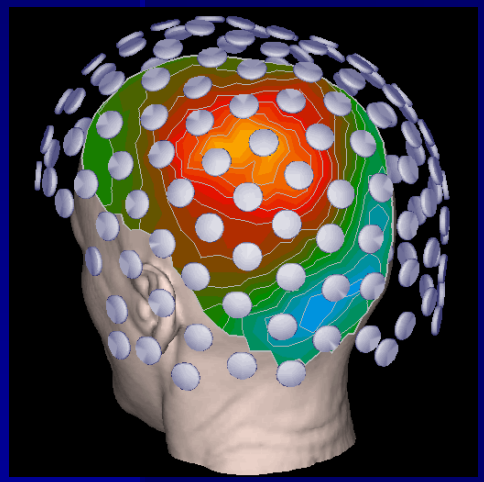
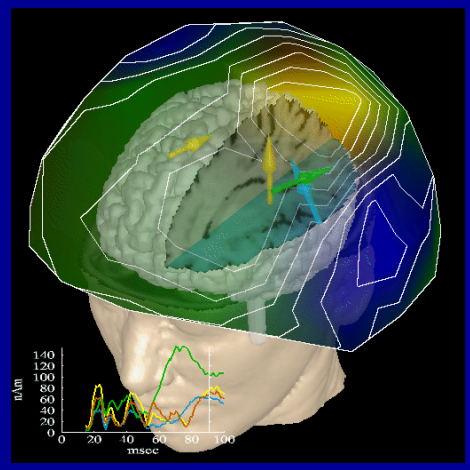
Neurodynamic imaging in the assessment of sensory and cognitive functions in health and disease



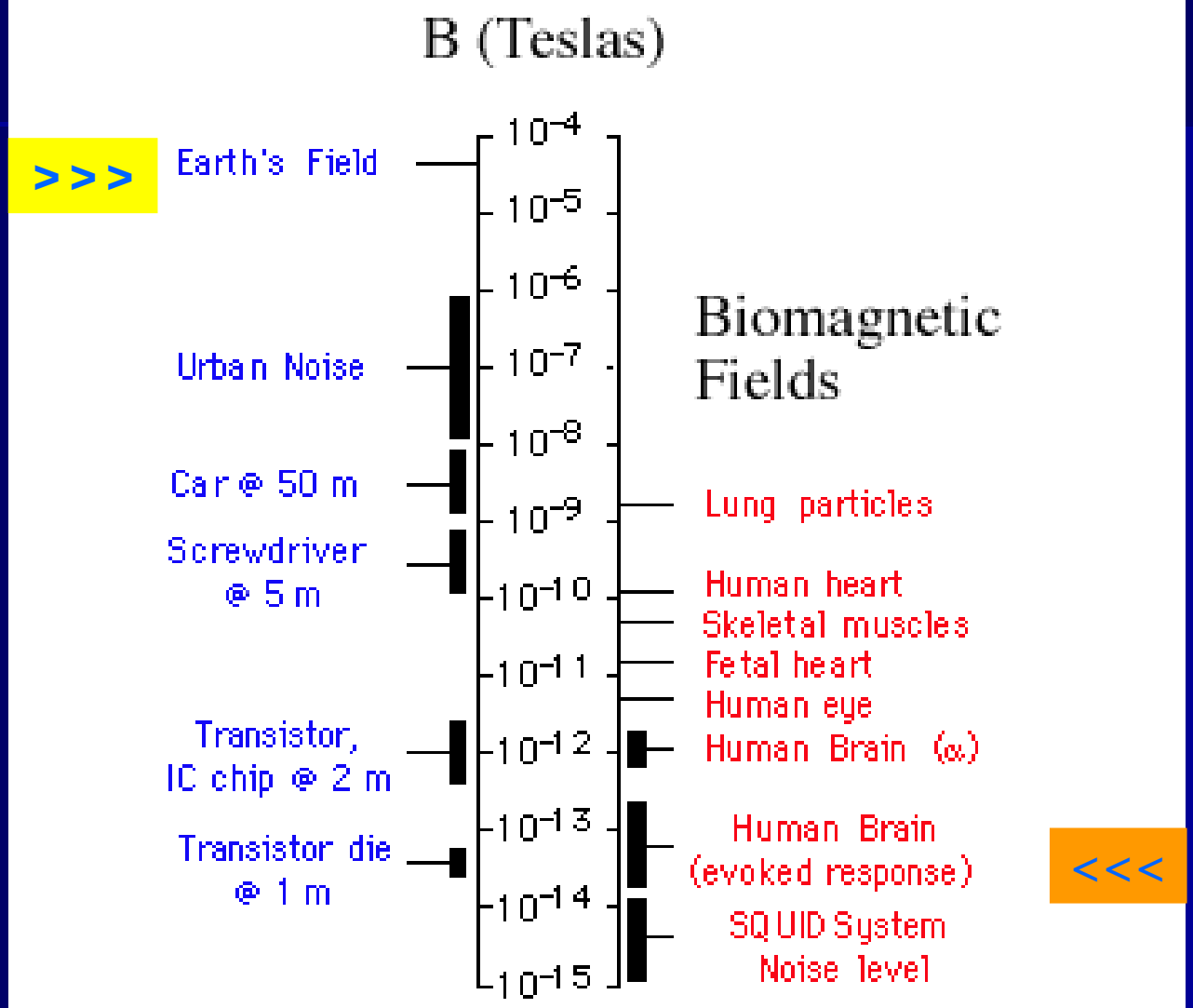
S e l m a S u p e k

University of Zagreb
Faculty of Science
Department of Physics



First Symposium "Toward translational research in brain and heart studies: Achievements and challenges in knowledge and technology transfer"
February 18, 2008, Zagreb, Croatia

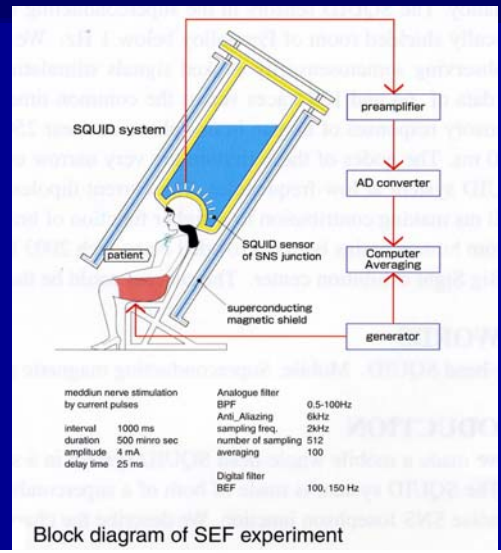
Magnetic Fields



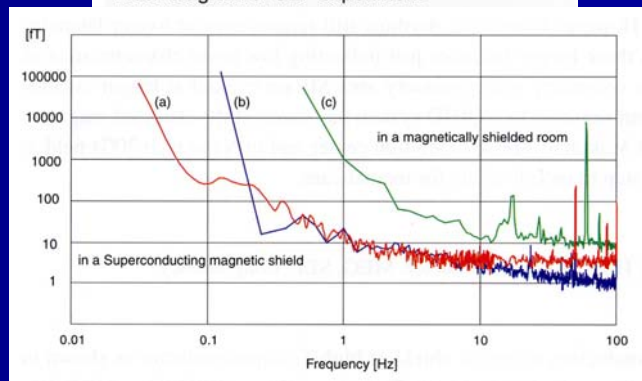
BIOMAG2004

Whole-head SQUID System in a Superconducting Magnetic Shield

National Institute of Information and Communication Technology
Tokyo Denki University



Block diagram of SEF experiment

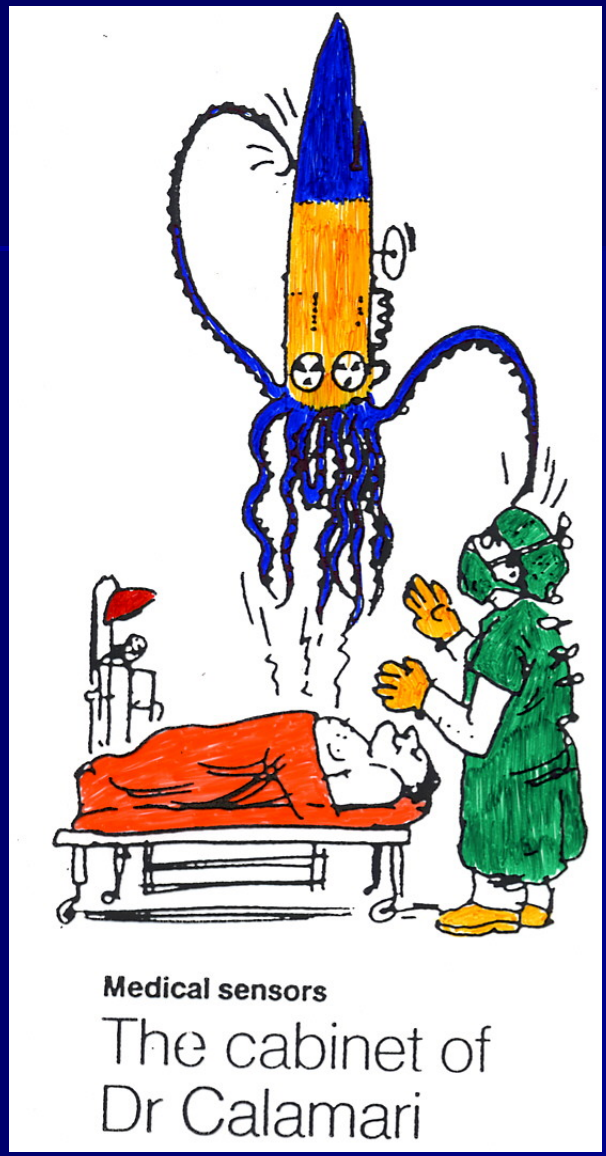


Noise spectra of a SQUID sensor both in the superconducting magnetic shield and in the magnetically shielded room of Permalloy.

The first step toward a mobile clinic for mental care!

