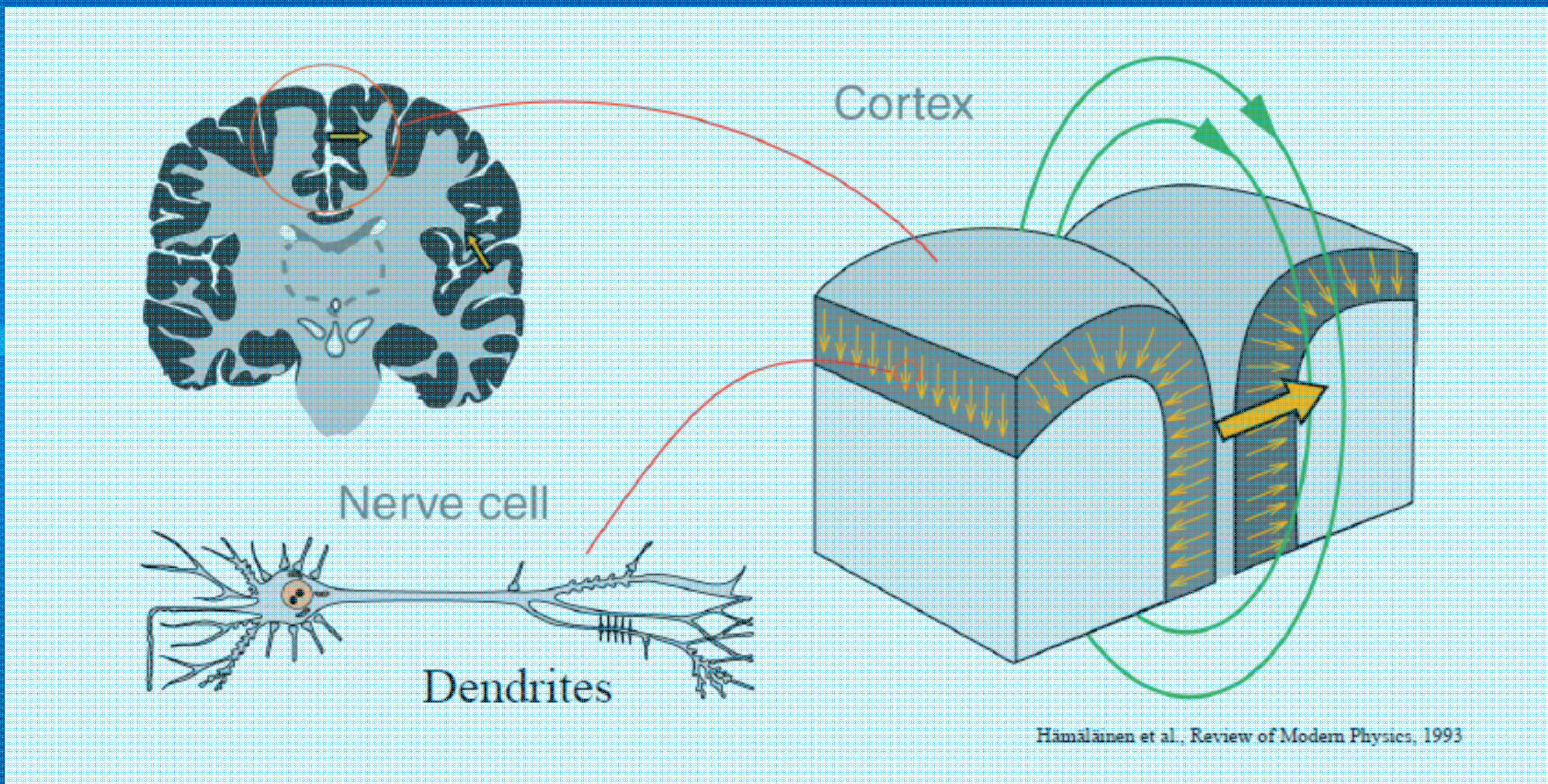
Epileptiform Patterns on Scalp EEG and MEG: Physiologic Basis and Principles of Localization



Cleveland Clinic

Richard C. Burgess, MD, PhD

Epileptiform Patterns on Scalp EEG and MEG: Physiologic Basis and Principles of Localization

OVERALL OBJECTIVES

- Understand the physiologic basis of the neurophysiological signals recorded from the brain
- Appreciate the basic physics and technical principles underlyng the recording instrumentation
- Become familiar with the fundamentals of source localization
- Understand the advantages and disadvantages of EEG and MEG for source localization

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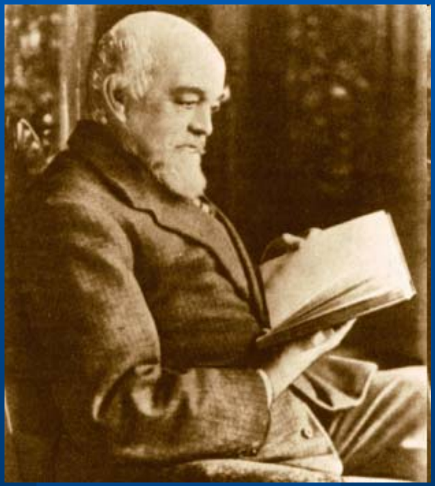
Definitions

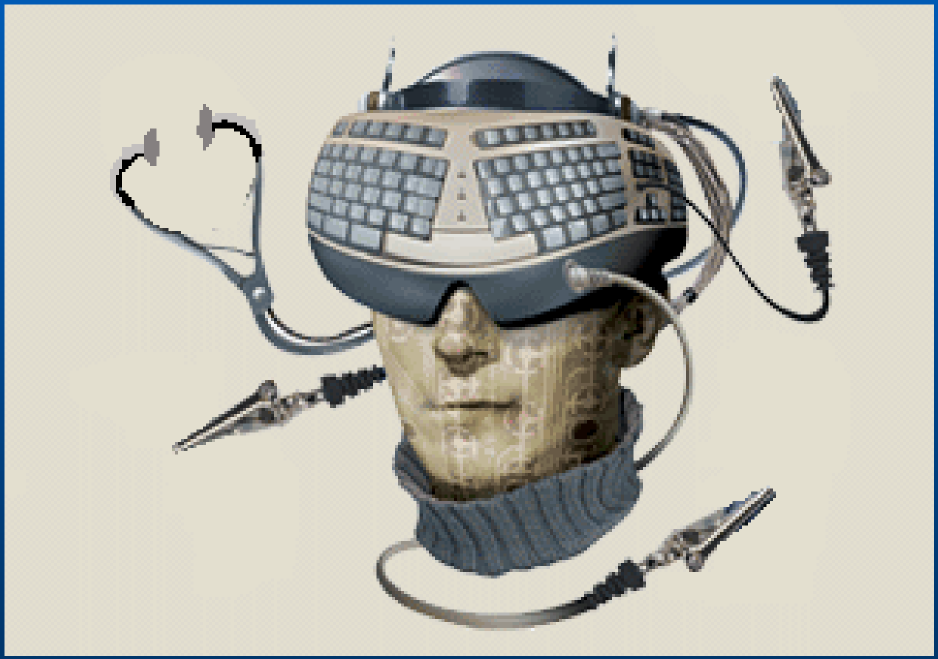
- Electroencephalography – EEG, recording of the brain's electrical activity
- Magnetoencephalography – MEG, recording of the brain's magnetic activity
- Source Imaging – pinpointing the location of the brain activity in three-dimensional space
  - ESI: electrical source imaging
  - MSI: magnetic source imaging

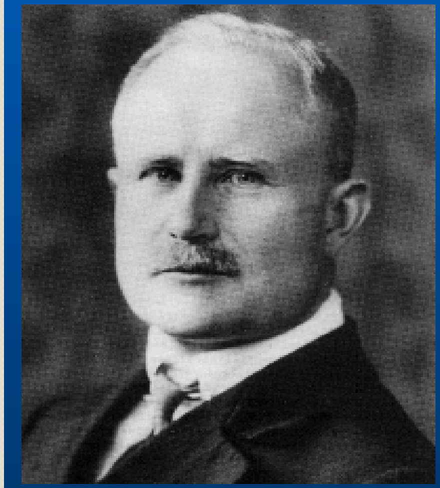
These two are neurophysiological techniques; they are not imaging methods, despite the names !

From where do the EEG and MEG signals originate?



Richard Caton

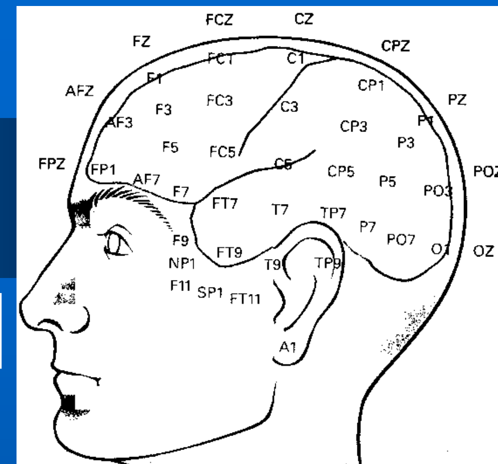


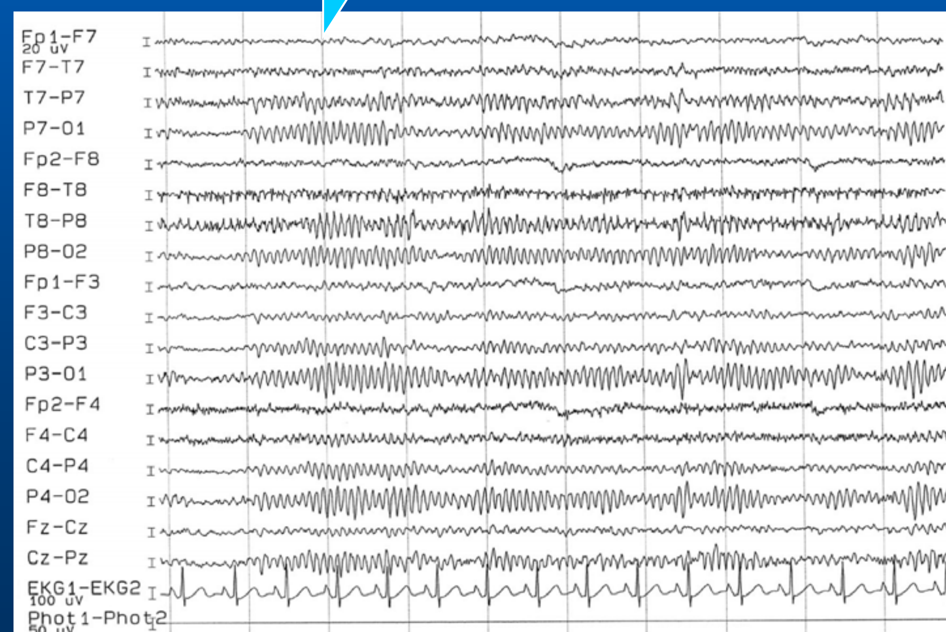


Hans Berger

What is EEG?

- The EEG is a measure of cerebral <u>electrical activity in the cortex</u>
- The summated <u>post-synaptic potentials</u> are the main generators of the recorded scalp EEG
- The electrical potentials reach the surface through volume conduction, a process of:
  - Origination,
  - Spread through a conductive medium, and
  - Pickup by a distant recording electrode.



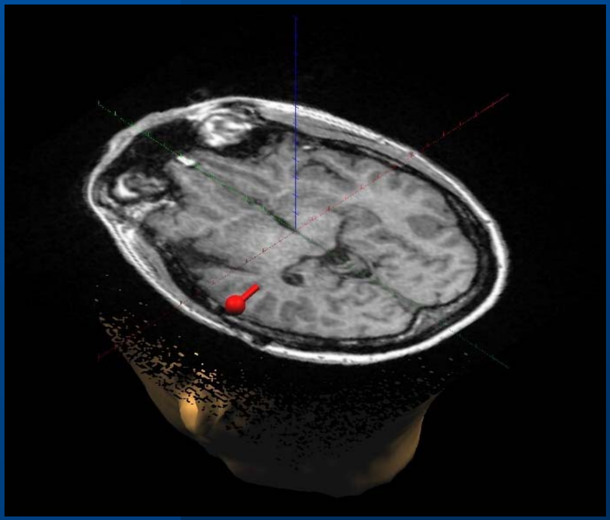


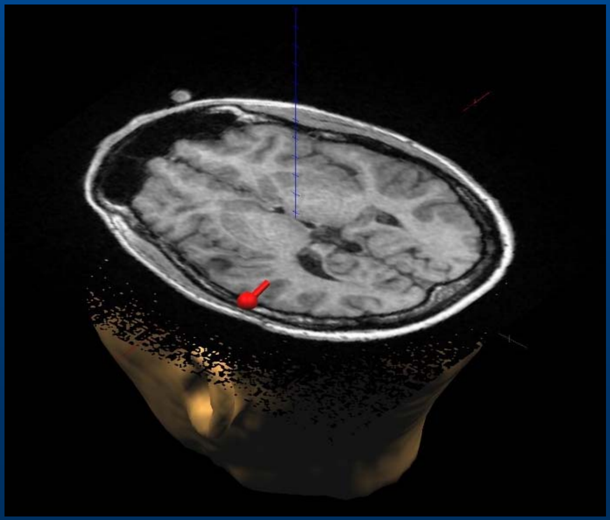
What is MEG?

- Based on recording of incredibly small magnetic fields (10^{-12} T).
- Easy acquisition of very high density (100-300 channels) wideband (DC – 2000 Hz) recordings of currents within the brain.

