Interpreting MEG data in terms of “distributed sources”: under the cover of MNE

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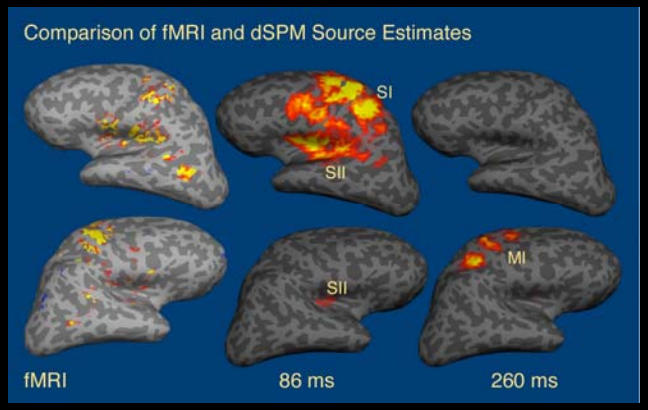
The Aim

and the weapon of choice

What do these activity maps & comparisons mean? What is a reasonable interpretation?



No pain, no MNE…

- Unpleasant information causes pain & stress.
  - This presentation contains unofficial inverse solution information!
  - I try to cover topics not typically covered.
- Why bother?
  - Intuition on estimates > Avoid pitfalls > Better interpretations > Fame & money >…
  - Interpretation of MNEs is not straightforward. It’s not safe to think anything else.
- You might even think about the MNE estimates when designing the experiment!
  - Will the MNE likely tell the difference I’m trying to prove?

And then some gain!

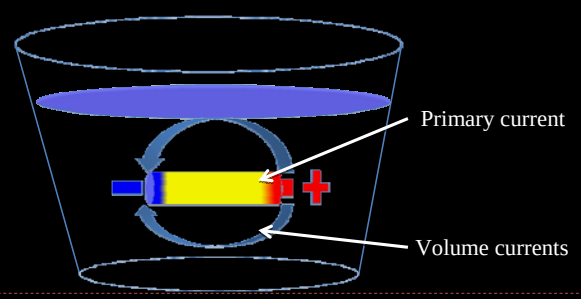
- The underlying physics & math is not so complicated!
  - Some intuition can be quite easily developed.
  - Clinical people using M/EEG solve the inverse problem also just mentally.
- Of course, real life numerical computations look complicated.
  - The same basic principles apply, implementation becomes tedious.
  - For MEG, even the simplest models give good answers.

Review of the current dipole

The hero of our story

What is the dipole in real life?

- To get 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.



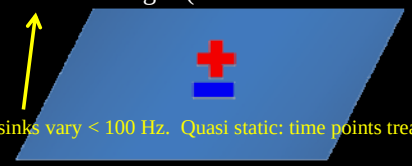
Relationship of quasi-static E-field & B-field

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

- Quasi-statics: slow electric & magnetic phenomena
  - Electromagnetic "waves/radiation" play no role.
- The dipole (*i.e.*, "battery") E-field drives passive (*i.e.* 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.

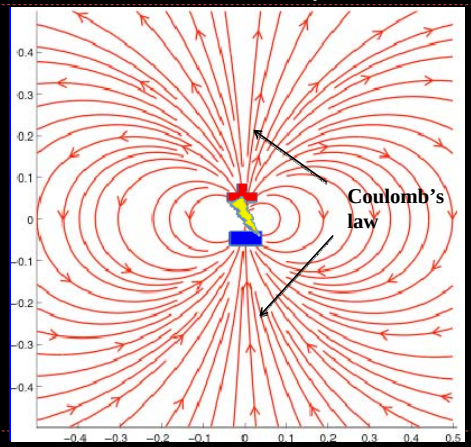
How to find a “matching” outside current for a given current dipole?