Novel ultrasensitive sensor device made medical uses possible

since 1963

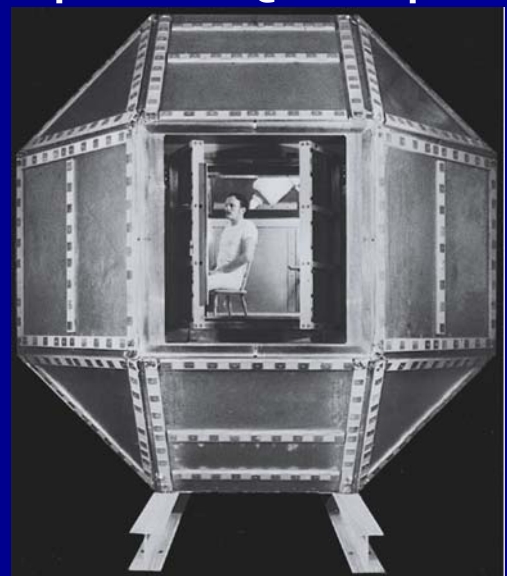


Cohen et al.

April 1, 1970

Pre-SQUID....

....and post-SQUID period



A NEW FIELD OF BIOMAGNETISM April 1, 1970

JAMES ZIMMERMAN
developed at Ford Superconducting QUantum Interference Device – SQUID
NYU – Biomag89:
Zimmerman recalled that his colleagues developed the popular passtime of
Watching the SQUID signal change as he moved the lab's metal chairs back and forth.

"It was obvious", he said, "that we had an extremely sensitive detector of lab chairs".

DAVID COHEN from high energy physics to study of bioelectricity
shielded room and induction coil device
"It was like trying to explore a new continent for the first time using a rowboat. "

EDGAR EDELSACK
an Office of Naval Research official who was funding both Zimmerman and Cohen:
"Why not get Zimmerman with his ultrasensitive lab chair detector together with his Shielded room and biomagnetic projects? "

First MCG, April 1, 1970, Journal of Applied Physics:
"These results suggest new medical uses for this magnetometer. "

Biomag2010
in DUBROVNIK, Croatia

March 28 - April 1, 2010

40th Anniversary of ''the medical uses of SQUID-based magnetometers''

ISACM 2007

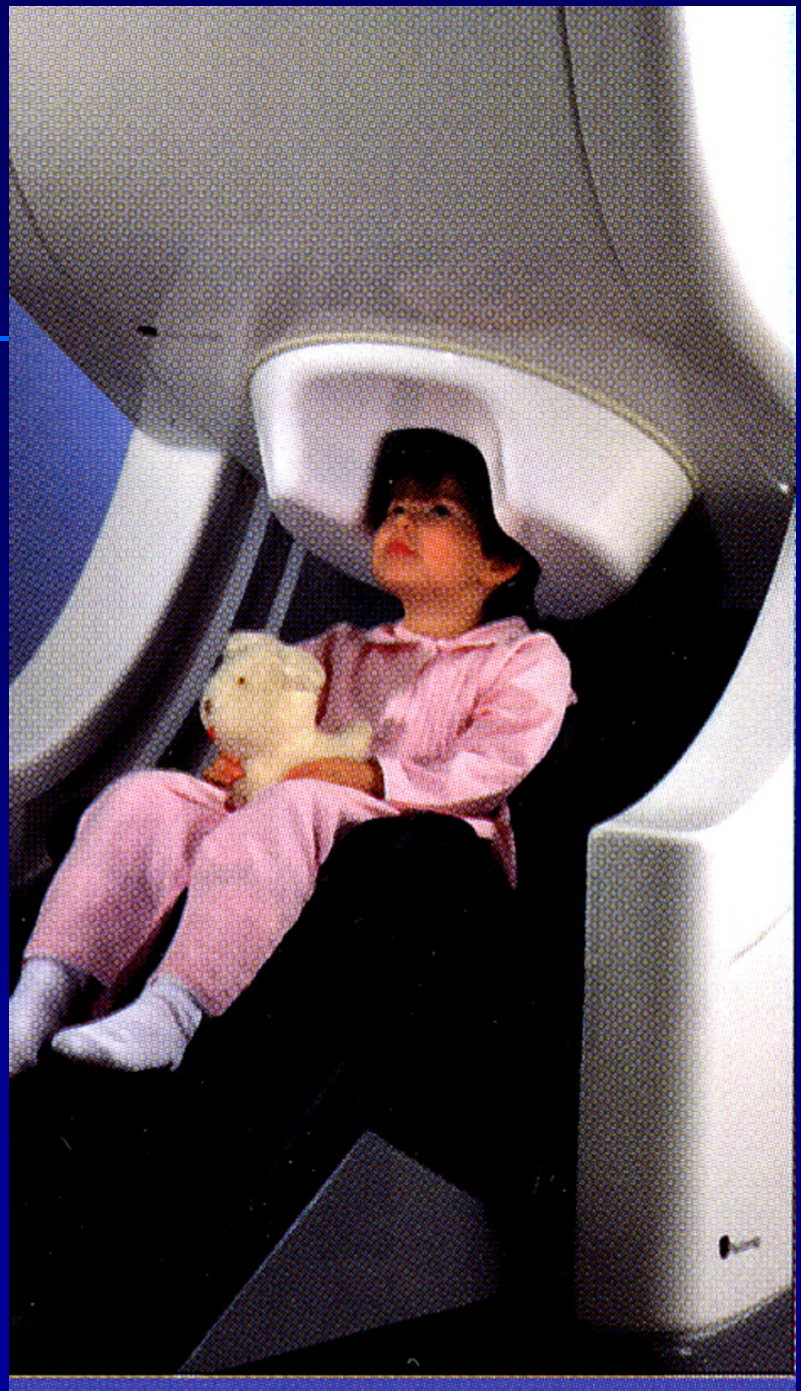
First Conference of the

International Society for the Advancement of Clinical MEG

August 27-30, 2007 Matsushima Bay Resort, Japan

http://www.knt.co.jp/ec/2007/isacm/

100 MEG whole-head systems vs 22 000 MRI systems



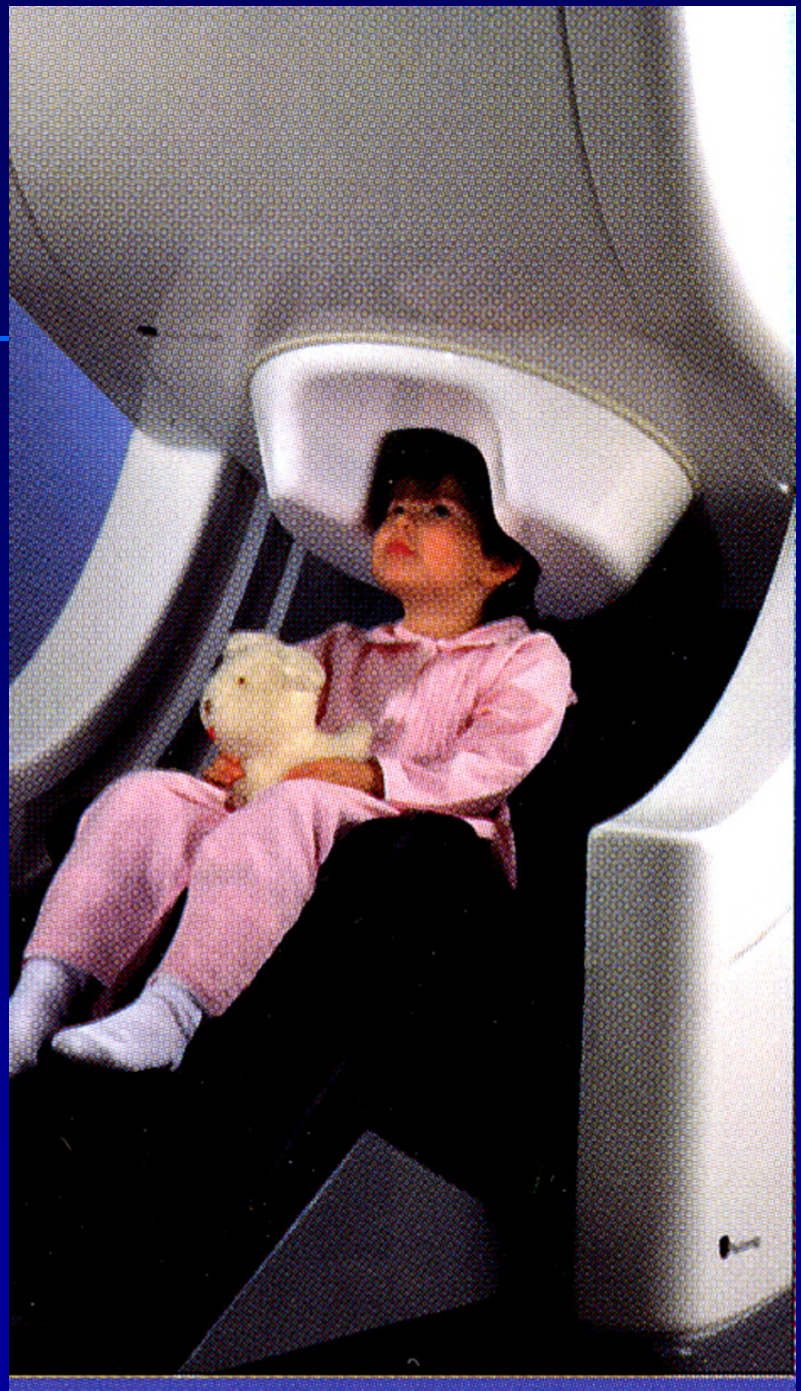
MEG – no field, no substance exposure

- repetitive measurements OK
- intersubject variability
- single subject analysis

Non-invasive insight into

sensory and cognitive development

in health and disease



Magnetoencephalography in Children:
Routine Clinical Protocol for Intractable Epilepsy at the Hospital for Sick Children

-Clinical MEG lab established in 2000
-303 routine clinical patients, 2-18 years
(August 2000 – August 2005)

Assessment of patients with epilepsy

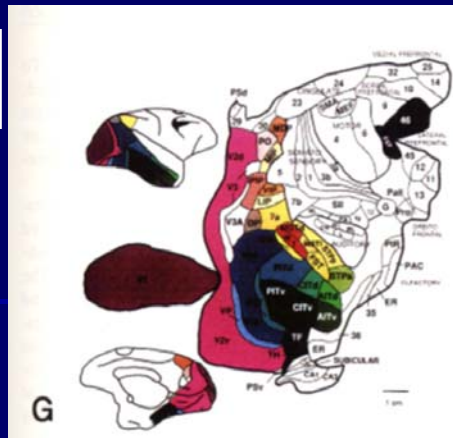
-Simultaneous MEG/EEG - at least 15 two minutes recordings (visual identification of the spikes, MEG spike source localization)

