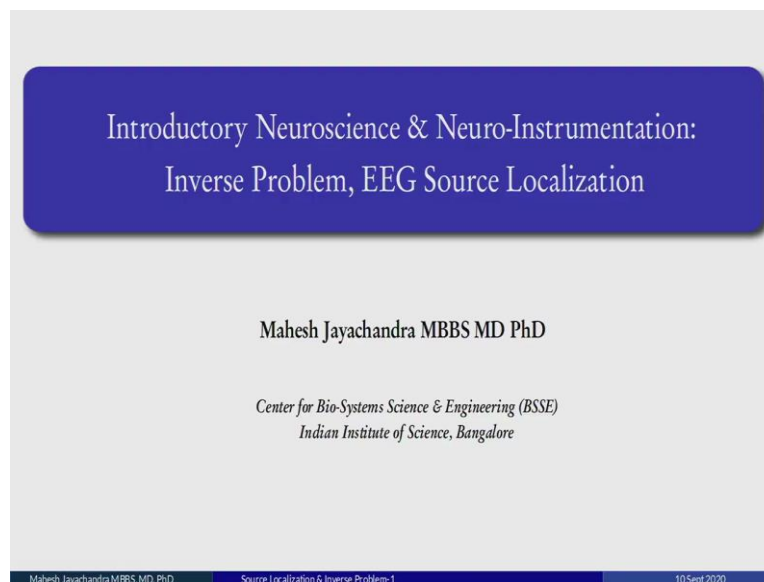


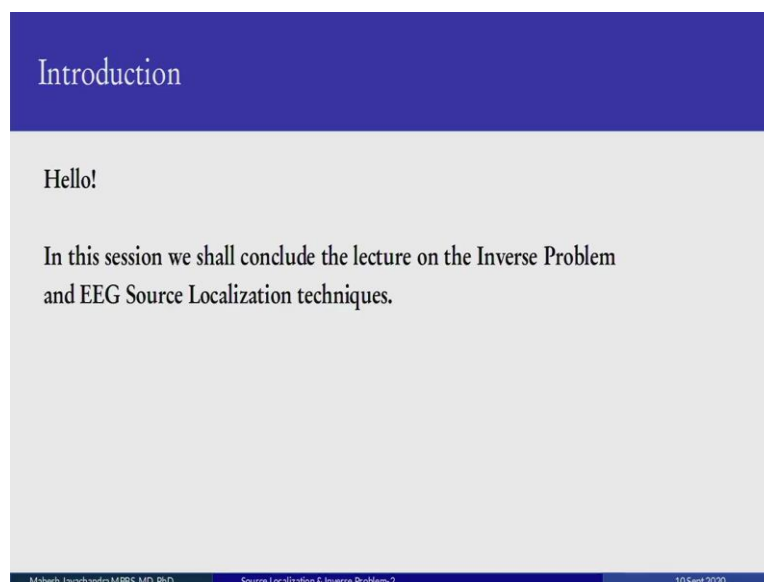
Introductory Neuroscience and Neuro-Instrumentation
Professor Mahesh Jayachandra
Center for Bio-Systems Science and Engineering
Indian Institute of Science, Bangalore
Lecture 28
Inverse Problem, EEG source localization 2

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Introductory Neuroscience and Neuro-Instrumentation: Source localization, Part 2.

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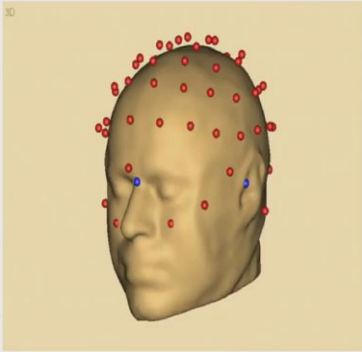
So in this session, we shall conclude the lecture on the inverse problem and EEG source localization techniques.

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Co-registration of EEG electrodes with the Head model

The head model is constructed from the MRI image (of the subject) which has a different 3D coordinate system than the EEG scalp electrodes.

Thus, it is necessary to align the EEG electrode locations to the subject's MRI in a common coordinate system, to solve for electric potentials.



