Bayesian multi-dipole models in M/EEG: static and dynamic inference

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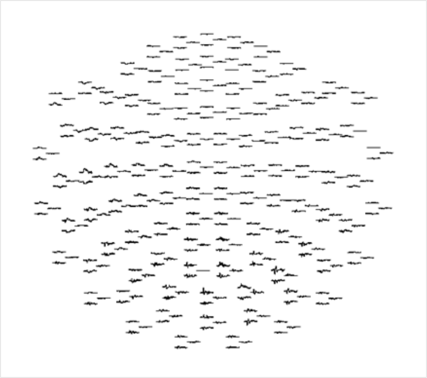
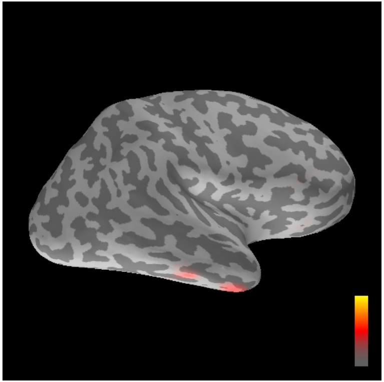
Bayesian Estimation for Engineering Solutions s.r.l.

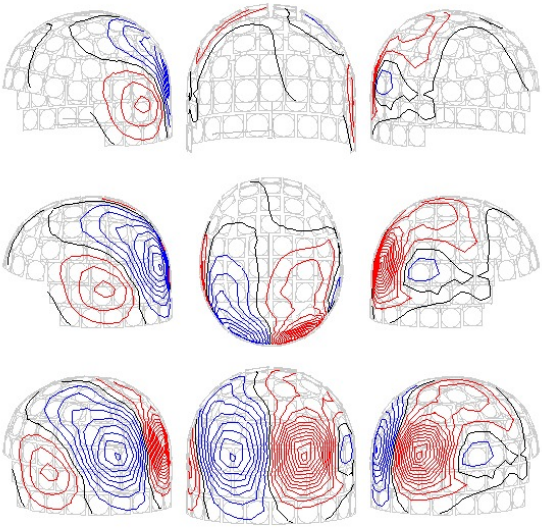
Source reconstruction





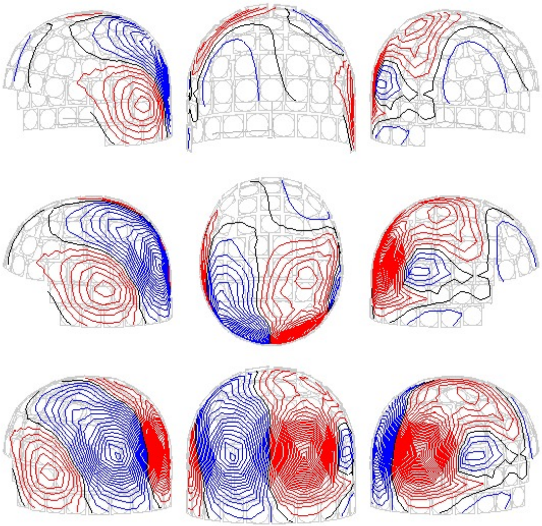
From data ... ... to sources

Multi–dipole modelling (in 2003)



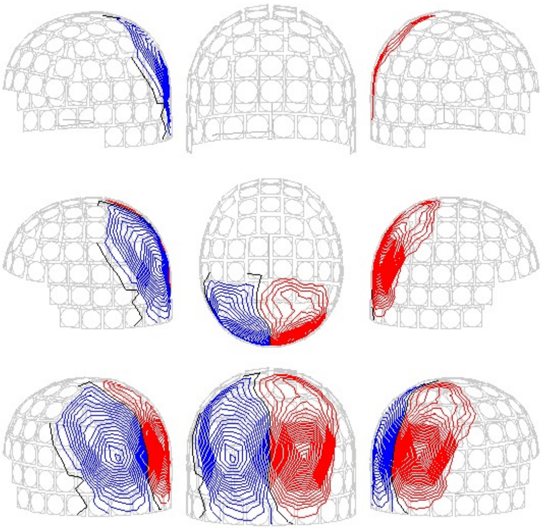
Look at the evolution of the field pattern and find dipolar patterns