Mapping of functional cortices

- Somatosensory Evoked Fields (SEF) – hand and foot areas localized by stimulation of the median and posterior tibial nerves
- Auditory Evoked Fields (AEF) – tones (1kHz, 80DB, 1s ISI, 100 trials) presented monaurally
- Visually Evoked Fields (VEF) – binocular hemi-field responses to a reversing (2Hz) black-and-white checkerboard stimuli

MAPS OF THE VISUAL SYSTEM

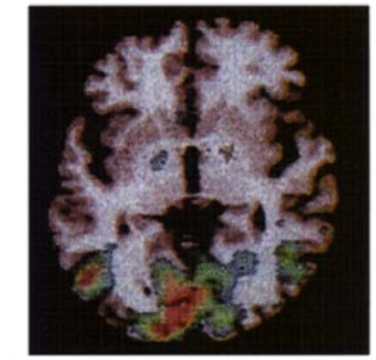
Cortical areas in the macaque
Van Essen, 1991



Hierarchy of 32 visual areas
(187) linkages

Activation of the visual cortex
fMRI (Belliveau et al, 1991)

Activation of visual cortex
PET (Fox et al., 1986

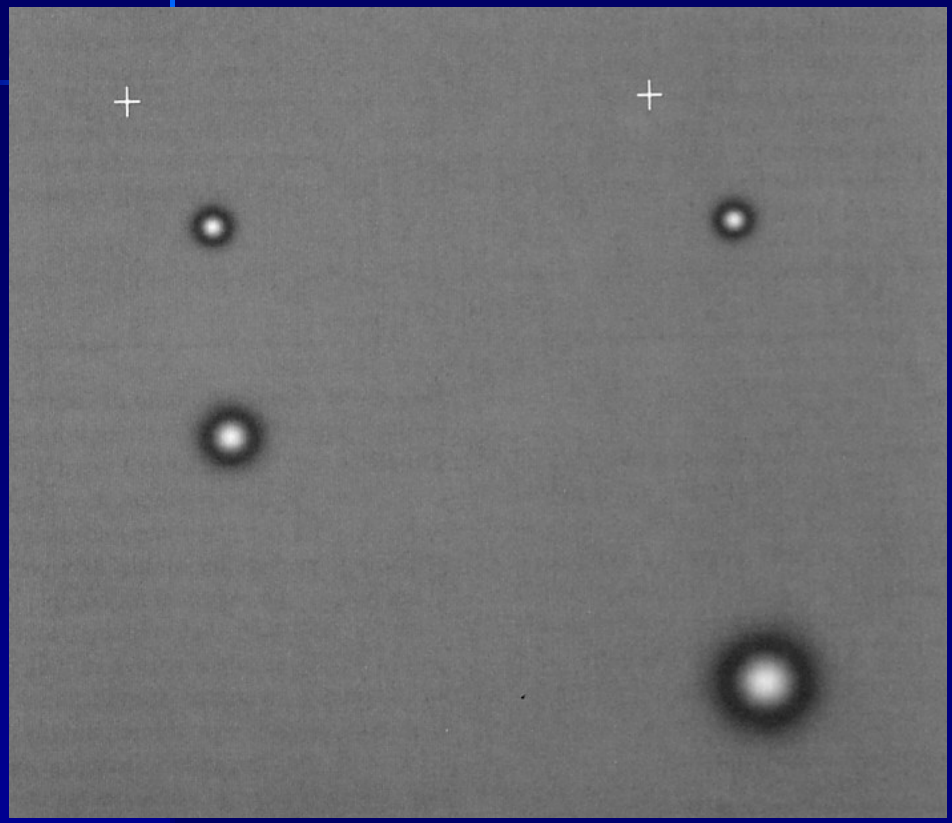


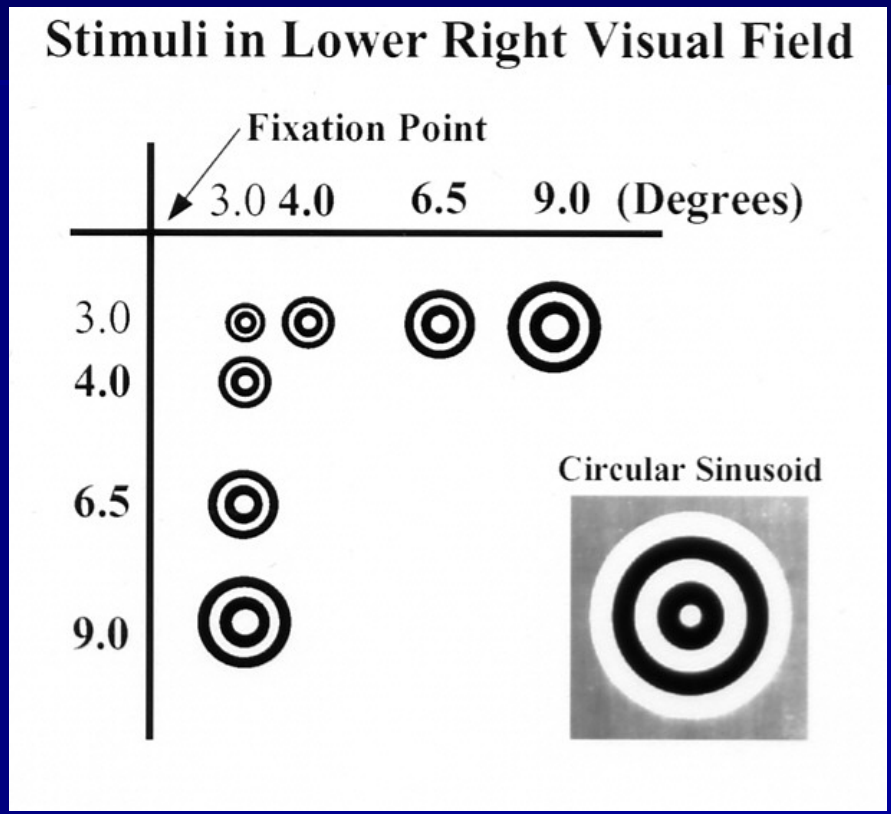
Retinotopic organization of multiple visual areas of the human cortex