The image shows a 3D model of a human head. The head is rendered in a light yellowish-brown color. Numerous red dots are placed on the scalp, representing EEG electrode locations. Three blue dots are placed on the head: one on the nose (nasion), one on the back of the head (inion), and one on the ear (pre-auricular ridge). These blue dots serve as fiducial markers for aligning the EEG electrode locations with the subject's MRI image.

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We were talking about models. So let us consider the head model. So we need the MRI image of the subject which has the different 3D coordinate system. Then the EEG electrodes, the subject. So we need to align the EEG electrodes with the subject's MRI in a common coordinate system to solve for these problems. So if you look at the picture on the right, the blue dots are the fiducial markers for MRI.

So you have the nasion, it is on the nose. You have an inion, you cannot see this here but the back. Then you have two points over the pre-auricular ridges for the ear. The red dots are all EEG electrodes. So we have to synchronize both these; otherwise, we will not be able to get the right solution if the EEG electrodes are not synchronized with the MRI image. There the physiology has to be synchronized with the anatomy.

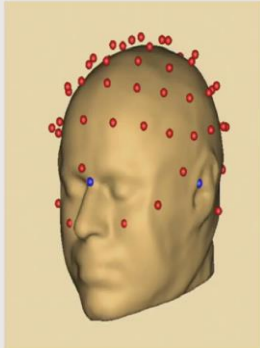
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Co-registration of EEG electrodes with the Head model (2)

This procedure is done using fiducial markers, which are known anatomical locations (blue dots) as reference:

- 1) Nasion
- 2) Inion
- 3) Ear - pre-auricular location

The red dots are the EEG electrodes (10-20 system).



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So as I mentioned this procedure is done using fiducial markers, which are anatomical locations. This point over here is the nasion. A similar point at the back, there is a ridge, is called the inion. And then you have the two pre-auricular ridges. So these are the anatomical landmarks for the MRI. The red dots are the EEG electrodes and they are arising from the, usually from the 10-20 system.

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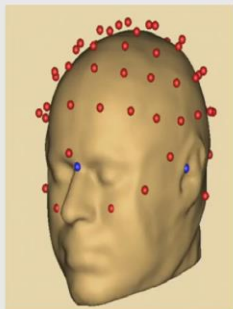
A simplified Head Model

Now we can model the measured EEG data as:

$$y = Lq + n$$

where,

- q is the time-course of the unknown dipole
- r is the dipole location
- L is a matrix capturing how currents from the dipoles are transformed into EEG recorded at the scalp electrodes
- n is measurement noise (from baseline recording)



We have to estimate q (given L, y, n)

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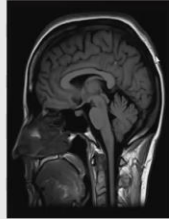
So once we have this, now we can model the measured EEG as so, y is equal to Lq plus n where q is the time course of the unknown dipole, r is the dipole location. L is the matrix capturing how the currents from the dipoles are transformed into EEG recorded at the scalp

electrodes and n is the noise, the measurement noise from the baseline recording. So essentially, we have to estimate q given L , y and n .

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Sources of Error

1. All the assumptions of the Inverse Problem.
2. Accuracy of the head model: a 4-layered model including brain, skull, CSF and skin is a good starting point. *3-layers can work, but 6-layers are computationally intensive.*
3. Recognizing different tissues from the MRI - non-trivial in effort or time.



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Source Localization & Inverse Problem 2

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So what are the sources of error? So all the assumptions of the inverse problem if they are off or you have not taken them into account, you will have a huge error. Then we need the head model has to be accurate. So usually, neuroscientists use a 4-layered model, that is the brain, the skull, the cerebrospinal fluid and the skin. This is a good starting point.

3 layers can also work but it is not so good while 6 layers is good but is computationally very intensive. The computer will keep modeling it for days. The other thing is we have to recognize the different tissues in MRI, I mean which is the skull exactly, which is the skull, which is the bone, which is the skin, how thick is the CSF layer, so on and so forth. This is nontrivial, you need to be an expert and it also takes a long time.

