Interpreting the MEG signals by using source models

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Background

Some relevant numbers & scales

- Magnetic fields:
  - Conventional MRI scanner ~1 Tesla.
  - Earth's magnetic field ~10^{-6} Tesla.
  - Magnetic field of MEG evoked response ~10^{-14} Tesla.

- Neuronal currents:
  - Intracellular postsynaptic current density[1] ~ 10^{-7} Ampere/mm^2
  - Estimated cortical area needed for producing measurable signal[1] ~40 mm^2

[1]From Hamalainen et al, *Rev. Mod. Phys.*

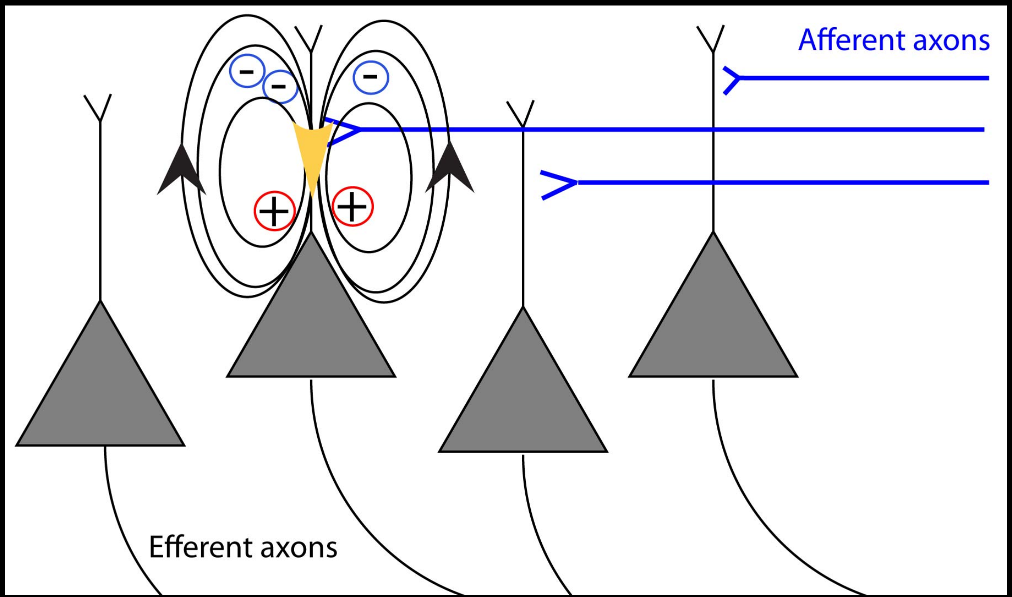
What MEG measures?

- MEG measures magnetic fields with highly sophisticated sensors.
  - SQUID=Superconducting QUantum Interference Device.
    - Presently the only technology for sufficiently sensitive sensors.
  - MEG sensors must be cooled, shielded, tuned…
    - Instrumentation becomes expensive.

- Magnetic fields can be generated by:
  - Magnetic materials (permanent magnets, etc.).
    - In MEG these are big trouble!
  - Electric currents = charged particles in motion.
    - Neuronal currents can be detected outside the head.

How neuronal population can elicit a measurable signal outside the head?

- Temporal and spatial summation is needed!
  - Large number of neurons must be synchronously active.
  - Direction of neuronal currents must not cancel.
  - Mostly post-synaptic currents contribute.
    - Apical dendrites of pyramidal neurons believed important:

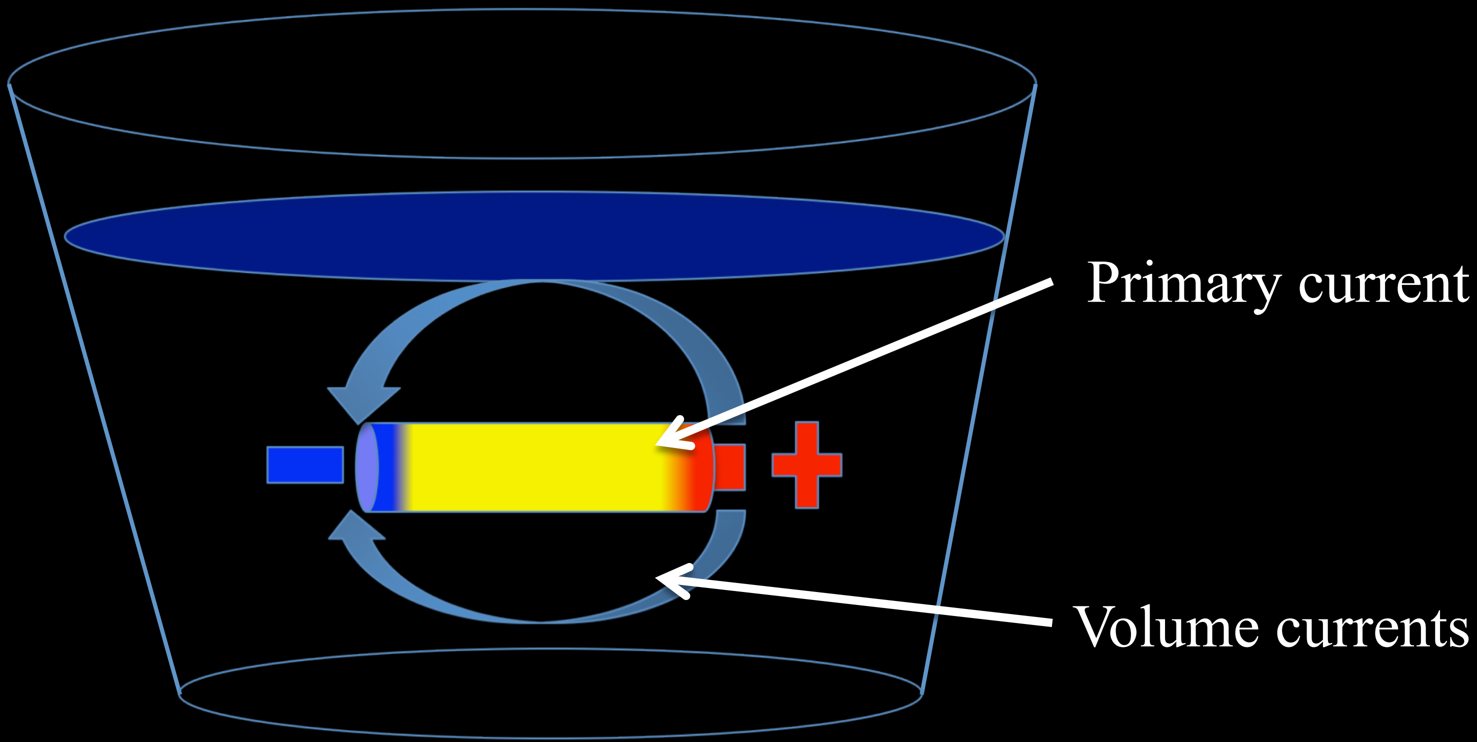


Modified from Purves et al, *Neuroscience*

Review of the current dipole

What is a current dipole?

- To get charges going, we must have a current source.
- What happens if a battery gets into salt water?
  - Currents in the water flow to close the circuit.



Relationship of quasi-static E-field & B-field

E-field = Electric field,   B-field =Magnetic field

- Quasi-statics: slow electric & magnetic phenomena.
  - Electromagnetic "waves/radiation" play insignificant role.
- The dipole (= "battery") E-field drives passive (Ohmic) currents.
  - Ohm: Current is proportional to E-field.
  - The proportionality constant = conductivity.
- The total current then determines B-field:
  - Given by the law of Biot & Savart.

How to find a "matching" outside current for a given current dipole?