What is MEG?
MEG is a Localization Tool

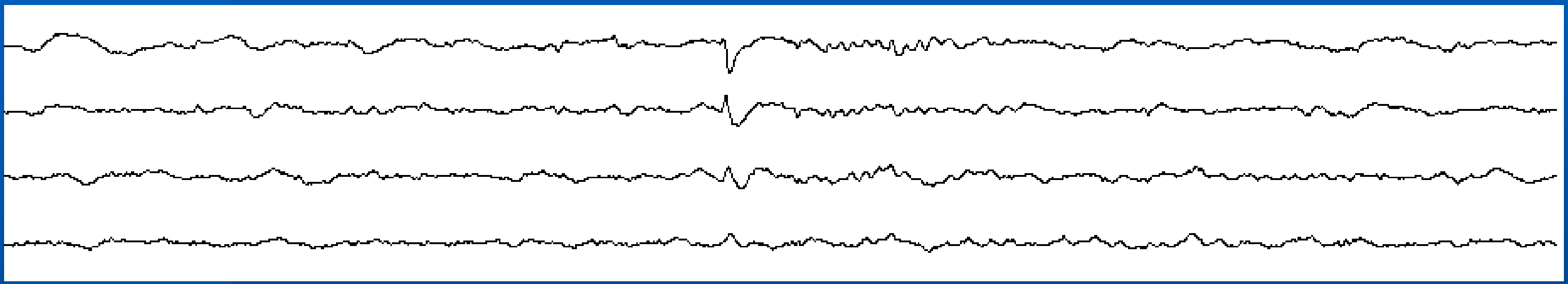
- **Based on solid theoretical reasons, MEG has localization accuracy better than scalp EEG**
  - **Greater number of sensors typically employed**
  - **Simpler source modeling and calculation**
  - **Anatomical co-registration with 3D-MRI**



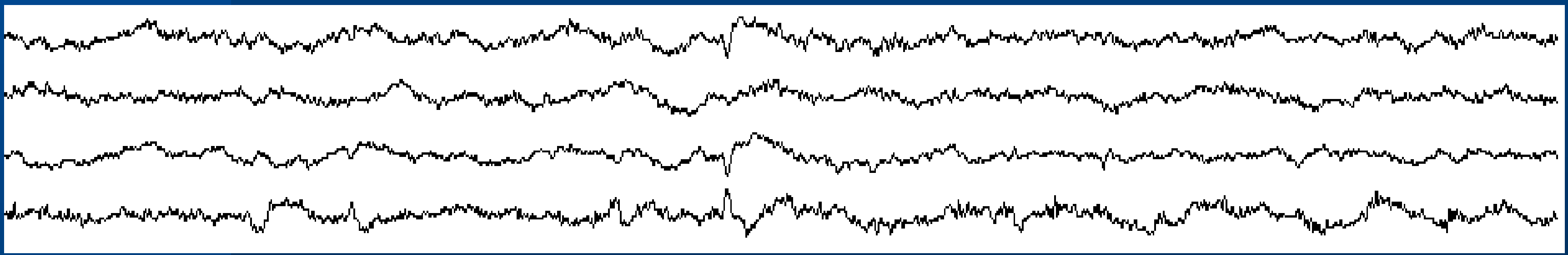


EEG and MEG Waveforms

EEG



MEG



Origin of signals recorded by EEG and MEG:

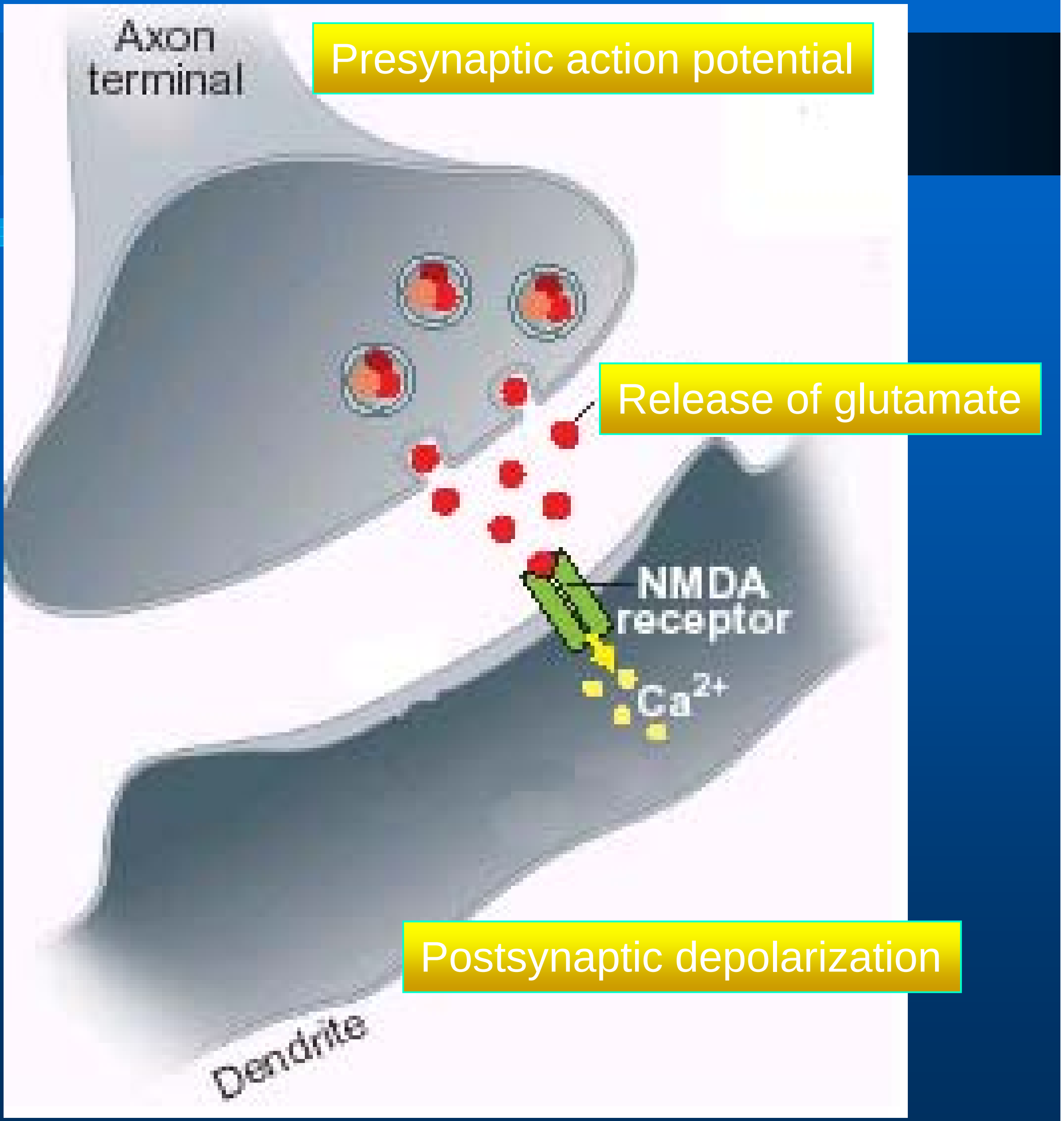
Main source is current flow from long apical dendrites of cortical pyramidal cells which are created from:

- 1. Gray matter synaptic potentials
- 2. Propagated action potentials in white matter fiber tracts (minimal contribution)

Consist primarily of:

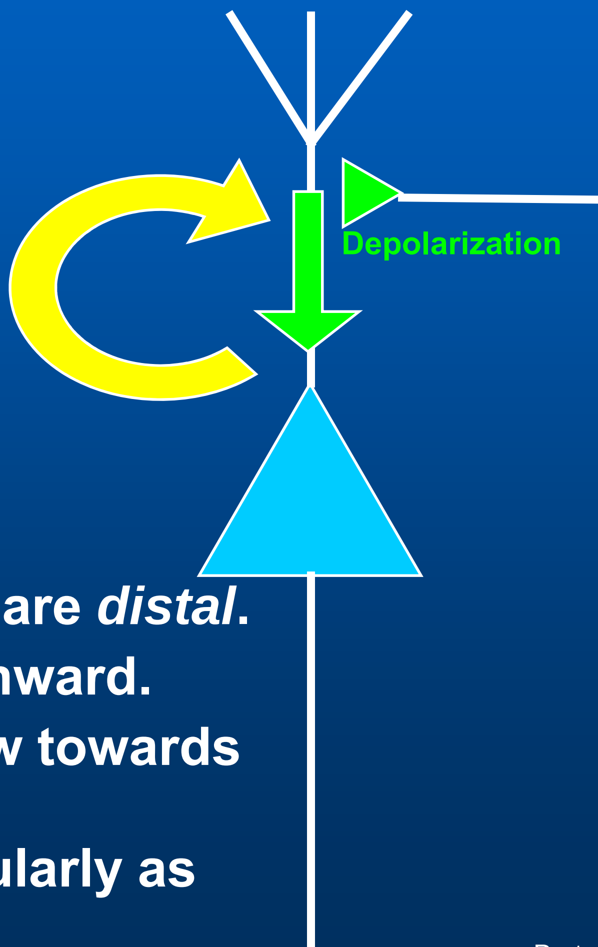
- Extracellular current resulting from summated IPSPs and EPSPs

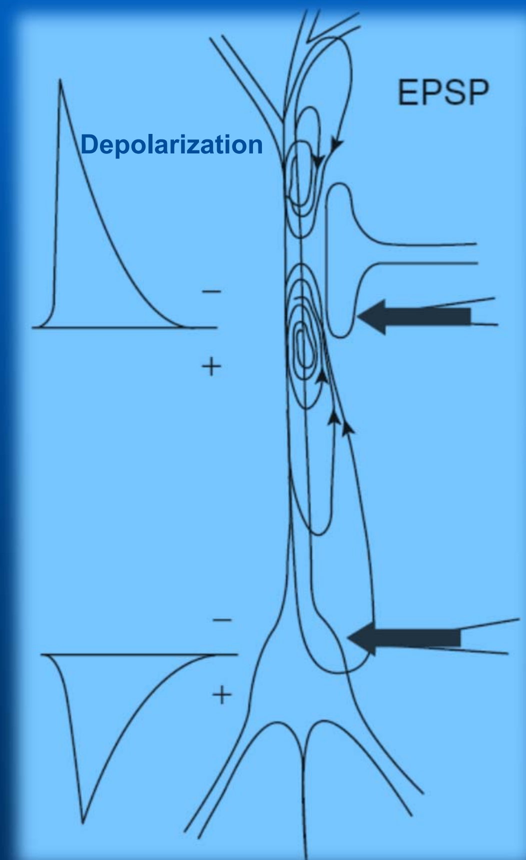
Excitatory Postsynaptic Potential (EPSP)



Pyramidal neuron excitation

- **Intracellular current**
- **Extracellular current**

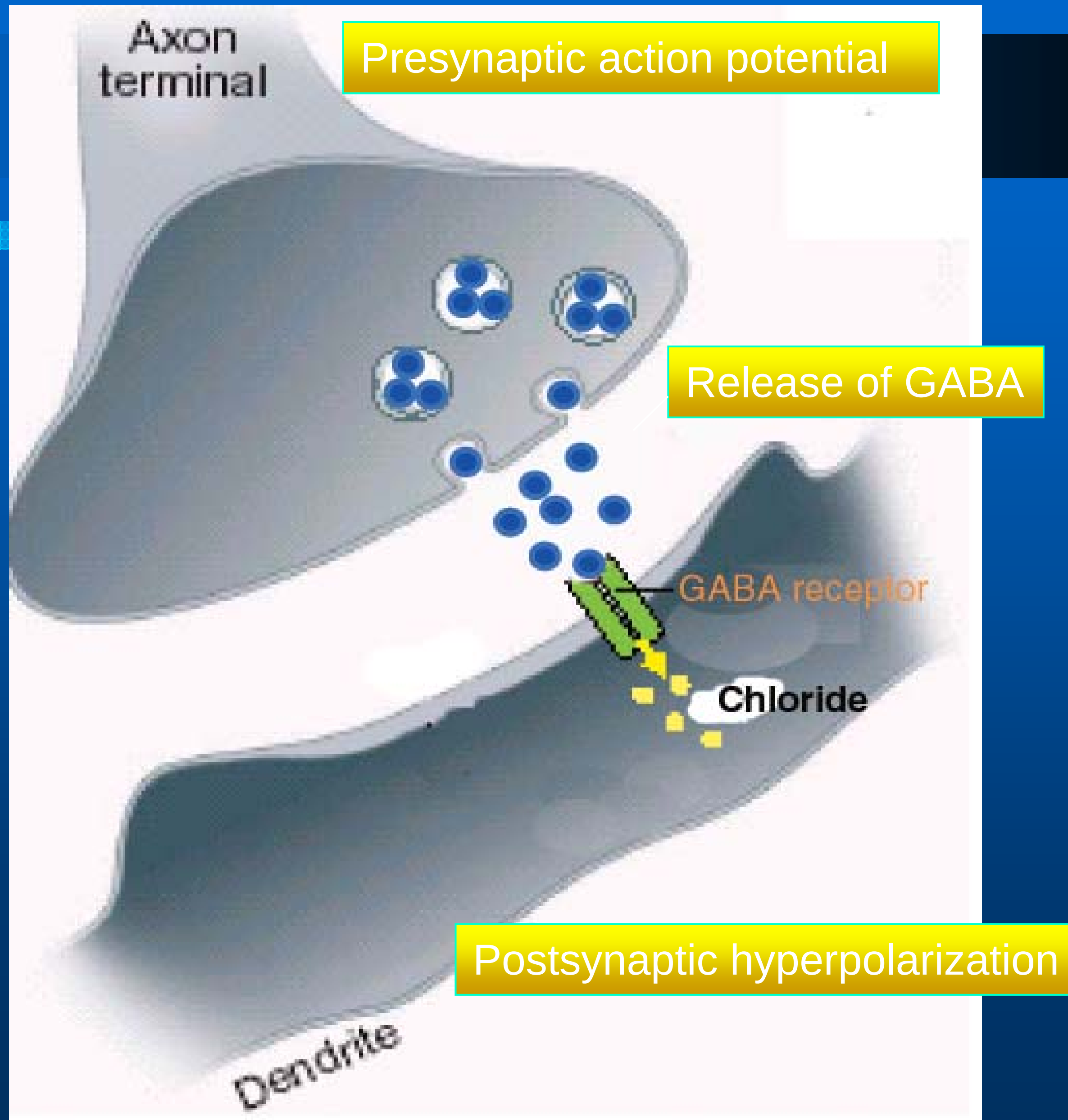




- **Excitatory synapse are *distal*.**
- **Positive ions flow inward.**
- **Induces current flow towards the soma.**
- **Measured extracellularly as *negative*.**

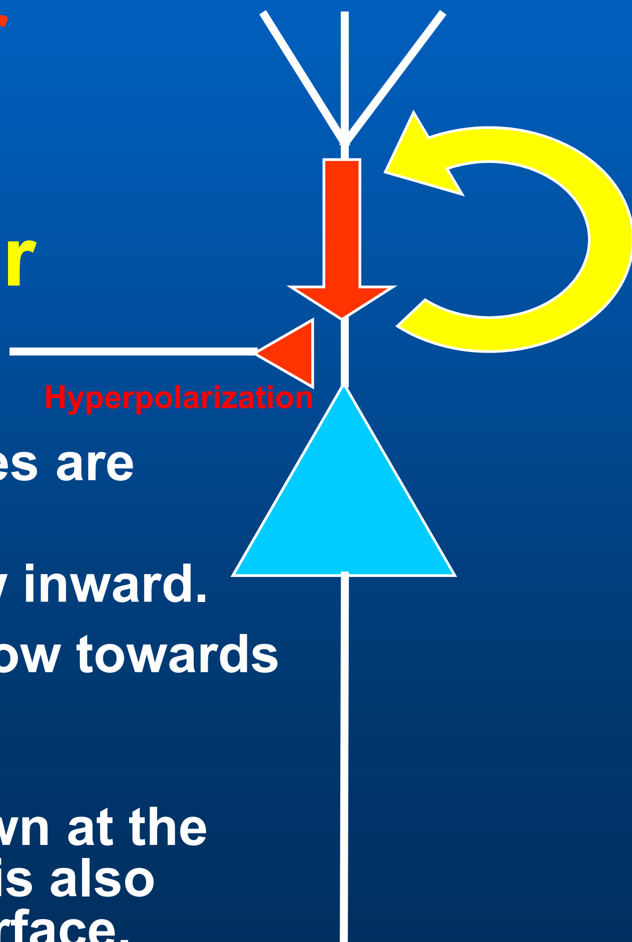
Part of illustration adapted from Hansen PC, Kringelbach ML, Salmelin R (eds). MEG: An Introduction to Methods.