Multi–dipole modelling (in 2003)



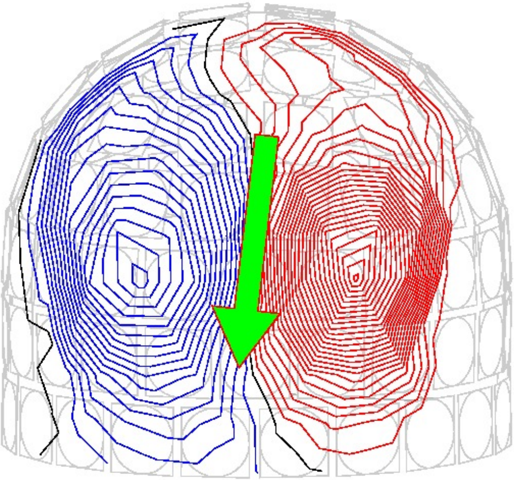
Look for the time
when it is stronger

Multi–dipole modelling (in 2003)



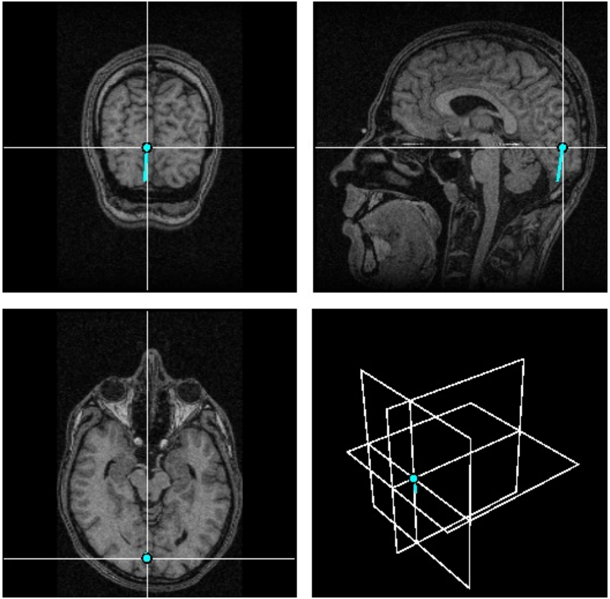
Select the channels exhibiting the dipolar pattern

Multi–dipole modelling (in 2003)



Fit a dipole

Multi–dipole modelling (in 2003)



Check that the fitted location makes sense

Repeat the process to identify more sources

In summary

- time consuming procedure
- many subjective choices
- many difficult choices
- results highly dependent on subjective choices
- perhaps the most difficult question: how many dipoles?

Can we make this procedure fully automated and statistically sound?

Our settings: a Variable–dimension model

Let

- N be the (unknown) number of dipoles;
- $r^{(i)}$ the location of the i-th dipole
- $q^{(i)}$ the dipole moment of the i-th dipole

so our unknown x is

$$x = \{N, (r^{(1)}, q^{(1)}), ..., (r^{(N)}, q^{(N)})\}$$

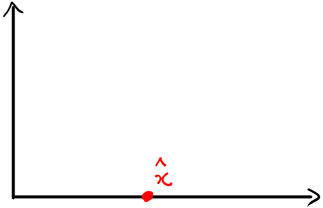
x belongs to the following state–space:

$$\mathcal{X} := \bigcup_{N=0,1,\dots} \{N\} \times \left(\mathbb{D}^N / \sim\right)$$

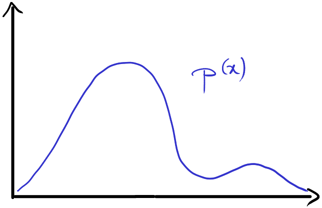
where $\mathbb{D}$ is the parameter space of a single dipole and $\sim$ makes all permutations equivalent (e.g., $(d_1, d_2) \sim (d_2, d_1)$).