UNKNOWN

RETINOTOPIC ORGANIZATION OF THE HUMAN VISUAL CORTEX

Los Alamos National Laboratory

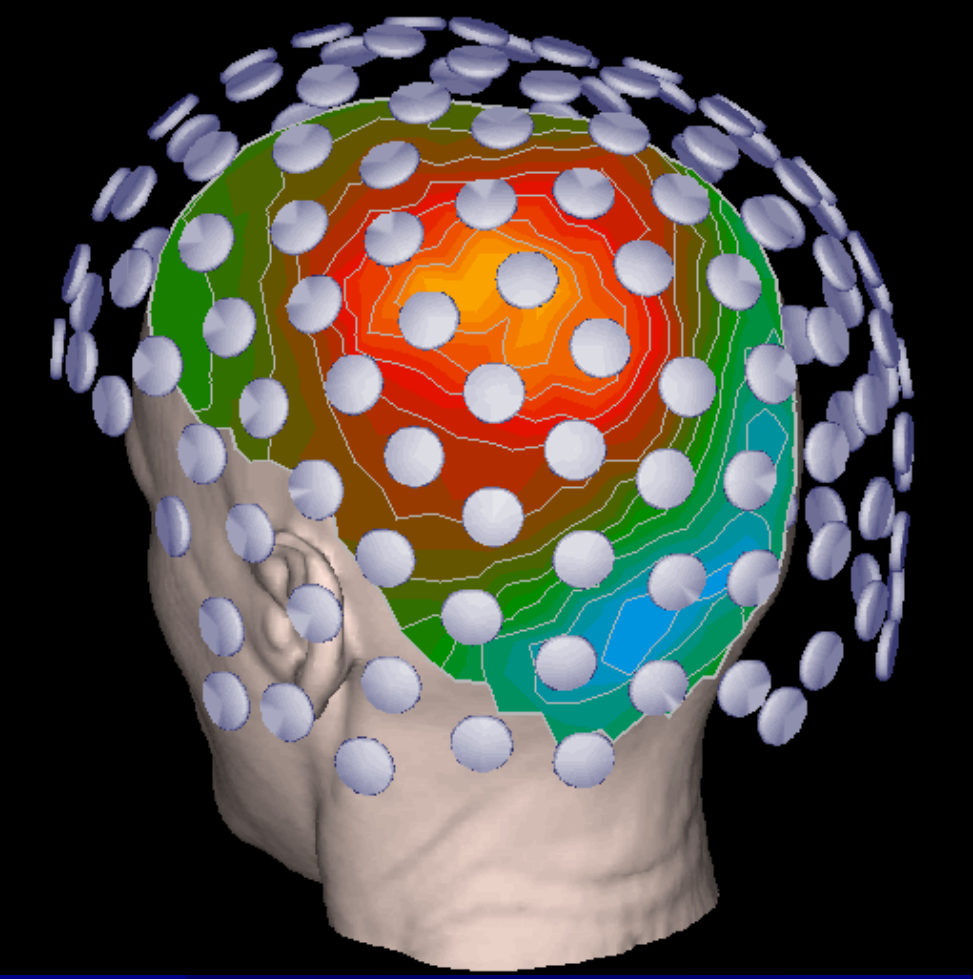




DOG = difference of gaussians

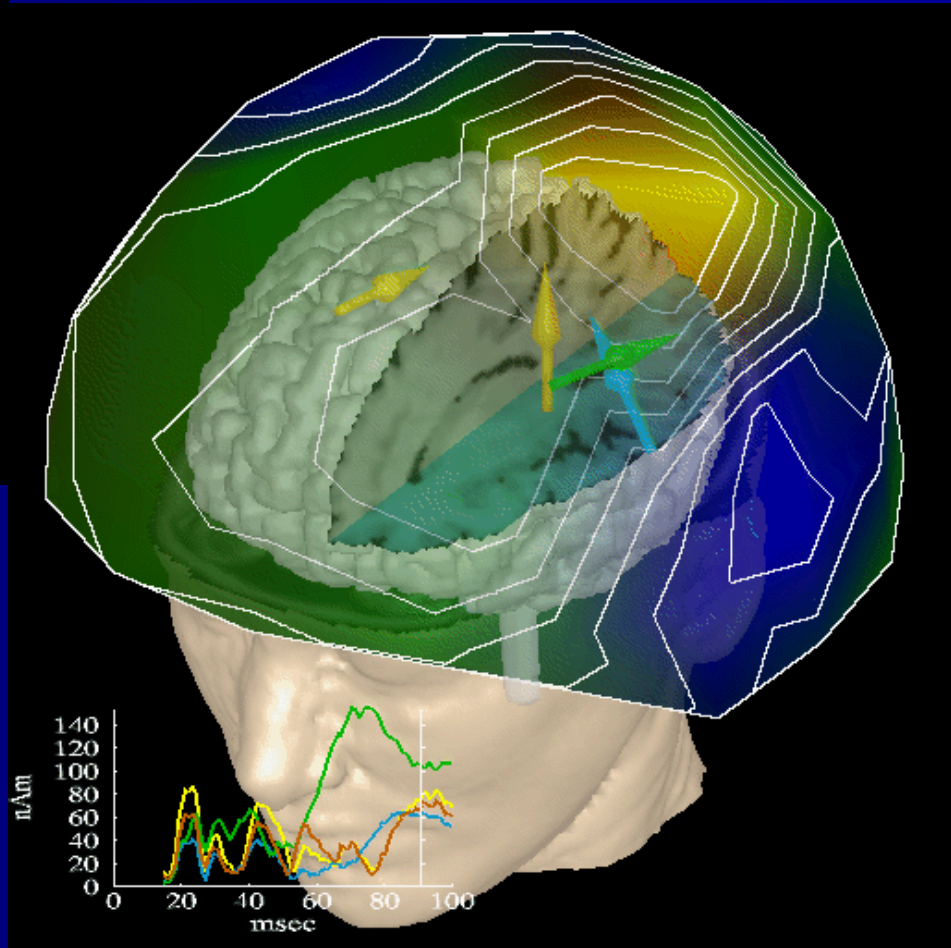
Supek at al., Brain Research, 1999

Aine, Supek, et al., Cerebral Cortex, 1996



Neuromagnetic contour map

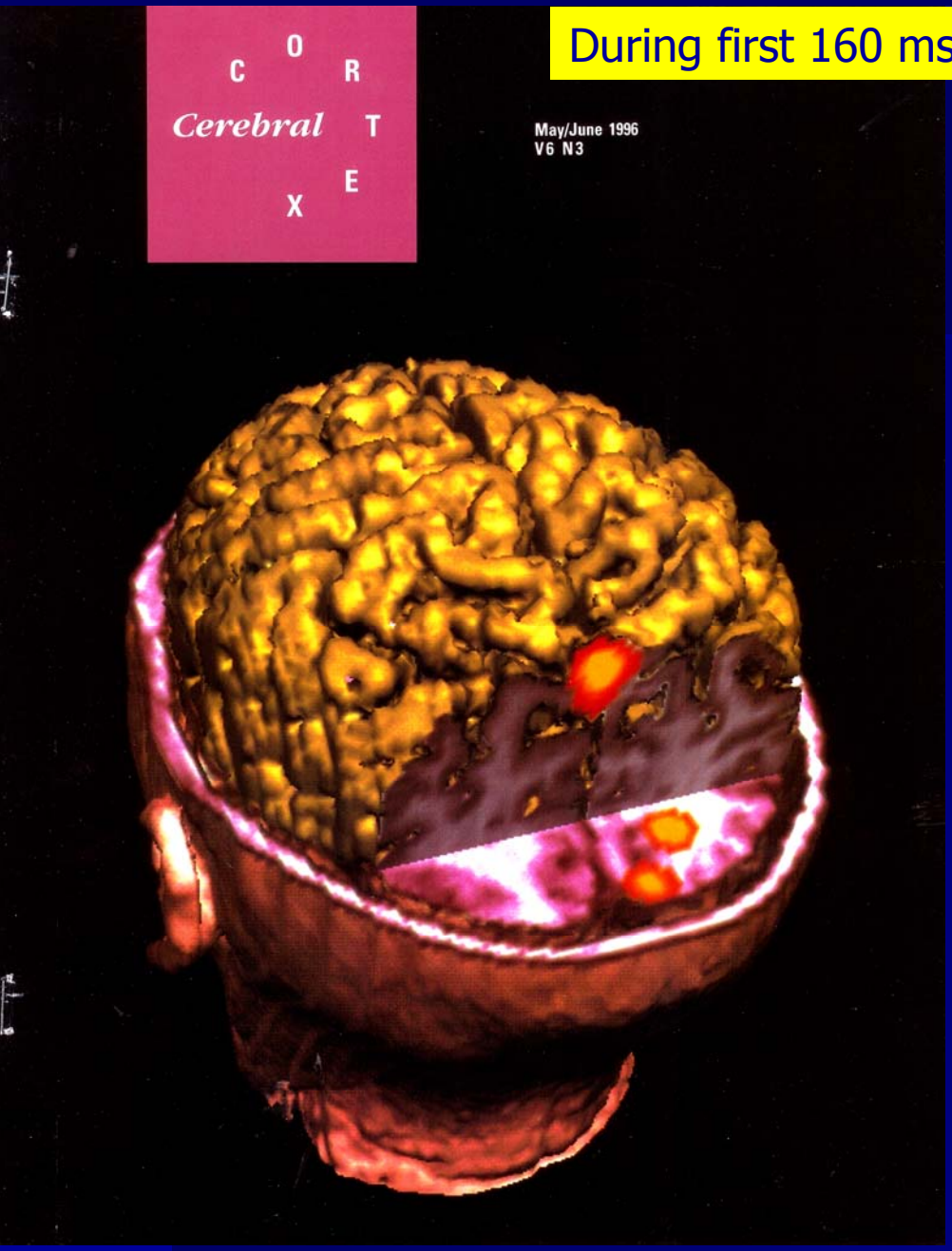
Measured field values at a single instant in time