- First, how to find the electric field generated by a dipole?
  - Ohm then gives us the currents.
- Let’s assume a 2D homogeneous conductor.
- The E-field of current dipole is equivalent to two closely spaced “static” charges (current source & sink):



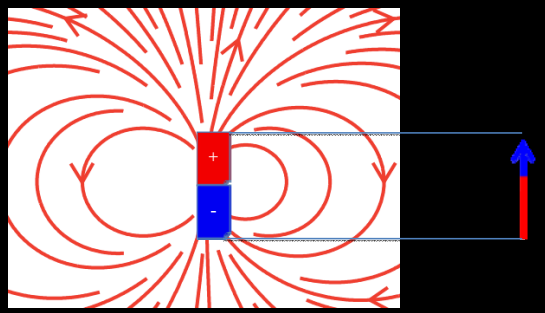
Sources & sinks vary < 100 Hz. Quasi static: time points treated separately!

The E-field of the current dipole



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

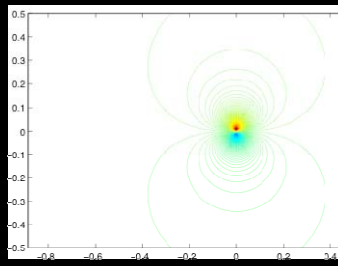
Total current = Volume (outside) + Primary (inside)



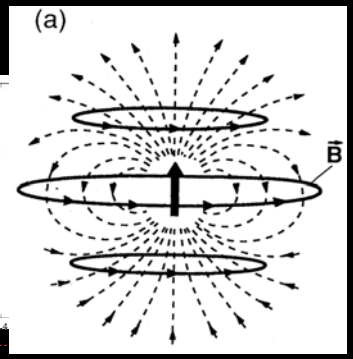
We know everything now!

- We know potential, all currents, we can calculate magnetic fields…

The “EEG’’ (E-potential)

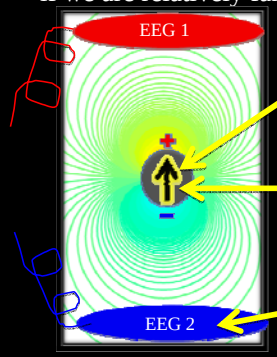


The “MEG’’ (B-field)



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 "sum", if we look form a distance.

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

And of course another things…

- The realistic conductivity models:
  - BEM (Boundary Element Model, brain/skull/scalp).
  - FEM (Finite Element Model, white matter conductivity anisotropy possible to handle).
- Rules of thumb:
  - EEG is more sensitive to conductivity than MEG.
  - Currents in skull are small (skull has poor conductivity).
    - MEG does not know/care much about these currents.
  - The potential has to be figured out all the way through the skull to the scalp.
    - EEG is sensitive to the thickness of the skull.

Minimum-norm estimate (MNE)

The timeless classic!

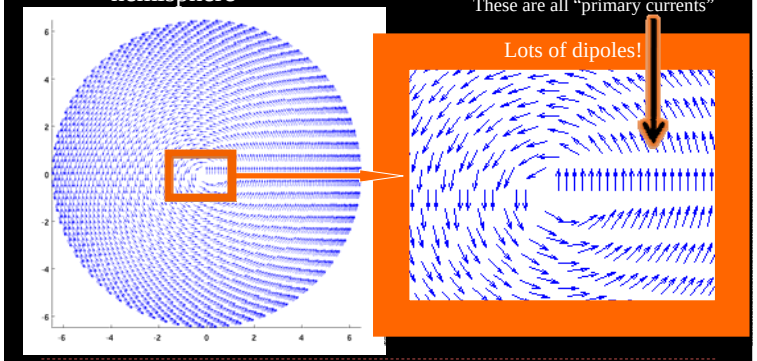
MNE: computational motivation

- 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!

Let's try this with spherical model!

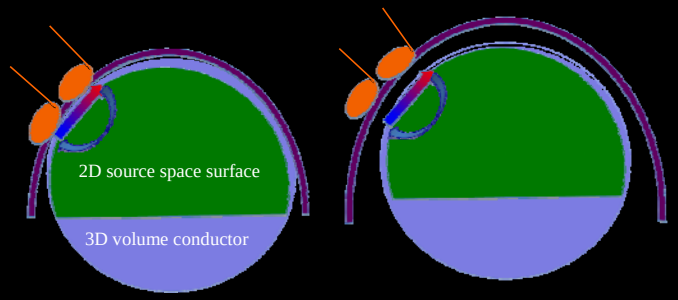
Assume that the source space is surface of a hemisphere