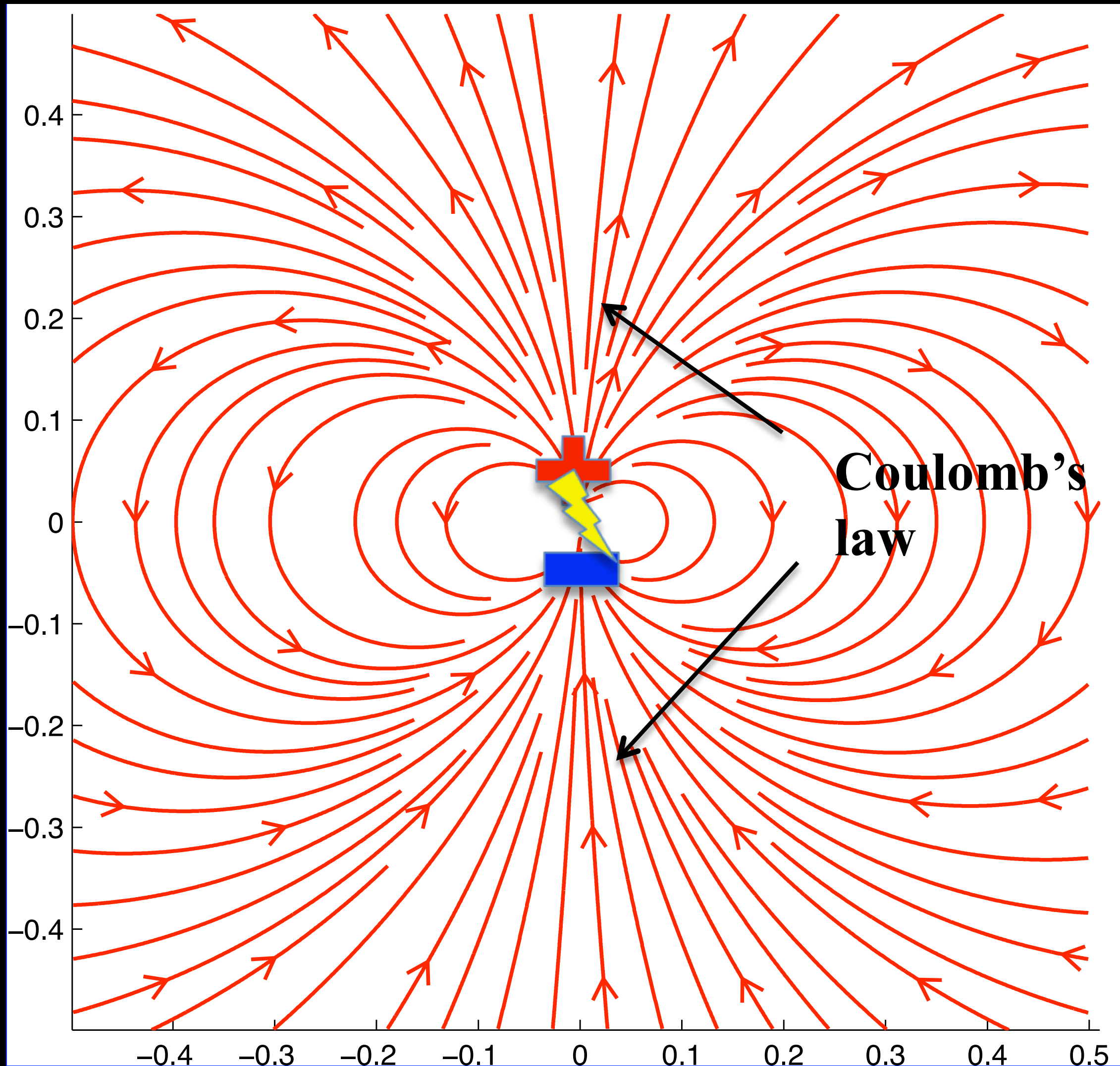
- First, how to find the electric field generated by a dipole?
  - Ohm then gives us the currents.

- Toy example: Let's assume a 2D homogeneous conductor.

- The E-field of current dipole is equivalent to two closely spaced "static" charges (current source & sink):

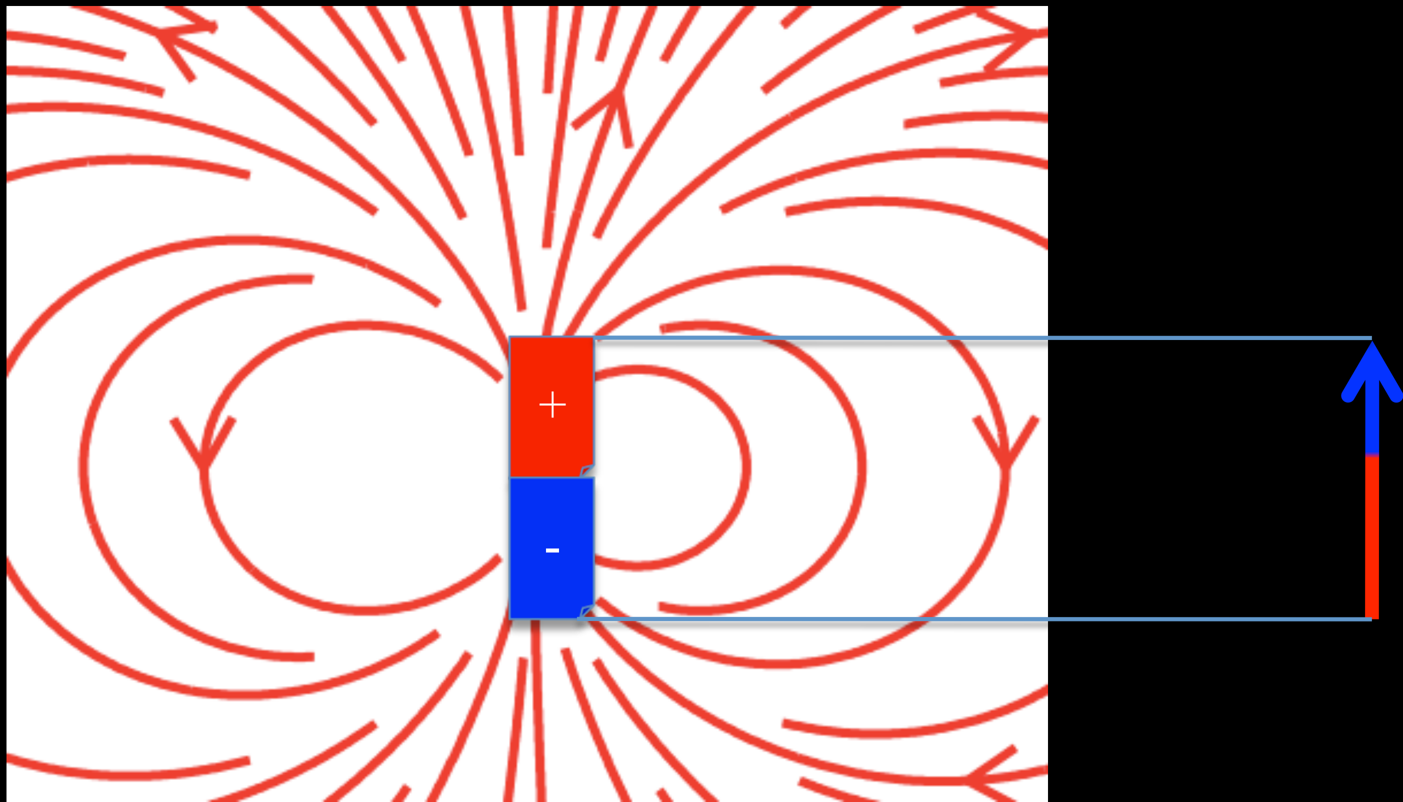
Sources & sinks vary < 100 Hz. Quasi static: time points treated separately!