Inhibitory Postsynaptic Potential (IPSP)

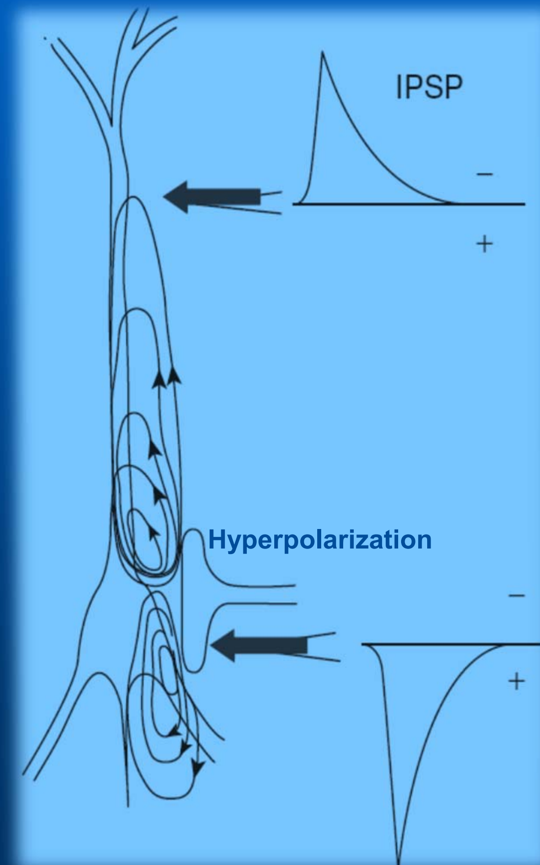


Pyramidal neuron inhibition

- **Intracellular current**
- **Extracellular current**



- **Inhibitory synapses are *proximal*.**
- **Negative ions flow inward.**
- **Induces current flow towards the soma.**
- **Measures positive extracellularly down at the synapse, but this is also *negative* at the surface.**



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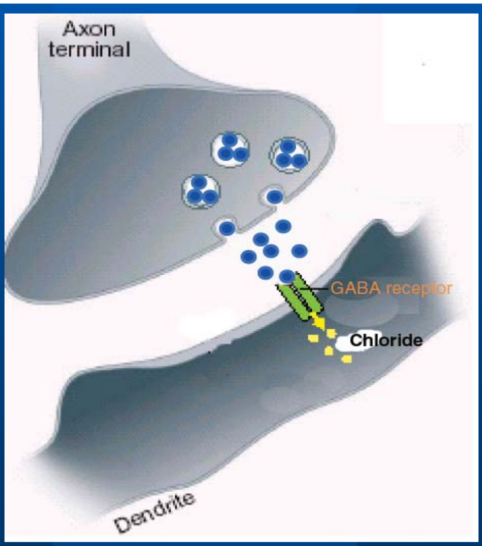
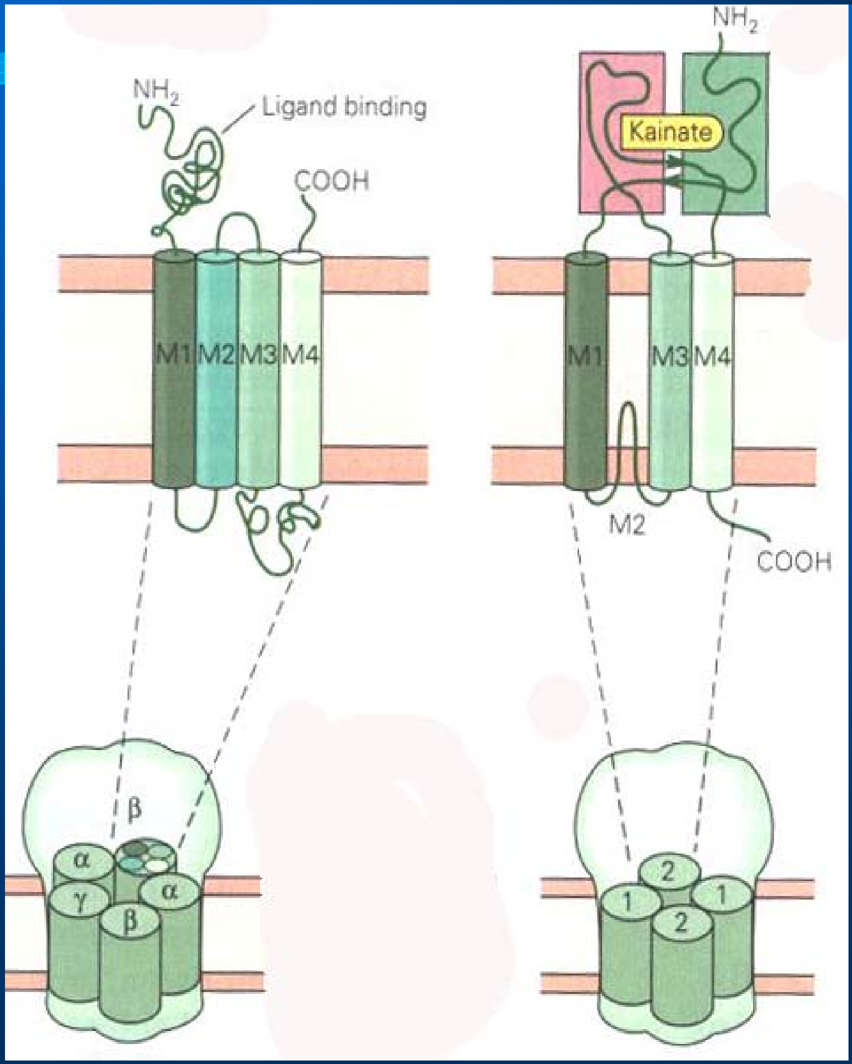
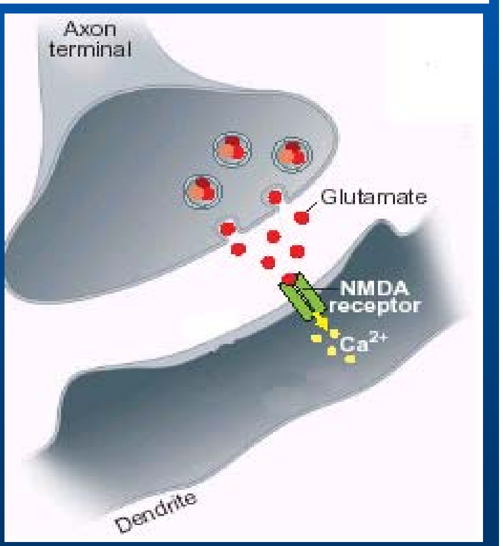
Synaptic Summary

Inhibitory Synapse
GABA





Excitatory synapse
Glutamate



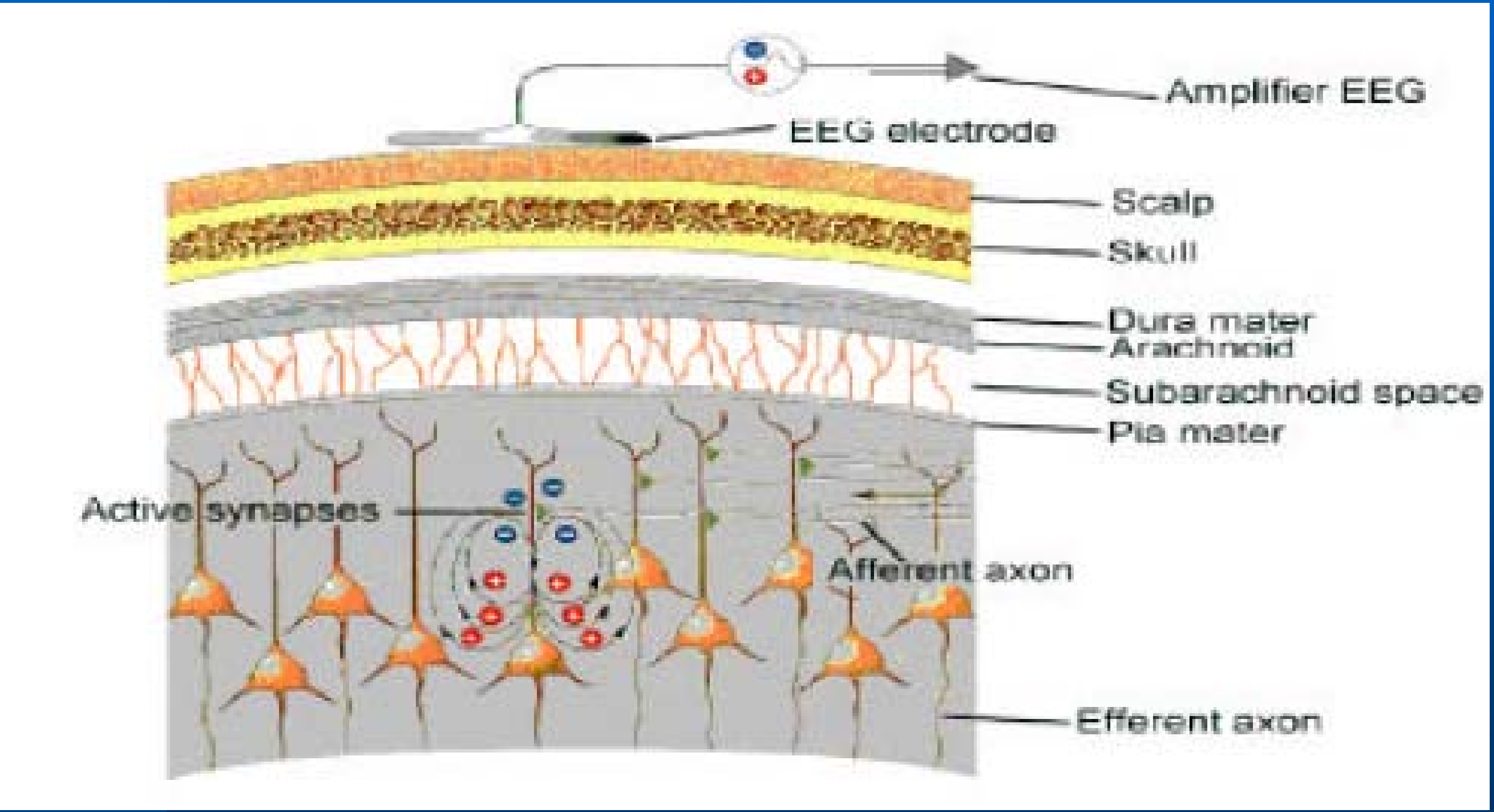
Non-Invasive recording of PSPs

- Tiny signals:
  - Signal from a single post-synaptic potential (PSP) lasts ~10 msec.
  - Too brief and too small to be detected non-invasively.
- Net effect of summated activity:
  - Thousands of adjacent pyramidal neurons.
  - Activated within more or less the same time window.

EEG and MEG Signals

A current dipole creates a magnetic field

Pyramidal Cells Act as Sheets of Dipoles in the Cortex



Cortical macrocolumn of diameter 3-4 mm contains:

10^6 neurons, 10^{10} synapses.

Presurgical Epilepsy Evaluation

- **Goals**
  - **Locate the epileptogenic zone.**
  - **Assess whether it *can* be resected to achieve seizure freedom.**

- **Multi-modality investigative tools:**
  - **Video-EEG monitoring +/- sphenoidals**
  - **MRI**
  - **PET/SPECT**
  - **Neuropsychology**
  - **Wada/fMRI**
  - **EEG and/or MEG source localization**
  - **Invasive Monitoring**

- **Additional hopes for source localization:**
  - **Avoidance of invasive recording if possible** ***OR***
  - **Better placement of invasive electrodes**

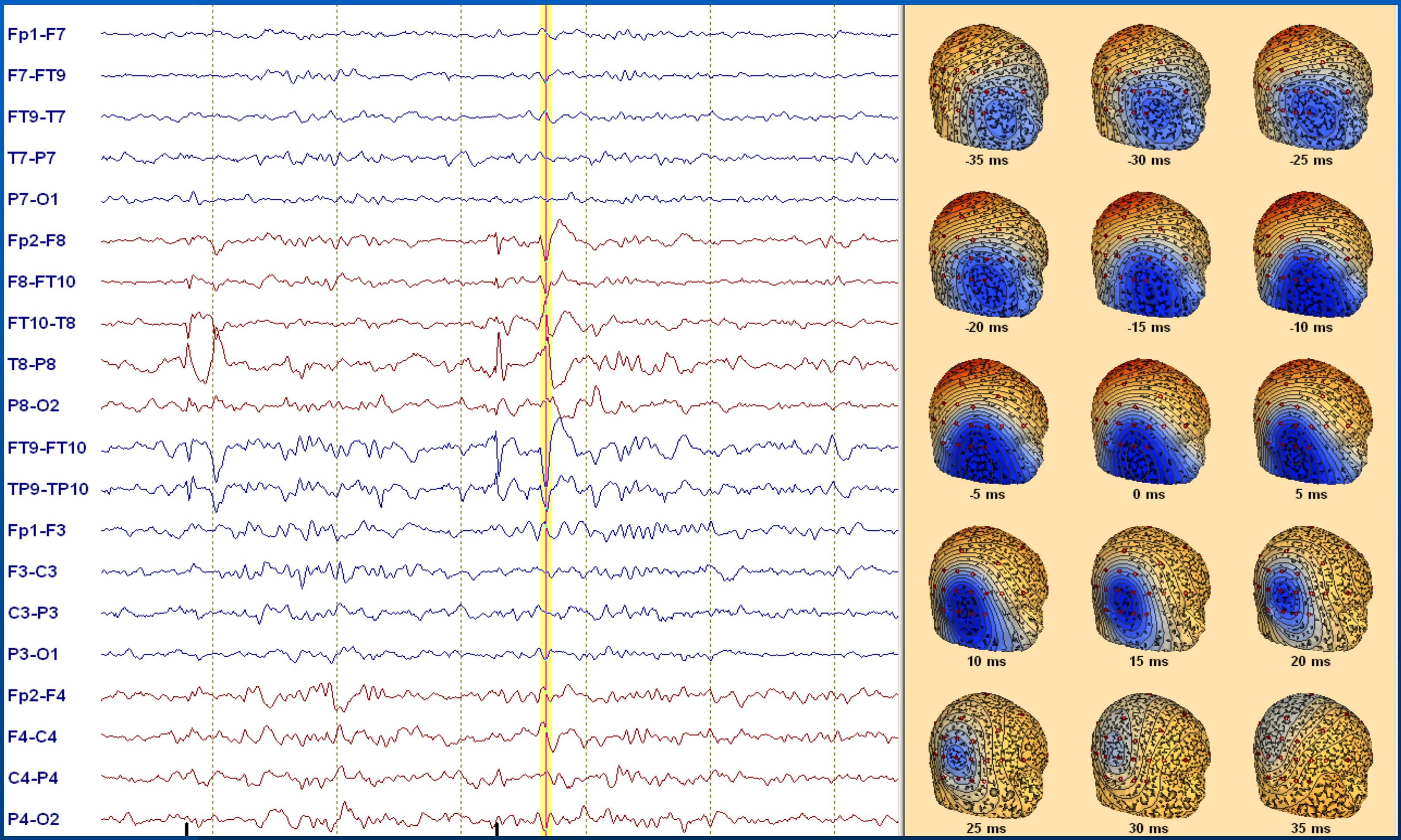
What is the Electroencephalographer or Magnetoencephalographer's Task?