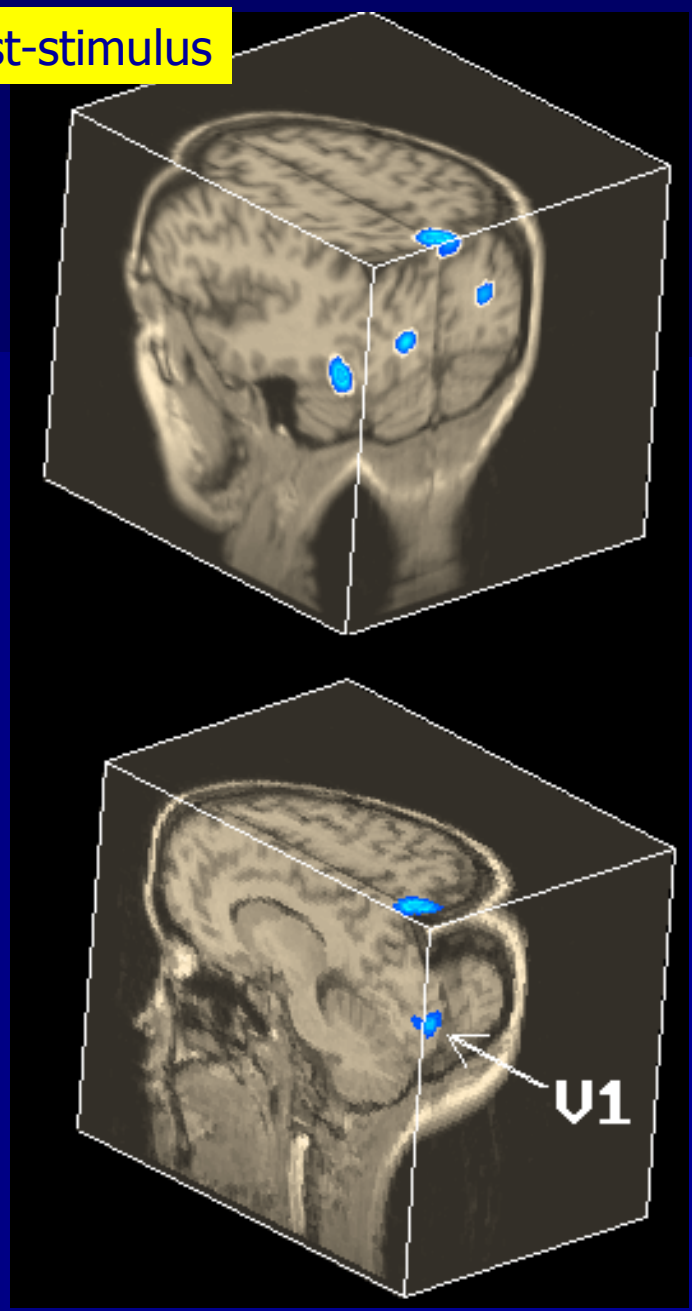


Functional source localization ------→

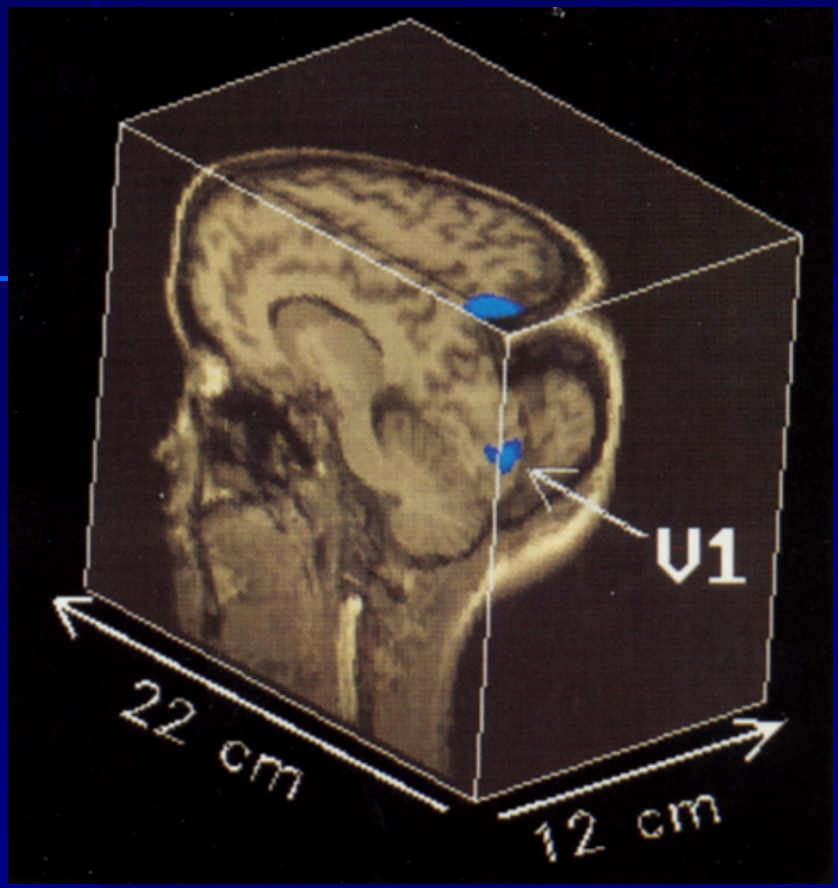
Estimated locations and timecourses

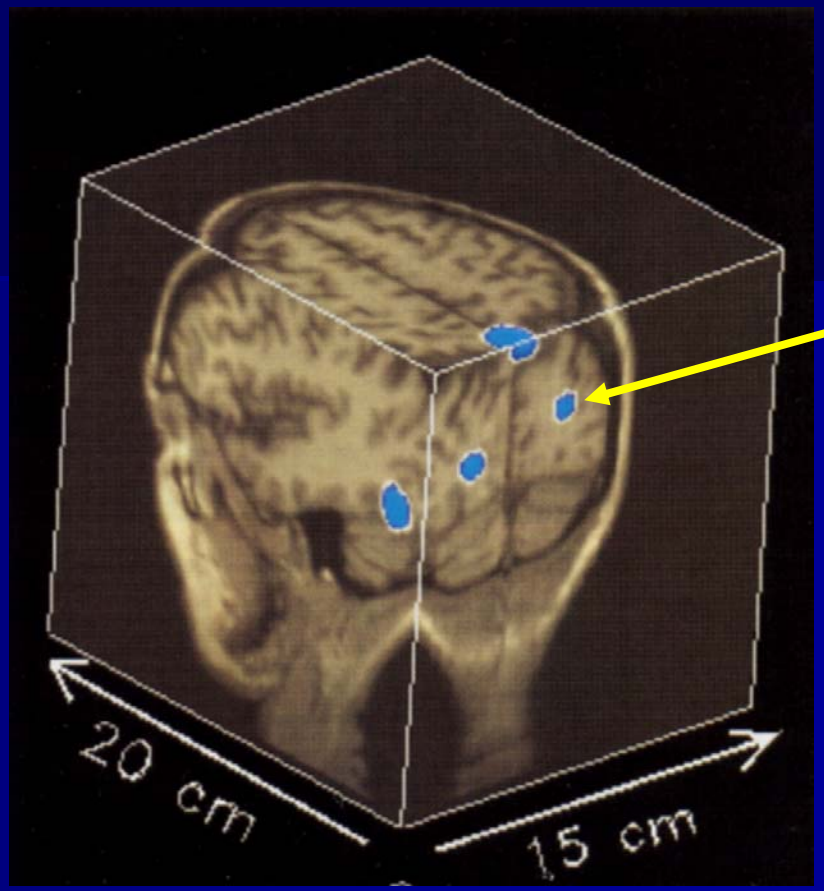
During first 160 ms post-stimulus





Aine, Supek….Wood, 1996

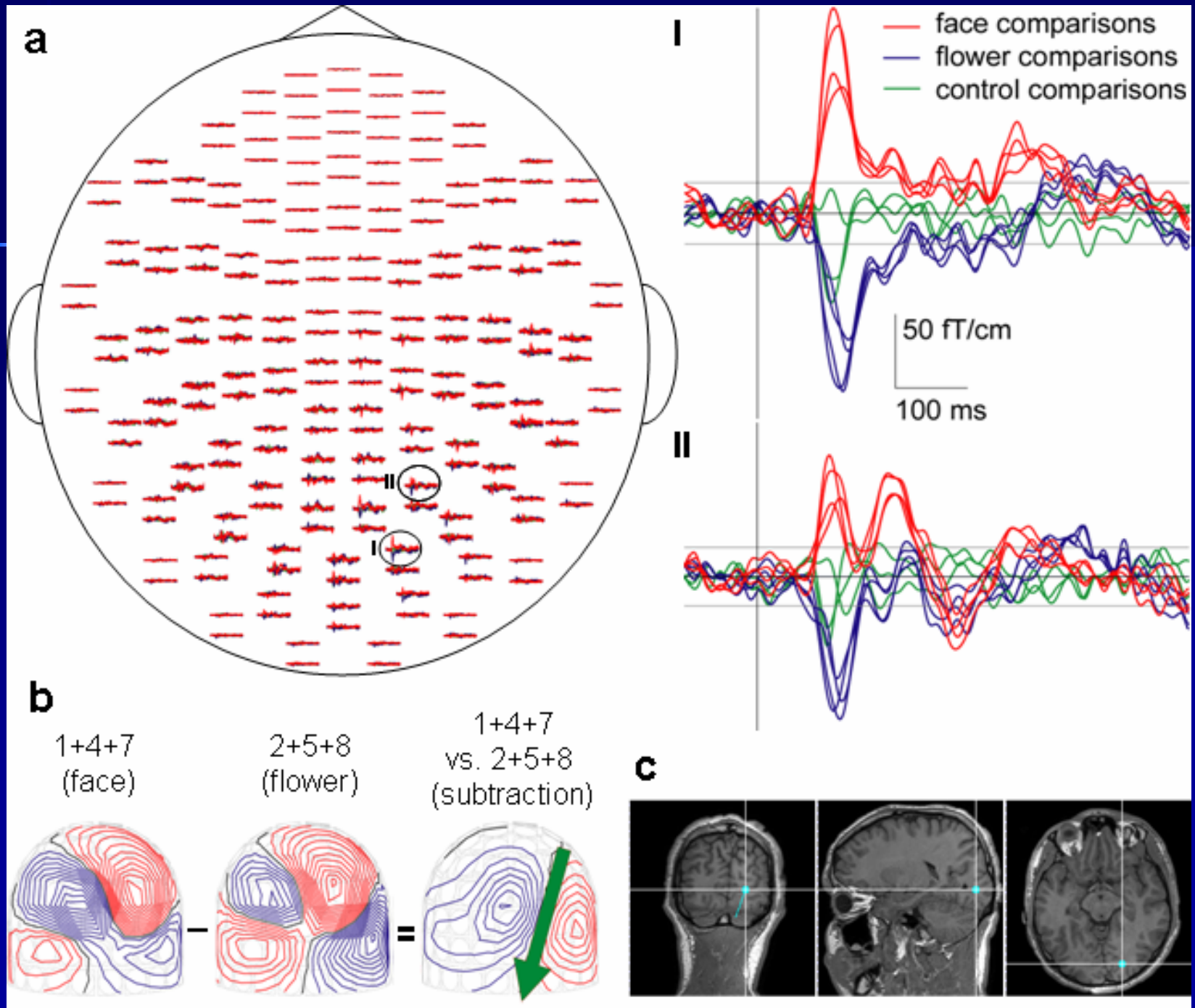




Target stimuli

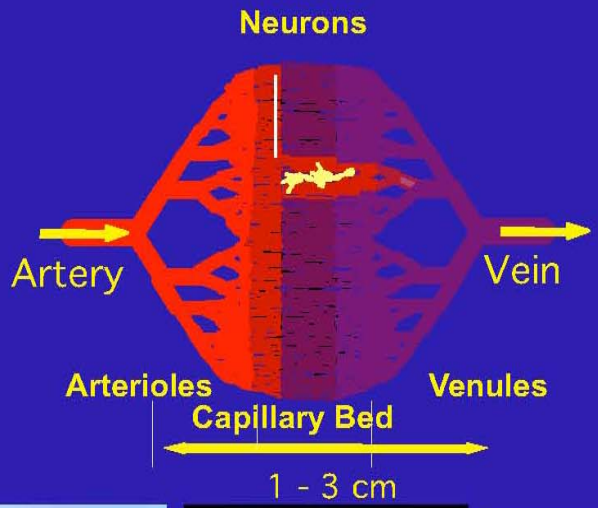
FIVE active sources during first 170 ms: V1, V2, parietal, temporal, ipsilateral

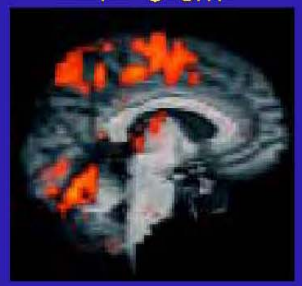
Aine, Supek, et al., Cerebral Cortex, 1996

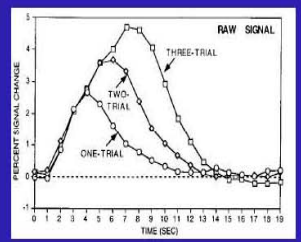

a
I
face comparisons
flower comparisons
control comparisons
50 fT/cm
100 ms
II
b
1+4+7
(face)
2+5+8
(flower)
1+4+7
vs. 2+5+8
(subtraction)
c

Functional Imaging: Physics and Physiology of Hemodynamic (fMRI, PET, DOI) and Electromagnetic (MEG, EEG) Techniques

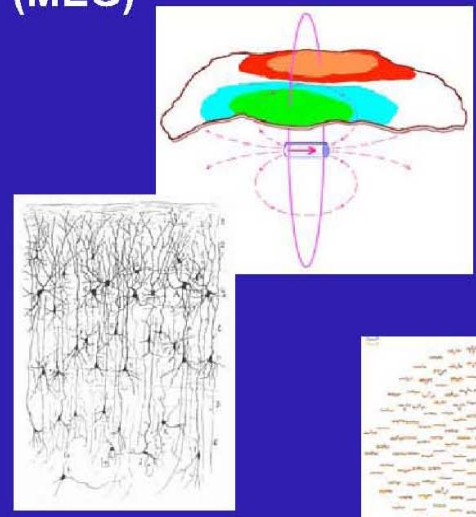
Functional Magnetic Resonance Imaging (fMRI)