The E-field of the current dipole



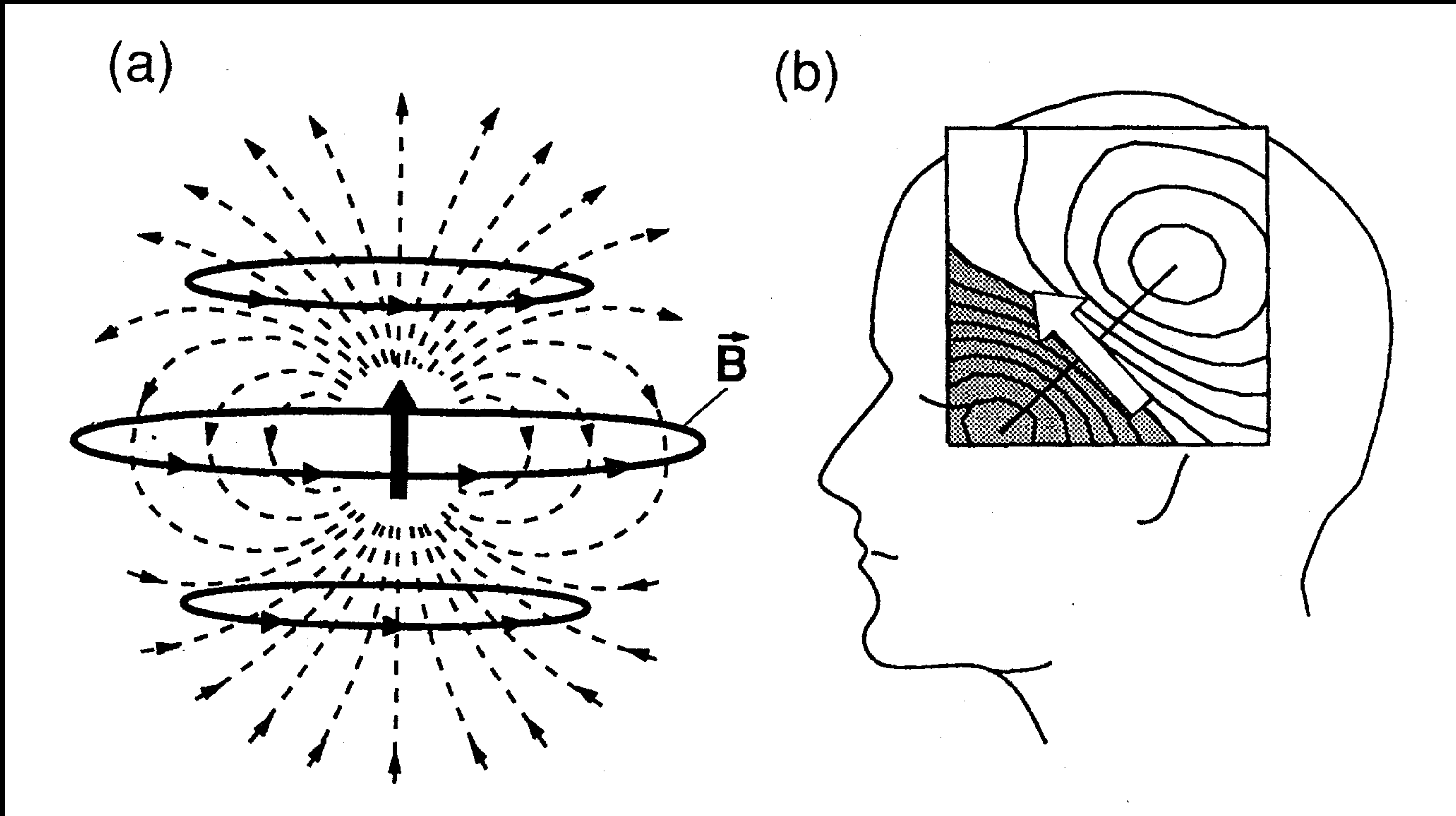
Quasi-statics: The total current must form a closed loop!

Total current = Volume (outside) + Primary (inside)



Magnetic field of the current dipole

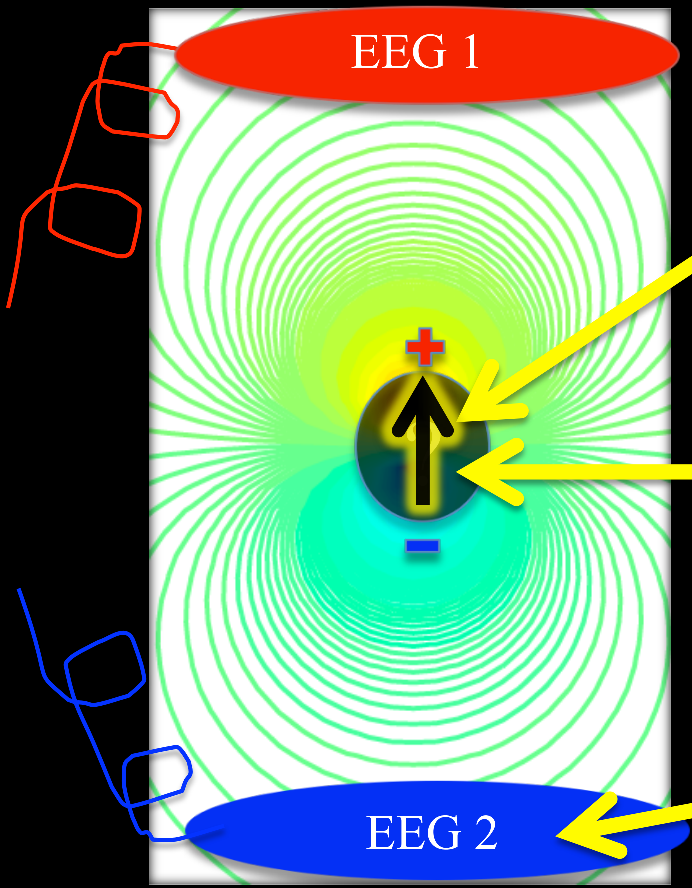
- The B-field circulates the dipole in right-hand sense.



From Hamalainen et al, *Rev. Mod. Phys.*

There's just one more thing…

- The "point-like dipole" approximation is meaningful only if we are relatively far away from the sources.



The actual sources live on the cellular level. Not necessarily "point dipoles"!

A point dipole is a reasonable model for this kind of a "lumped current", if we look form a distance.

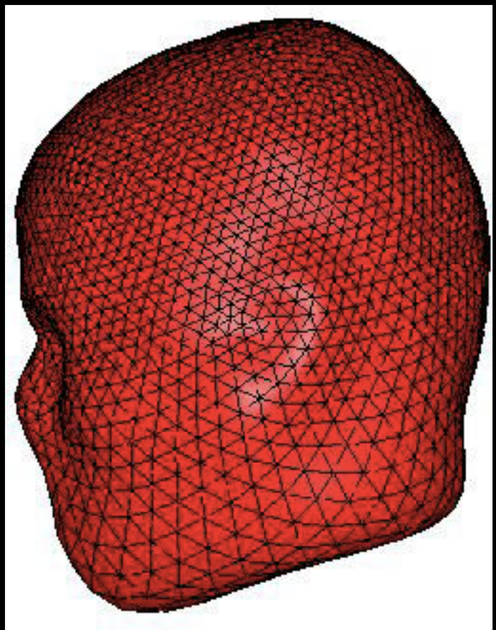
We measure/see the effects of "summed" currents on a macroscopic level.

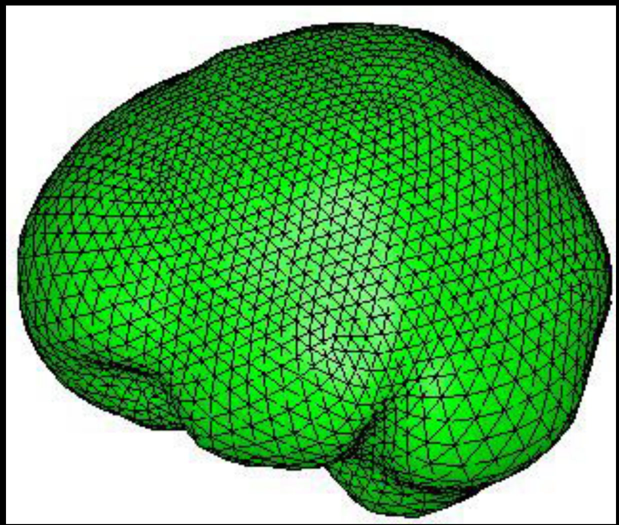
Why bother with MEG (instead of just EEG?)