<u>Examining the surface evidence of electrical currents, estimate the:</u>

- Magnitude,
- Location, and
- Distribution

Of the underlying source(s) producing the recorded field.

Topographic Mapping: Amplitude vs Time



Source Localization is Based on Computerized *Modeling*

- **Source model**
  - **number**
  - **type**
  - **location**

- **Head model**
  - **homogeneity**
  - **number of layers**
  - **shape**

Models of the Brain Electrical Activity *Sources*

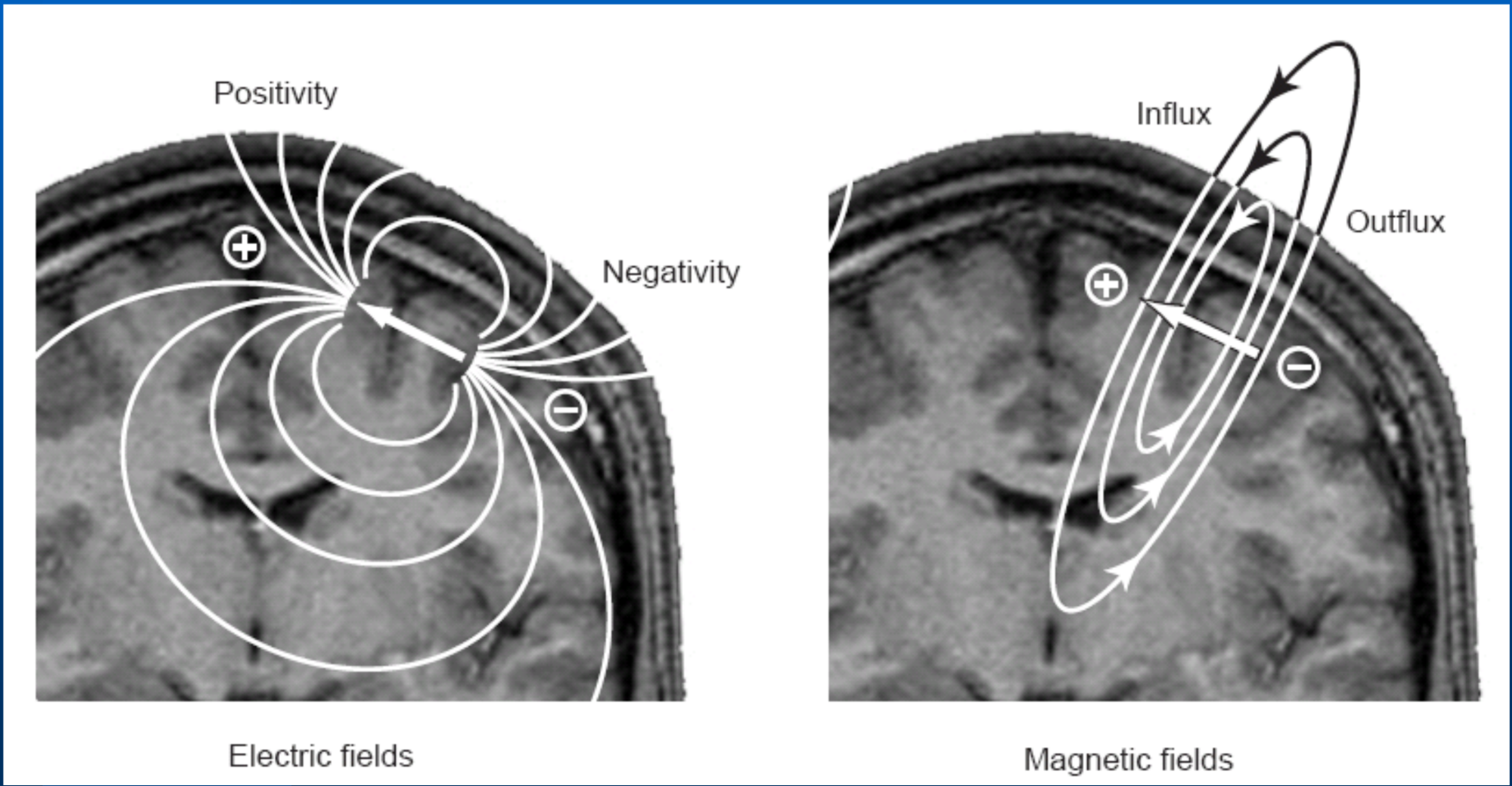
Equivalent Current Dipole Model (Simpler)

- Examples: Single Equivalent Dipole
- Multiple Signal Classification (MUSIC)

Distributed Model / Current Density Reconstruction Model (Computationally Intensive)

- Examples: Minimum Norm Estimate
- LORETA (Low resolution electromagnetic tomography)
- FOCUSS (Focal undetermined system solver)

Electric fields and magnetic fields generated by a current dipole.



What is an “*Equivalent* Dipole” ?

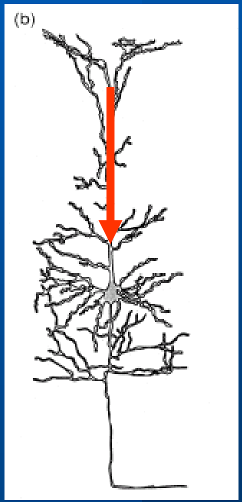
It is *not* the “centroid” of the electrical activity.

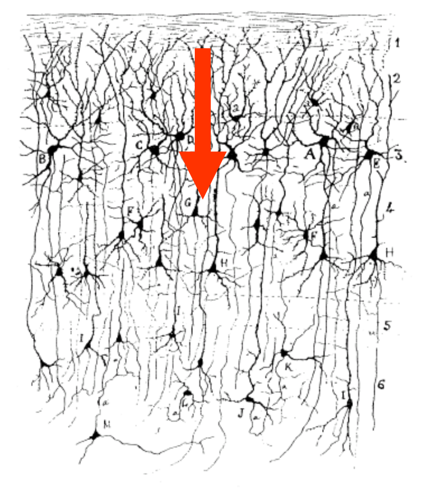
(In fact, it is frequently found in white matter below the spiking cortex.)

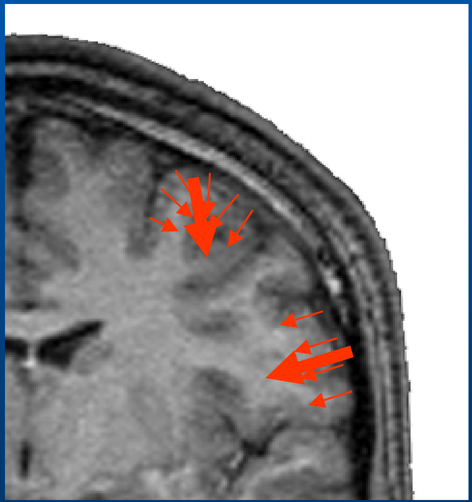
It is a device which, if it existed, *could* produce the field distribution of the activity under study.

Dipolar Representation in MEG and EEG

- The signals picked up by scalp electrodes or MEG sensors are generated by synchronized activity from many neurons:
  - Postsynaptic potentials produce intracellular laminar currents
  - Neocortical pyramidal neurons arranged in a palisade structure
  - Typically seen as a current dipole perpendicular to the cortical surface





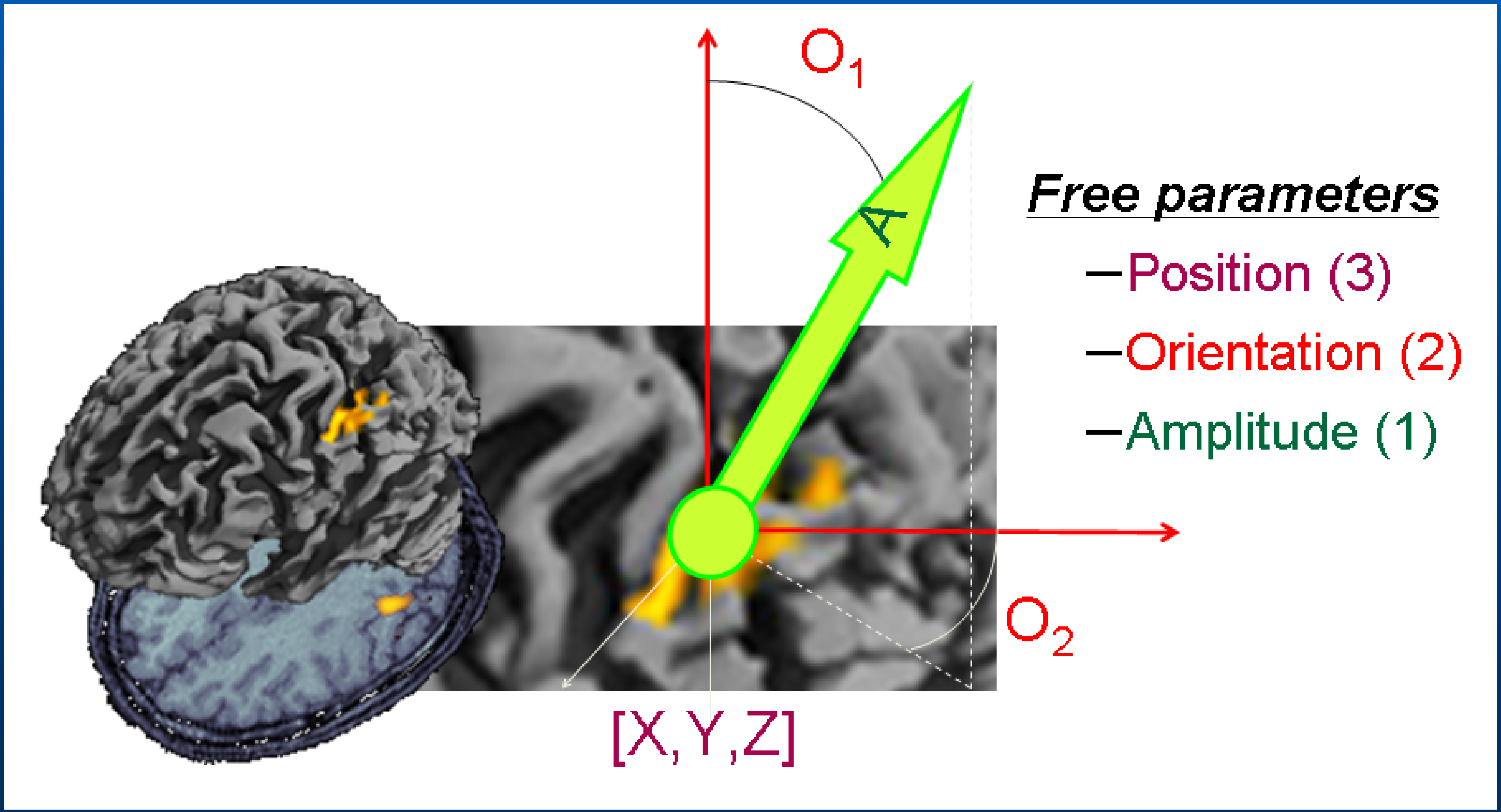


- Dipolar models are based on the assumption that:
  - Coherent activation of a large number of pyramidal cells can be represented by a point source
  - A small number of current sources (multiple dipoles, sheets of dipoles) in the brain can adequately model surface measurements

Current Dipole Model

Current dipole:

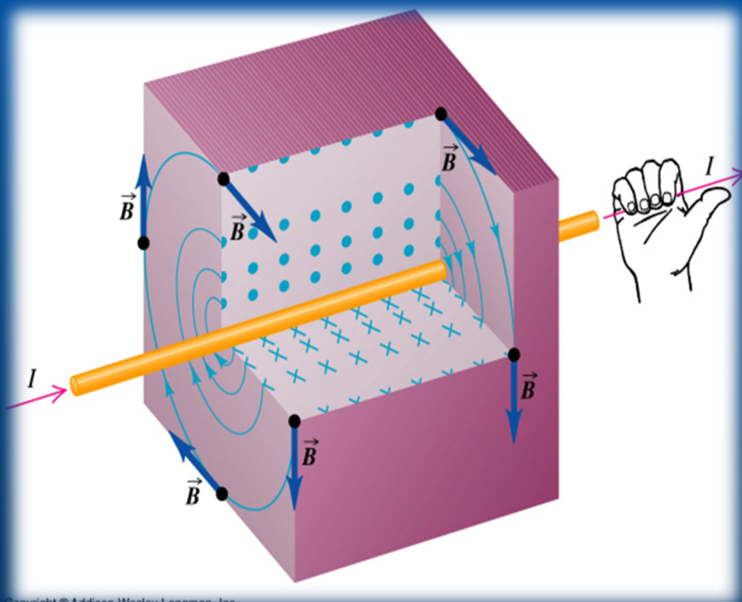
- Representation of an electric current travelling from – to + over a short distance (Ohm's law)
- Has a strength and orientation



