}^{M} (x_{j}(t) - \hat{x}_{j}(r_{i}, q_{i}, t))^{2} + \lambda f(r, q)
\]

\[f(r, q) > 0\] is used to regularize the solution
\[\lambda > 0\] trades fit against regularization

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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

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www.brainmapping.org
Source Localization Stability (LORETA)

Change in LORETA Calculation When Electrodes are Zeroed

Nominal EEG Amplitude: 18

From Alex Korb (unpublished)
Source Localization Stability (LORETA)

Error in Localization as a function of noise

Error in Peak Location (mm)

Noise Level

0 12.5% 25% 37.5% 50%

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

RF Noise

- Properly-shielded Amplifiers
- Softened Logic Pulses

Magnetic Field Distortion

Non-magnetic material such as Silver

Signal Losses

- Careful Lead Dress
- Eliminate RF Loops
A Method for Removing Imaging Artifact from Continuous EEG Recorded during Functional MRI

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

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Receiver Saturation

150 mV

DC offset

Time (sec)

1 2

150 mV

OUT

IN

Time (sec)

1 2

2 Hz
Artifacts During Scanning
Logothetis (recording method)
BOLD response reflects synaptic activity

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

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.

Logothetis, 2001
Inductive Pickup by EEG leads

Imaging Field Gradients

Ballistocardiogram
Ballistocardiogram

Jan de Munck
Can We Simply Filter?

BCG Power Spectrum

0  20  40  60  80  100 Hz
Ballistocardiogram Subtraction

Goldman, et al., Clinical Neurophysiology, 2000
EEG after Ballistocardiogram Averaging

Jan de Munck
Model the BCG as the superposition of basis functions

Basis 1

Basis 2

Basis 3
Spectral Suppression

MR Artifact

Artifact Spectrum

\[ \log_{10}(\text{Amplitude}) \]

Frequency

[Graph showing a waveform and its corresponding frequency spectrum]
Approach to MR Artifact Removal

This approach requires that:

- \( \text{EEG}_k \) and \( \text{Artifact} \) are uncorrelated
- \( \text{EEG}_k \) and \( \text{Artifact} \) add linearly
- \( \text{Artifact} \) is identical at each time (\( k \))
Fast Sampling is NOT enough

Raw Signal

After Subtraction of Averaged Artifact

Sampling rate: 10 kHz
Sampling and Nyquist

Scanner Artifact (simulated)

1 msec
Sampling and Nyquist

Scanner Artifact (simulated)
Digital Sampling >5X Nyquist

1 msec
Sampling and Nyquist

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

1 msec
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

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

Scanner Artifact (simulated)
Sub-Nyquist Sampling
Synchronized Sampling

Scanner Artifact (simulated)

Sub-Nyquist Sampling

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

1 msec
Allen Method

Digitized EEG  \[ \sum_{n}^{k} S_k \nfrac{1}{N} \]  Interpolation  Averaging  Interpolation  +  Smooth and Downsampling  Low-pass Filter  +  EEG

Slice-timing Signal  

Adaptive Noise Cancellation

Reference Signal  +  Slice Timing

Corrected EEG  -  Primary Signal

**Reference**


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

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

\[ \epsilon = \cos(2\pi ft) - \cos(2\pi ft - \varphi) \]
\[ = \cos(2\pi ft) \cos(\varphi - 1) - \sin(2\pi ft) \sin \varphi \]

...where:
- \( f \) is the frequency of the artifact
- \( \varphi \) 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 \( \varphi \)) the error, \( \epsilon \), is linearly proportional to the sampling frequency.
Synchronized Correction

EEG

+  RF Filter

−

Trigger once per tr

Scanner Master Clock

24 bit Digitizer

Σ

−

Corrected EEG

+
Artifacts During Scanning

The graph shows EEG data with various electrode labels such as FP1, FP2, AF3, AF4, F7, F3, FZ, F4, F8, FC5, FC1, FC2, FC6, T7, C3, CZ, C4, T8, CP5, CP1, CP2, CP6, P7, P3, PZ, P4, P8, PO7, PO3, PO4, PO8, O1, OZ, O2, and ECG. The vertical scale is marked with 100 µV.
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
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
EEG during Sleep (corrected)
EEG Spectral Content

Goldman, et al., Clinical Neurophysiology, 2000
Alpha Mapping

Spectral power in the alpha band

Predicted BOLD response
Alpha Rhythm and BOLD

Alpha Tomograms

Correlation of EEG and fMRI data

Alpha
\( r^2 = 0.83 \)
\( p < 0.05 \)

Theta
\( r^2 = 0.56 \)
\( p \approx 0.07 \)

Gamma
\( r^2 = -0.03 \)
\( p = \text{n.s.} \)
JackKnife pseudo t-image

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.
Application

- Temporal-Lobe Epilepsy Depth Electrode and Microwire Array

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

Novel Implantable Design

- Small diameter < 2 mm
- Prioritize homogeneity magnetic flux density
- Orthogonal to static magnetic field
- \( f_{\text{coil}} > 3 \cdot f_{\text{operating}} \)
- Maximize
  \[
  Q = \frac{(2 \cdot \pi \cdot f_{\text{operating}}) \cdot L}{R}
  \]
  
  \( f = \) frequency, \( L = \) inductance, \( R = \) resistance

Transform NMR microcoil into implantable design

NOVEL: INTRACRANIAL MRI MICROCOIL

Imaging Set-up

Lewis Center for Neuroimaging, University of Oregon

Experimental Results

3-Tesla Magnetom Allegra (Siemens, Erlangen, Germany)
Butcher-grade Ovis aries
Turbo Spin Echo, TR/TE 4000/22 ms, slice 0.4 mm, FOV 26 × 25 mm, 256 × 256

Experimental Results

Butcher-grade *Ovis aries*

3-Tesla Magnetom Allegra (Siemens, Erlangen, Germany)

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