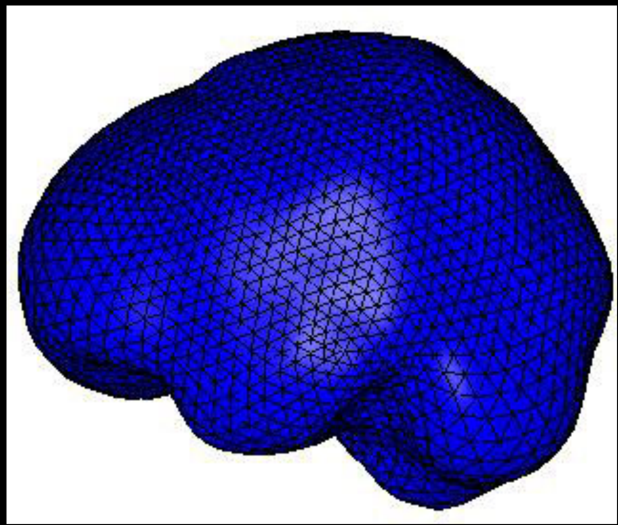
- Both MEG and EEG see effects of post-synaptic currents.
  - EEG is more sensitive to conductivity profile than MEG.
- The potential in EEG has to be figured out all the way through the skull to the scalp.
  - EEG is sensitive to the fine structure of the skull.
    - Current follow “paths of least resistance”.
- Currents in skull & skin are small (skull has poor conductivity)
  - MEG does not know/care much about these currents.
  - The skull is “transparent” to the magnetic fields (no distortions).
- MEG and EEG combined gives best results in theory!

Practical calculations: The BEM

- BEM = Boundary Element Method (or Model)
  - In present "standard approach" 3 layers (compartments):
    - Scalp, Skull & Brain (Outer skin , Out. skull, Out. Brain=In. skull)
  - Conductivity of each layer assumed homogeneous & isotropic
    - Conductivity values : ~0.3 S/m (Scalp & Brain) ~0.006 S/m (Skull)





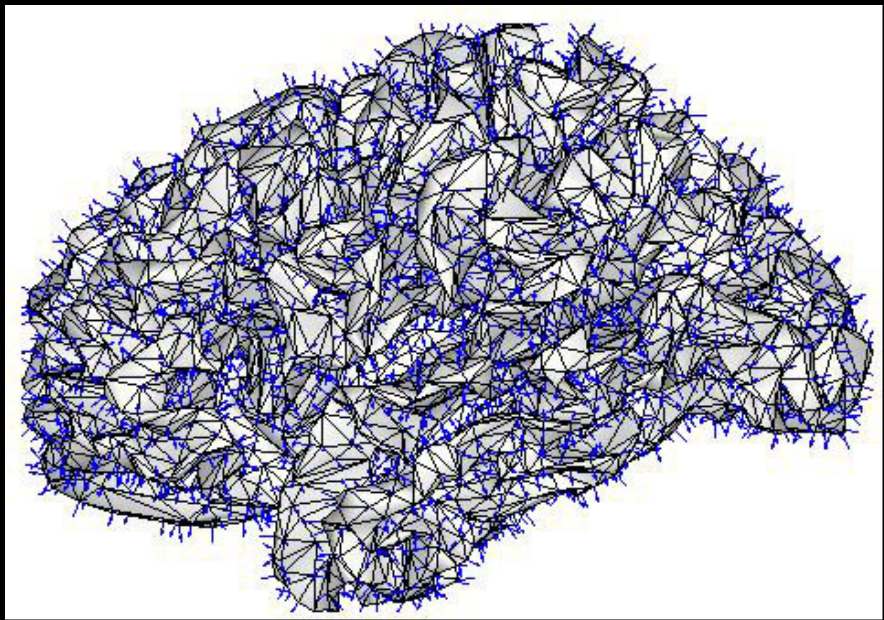


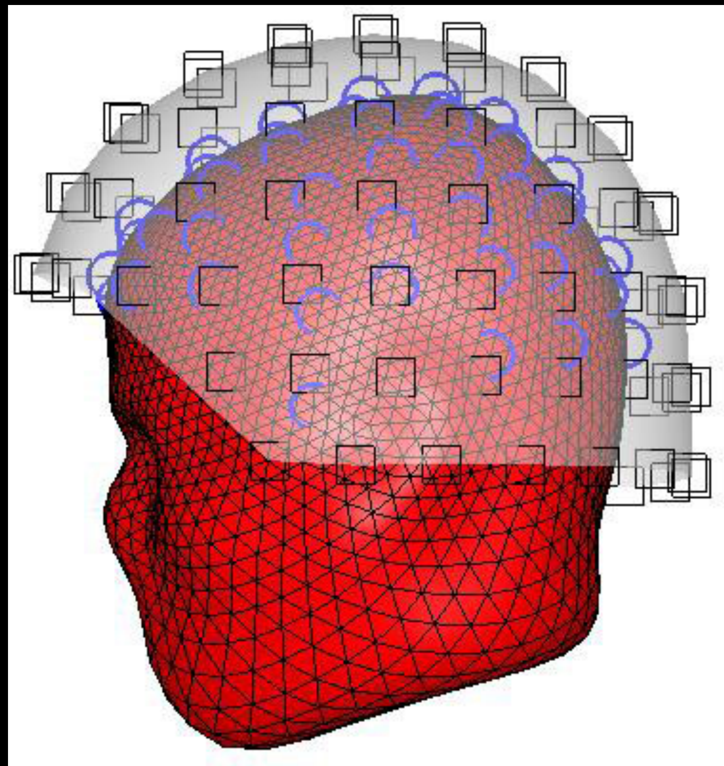
The source & sensor spaces

Dipoles: ~ 4000 locations on GM-WM boundary

MEG: 102 sensor triplets

EEG: 60 channels

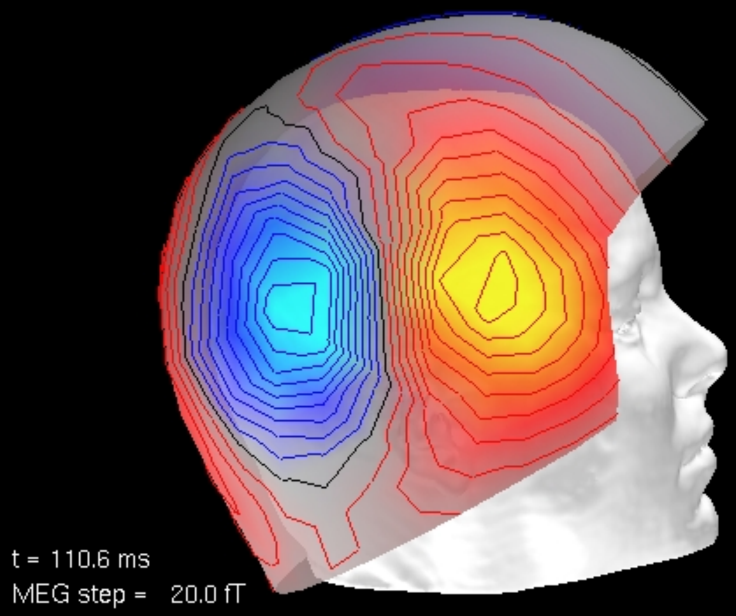




Dipole modeling

Why dipoles?

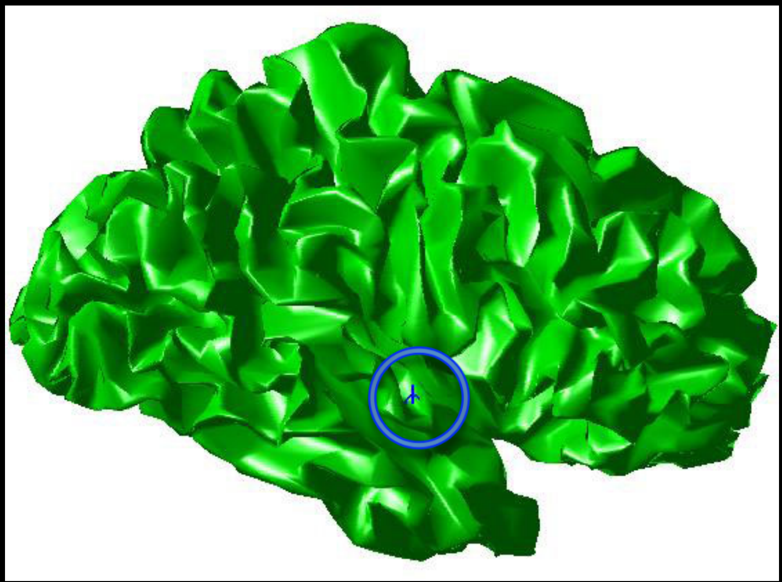
Auditory response about 100 milliseconds after stimulus.