Magnetic Field Produced by a Current Dipole

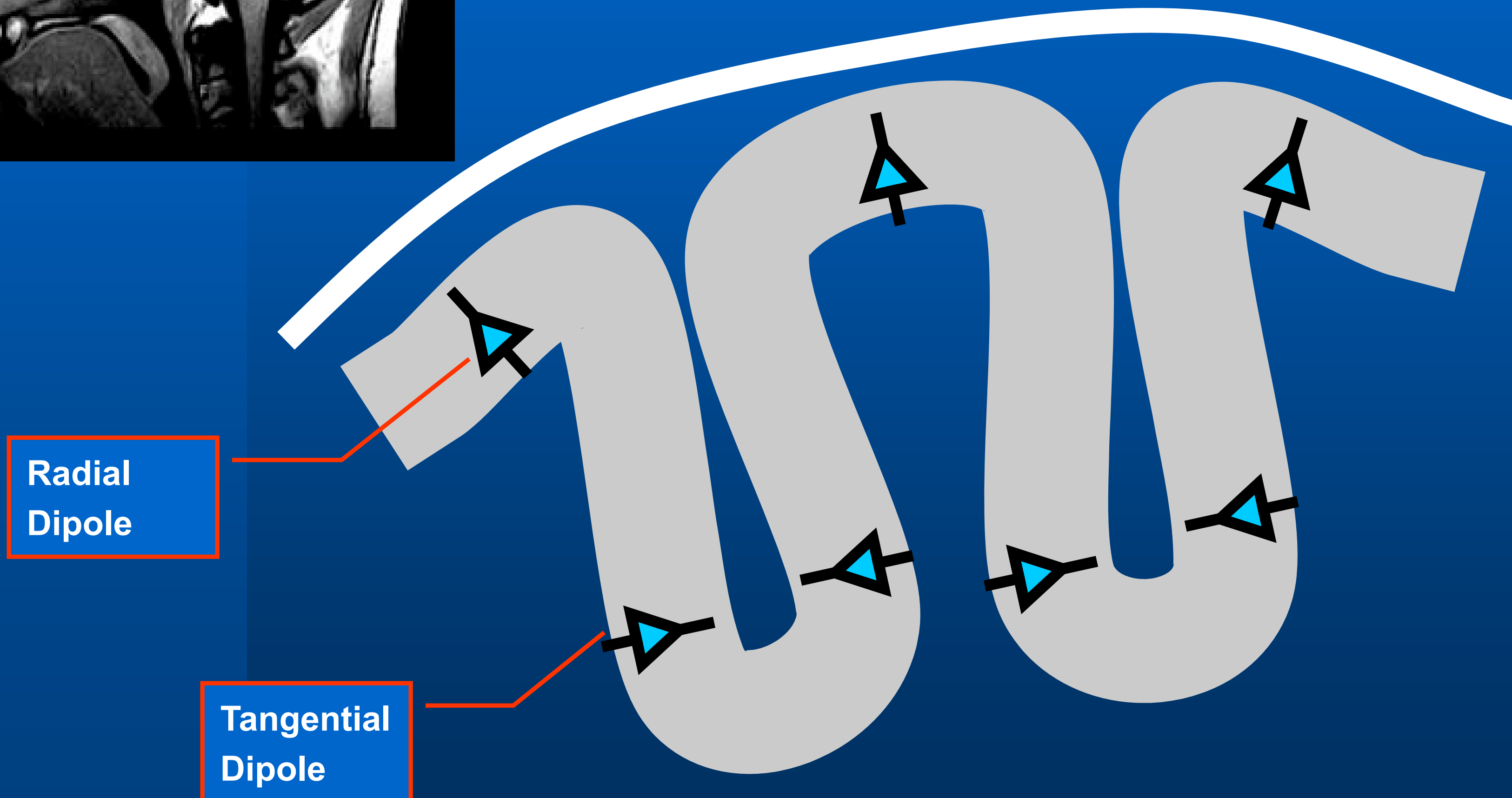
Magnetic fields produced by current dipole:

- Follow the "Right-hand rule":
  - When the right hand thumb points to direction of the current, the fingers curl in the direction of the magnetic fields.



- Biot-Savart's law:
  - Forward solution
  - Field strength decreases in proportion to the square of the distance from the dipole

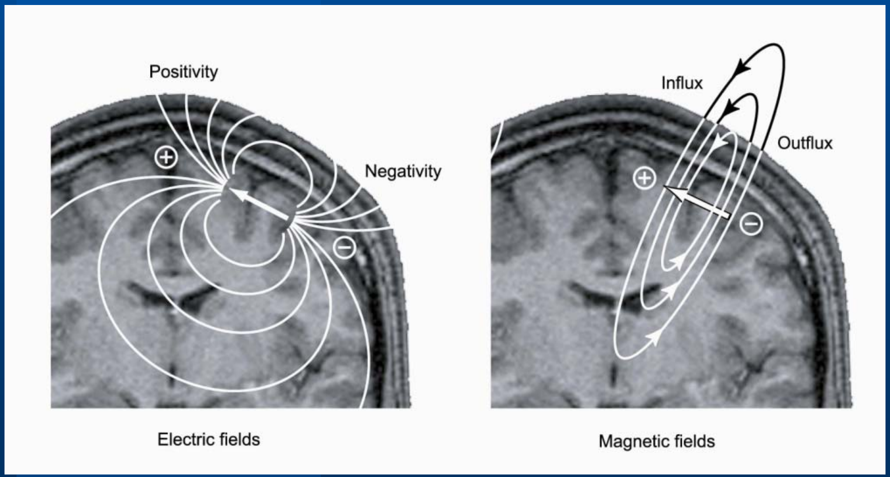
Radial & Tangential Sources



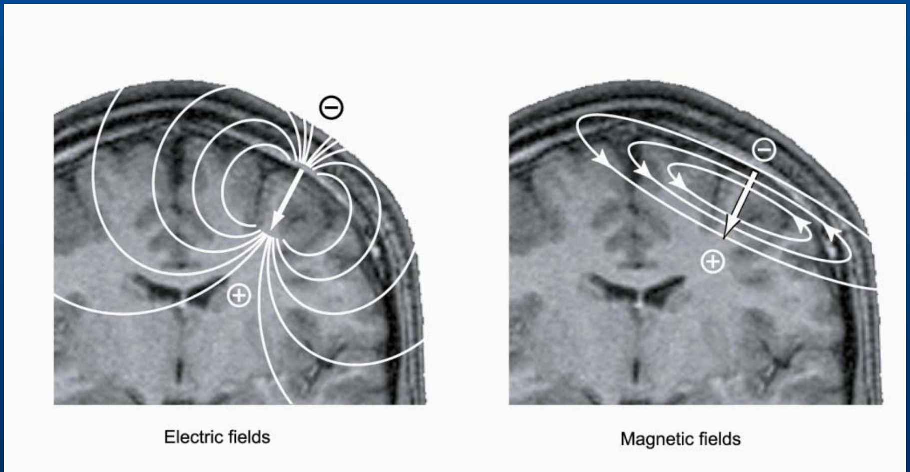
Differences Between EEG and MEG in Sensitivity to Current Dipole Orientation

- **Scalp EEG is relatively sensitive to vertical dipoles**
- **MEG is exclusively sensitive to tangential dipoles (neglects the vertical component of the dipole vector)**

Tangential dipole



Vertical dipole



** **

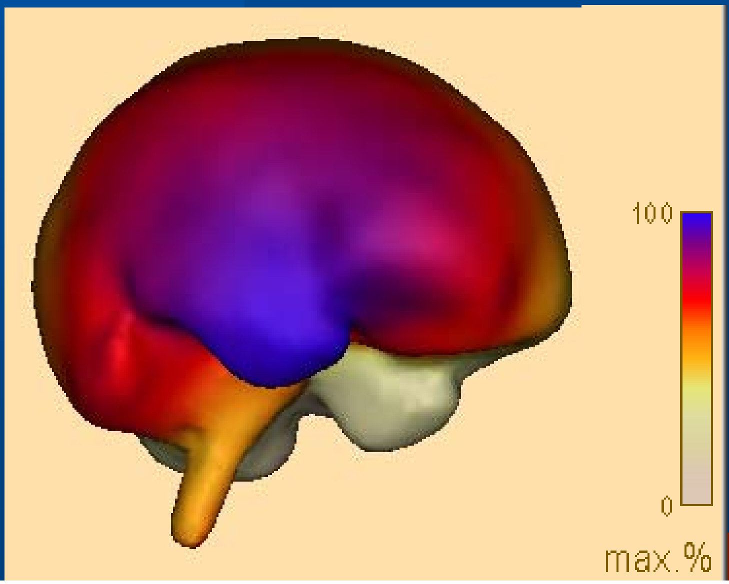
Determining the Best Model

- In fact, many sources are not dipolar, but rather are extended or complex.
- Therefore this becomes an even more difficult and elaborate — but educated — estimation, which draws on an extensive body of mathematical work on the inverse problem.
- The solutions are usually constrained in some rational way, therefore the sources found will depend on the assumptions used.

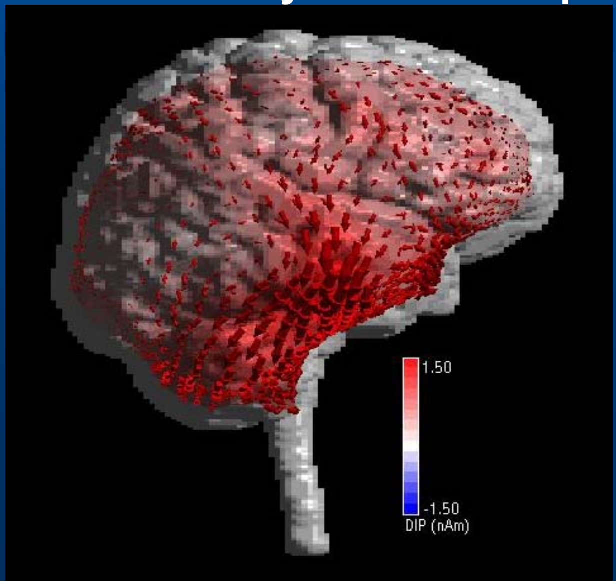
Source Localization: Linear Models

- Minimum norm estimation
  - Predetermined set of dipoles (usually 1000 to 10,000)
  - All have fixed positions and orientations (usually constrained to the cortical mantle
  - Calculate a combination of dipole strengths to explain the measured fields.

- Distributed results
  - Looks realistic



- Requires no initial guess
  - No bias by human interpretation



Models of the *Head*

Sphere Model

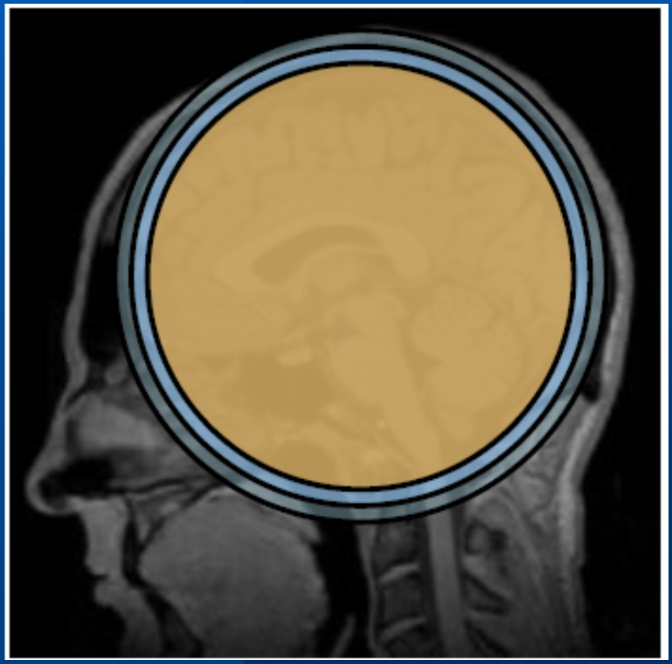
- **Concentric spheres (most common)**
- **Multiple spheres**

Realistic Head Model

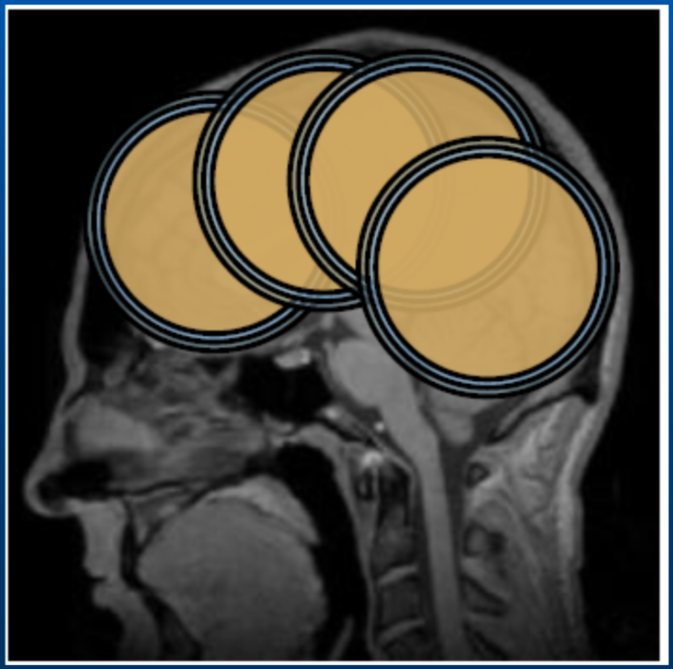
- **BEM (boundary element method)**
- **FEM (finite element method)**
- **Head shape from MRI**
- **Image segmentation in 3D**

Head Models

Single Sphere



Multiple Spheres



EEG: Complicated Concentric Sphere Model

Layers:

Head consists of series of roughly concentric layers separating brain from scalp surface, each of which presents different electrical characteristics to the currents which conduct the EEG to the surface:

- **CSF**
- **meninges**
- **bone**
- **skin**

Effects:

- **smearing and blurring**
- **attenuation**

Model:

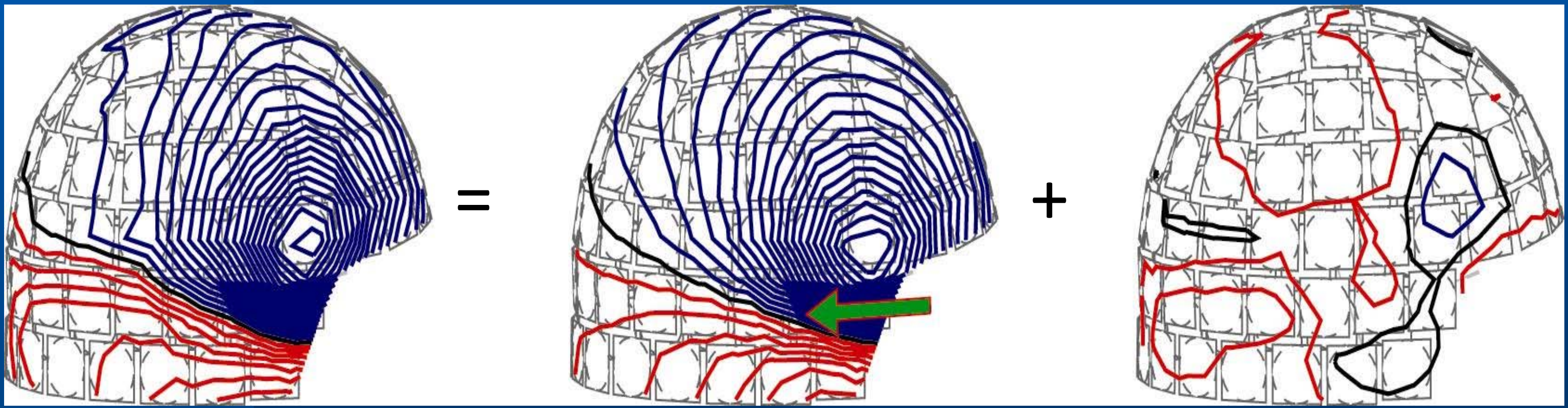
3- or 4-layer compartment head model necessary in EEG to take inhomogeneous conductivity into account

MEG: Simple Single Sphere Model

- **MEG requires a simple conductor (head) model and therefore a lower calculation burden than EEG for computerized source modeling.**
- **Magnetic fields are conveyed transparently through all of the cranial tissues.**
- **Effects on the magnetic fields of volume conduction and skull defects are negligible or small.**

With models for both the source and the head, we can carry out *source localization*

Iteratively search possible dipoles for best fit to the actual field distribution



Measurement Model Residual

How Does MEG Recording Work?