These are all "primary currents"

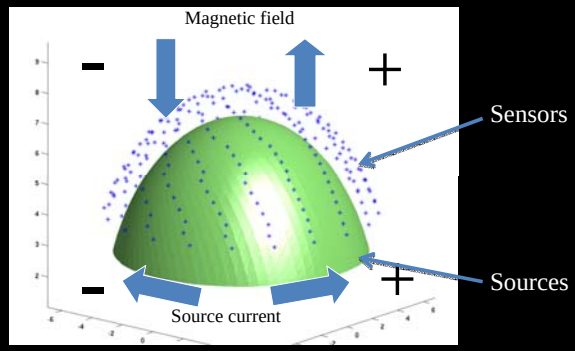


Two cases: 2 cm and 5 cm above sources

Case 1: MEG sensors near **Case 2: MEG sensors far**

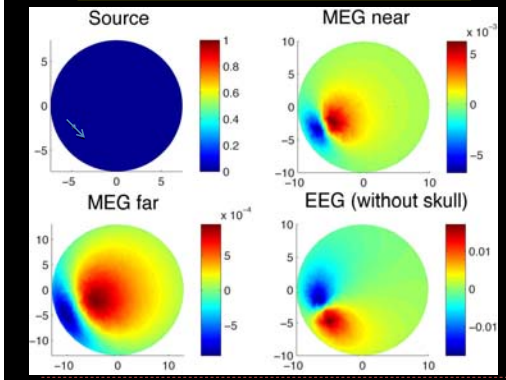


Plotting conventions



"Image reconstruction perspective": point-like source is observed as very non-point-like field pattern.

The dipole field dies off ~ 1 / (distance)^2



Inverse setup

Number of little dipoles = number of unknowns ~ 10^3

>>

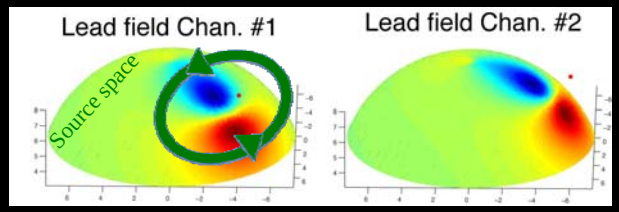
Number of MEG channels = number of equations ~ 10^2

Adding channels beyond some point does not help:

- spatial correlations in the signals -> sensors not independent

The MNE “trick”: sensitivity profile basis

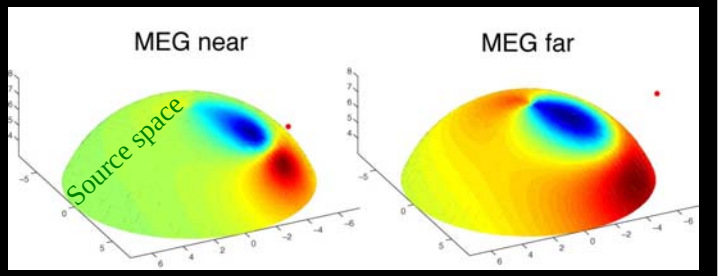
- Each channel has a sensitivity profile (lead field), which tells how well each source point shows up in that sensor.
- MNE assumes that solution can be formed as linear combination of these lead fields. Then, automatically:
  - Number of unknowns (#lead fields) = Number of equations (#channels)



Lead field as a function of distance

This is kind of a “reciprocal” way of looking the dipole magnetic field $\propto 1/(\text{distance})^2$.

Overall sensitivity of the whole sensor array has more complicated characteristics.

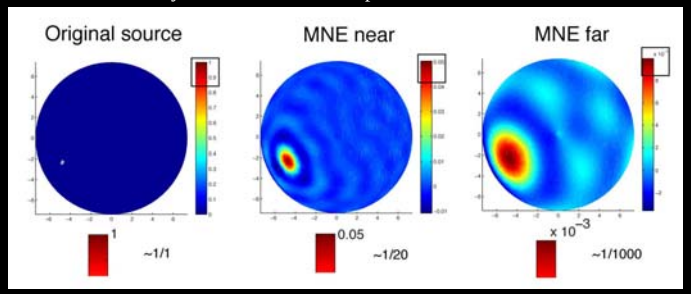


MNE: So, you ask for a distributed source….