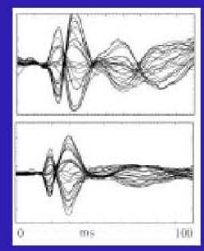






Magnetoencephalography (MEG)





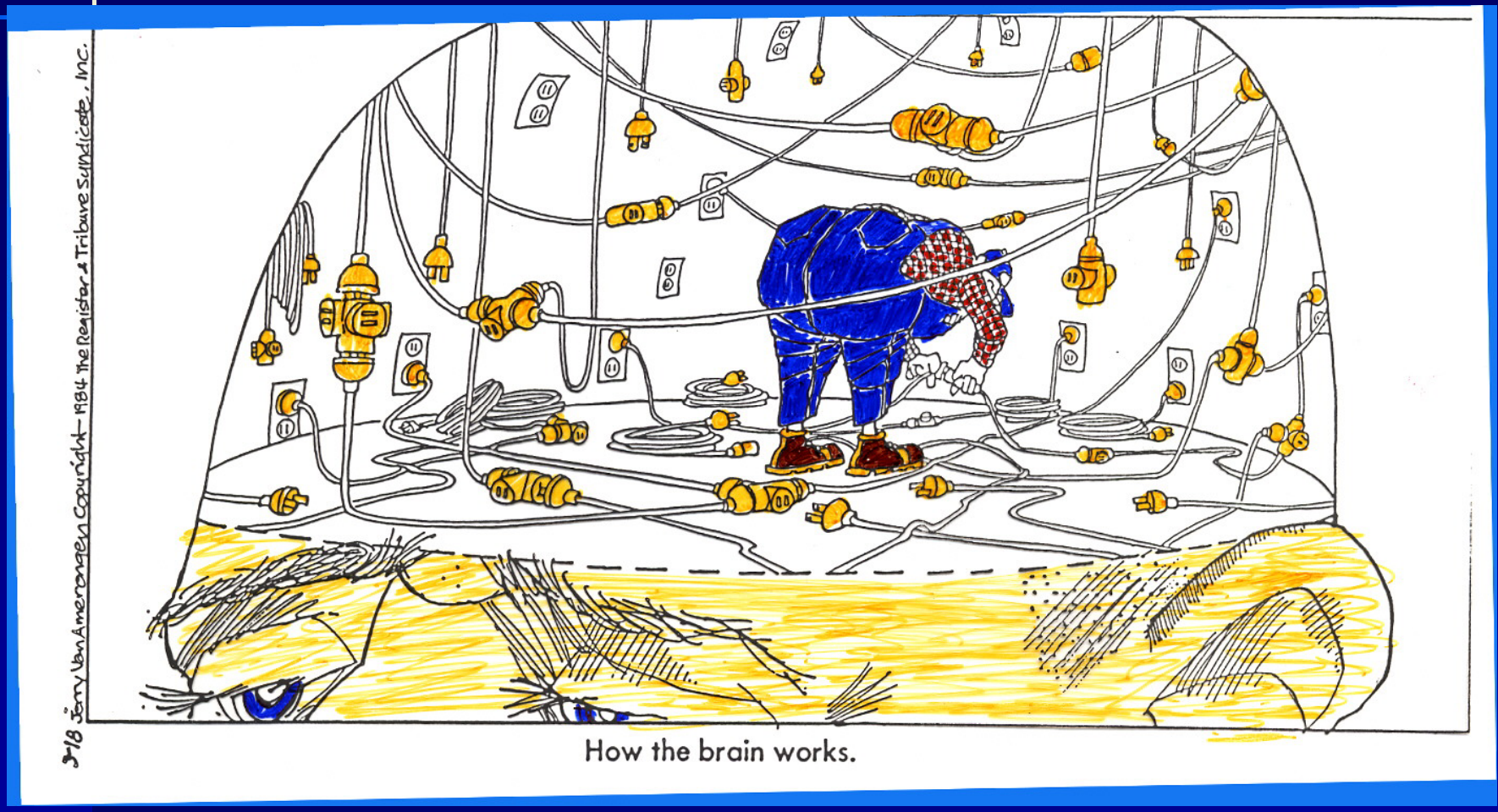
Measurement space – mm

- Excellent spatial coverage, spatial resolution, and spatial specificity
- Response timecourse on the order of seconds

Source space – mm – cm

- Excellent temporal resolution (sub-millisecond)
- Spatial resolution and specificity are model-dependent