MEG Instrumentation

- **SQUID**
- **Flux transformers**
- **Shielded room**
- **Head position indicator**

Relative Magnetic Field Strength

BRAIN SOURCES
Evoked cortical fields: 10 fT
Alpha rhythm: 1000 fT

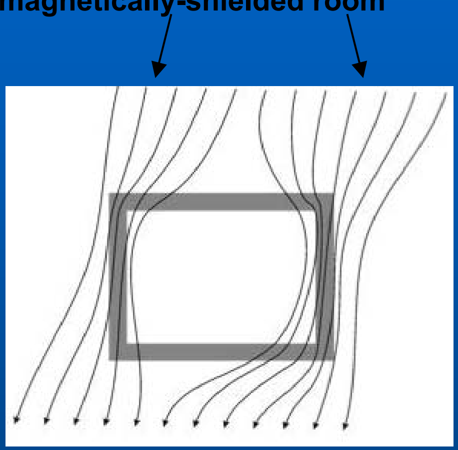
NOISE SOURCES
Earth's magnetic field: ~50 µT
Field from home appliances and wiring: <10 µT
Urban environmental noise: 10^8 fT

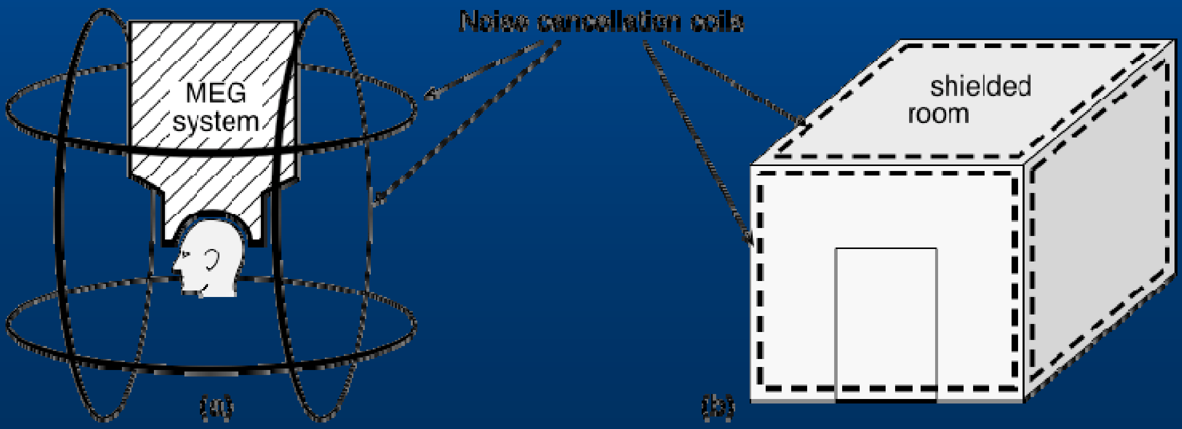
(fT = femto Tesla or 10^{-15} Tesla)

Magnetically Shielded Room

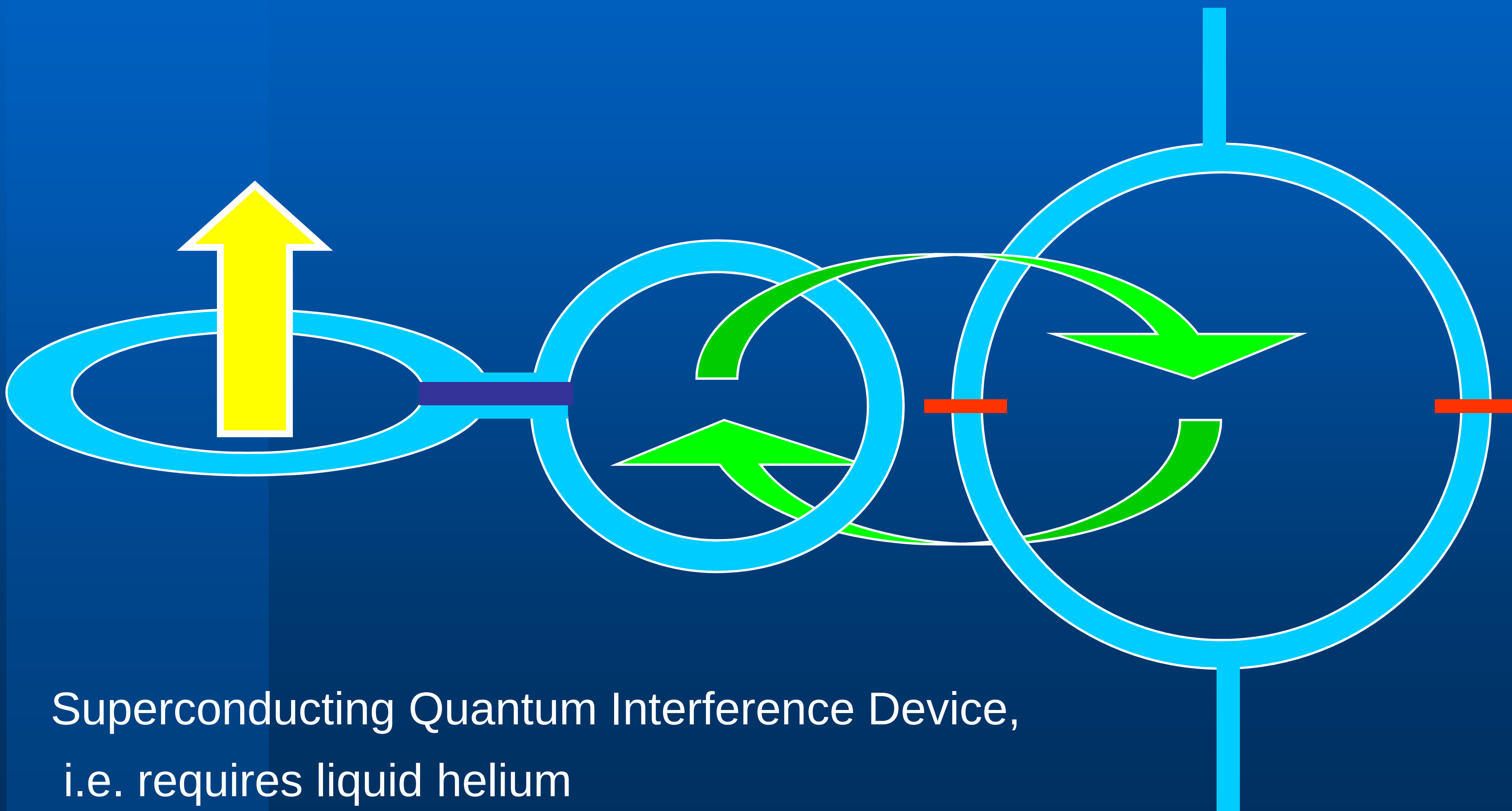
- Passive magnetic shielding using Mu-metal (alloy)
- May employ coils for active noise cancellation

External magnetic field is guided around the boundaries of the magnetically-shielded room





SQUID & Flux Transformer

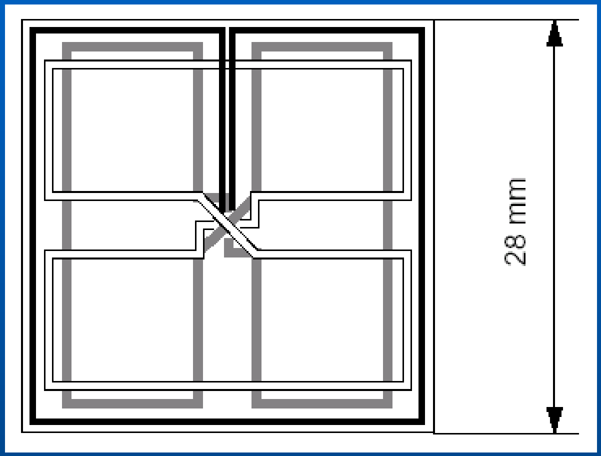


Superconducting Quantum Interference Device,

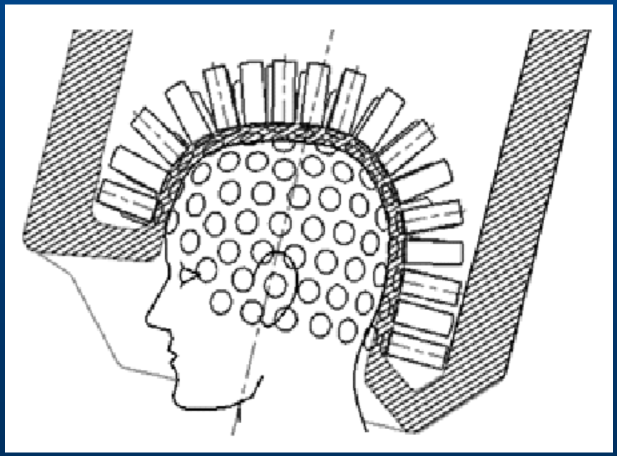
i.e. requires liquid helium

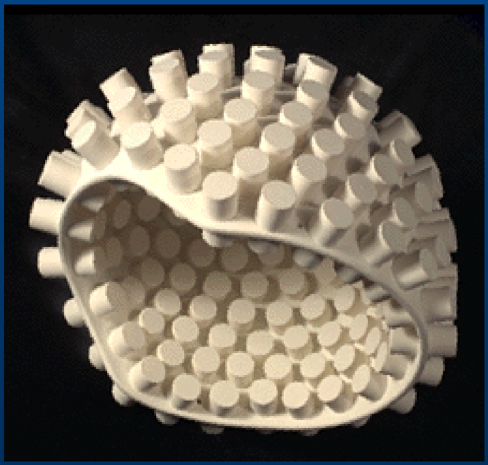
SQUID Sensors Arrayed Around Head

Planar Gradiometers



Axial Gradiometers

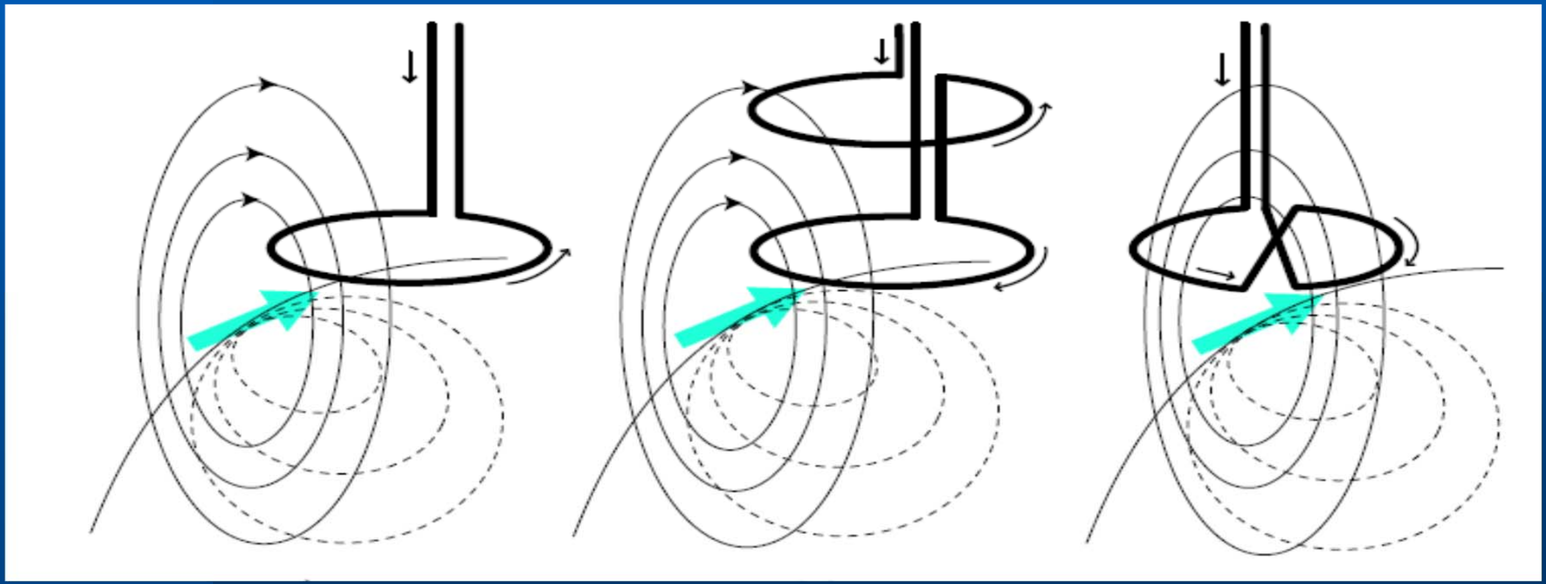




Gradiometers vs Magnetometers

- **Measuring gradients (relative differences), rather than absolute magnetic field, helps subtract background noise**

- **Requires two coils oriented to subtract overall global field, with the difference representing <u>local</u> gradients**



Magnetometer

Axial Gradiometer

Planar Gradiometer

Tanzer, PhD Thesis, Helsinki

Source Analysis

- **Forward problem:**
  - –**Has a unique analytic solution**
  - –**Poisson's equation** $\nabla^2 \Phi = -\rho / \varepsilon$

(von Helmholtz H. Bereinige Gesetze der Vertheilung elektrischer Stroeme in koeperlichen Leitern, mit Anwendung auf die thierisch-elektrischen Versuche. Ann Phys Chem 89:211-33, 353-77. 1853.)