Our settings: a Bayesian approach

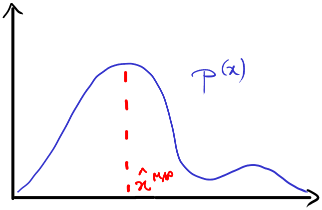
NB: not half Bayesians
find $\hat{x} = \arg\max(p(x|y))$



but fully Bayesian:
characterize the posterior probability



Why should I go fully Bayesian?



You can:

- compute best estimate
- easily include prior information
- estimate uncertainty
- find multiple solutions [a big part of inverse problems!]

The dilemma

Our aim:to approximate the posterior distribution

$$p(x|y)$$

with

$$x \in \mathcal{X} := \bigcup_{N=0,1,\ldots} \{N\} \times \left(\mathbb{D}^N / \sim\right)$$

and y the electric/magnetic field

But: x and y depend on time! How to treat this?

1. Dynamic dipole:
   Number of dipoles and dipole locations and moment can change every sampled time
2. Static dipole:

   Only dipole moments change in time

Hidden Markov Models

A pair of processes:

- a Markov process X, not observed directly:

$$p(x_t|x_{1:t-1}) = p(x_t|x_{t-1})$$

- a measurement process Y generated by X:

$$p(y_t|x_{1:t}, y_{1:t-1}) = p(y_t|x_t)$$

In practice, the following graphical structure

$$\begin{array}{ccccccc} X_1 & \longrightarrow & X_2 & \longrightarrow & \dots & & X_t \\ \downarrow & & \downarrow & & & & \downarrow \\ Y_1 & & Y_2 & & & & Y_t \end{array}$$

Bayesian Filtering

Assume knowledge of:

- Initial distribution
$$p(x_1)$$
- Likelihood
$$p(y_t|x_t)$$
- Transition kernel
$$p(x_t|x_{t-1})$$

Simple case: approximate the *filtering* distribution in a two-step algorithm:

$$p(x_t|y_{1:t}) = \frac{p(y_t|x_t)p(x_t|y_{1:t-1})}{p(y_t|y_{1:t-1})}$$

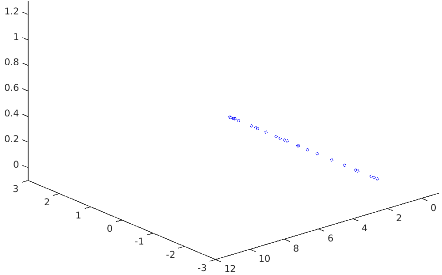
$$p(x_{t+1}|y_{1:t}) = \int p(x_{t+1}|x_t)p(x_t|y_{1:t})dx_t$$

known as *bootstrap filter*

Particle Filtering

Produce a sequential Monte Carlo sampling of the filtering distributions:

- sample $X_1^{(i)} \sim p(x_1|X_0^{(i)})$;
- assign weigths $w(X_{0:1}^{(i)}) \propto p(y_1|X_1^{(i)})$;
- possibly resample;
- sample $X_2^{(i)} \sim p(x_2|X_1^{(i)})$;
- assign weigths $w(X_{0:2}^{(i)}) \propto w(X_{0:1}^{(i)})\ p(y_2|X_2^{(i)})$;
- ...



A particle filter for M/EEG

S. et al. (2009) **Human Brain Mapping**

Prior $p(x_1)$

$$p(x_1) = p(N_1) \prod_{i=1}^{N_1} p(r_1^{(i)}) p(q_1^{(i)})$$

- $N_1 \sim$ Poisson.
- $p(r_1^{(i)})$ dipole location uniform in the brain.
- $p(q_1^{(i)})$ dipole moment Gaussian.

Likelihood $p(y_t|x_t)$

$$y_t = \sum_{i=1}^{N_t} G(r_t^{(i)}) \cdot q_t^{(i)} + \epsilon_t$$

ϵ_t Gaussian noise (but G non–linear).