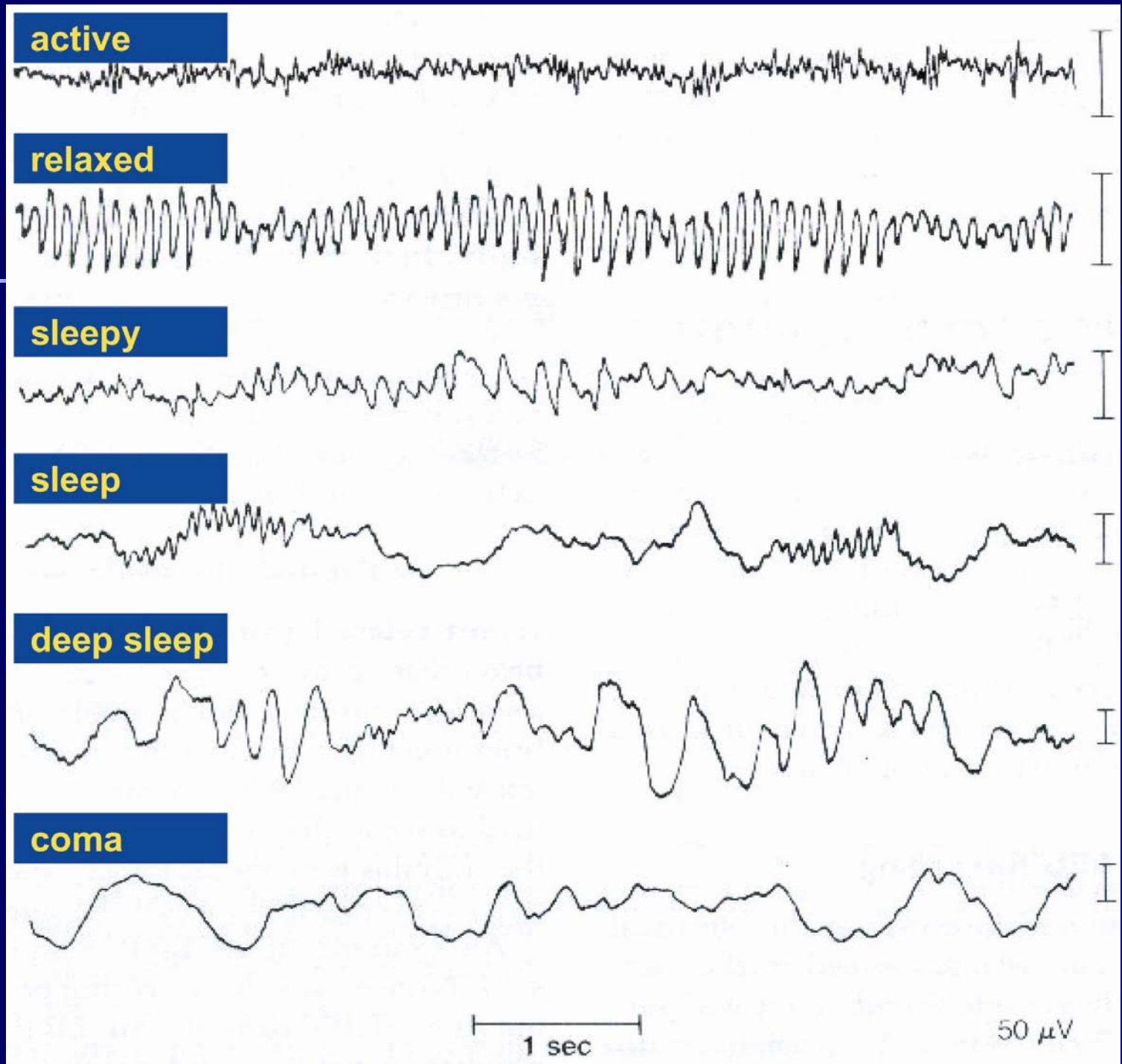
WHEN? WHERE? **HOW MANY?**

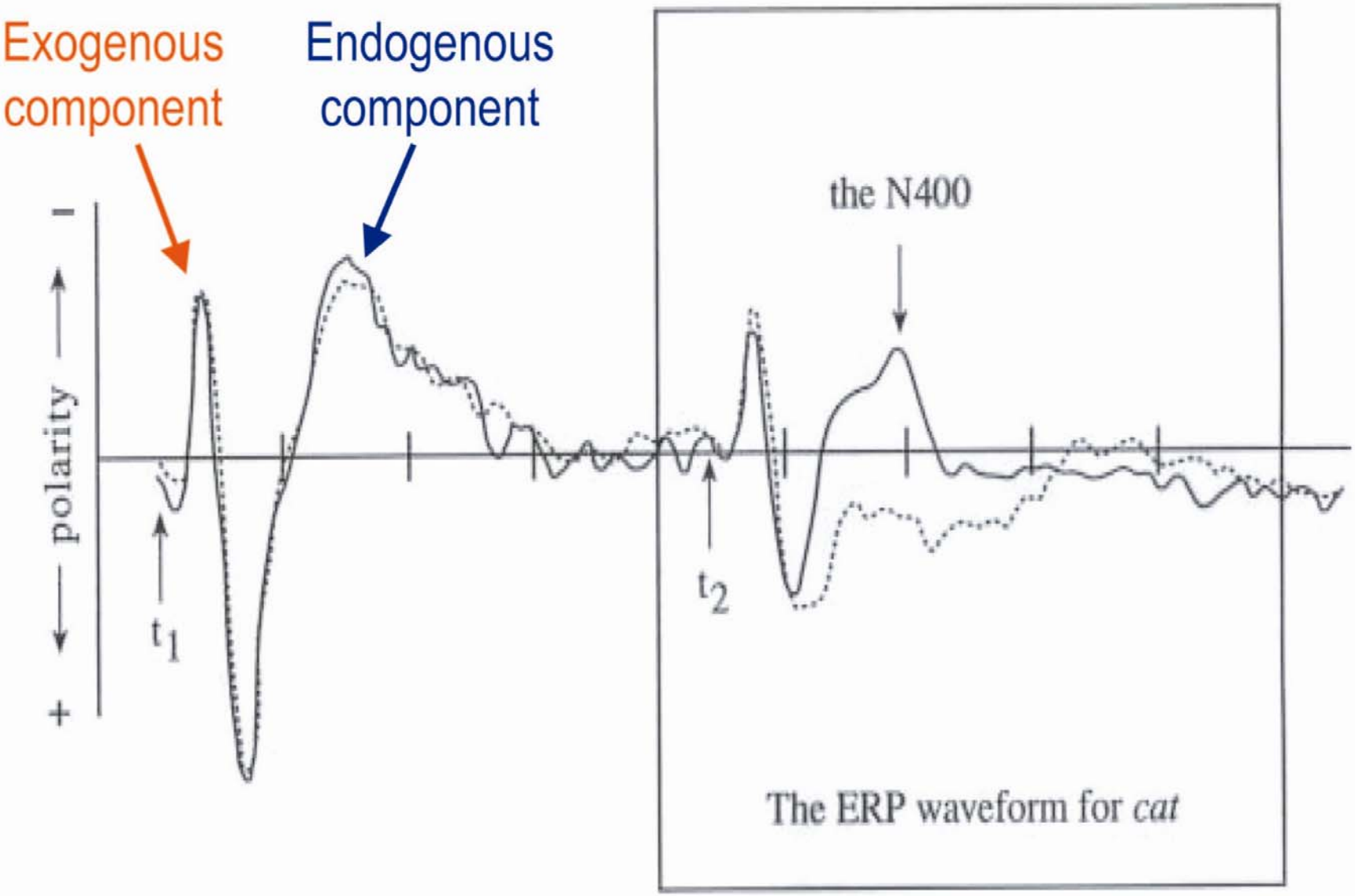


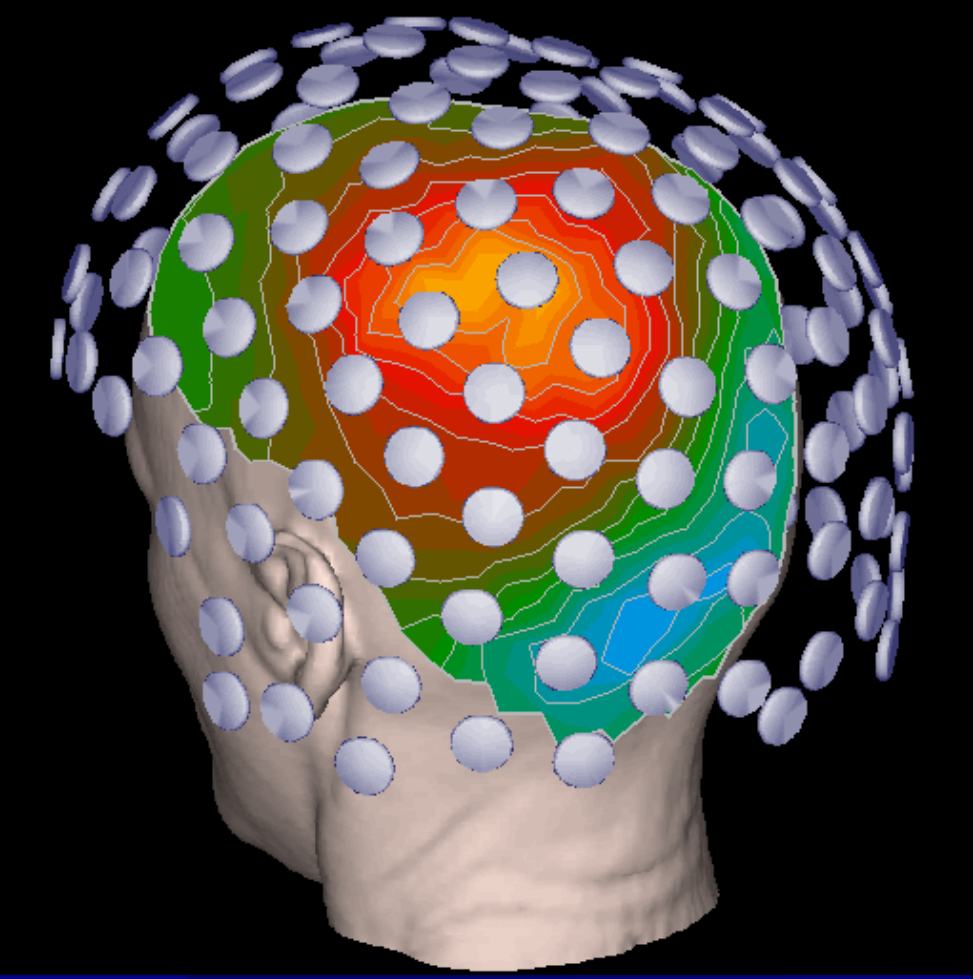
How the brain works.

Cognitive neuroscience

Cognitive neurodynamics

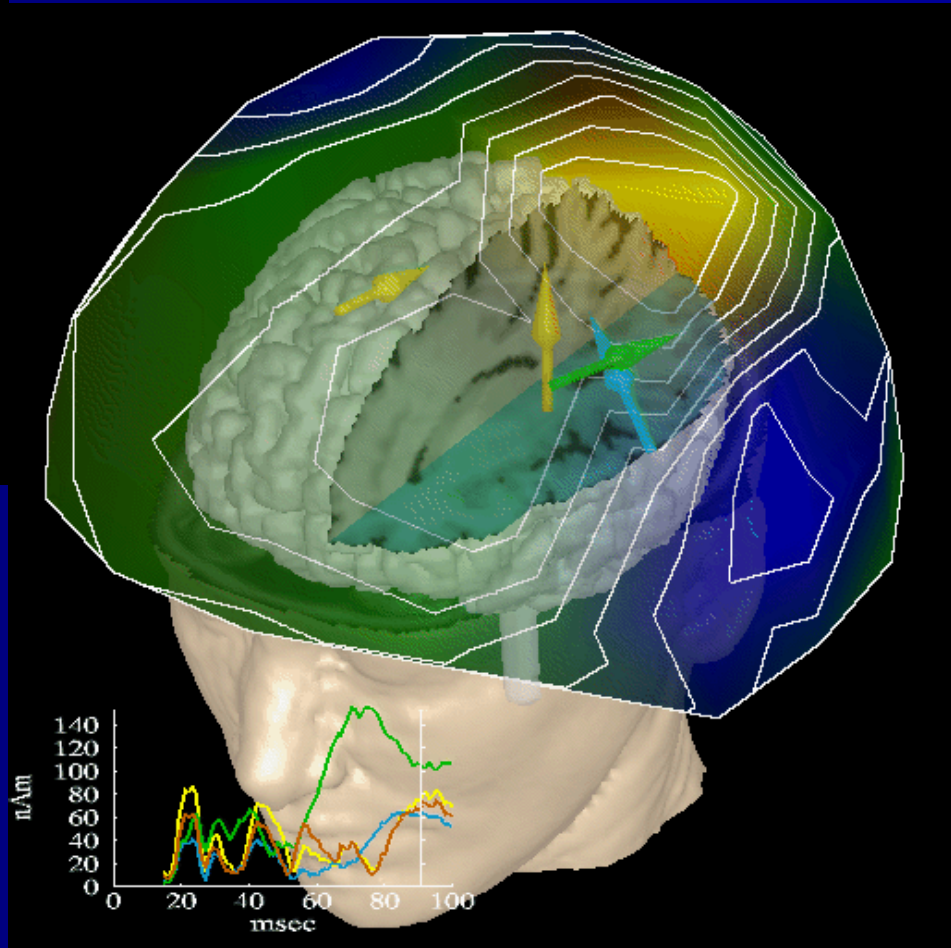

active
relaxed
sleepy
sleep
deep sleep
coma
1 sec
50 μV


Exogenous component
Endogenous component
the N400
+ polarity −
t_1
t_2
The ERP waveform for *cat*