Source Analysis

- **Forward problem:**
  - –Has a unique analytic solution
  - –Poisson's equation $\nabla^2 \Phi = -\rho / \varepsilon$
- **Inverse problem:**
  - –Has a theoretically infinite number of solutions
  - –Impossible to find a unique solution
  - –THIS IS THE EEGer or MEGer's ACTUAL PROBLEM

(von Helmholtz H. Bereinige Gesetze der Vertheilung elektrischer Stroeme in koeperlichen Leitern, mit Anwendung auf die thierisch-elektrischen Versuche. Ann Phys Chem 89:211-33, 353-77. 1853.)

Source Localization Parallels: MEG and EEG

- Both EEG and MEG can employ similar models (e.g. equivalent current source dipole).
- Substrate
  - MEG: 3.5 cm^2
  - EEG: 6 cm^2 *or*

    20-30 cm^2 depending on location (lateral convexity vs anterior temporal) and consideration of background
- Both can utilize patient-specific anatomic models (CT, MRI).

Differences and Similarities: EEG and MEG

- **Similarity**
  - Record the same phenomenon
    - Same time-resolution
    - Spontaneous activities (epileptic spikes, non-epileptiform physiological), evoked responses (SEP, VEP, AEP)
  - Sensitivity to brain volume and depth
- **Differences**
  - Sensitivity to the current dipole orientation
    - Tangential or vertical to the scalp surface
  - Complexity of the forward model
    - Feasibility of the computerized source estimation
  - Analysis
  - MEG is reference-free
  - Number of sensors
  - Duration of the recording
  - Different sensitivity to external noises
  - Cost
  - Established knowledge

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  - Analysis
  - MEG is reference-free
  - Number of sensors
  - Duration of the recording
  - Different sensitivity to external noises
  - Cost
  - Established knowledge

Advantages of MEG

1. Inherently higher source resolution and accuracy.
2. Better detection yield.
3. Reference – free.
4. Signals not attenuated or distorted by bone and scalp, or other inhomogeneities that exist between brain and surface.
5. Therefore for source analysis, the head modelling problem is significantly simpler.
6. Easy to obtain multichannel, whole-head, high spatial-density recordings.
7. No exposure to radiation, magnetic field, or other active device.

Source Localization Accuracy

What is clinically acceptable?

- In 1997, Baillet recommended a spatial accuracy of better than 5 mm.

Source localization accuracy is higher for MEG than for EEG.

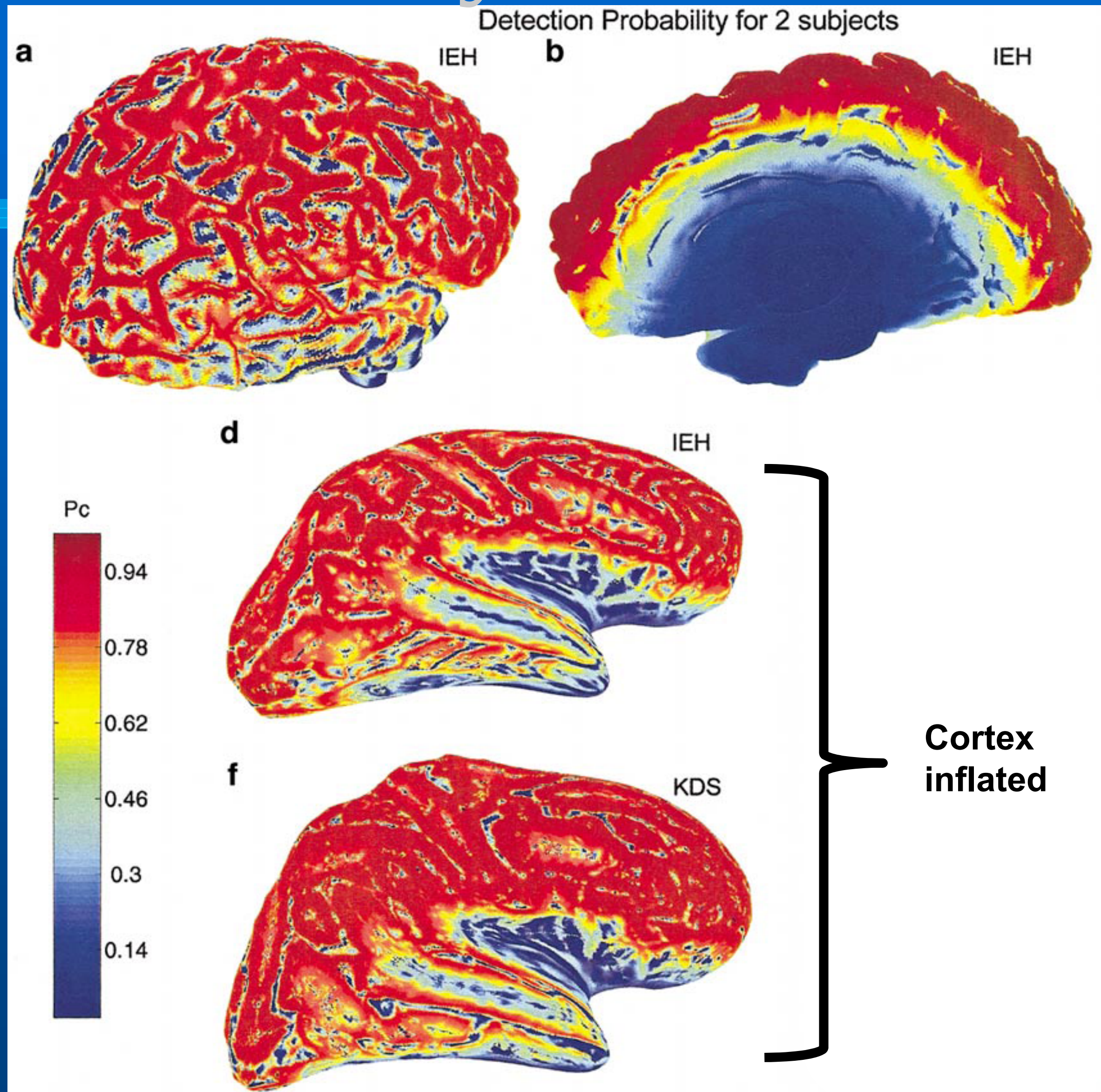
Authors	Year	EEG	MEG
Cohen D and Cuffin BN[2]	1991	10 mm	8 mm
Leahy RM, Mosher JC, Spencer ME, Huang MX, and Lewine JD[3]	1998	7-8 mm	3 mm

[1] A Bayesian Approach to Introducing Anatomo-Functional Priors in the EEG/MEG Inverse Problem. Baillet S, Garnero L: IEEE Transactions on Biomedical Engineering 1997, 44(5):374-385.

[2] EEG versus MEG localization accuracy: Theory and experiment Brain Topography Springer Netherlands Vol 4, No 2; December 1991.

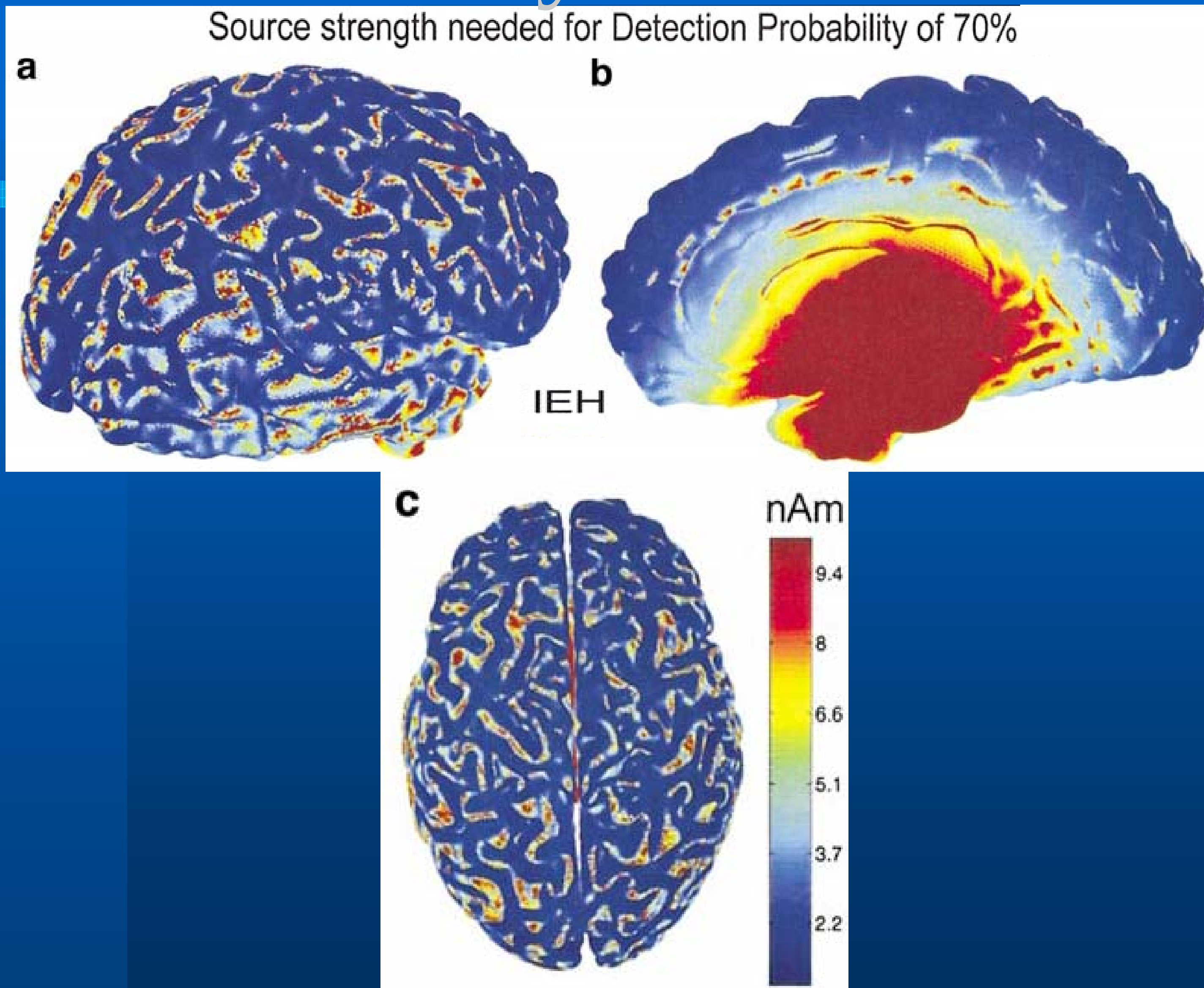
[3] A study of dipole localization accuracy for MEG and EEG using a human skull phantom. Electroencephalogr Clin Neurophysiol 1998;107:159-173.

MEG Sensitivity: Geographic detection probability



(Adapted from Hillebrand A and Barnes GR, NeuroImage 16, 638-650, 2002)

MEG Sensitivity: Required source strength



(Adapted from Hillebrand A and Barnes GR, NeuroImage 16, 638-650, 2002)

What do we know about MEG in Epilepsy?

- **The <u>yield</u> of MEG is higher than scalp EEG.**
  - **(Yoshinaga et al, 2002; Iwasaki et al, 2005; Ossenblok et al, 2007; Goldenholz et al, 2009)**
- **MEG provides <u>additional</u> localizing information.**
  - **(Wheless et al, 1999; Stefan et al, 2003; Pataraia et al, 2004)**
- **MEG results <u>change</u> the electrode coverage decisions for intracranial EEG.**
  - **(Knowlton et al, 2009)**

ACMEGS Clinical Practice Guidelines

Burgess, Richard C.; Barkley, Gregory L.; Bagic, Anto I.; Turning a New Page in Clinical Magnetoencephalography: Practicing According to the First Clinical Practice Guidelines. Journal of Clinical Neurophysiology. 28(4):339-340, August 2011.

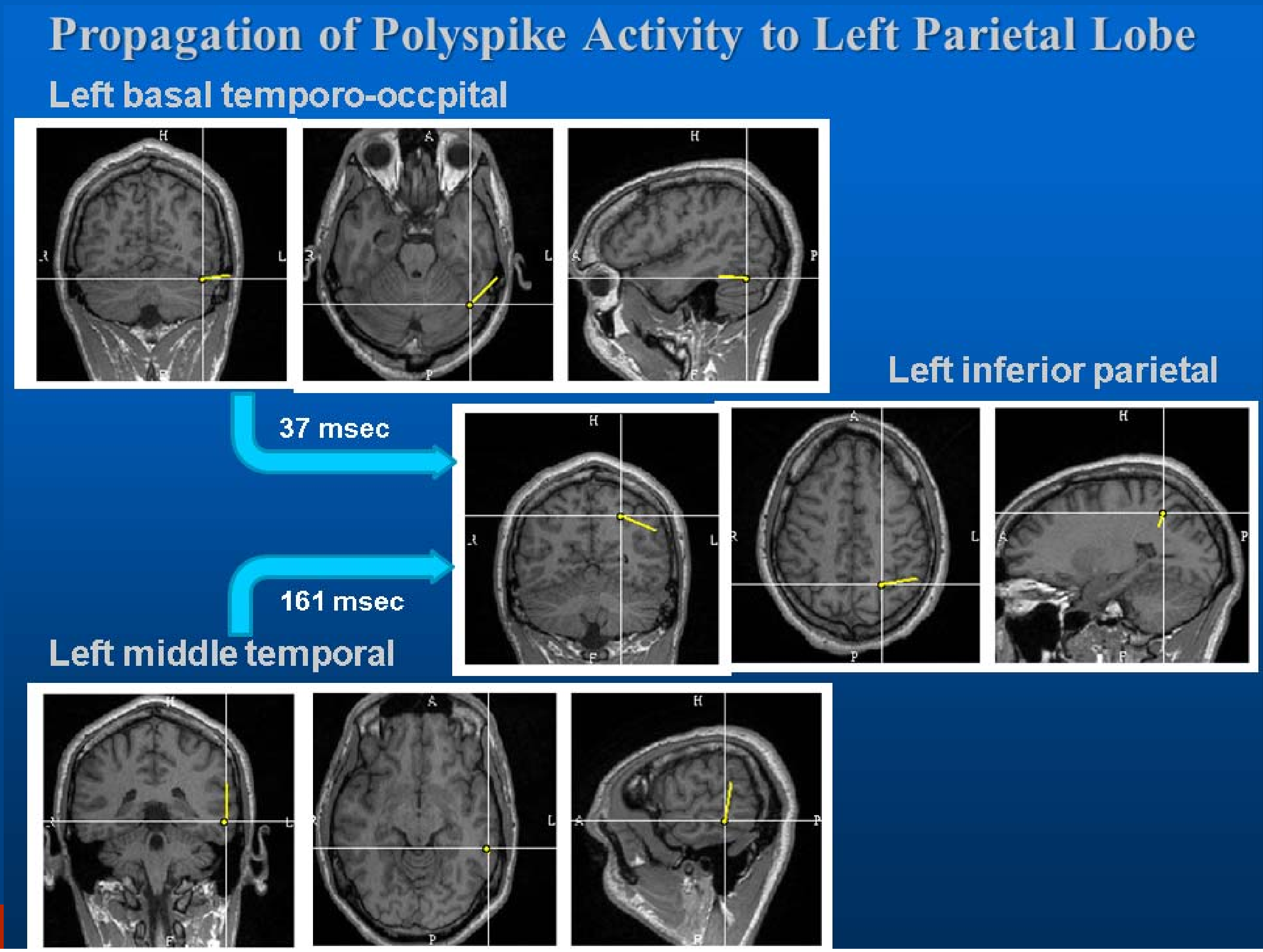
Bagic, Anto I.; Knowlton, Robert C.; Rose, Douglas F.; Ebersole, John S.; American Clinical Magnetoencephalography Society Clinical Practice Guideline 1: Recording and Analysis of Spontaneous Cerebral Activity. Journal of Clinical Neurophysiology. 28(4):348-354, August 2011.