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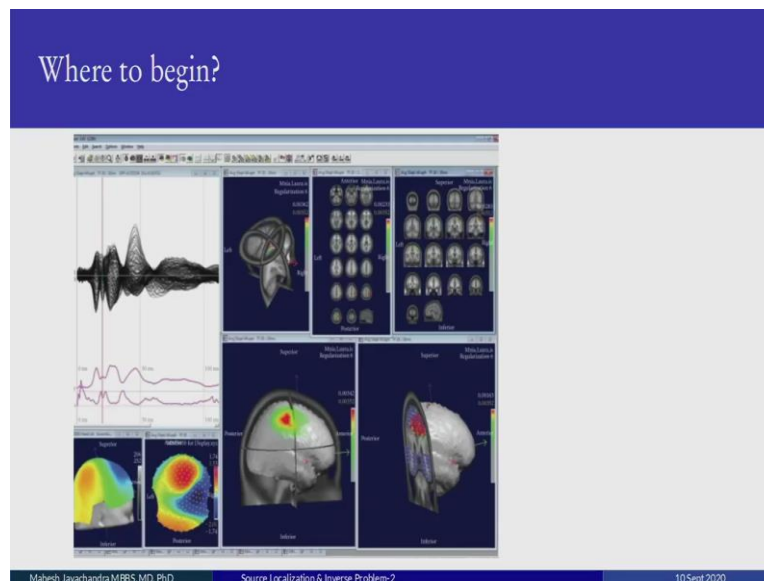
Source modeling software, both free and commercial		
Name	Website	Inverse models
ACADEMIC SOFTWARE PACKAGES		
Brainstorm	https://neuroimage.usc.edu/brainstorm	Dipole modeling, Beamformer, sLORETA, dSPM
Cartool	https://sites.google.com/site/cartoolcommunity/	Minimum Norm, LORETA, LAURA, Epifocus
EEGLab	https://scoo.ucsd.edu/eeqlab/index.php	Dipole modeling
Fieldtrip	http://www.fieldtriptoolbox.org/	Dipole modeling, Beamformer, Minimum Norm
LORETA	http://www.uzh.ch/ley/inst/loreta.htm	LORETA, sLORETA, eLORETA
MNE	https://martinos.org/mne/stable/index.html	MNE, dSPM, sLORETA, eLORETA
NUTMEG	https://www.nitrc.org/projects/hutmeg	Beamformer
SPM	https://www.fil.ion.ucl.ac.uk/spm/	dSPM
COMMERCIAL SOFTWARE PACKAGES		
BESA	http://www.besa.de/products/besa-research/besa-research-overview/	Dipole modeling, RAP-MUSIC, LORETA, sLORETA, LAURA, SSLOFO
brainvision analyzer	https://www.brainproducts.com/	LORETA
BrainVoyager	https://www.brainvoyager.com/	Beamformer, Minimum Norm, LORETA, LAURA
GeoSource	https://www.usa.philips.com/healthcare/solutions/neuro/neuro-research-applications	Minimum Norm, LORETA, sLORETA, LAURA
CURRY	https://compmediscneuroscan.com/curry-source-reconstruction/	Dipole modeling, MUSIC, Beamformer, Minimum norm, sLORETA, eLORETA, SWARM

So source modeling software, usually, nobody writes it from scratch and it is really good numerical analysis and coding. There are open source academic software packages and there are commercial packages. So some of the academic packages which we have some experience with both of the institution at St. John's include EEG Lab, it is from the University of California, San Diego. And this has reached to the test of time and it is very, very majorly supported and I advise any newbie in this field to first check it out.

There is also newer software which is available, which integrates both the MRI as well as the EEG data. So one is Brainstorm which we have begun playing with at St. John's. Then there is one called Cartool and then there is FieldTrip which is a set of packages which runs on MATLAB, so does EEG Lab it runs on MATLAB. Then there is low-resolution electromagnetic tomography which we will consider just in a minute.

As far as commercial software packages are concerned, BESA is the most popular, it is little expensive but it is considered very, very good in its field and also CURRY which is from Neuroscan which has a source modeling module. I am not familiar personally with the rest of the software but you can check them out.