The dynamic model

Easiest assumption: sources perform a random walk (i.e. they can move a bit); resulting transition kernel:

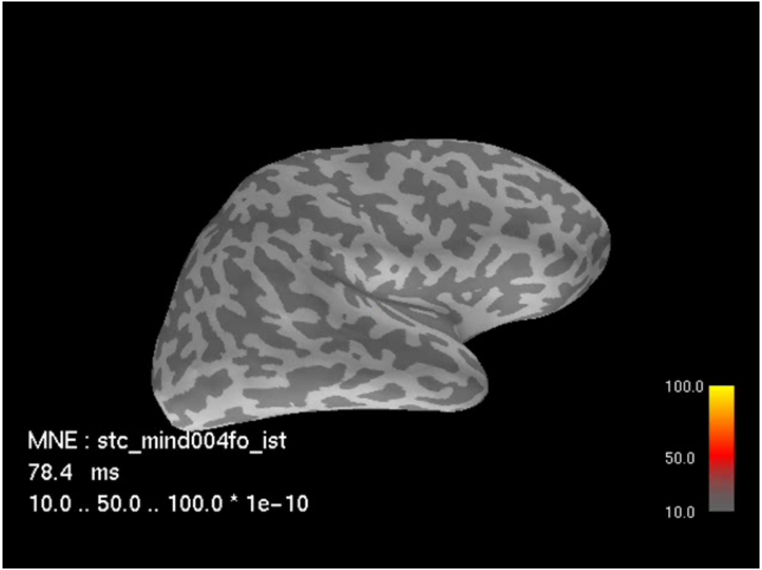
$$p(x_t|x_{t-1}) = P_{\text{birth}} \times U_{R_{\text{grid}}}(r_t^{(N_t)})\mathcal{N}(q_t^{(N_t)}; 0, \Delta) \times \prod_{n=1}^{N_{t-1}} \mathcal{N}(r_{t+1}^{(n)}; r_t^{(n)}, \Delta_r)\mathcal{N}(q_t^{(n)}; q_{t-1}^{(n)}, \Delta_q)+$$

$$+P_{\text{death}} \times \frac{1}{N_{t-1}} \sum_{j=1}^{N_{t-1}} \prod_{n=1}^{N_{t-1}-1} \mathcal{N}(r_{t+1}^{(a_{j,n})}; r_t^{(a_{j,n})}, \Delta_r)\mathcal{N}(q_t^{(n)}; q_{t-1}^{(a_{j,n})}, \Delta_q)+$$

$$+(1 - P_{\text{birth}} - P_{\text{death}}) \times \prod_{n=1}^{N_{t-1}} \mathcal{N}(r_{t+1}^{(n)}; r_t^{(n)}, \Delta_r)\mathcal{N}(q_t^{(n)}; q_{t-1}^{(n)}, \Delta_q)\,.$$

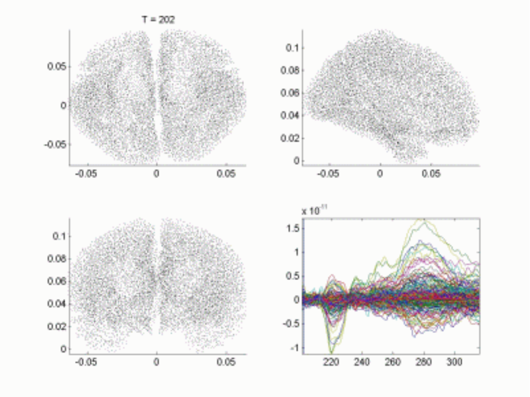
It works!

Example: auditory data (from S. et al. 2009)



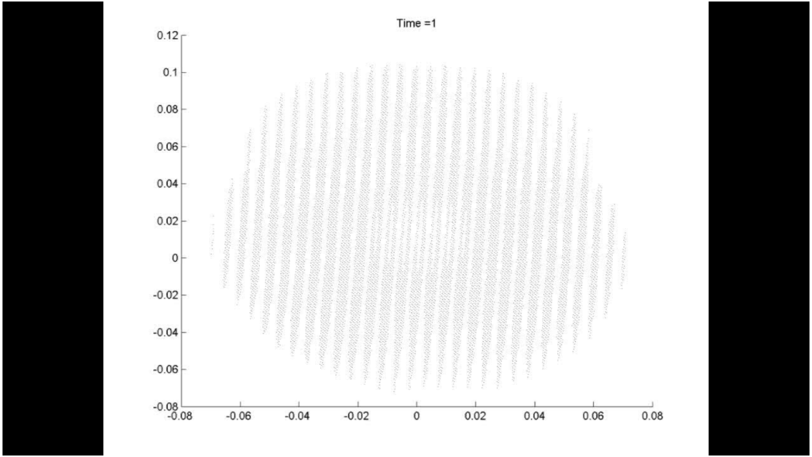
Main issue of random walk

Sources tend to move even when they shouldn't



Main issue of random walk

Sources tend to move even when they shouldn't (**True** and **Estimated** locations)