The point-like source is smeared across whole source-space.

This is a picture of the point-spread function of MNE at one location.

We essentially see a somehow “low-pass filtered/smoothed” source.



How to interpret the MNEs?

“Linearity is our friend”

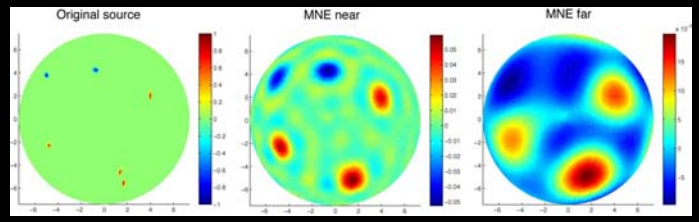
-KC

Why do we use MNE?

- M/EEG people also want to visualize the activity on cortex.
  - Why should only fMRI people have nice color pictures? It's not fair!
- MNE is an inverse method with a closed-form solution.
  - Computationally very efficient. One-liner in MATLAB.
  - Basically it is 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.

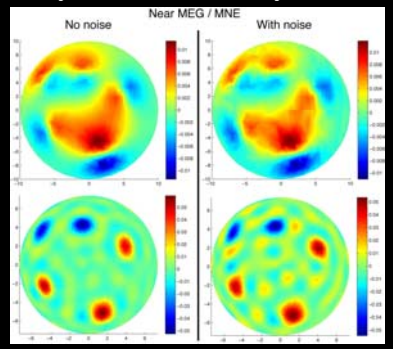
Clueless about possible activations?

- No worries, MNE gives you an answer!
  - This is the MNE appeal…
- Basic question: How "many" activations are there?
  - The "ripples" from sources can sum up coherently!
  - Smaller real sources and ripples may look alike.

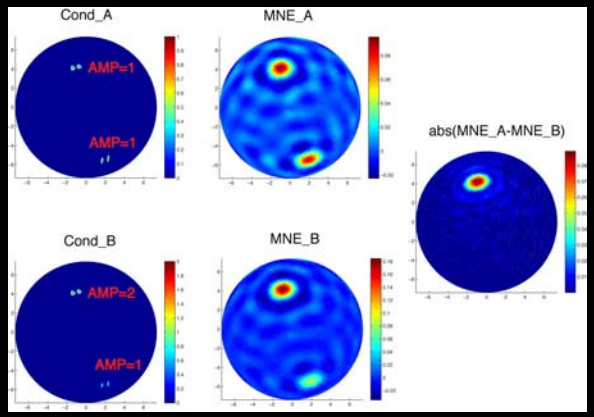


Got noisy data?

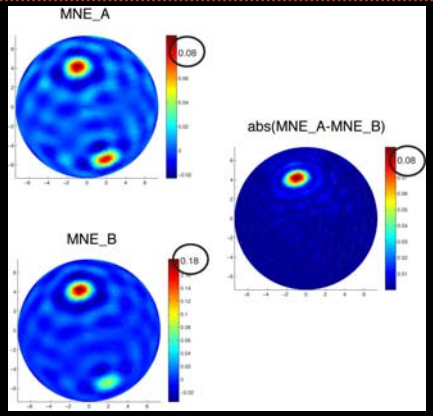
No worries, MNE is linear and straightforward to regularize. Stability can be rather easily obtained.



Comparing two "experimental conditions":



What happened? Let's take a closer look…



How to misinterpret the MNEs?