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So where to begin? Because you have a whole bunch of data you have the EEG data and typically you do not have one or two electrodes, it is minimum of 64 electrodes or 128 or 256 channels. And then you have to superimpose this after doing all the modeling and stuff on fMRI datasets which are vast, very big to begin with. EEG datasets are much smaller than fMRI data because, and then MRI data because there they go into gigabytes. And then you need a computer to handle all this, lots of RAM, a fast processor and lots of hard drive space because it quickly fills up.

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CARTOOL Source Imaging

Michel CM and Brunet D (2019) EEG Source Imaging: A Practical Review of the Analysis Steps. Front. Neurol. 10:325.

- This review describes in detail the different steps needed to estimate the distribution of the underlying neuronal sources, derived from EEG.
- It explains the logic underlying each step and the requirements needed to be fulfilled to perform them.
- All these steps are implemented in a stand-alone software: *Cartool*.

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So one suggestion is to start with Michel and Brunet's 2019 paper, it is over here and they describe CARTOOL which is open source software for source imaging. So this review is

good because it describes in detail the different steps needed to estimate the distribution of underlying neuron sources derived from EEG, all the dipoles. It also explains the logic underlying each step and the requirements needed to be fulfilled to perform them.

And all these steps are implemented in a standalone software called CARTOOL. So I suggest if you are interested in source imaging and modeling, to please check this out and you do not have to collect data. There are demo datasets which come with these programs and also you have many groups all over the world who have put up their data, real data which is recorded from real subjects, not simulated data on the internet which you are free to use and to analyze. The only condition being that you have to acknowledge them in your paper's presentation.

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Low-resolution brain electromagnetic tomography (LORETA)

LORETA calculates current distribution throughout the brain volume.

Advantages:

- 1) Provides basic localization solution with easy-to-follow procedures.
- 2) LORETA can localize the boundary and deep sources, unlike earlier minimum norm estimation solutions.

Disadvantage: Low spatial resolution, undesirable for source localization.

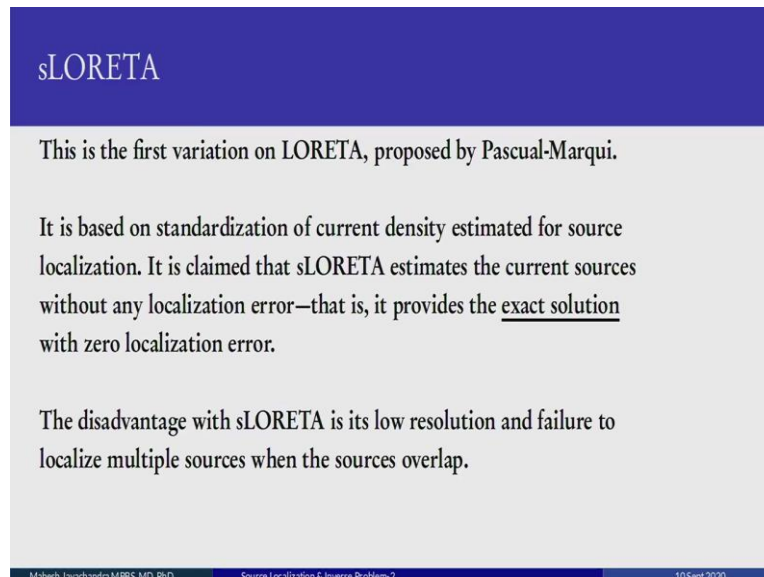
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So coming to LORETA, so LORETA is low-resolution brain electromagnetic tomography and it calculates the current distribution throughout the brain volume. Not just on the surface but throughout the brain volume. So it has advantages, one is it provides basic localization solution with easy to follow procedures. It is much simpler than CARTOOL and it is also open-source, so you can download it and use it.

And it can localize boundary and deep sources unlike earlier solutions because if you just look at EEG per say, it is just the 2 centimeters below the scalp and after that you cannot really say anything unless you use MEG in which case you get deep sources but you do not get the superficial sources. So one way to have best of both worlds is to do simultaneous recordings or recordings of both EEG and MEG in a given subject and integrate the data.

Now that is difficult because EEG while relatively freely available MEG is not. And there are very few sites, I am not sure if there is any place in India which does MEG on a routine basis. The disadvantage of LORETA is that its spatial resolution is low and that makes source realization, localization difficult.