Burgess, Richard C.; Funke, Michael E.; Bowyer, Susan M.; Lewine, Jeffrey D.; Kirsch, Heidi E.; Bagic, Anto I.; American Clinical Magnetoencephalography Society Clinical Practice Guideline 2: Presurgical Functional Brain Mapping Using Magnetic Evoked Fields. Journal of Clinical Neurophysiology. 28(4):355-361, August 2011.

Bagic, Anto I.; Knowlton, Robert C.; Rose, Douglas F.; Ebersole, John S.; American Clinical Magnetoencephalography Society Clinical Practice Guideline 3: MEG–EEG Reporting. Journal of Clinical Neurophysiology. 28(4):362-365, August 2011.1

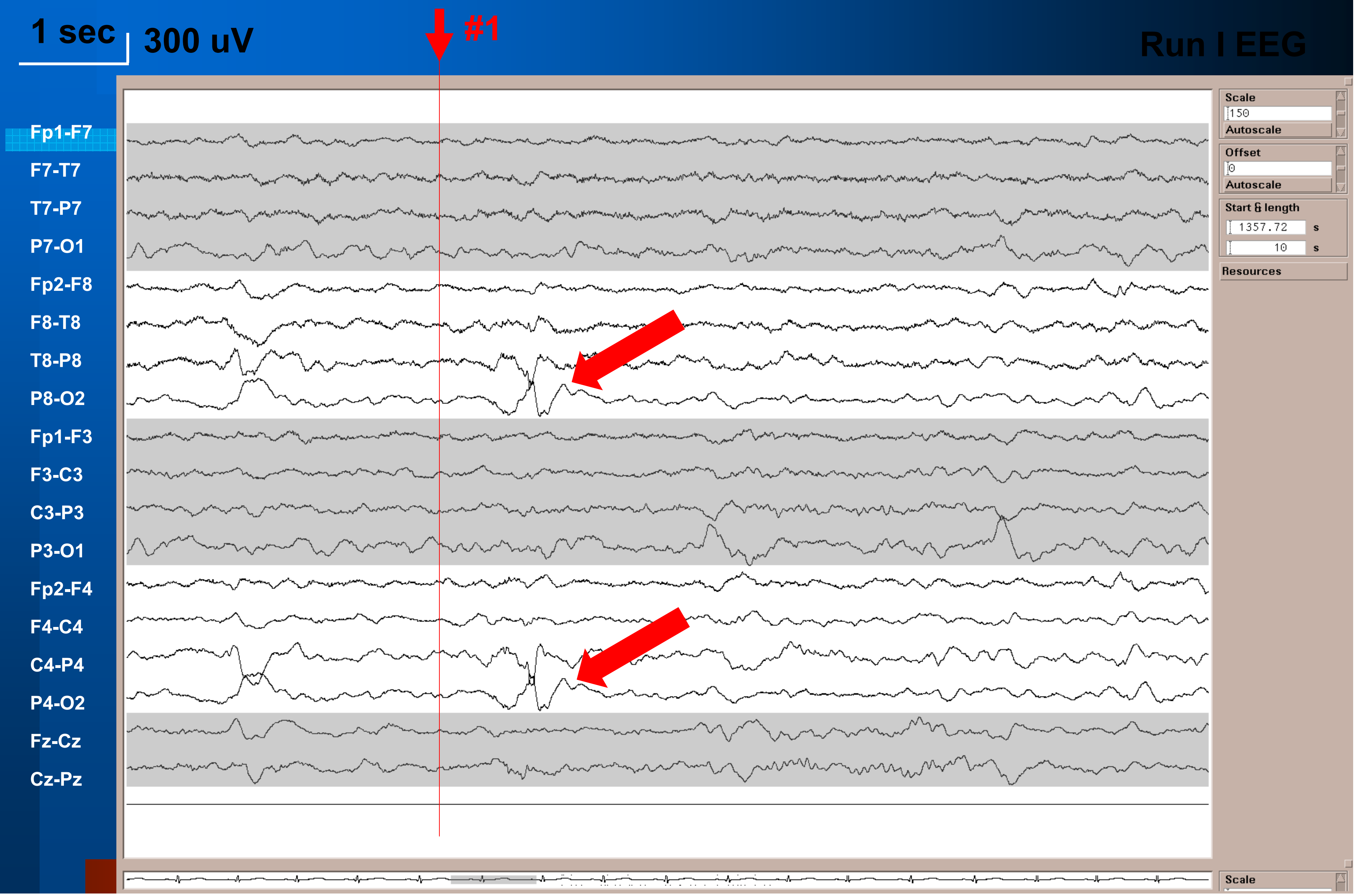
Bagic, Anto I.; Barkley, Gregory L.; Rose, Douglas F.; Ebersole, John S.; American Clinical Magnetoencephalography Society Clinical Practice Guideline 4: Qualifications of MEG–EEG Personnel. Journal of Clinical Neurophysiology. 28(4):364-365, August 2011.

What Should the Referring Physician Expect from a MEG Report?

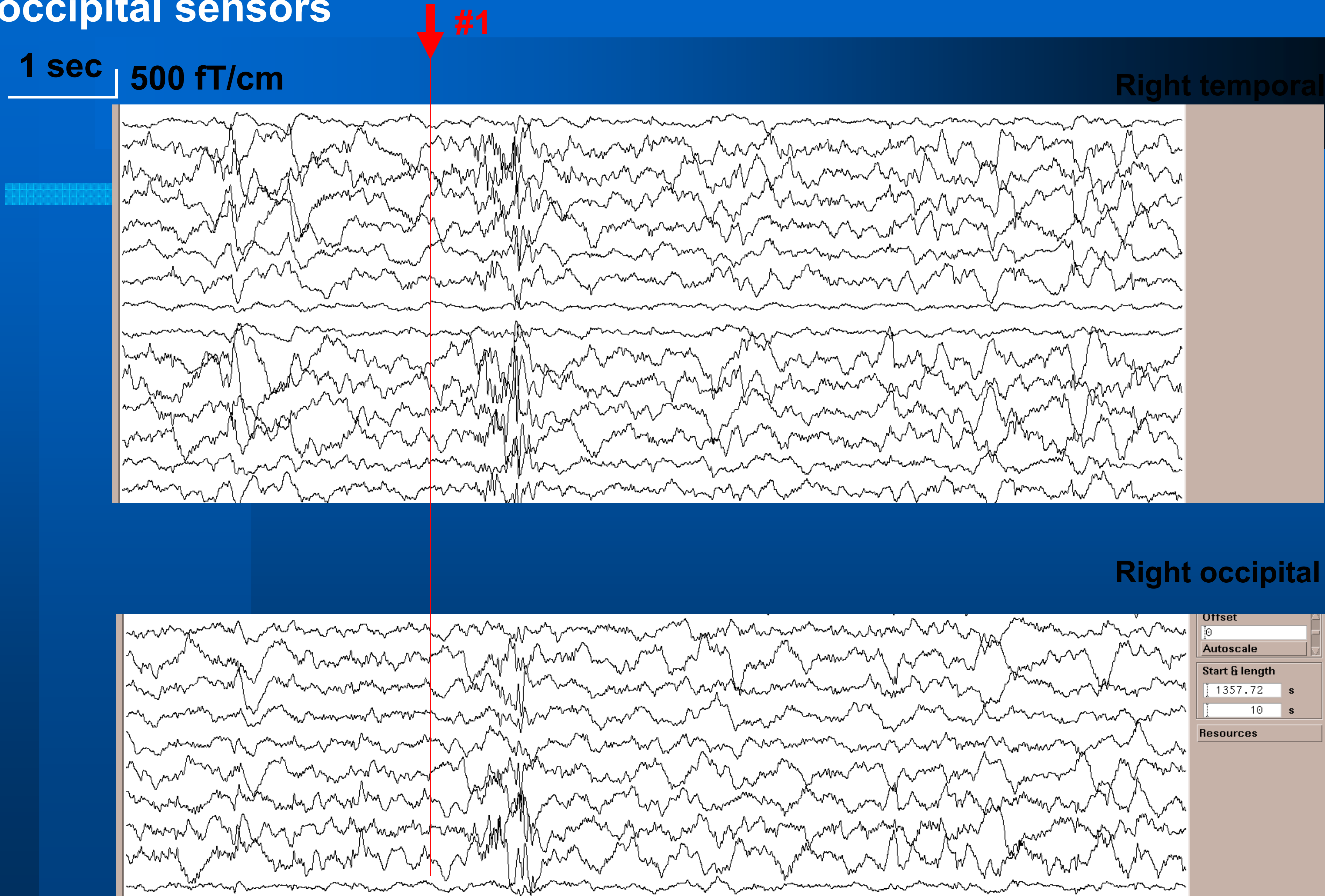


Example Waveforms Showing the EEG Correlate to the MEG Discharge

EEG dipole #1: Spike regional right posterior quadrant

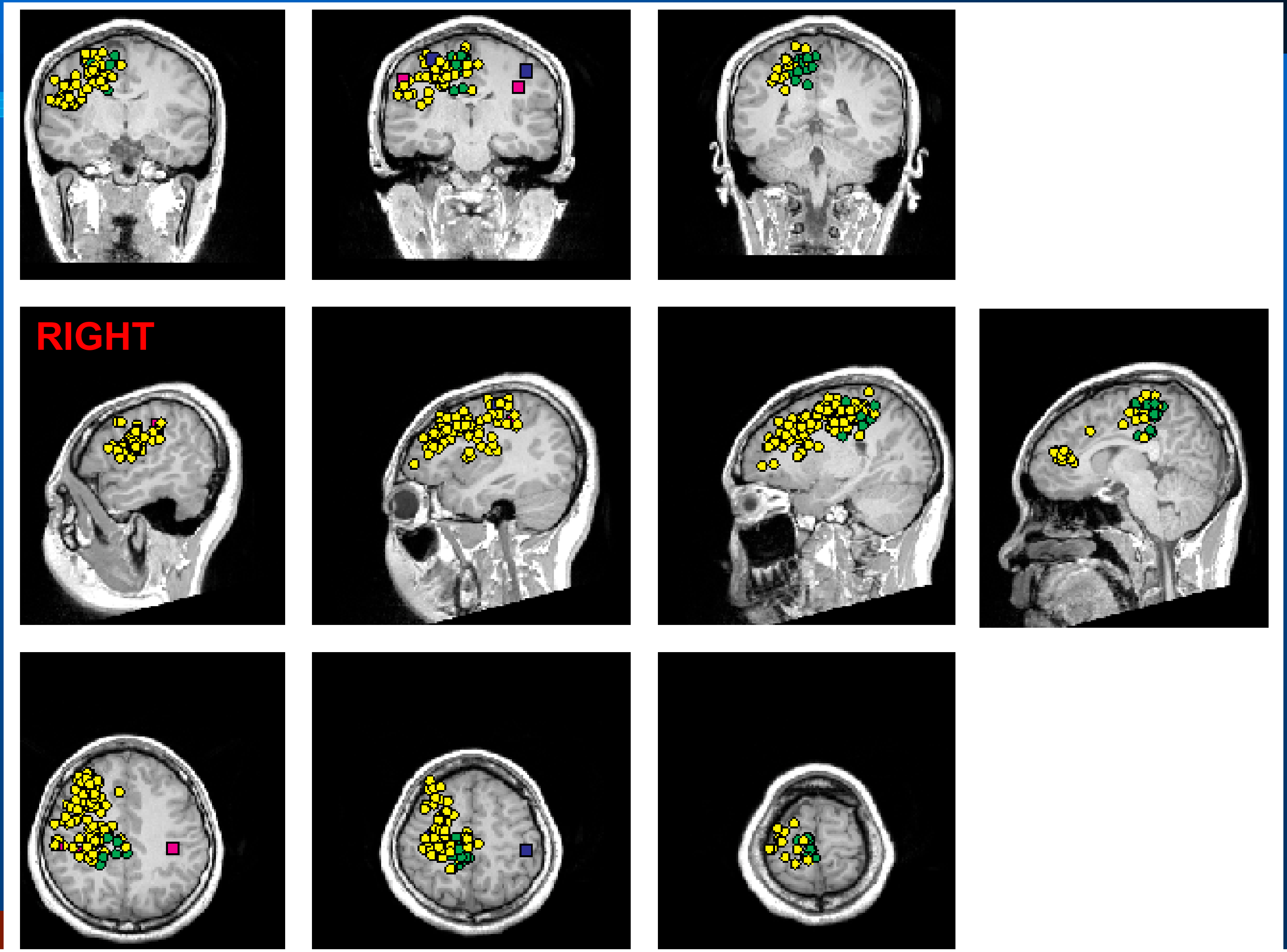


MEG dipole #1: Poly spikes maximum in the right temporal > occipital sensors



Summary Slide Showing Epileptic and Functional Results

Ictal and interictal dipoles with SEF and MEF dipoles

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