Particle filtering with static model

Want to fix dipoles

$$p(x_t|x_{t-1}) = P_{\mathrm{birth}} \times U_{R_{\mathrm{grid}}}(r_t^{(N_t)})\mathcal{N}(q_t^{(N_t)}; 0, \Delta) \times \prod_{n=1}^{N_{t-1}} \delta(r_{t+1}^{(n)}; r_t^{(n)})\mathcal{N}(q_t^{(n)}; q_{t-1}^{(n)}, \Delta_q) +$$

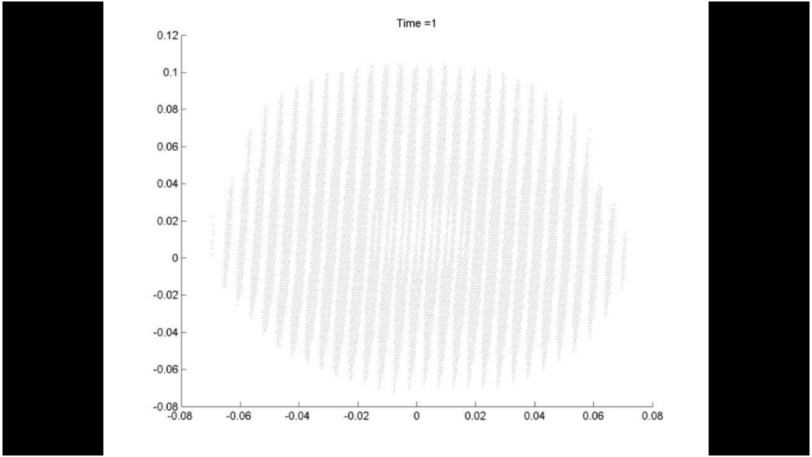
$$+P_{\mathrm{death}} \times \frac{1}{N_{t-1}} \sum_{j=1}^{N_{t-1}} \prod_{n=1}^{N_{t-1}-1} \delta(r_{t+1}^{(n)}; r_t^{(n)})\mathcal{N}(q_t^{(n)}; q_{t-1}^{(a_{j,n})}, \Delta_q) +$$

$$+(1 - P_{\mathrm{birth}} - P_{\mathrm{death}}) \times \prod_{n=1}^{N_{t-1}} \delta(r_{t+1}^{(n)}; r_t^{(n)})\mathcal{N}(q_t^{(n)}; q_{t-1}^{(n)}, \Delta_q) \,.$$

Particle filtering with static model

S. et al. (2013) **Annals of Applied Statistics**

Some technical details to be adjusted (no bootstrap, different sampler)



Limitation of Particle Filtering

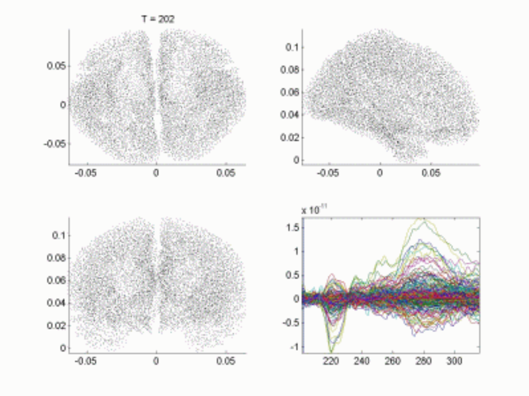
At source appearance, the filtering distribution

$$p(x_t|y_{1:t})$$

has little information on the new source.

This is particularly tedious for some applications (epilepsy)

Of course there is more information in the future...