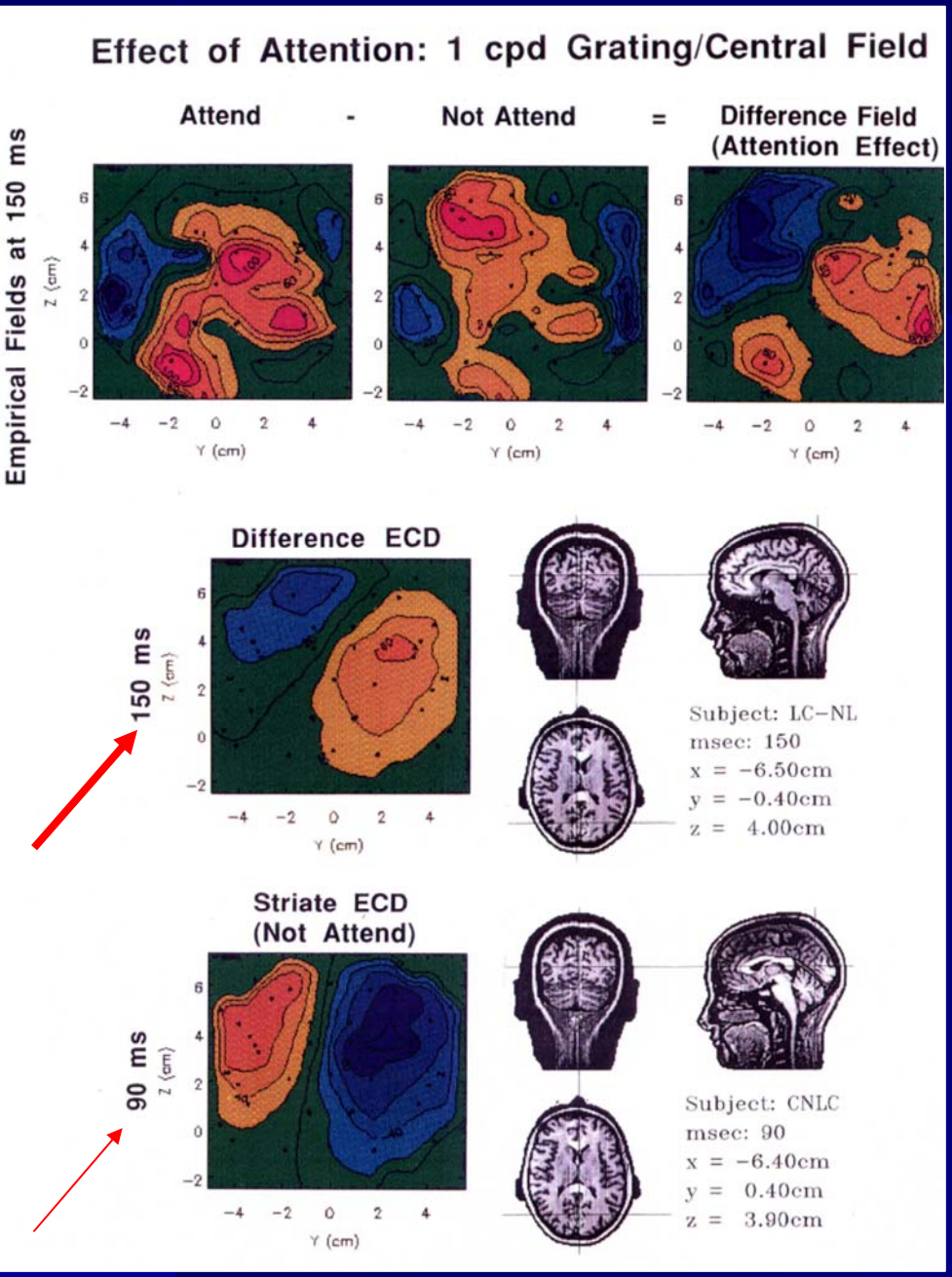
Neuromagnetic contour map

Measured field values at a single instant in time



Functional source localization ------→

Estimated locations and timecourses



Temporal dynamics of attention

Aine, Supek, George: Intern. J. Neurosci., 1995

First evidence

of early selective visual attention effects in V1

Aine et al., 2004, BIOMAG2004

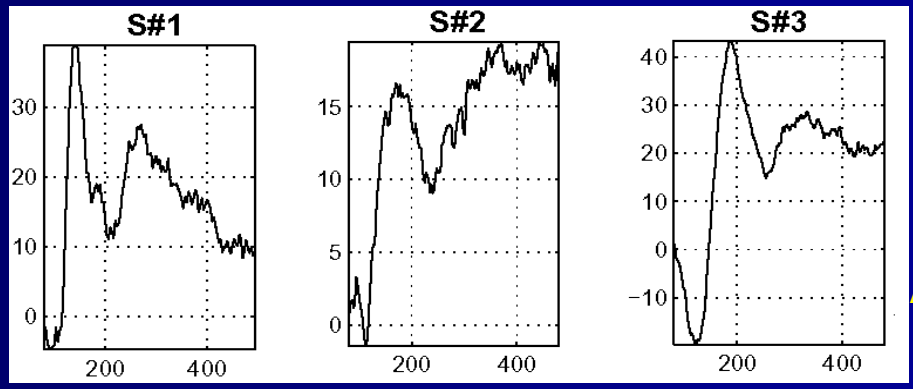
SPATIAL SELECTIVE ATTENTION

Can striate cortex (V1) be modulated by selective attention?

Early studies of spatial attention in monkeys suggested that V1 was not influenced by spatial attention, unlike extrastriate areas (e.g., Wurtz and Mohler, 1976; Moran and Desimone, 1985).

Activity in primary visual cortex and extrastriate regions can remain active for hundreds of milliseconds after stimulation, depending upon the task.

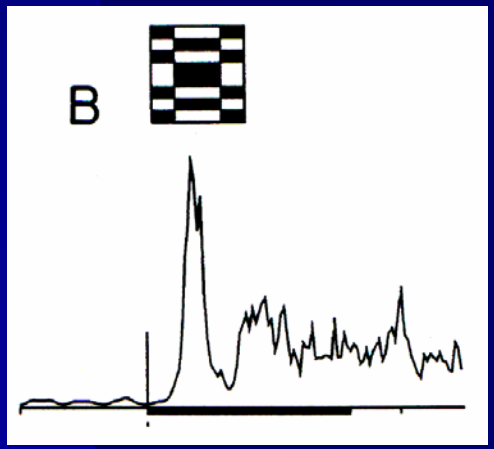
Human MEG Response Profiles—Medial Occipital Cortex

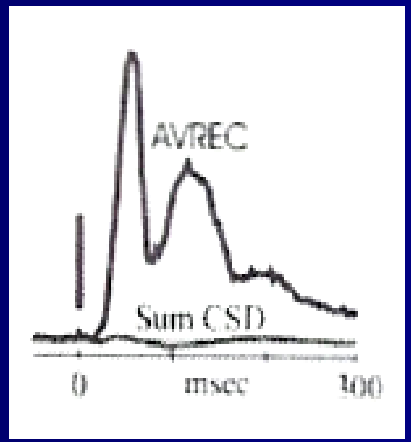


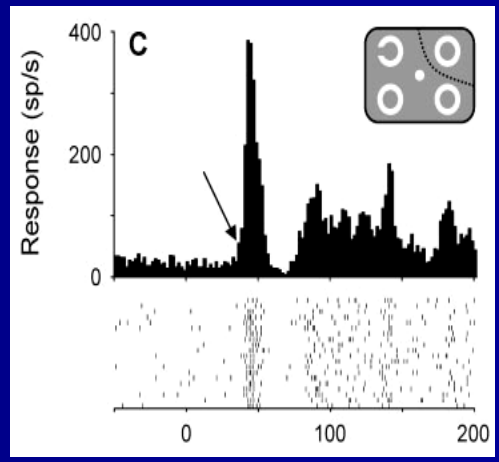
Aine et al., 2003

Response Profiles from Monkey V1

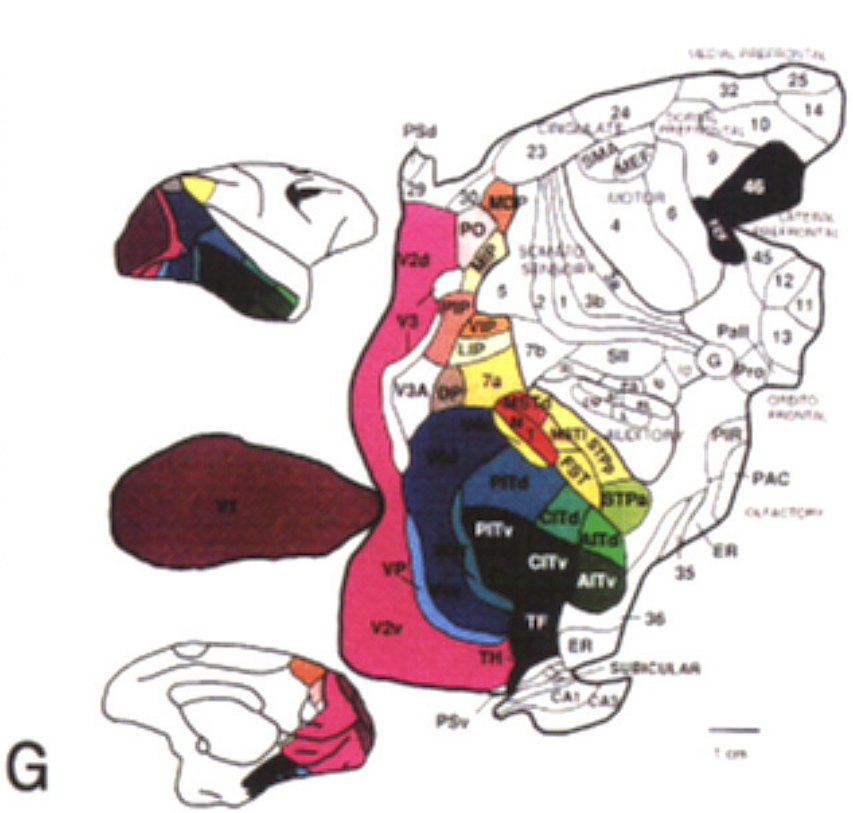
Monkey Parietal Cortex







Richmond et al., 1990 **Mehta et al., 2000** **Bisley et al., 2004**



MEG studies support the assumption that
distributed focal processes can adequately characterize
complex cognitive processes
as opposed to a strict serial and hierarchical arrangement.

NIH 5RO1 AG020302-03 C. J. Aine (PI)

"Functional Imaging of Aging and Alzheimer's Disease"

June 1, 2004 – May 31, 2009

longitudinal study

Goals:

1. to characterize functional networks of the normal brain engaged in episodic memory encoding/retrieval and working memory tasks using MEG/MRI methods

2. to develop new protocols to assess Mild Cognitive Disorder (MCI) and Alzheimer's disease in which medial temporal lobe dysfunction is known to occur

Alzheimer's disease (AD) – the most common form of dementia
- the third most costly disease to treat
- the prevalence of AD is expected to double by 2030

The clinical course of AD is characterized by gradual onset
and progressive decline in cognition
with sparing of motor, behavioral and sensory functions until later stages of disease

If untreated, the average duration of AD symptoms from onset to death is 8-10 years.

Structural imaging studies
Significant medial temporal lobe atrophy occurs before the diagnosis of mild AD

However, **earlier** diagnosis is necessary for novel anti-dementia treatements.

→ Functional neuroimaging studies

FUNCTIONAL NEUROIMAGING

MEG good spatial and temporal resolution
can disriminate early vs late activity
within subject analysis

MEG and anatomical MRI are used to follow a group of normal elderly (>65 years)

and a group of patients diagnosed as Mild Cognitive Impairement (MCI) or AD

in search of a neural pattern selective for mild AD

before detectable changes in cognitive decline are evident (i.e., preclinical)

Tasks ranging from **sensory** to various cognitive tasks are utilized in order to be more specific about the nature of the deficits found.

MEG results suggest that late activity associated with primary/secondary sensory regions is at risk early in the degenerative process (e.g., MCI)

and that early activity in these same regions
is compromised at mild to moderate stages of the disease (e.g., mild AD).

Sensory regions are not spared!

Sanja Josef Golubić – Physics PhD student

Analysis of the MEG auditory oddball data in progress.