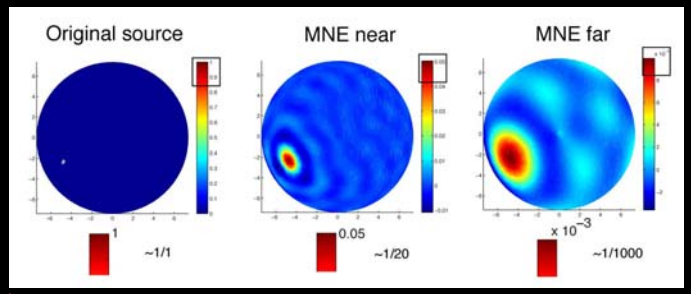
"Nonlinearities are hidden"
-Aapo

Unfortunately, M/EEG does not work like fMRI

- Well, not even fMRI works like fMRI…
- Due to the ill-posedness of the inverse problem, the MNE is "one possibility out of infinitely many".
- Nonlinear post-processing destroys the original linearity.
  - Thresholding and taking absolute values are nonlinear ops.
- We really do NOT have the millimeter resolution of the FreeSurfer surface:
  - The true resolution (~point spread) depends on various non-linear factors (SNR, source location, orientation).

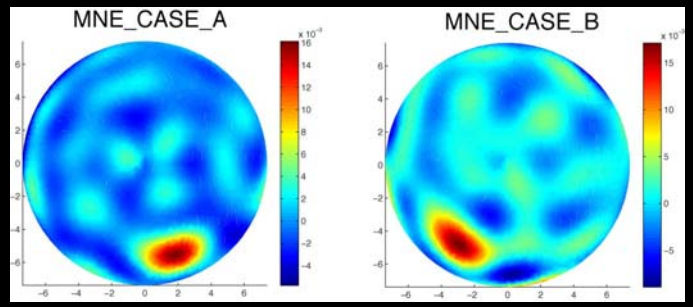
The extent and amplitude of MNE do not have a direct relationship to those of the "activation".

- The spatial smearing and amplitude scaling of source estimate depend on distance between sensors & source.
  - More logically, the uncertainty about location should / could depend on this distance.

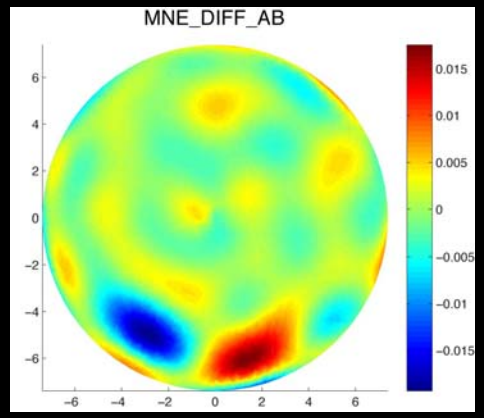


MNE interpretation contest!

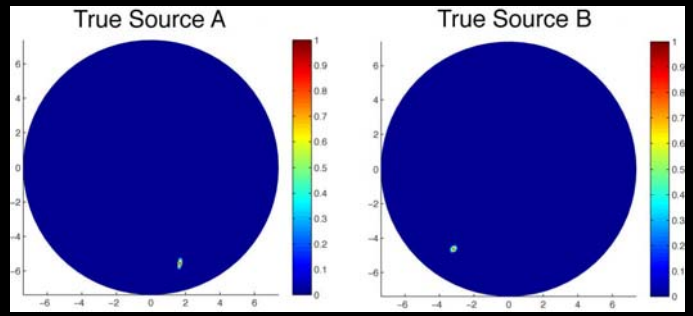
How many sources and where?



The difference across conditions…

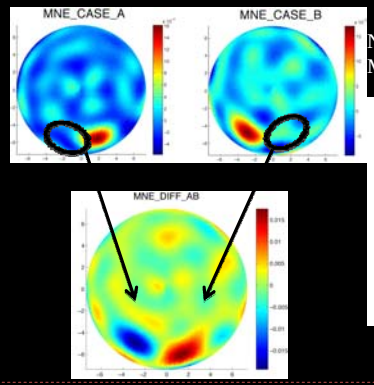


…And the Truth!

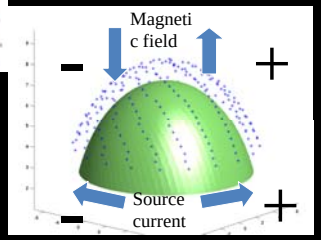


Remainder: the current has direction & magnitude!