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sLORETA

This is the first variation on LORETA, proposed by Pascual-Marqui.

It is based on standardization of current density estimated for source localization. It is claimed that sLORETA estimates the current sources without any localization error—that is, it provides the exact solution with zero localization error.

The disadvantage with sLORETA is its low resolution and failure to localize multiple sources when the sources overlap.

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So the original author of LORETA came up, Pascual-Marqui, professor Pascual-Marqui came up with a variation on LORETA called sLORETA. So this is based on standardization of current density estimated for source localization. It claimed, it is claimed that sLORETA estimates the current sources without any error. That is, it provides the exact solution of zero localization error. Again, the disadvantage is it has low resolution and it fails to localize multiple sources when they overlap especially.

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eLORETA

Exact LORETA is a method which focuses on deep sources with reduced localization error. Based on LORETA method but use different numerical analysis.

eLORETA is a reliable localizing method with no localization bias, providing zero error localization in the case of nonideal conditions—that is, the presence of noise.

Several studies show that eLORETA provides better results than sLORETA.

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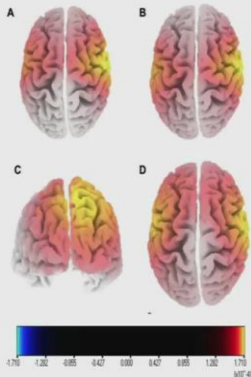
So then the group, the LORETA group came up with another variation called exact LORETA or eLORETA, which is a method which focuses on deep sources with reduced localization error. Is based on LORETA but uses different numerical analytical procedures. So it is supposed to be reliable localizing method with no bias, localization bias. And again, it provides zero error localization in case of non-ideal conditions that is in the presence of noise. Several studies have shown that eLORETA seems to provide better results than sLORETA but your mileage may vary.

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eLORETA Implementation

Mansi Saxena (ex-IISc, now at IIIT-D) is studying the mu-rhythm in spinal cord injury patients for developing BCI assistive devices.

M. Saxena, E. Sareen and A. Gupta, "Understanding Functional Brain Activation using Source Localization of EEG Signals in Motor Imagery Tasks," 2020 International Conference on COMMunication Systems & NETWORKS (COMSNETS), Bengaluru, India, 2020, pp. 58-63, doi: 10.1109/COMSNETS48256.2020.9027409.

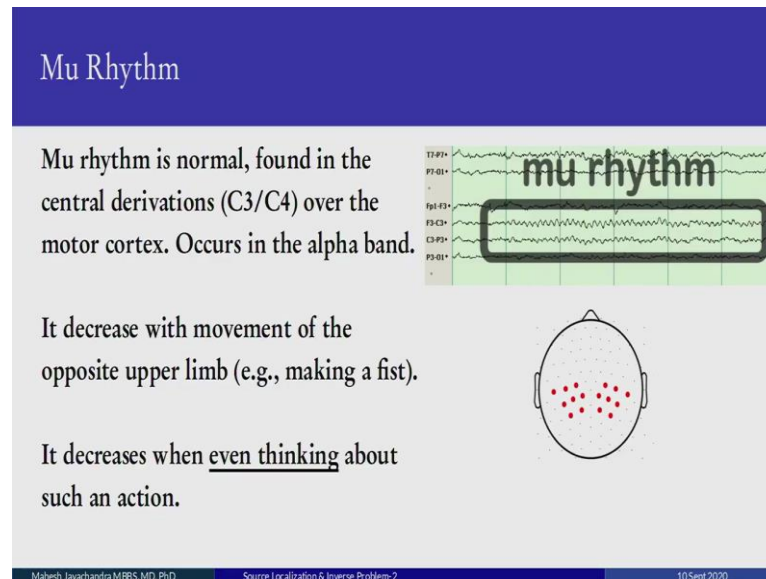


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So implementation, so one of our students at IISc, she is now at IIT-D. So she is studying the mu-rhythm in spinal cord injury patients for developing BCI assistive devices. We shall

consider the mu-rhythm in greater detail in our BCI lectures but essentially it is rhythm which comes in the alpha band and it is over the motor areas, central on both sides. And when you move or when you think of moving, it gets disrupted.