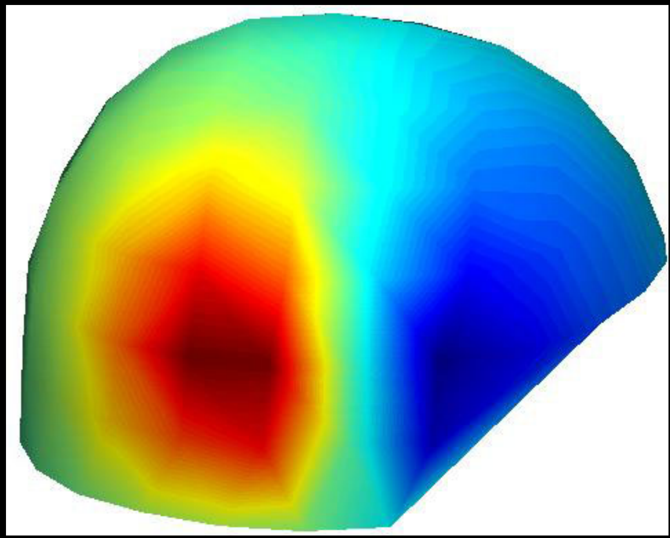
- Often the empirical field patterns look dipolar.
  - Especially the early responses from sensory cortices have this property.
- Find “Equivalent Current Dipole” (ECD).
  - A current dipole that best explains the data.
  - Supposedly reflects the location of the activation.

Let’s do a little simulation experiment!

- An auditory “activation”:
  - Single dipole pointing along z-axis (up)



- This is how MEG field pattern looks like:

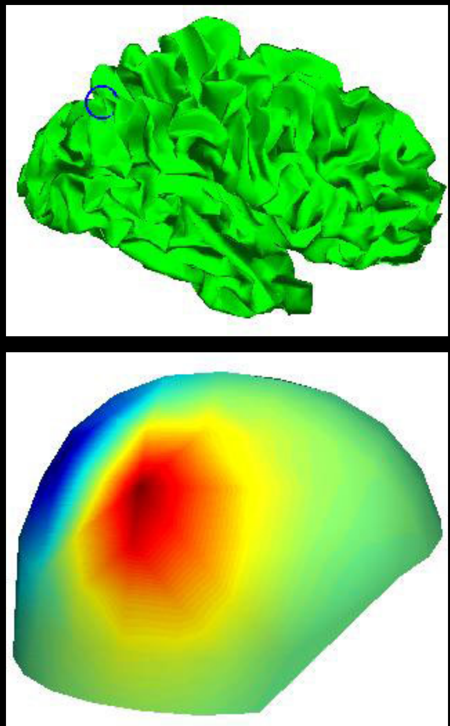


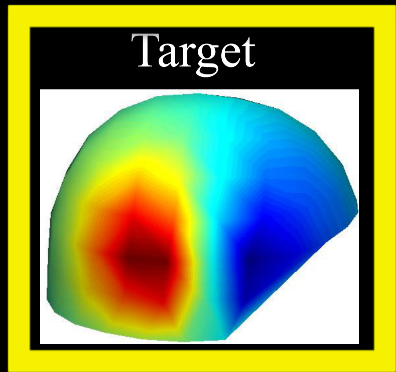
Try dipoles at different locations…

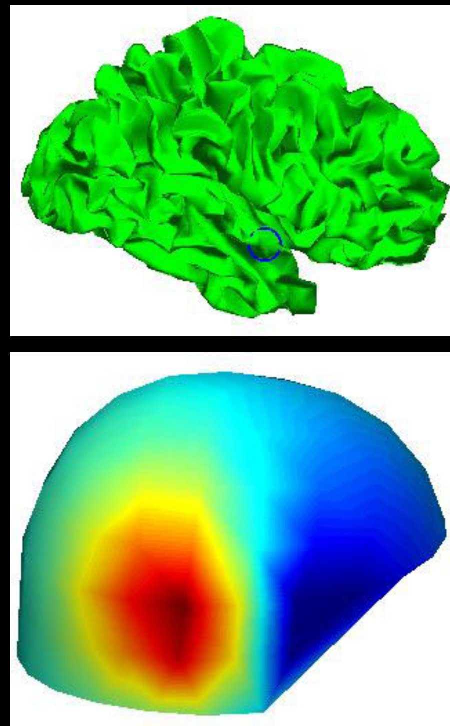
- Orientation constraint:
  Assume dipole orientation perpendicular to cortex.

Some of them give poor fits…

While some of them do a better job!

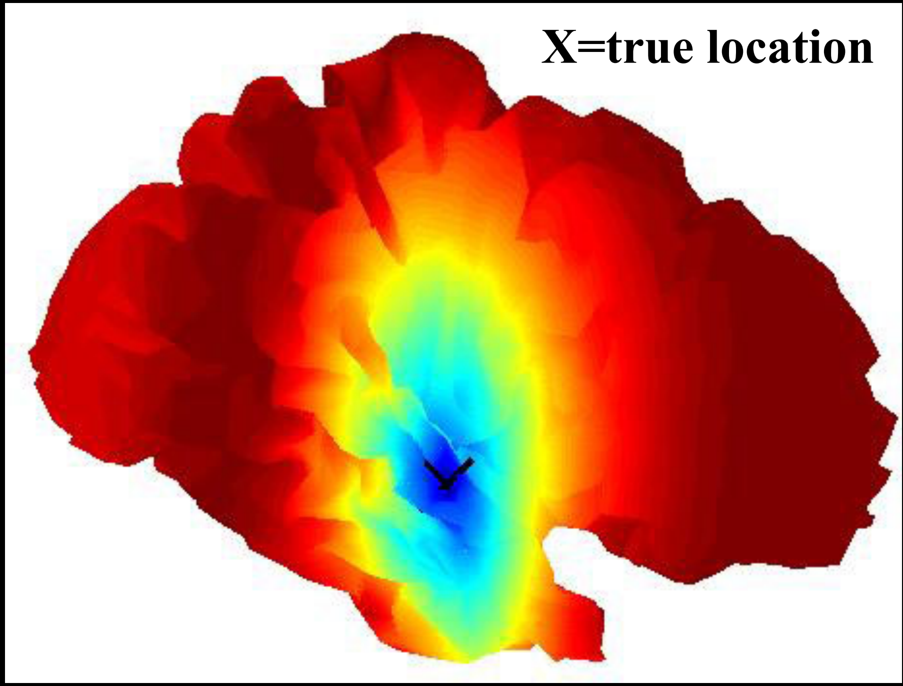






How to quantify the localization result?

Evaluate goodness-of-fit at each location:



What is sufficient goodness-of-fit?

Depends on:

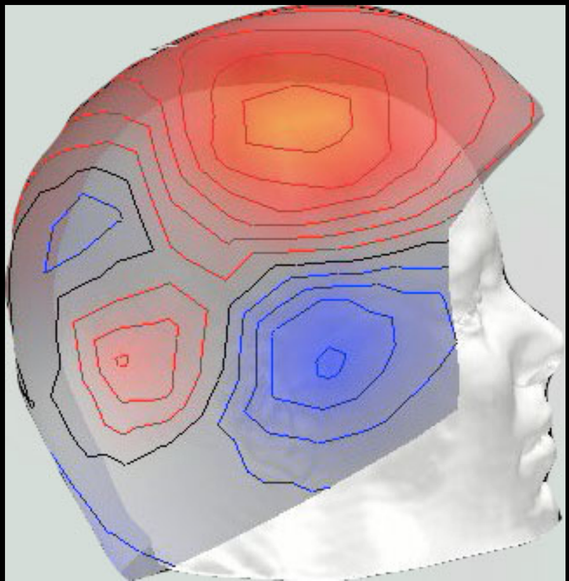
- •Noise levels / SNR.
- •How dipolar the MEG data
- •Quality of BEM
- •MRI-MEG co-registration

Most crucially in this case:

Is one ECD reasonable model?