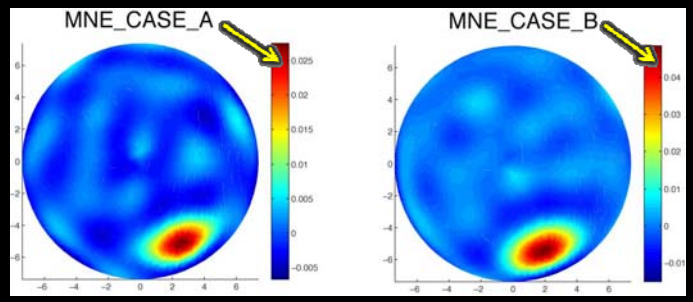
- You have to go back and check if "(case A left)<0"



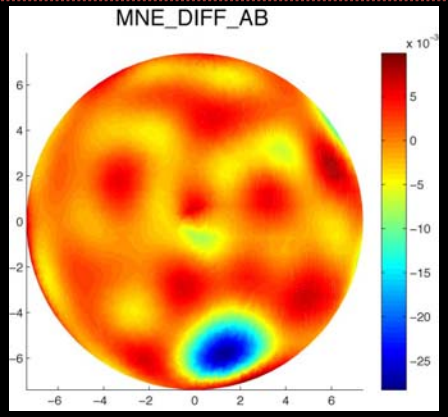
Negative current is NOT deactivation!
More negative current is "more".



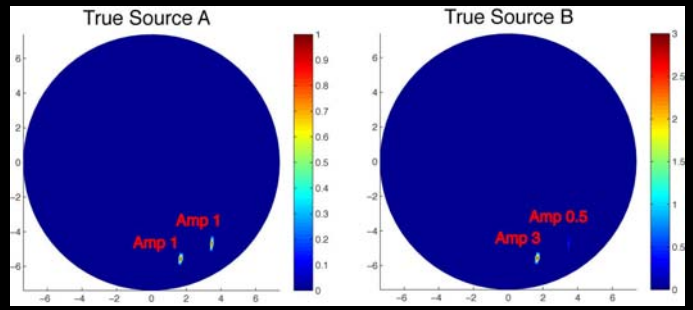
Let's do another!



And the difference of the MNEs…

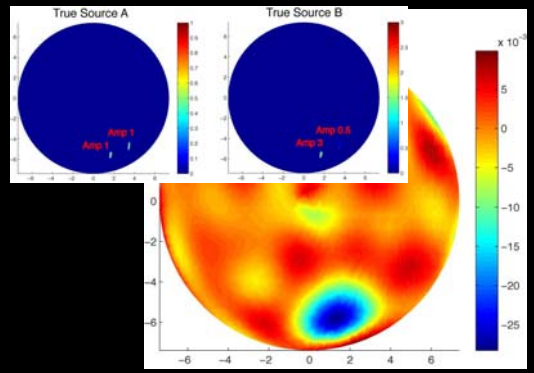


And the winner is…



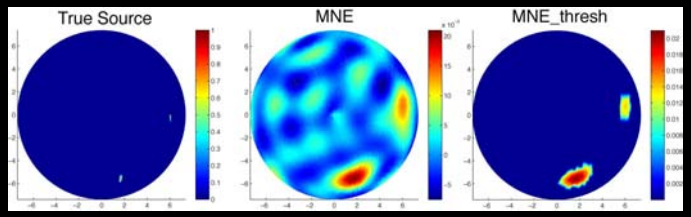
The decreased dipole is "lost in ripples".

Overall activation still larger in "Case B" = Useful & correct information!



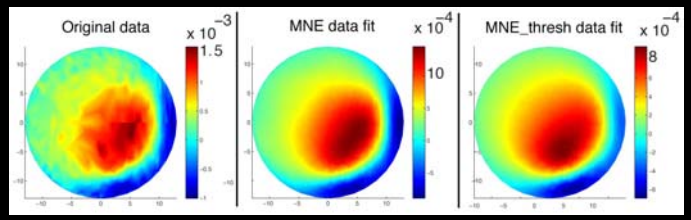
Nonlinear post-process: Thresholding…

What if we try to get rid of the ripples just by zeroing them?