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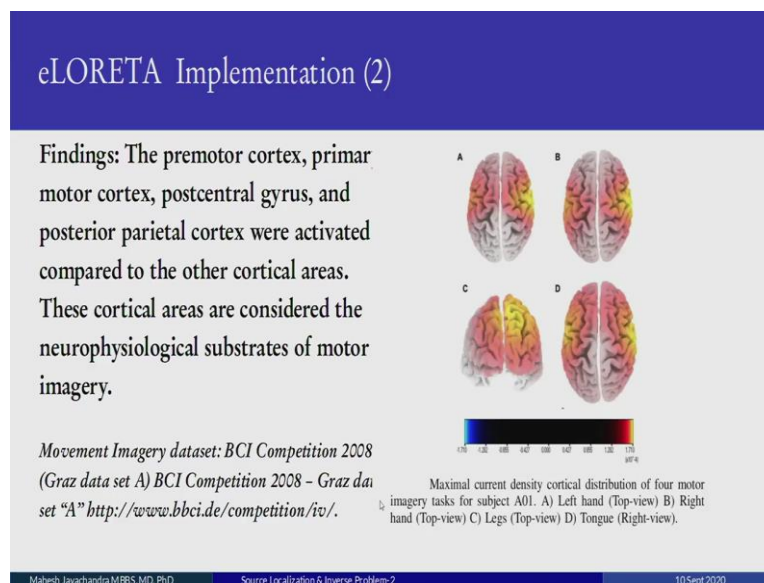


So these are the electrodes where the mu rhythm is mostly prominent over the motor areas, sensory-motor areas. And this is the typical mu rhythm. You see this regular thing and it occurs in the alpha band. So it could be easily be missed as alpha waves. But it is in the wrong area for alpha waves. Alpha waves are typically prominent in the occiput and when they occur, if they occur in all areas, they are most prominent in the occiput.

The mu rhythm on the other hand is localized only to the central and the parietal areas. Now the interesting thing about the mu rhythm is if you think of moving your hand, immediately the mu rhythm which is there, it is kind of an idling rhythm like your car being on neutral. It immediately gets disrupted and it becomes better. Now even if you think of moving your hand, you do not have to move it. if you think of moving your hand, it gets disrupted.

So that is the interesting thing about the mu rhythm and it can be possibly used for rehabilitation in stroke patients, make them, train them to keep thinking about this and the brain is plastic and there it keeps changing. They say your brain is not the same today as it was yesterday, it changes all the time. So this could possibly help in stroke rehabilitation.

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So what did Mansi and her group find? They found that the premotor cortex, the primary motor cortex and the postcentral gyrus and the posterior parietal cortex were activated compared to other areas. And these areas are considered the neurophysiological substrates for motor imagery. So consider her data, so A is moving the left hand, so on the, the left hand is represented contralaterally on the opposite side. So you see a lot of action over here.

B is moving to the right hand. You see some action here but you also see action on the left motor cortex. C is moving the legs and those are the leg areas. The hand areas are below, the leg areas on top. And D is moving the tongue. So each of these specific movements activates specific areas in the motor cortex. And she did not collect the data, she used a movement imagery database from this website. So please mark out, download this and you can do eLORETA. You can either use the LORETA software per say or you can use a software called FieldTrip which has LORETA implemented in it which runs on MATLAB.

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Field-Trip implementation eLORETA

Software: FieldTrip is a MATLAB toolbox for source modeling. It contains a set of separate (high-level) functions and visualization is via MATLAB.

Please see references to review papers and teaching material to get you started.

By far the best way to get hands-on experience with FieldTrip is by following the tutorials, the walkthrough and through the other documentation.

Also, FieldTripping is not something you do alone. Inform yourself about colleagues that use (or want to use) FieldTrip.

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So the FieldTrip implementation of eLORETA, FieldTrip is a MATLAB toolbox for source modeling. It contains a set of separate high-level functions and visualizations is via MATLAB. It does not have any EEG per say. And if you go to their website, please see references to the review papers and teaching material to get you started. And by far the best way to get hands-on experience you should go through the tutorials like everything else.