Challenges with multi-dipole models

Auditory response about 150 milliseconds after stimulus.



1) How many dipoles (model selection)?

- More dipoles give always better data fit!
- Model complexity vs. data fit.

2)How to find a solution (optimization)?

- Non-linear multidimensional problem
- Local minima, sensitivity to noise…

Minimum-norm estimate (MNE)

MNE: computational motivation

- Generally, with respect to the position & orientation of the dipole, the E- and B-field dependence is non-linear.
  - The field pattern looks different for a rotated/moved dipole.
  - If we want to fit multiple dipoles to the observed data -> optimization becomes difficult.

- With respect to dipole amplitude the field dependence is linear.
  - The MEG field pattern for different amplitudes stays the same.
  - If we take a grid and put a dipole to all points, the problem becomes linear -> mathematical convenience ensues!

Why do we use MNE in practice?

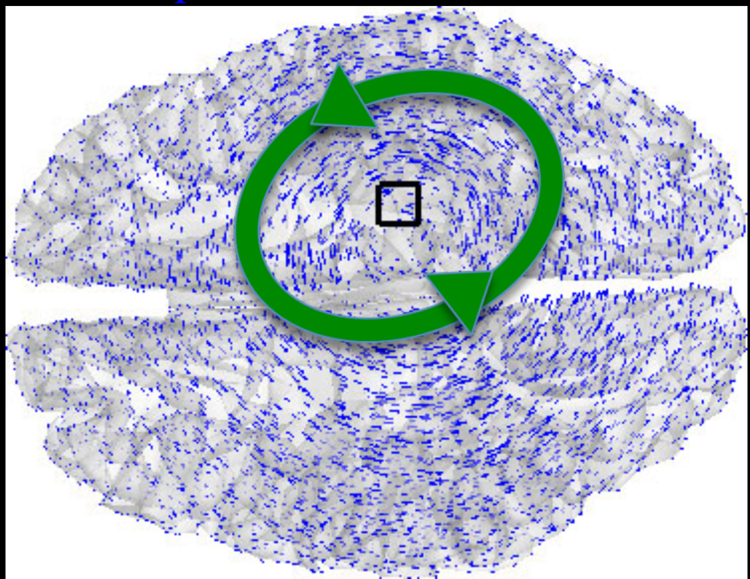
- MNE is an inverse method with a closed-form solution.
  - Computationally very efficient. One-liner in MATLAB.
  - Basically just a “pseudo-inverse” or “generalized inverse” of the so-called forward matrix.

- The MNE has appealing mathematical properties, such as linearity, geometrical interpretations etc.
  - In a certain technical sense it makes minimal assumptions of the source distribution.
  - Number of sources needs not to be known!

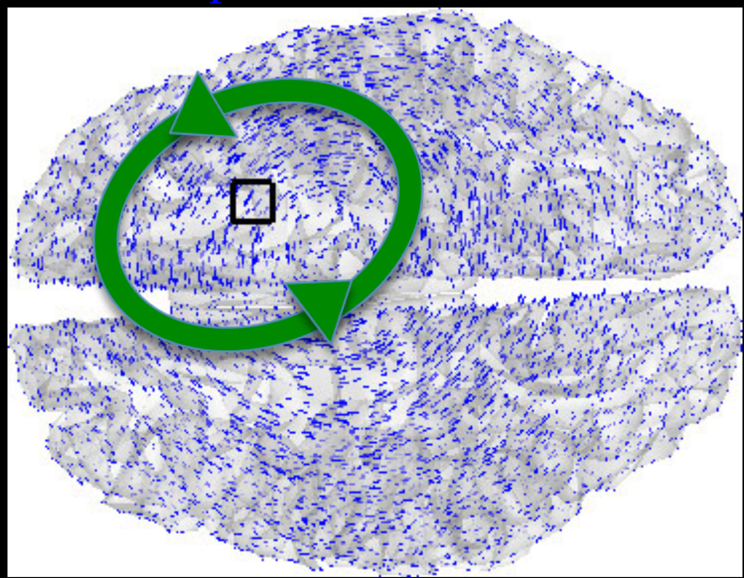
How to make an MNE: sensitivity profile basis

- Each channel has a sensitivity profile (lead field), which tells how well each point source shows up in that sensor.
- MNE assumes that solution can be formed as linear combination of these lead fields. Then, automatically:
  - Number of unknowns (#lead fields) = Number of equations (#channels)

Example lead field channel #1

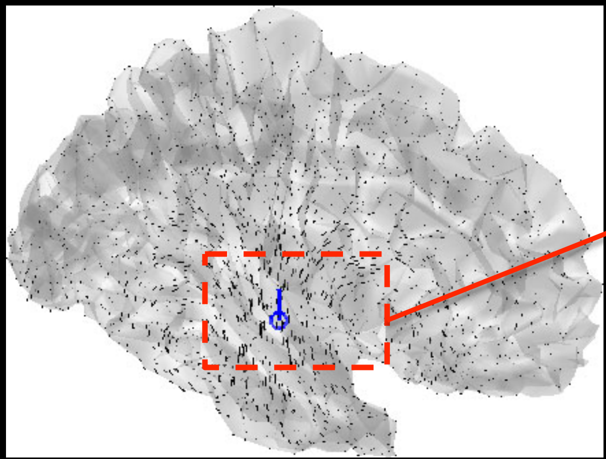


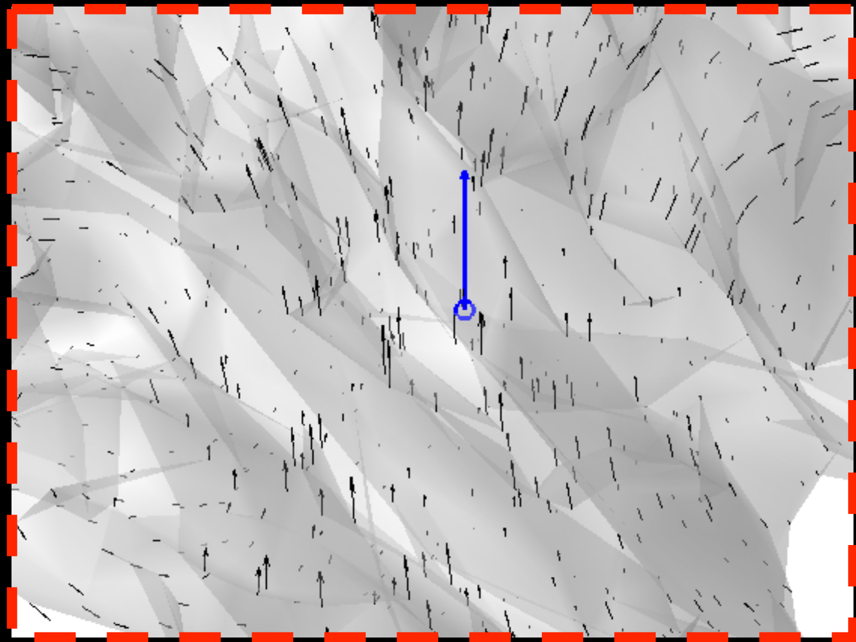
Example lead field channel #2



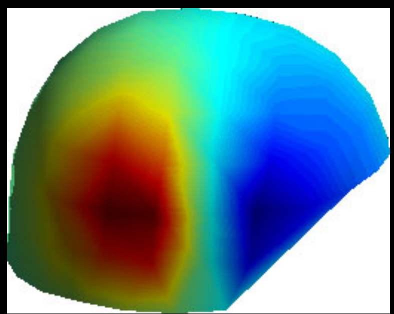
Simulated auditory data with MNE

The MNE solution (tiny black arrows):





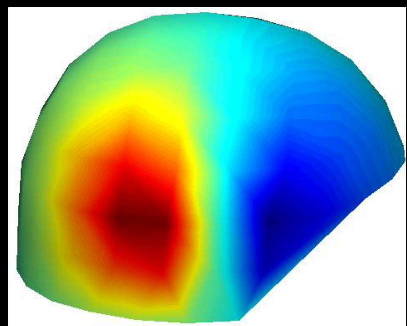
Single dipole



When summed up, the "small dipoles" give (almost) identical MEG data!