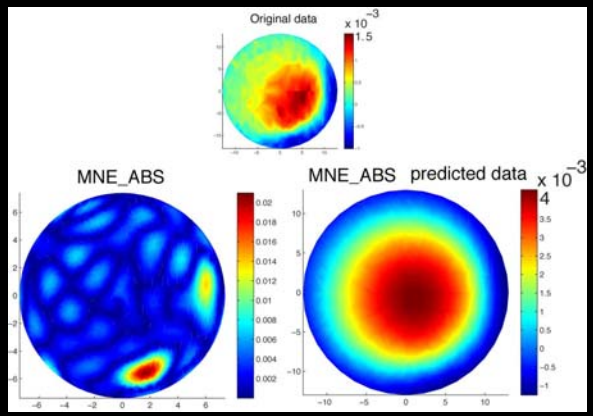


Thresholding is not a linear operation!

The MEG field pattern is both diminished and "twisted".



Taking absolute values: different inverse!



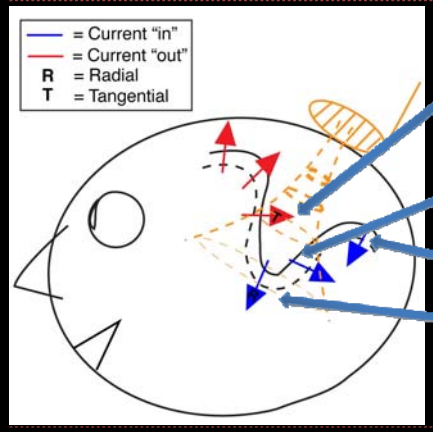
Point spread depends on location, SNR …

- The amplitude is decreased in different proportions for different locations.
  - The overall "MEG visibility" of source determines this.
  - The position of the subject's head vs. actual depth of the source.
  - Pattern of "ripples" in the MNE depend on location.
- The SNR in the two datasets A & B may be different!
  - Suitable regularization (and point spread) depends on overall SNR.
  - Selection of regularization IS nonlinear.
  - The noise "gets" to the estimates. The regularization prevents amplification.

Realistic cortical geometry, MEG & MNE

Getting closer to the real world

MEG & cortex geometry



MEG visibility rank:

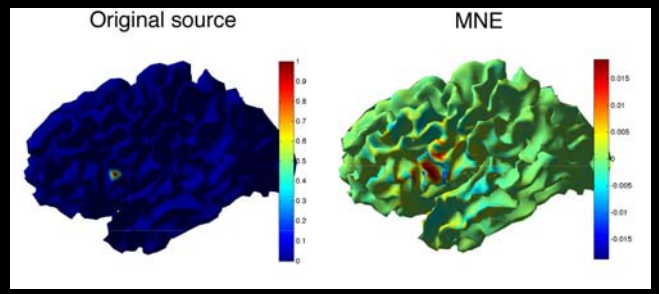
Superficial tangential

Deeper tangential

An example cortical MNE

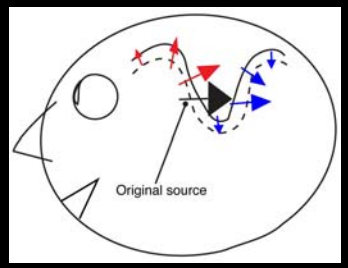
This is a pretty visible source location…

The ripples still go pretty far!



Still one more look the cortical solution

- The origin of the "plus-minus" alternation in the MNE: Opposite banks of a sulcus have opposite outward normal orientation.
  - True point-spread becomes hard to see…



Summary & Conclusions

And messages to take home to your sweetheart!

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.
- It is still "just" an interpretation, 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".
- If you really play linear, then you live with ripples!
  - Even simple operations (*e.g.*, thresholding) render the output nonlinear. You'll lose some of the touch with the data.

Practical advice

- Try to show your case with:
  - Basic regularized MNE. Try to make linear color-scale too.
  - MNE with thresholding.
  - MNE with thresholding and absolute-value taking.
- Remember to look at you data! See dipolar fields?
  - Dipolar fields are "easily localizable" by nature.
- Sequential activations easier to distinguish.
  - Can you tease out sources by experimental manipulation.
- The MEG realm is temporal!
  - More about this in the next tutorial…

Thanks for listening!

Questions?