And also, you shouldn't do it alone because you might make some mistakes and it is better to get course corrected right in the beginning. So it is better to work with a group of people or other people who have done FieldTrip in the past. By having said that it is free and as long as you have MATLAB, you can run it and get some good data.

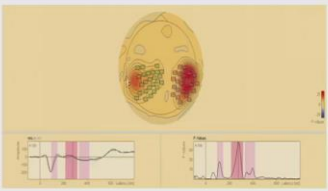
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Brain Electrical Source Modeling (BESA)

This is a commercial software from German scientists – Michael Berg and Paul Scherg.

It performs brain electrical source analysis (BESA) for estimating the parameters of the intracranial sources of ERPs.

BESA may not provide an exact solution. Its localization errors may range from extremely small to being on the order of 2-3 cm – it can miss real sources.



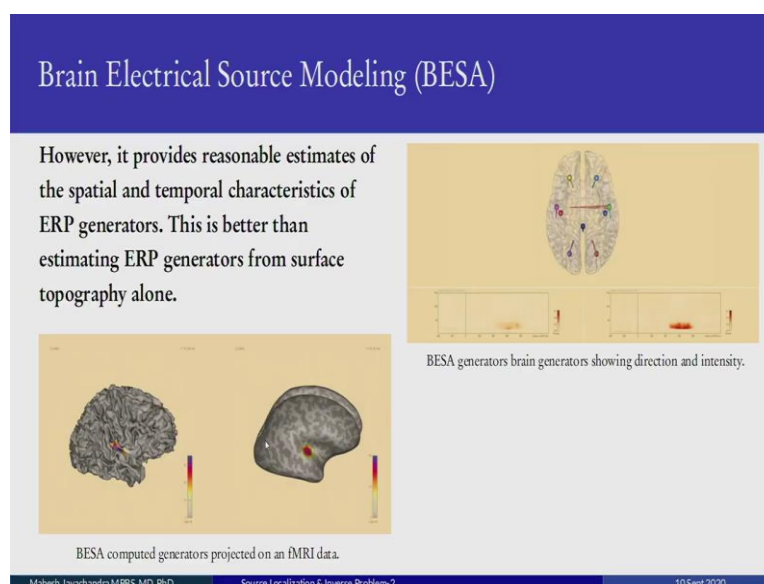
BESA ERPs lower panel. Computed brain generators above.

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Now we have to consider commercial software tool and BESA, brain electrical source modeling software is the one most commonly seen in cognitive neurophysiology labs, the proprietary software. And it was created by two German scientists, Michael Berg and Paul Scherg, Berg and Scherg. And it performs brain electrical source analysis for estimating the parameters for these intracranial sources of ERPs.

So it may not provide an exact solution and the errors may vary from very small to being on the order of 2 to 3 centimeters. So it may miss sources. But that is part of the inverse problem and it is not the thing of the software, the inverse problem is such that you never be able to sure that this is the exact solution of what we record on the scalp. So on the figure on the right you see the ERPs in the lower panel, different ERPs. And on the top you have the computer brain generators, it is on top.

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But given all its disadvantage it still provides BESA a reasonable estimate of spatial and temporal characteristics of ERP generators. This is better than estimating ERP generators from surface topography alone. It has got good math. So if you see the figure on the right, you see BESA brain generators and there are different spheres over there and they have a little rod sticking out of them, so it is a vector.

So it shows the direction and it also shows amplitude. And best of all, you can superimpose these data on fMRI data. Now fMRI is different from structural MRI where you look at the activation of areas in the brain and you estimate this by something called the BOLD signal, the blood oxygen level dependence signal. The assumption being that areas with, which are

active have more, use more energy and so the blood supply to them increases. So using EEG and fMRI is probably the most powerful way. EEG, fMRI and MEG is probably the most powerful way to figure out sources and generators in the brain.

So this has just been a brief introduction to source localization and modeling. This is neurobiophysics. There is a lot of physics and numerical analysis involved. So I strongly encourage you to read a lot with references given over here and also available on the internet. And the best way to do things is to get started. And if you have MATLAB in your institute or in your lab, please download and use EEG lab, ERP lab, FieldTrip and CARTOOL and you are on your way.