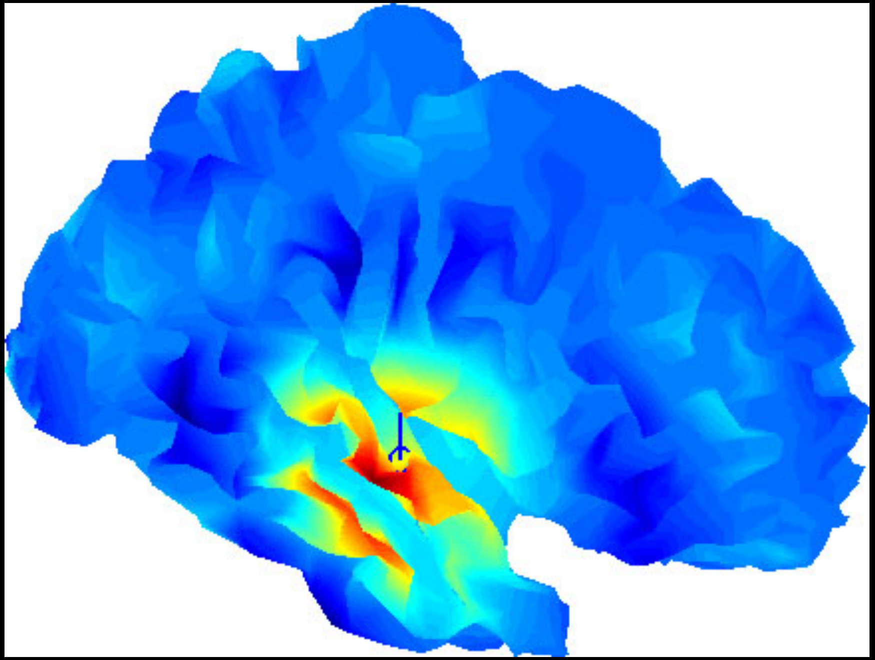
"Inverse problem: solution is non-unique"

MNE



MNE and point spread

A cortically constrained MNE

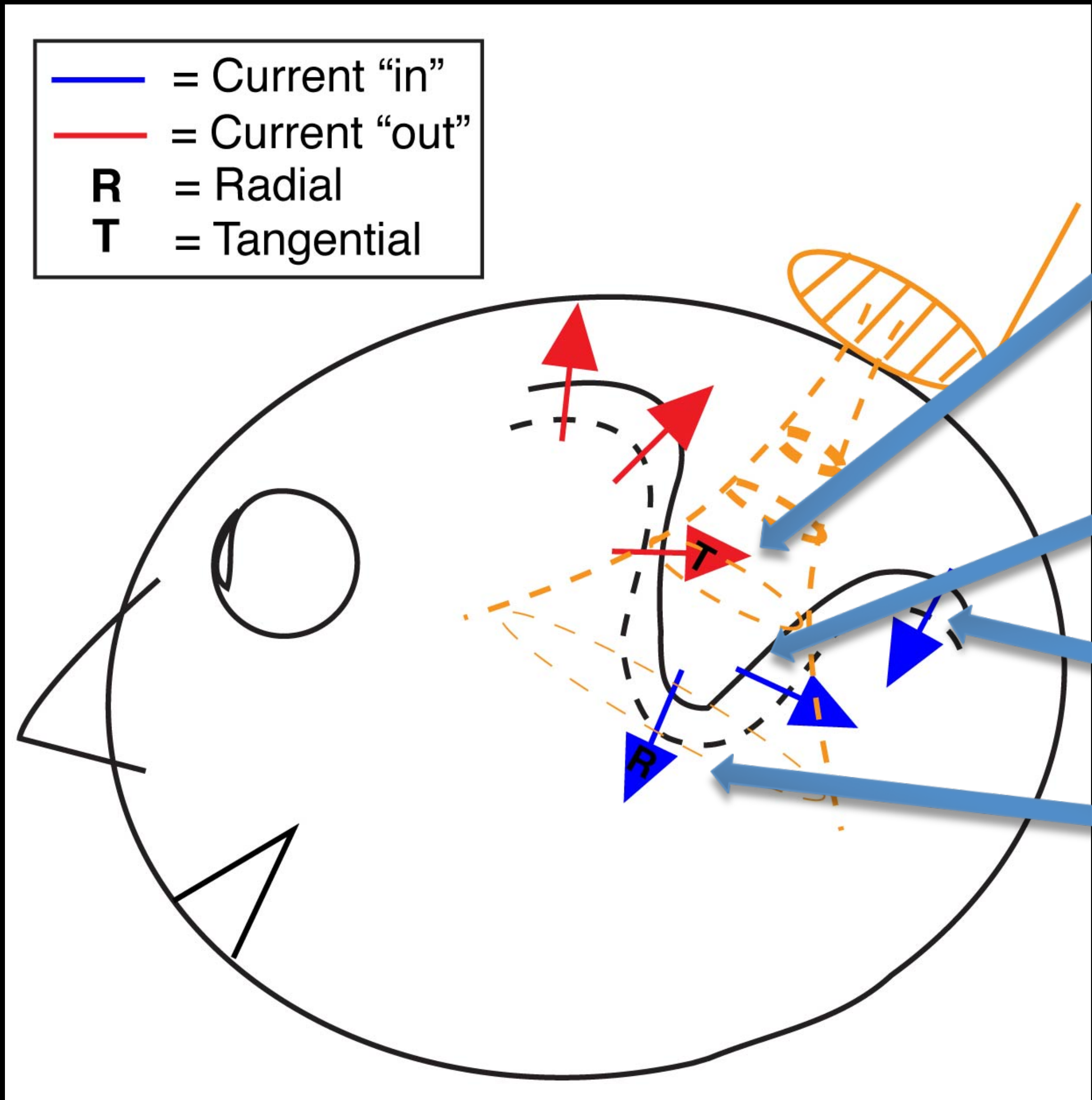


The point spread function

- How much a point source is blurred
- Tells something about "imaging resolution"
- For MEG / MNE, the point spread depends on source amplitude, location & orientation and noise levels…
- Deep and or radial sources get more blurred.

Cortical geometry, MEG & MNE

MEG & cortex geometry



MEG visibility rank:

Superficial tangential

Deeper tangential

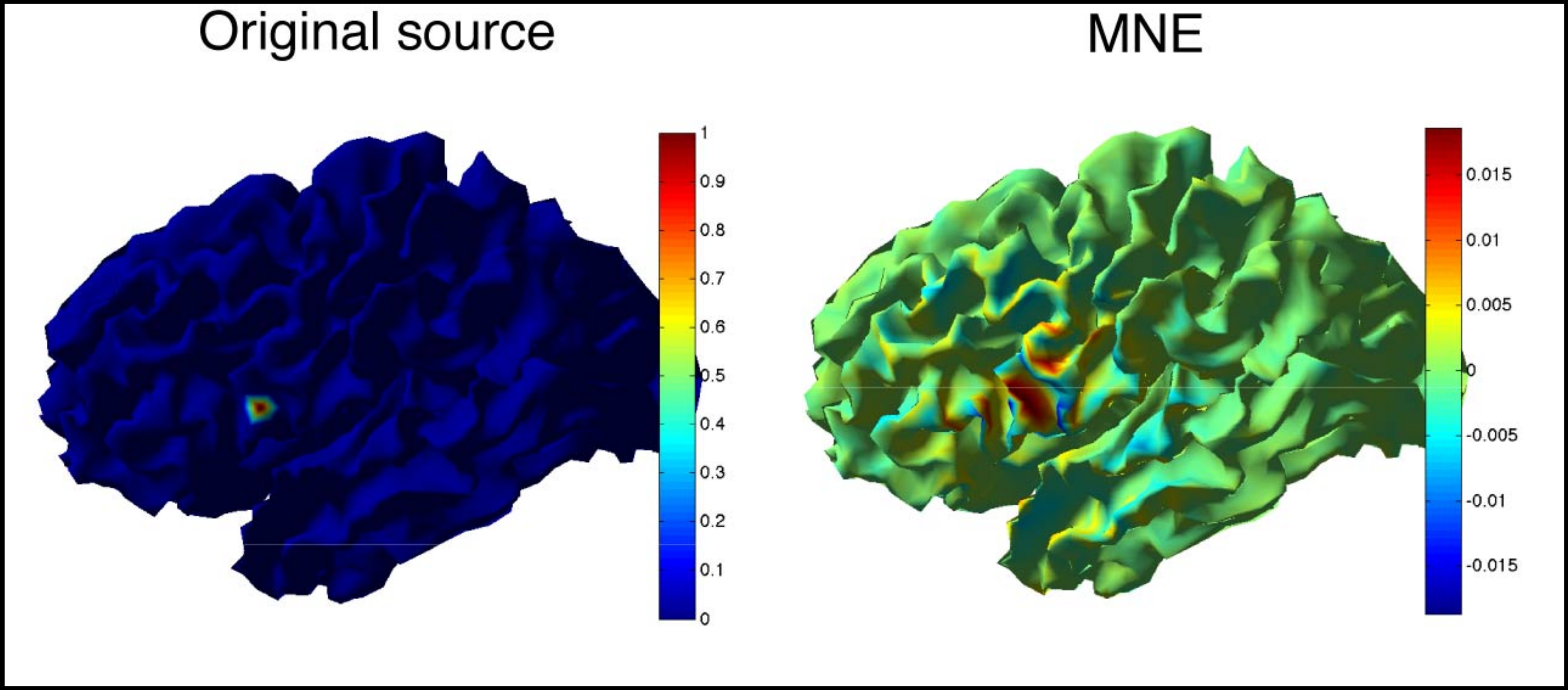
Superficial radial

Deeper radial

Another example cortical MNE

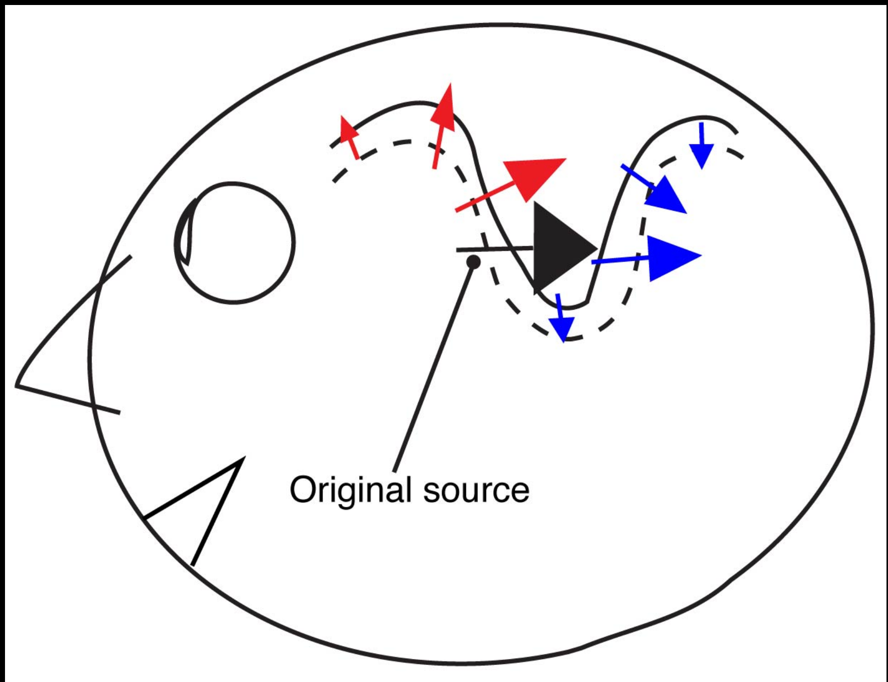
MNE gives you an "automatic estimate"…

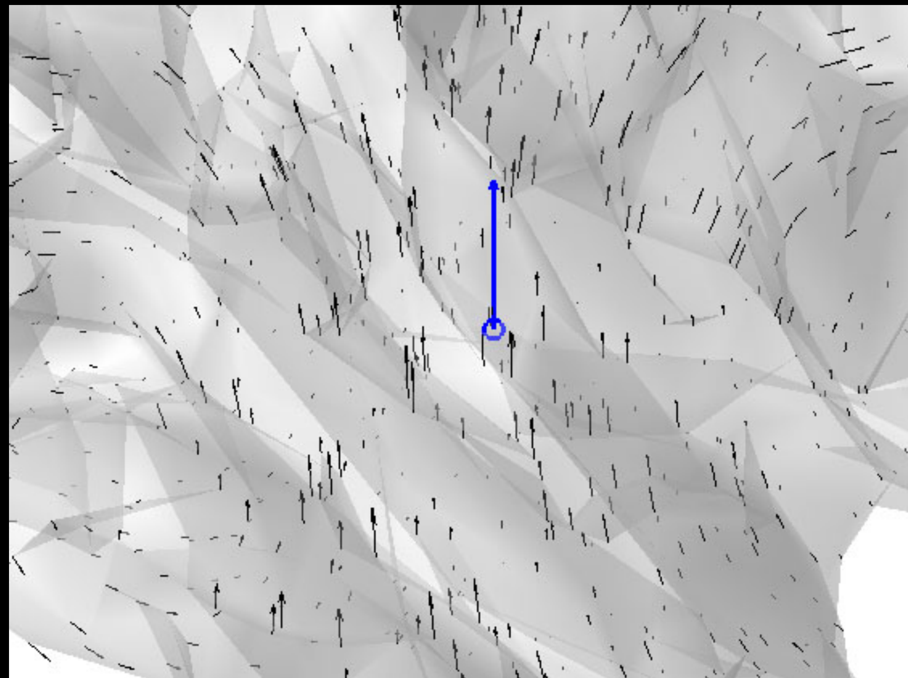
But does not really reflect source extent!



Still one more look the cortical MNE solution

- The origin of the “plus-minus” alternation in the MNE: Opposite banks of a sulcus have opposite outward normal orientation.





Summary & Conclusions

ALL models are wrong, but some are useful

- Beyond reasonable doubt, MNE has proven to be a useful tool for interpreting MEG/EEG data!
  - The MNE has been / is successfully used at MGH/Martinos Center and elsewhere, on various types of experimental data.
- MNE is still just one possible solution, sometimes deceptive!
  - Typically looks more "physiological" than a "point dipole".
  - This is mostly due to the blurring effect: The MNE assumes a grid of point dipoles.
  - The dipole is just a tool to model the fields "far away".
- Keeping in touch with the data.
  - Even simple operations (threshold, absolute value) render the output nonlinear. It does not fit the data any more!

Use clever experimental design

- Relative accuracy of MEG/MNE is better than absolute
  - Changes in source location or amplitude might be detected more easily.
  - Try to make most sources “constant across conditions”.
- Sequential activations are easier to distinguish.
  - Can you delay some sources by some manipulation?
  - Ideally you have only few sources active simultaneously.
- The MEG realm is temporal!
  - Timing of stimulus presentations etc. highly important.
  - More about this in “MEG analysis in practice”.

Look at the data!

- Is there something to “localize” to begin with?
  - See anything dipolar? A couple of dipoles maybe?
- Look at major peaks of time-courses in the data.
  - Do the field patterns look reasonable?
- Look at similar time-courses in the MNE solution.
  - This can give a clue about point spread!
- Look at field patterns across conditions
  - Does the field pattern change, or only the response magnitude?

Thanks for listening!

Questions?