Particle Smoothing

The *smoothing* distribution

$$p(x_t|y_{1:T})$$

is more difficult to approximate.

Two–filter smoothing relies on:

$$p(x_t|y_{1:T}) \propto p(x_t|y_{1:t-1})\color{red}{p(y_{t:T}|x_t)} \qquad (1)$$

but $p(y_{t:T}|x_t)$ is not a pdf in x_t.

Introduce auxiliary distributions γ_t and $\tilde{p}$

$$\tilde{p}(x_t|y_{t:T}) \propto p(y_{t:T}|x_t)\gamma_t(x_t) \quad ; \qquad (2)$$

to get

$$p(x_t|y_{1:T}) \propto \frac{p(x_t|y_{1:t-1})\tilde{p}(x_t|y_{t:T})}{\gamma_t(x_t)} \quad . \qquad (3)$$

Particle Smoothing

Two–step recursion for the backward filter:

$$\tilde{p}(x_t|y_{t+1:T}) = \int \tilde{p}(x_{t+1}|y_{t+1:T}) \frac{p(x_{t+1}|x_t)\gamma_t(x_t)}{\gamma_{t+1}(x_{t+1})} dx_{t+1} \tag{4}$$

$$\tilde{p}(x_t|y_{t:T}) = \frac{p(y_t|x_t)\tilde{p}(x_t|y_{t+1:T})}{\int p(y_t|x_t)\tilde{p}(x_t|y_{t+1:T}) dx_t} \quad . \tag{5}$$

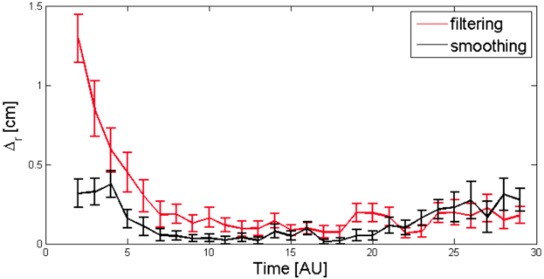
you can use Sequential Monte Carlo to approximate these distributions:

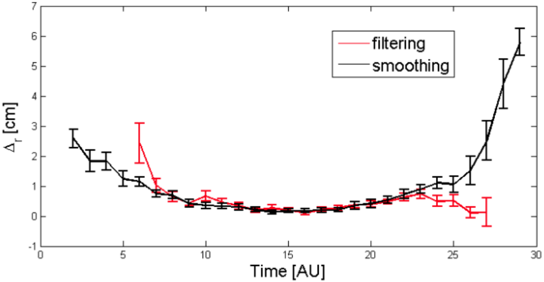
$$\begin{array}{ccccccc}
p(x_1|y_1) & \rightarrow & p(x_2|y_{1:2}) & \rightarrow & \ldots & \rightarrow & p(x_T|y_{1:T}) \\
\downarrow & & \downarrow & & & \downarrow & \\
p(x_1|y_{1:T}) & & p(x_2|y_{1:T}) & & & & p(x_T|y_{1:T}) \\
\uparrow & & \uparrow & & & \uparrow & \\
\tilde{p}(x_1|y_{T:1}) & \leftarrow & \tilde{p}(x_2|y_{T:2}) & \leftarrow & \ldots & \leftarrow & \tilde{p}(x_T|y_T)
\end{array}$$

It works (ish)

Vivaldi and S. (2016) **Inverse Problems**

Using synthetic data, localization error in time:





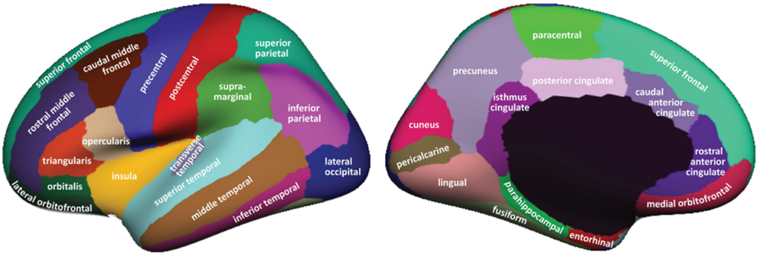
In progress

Moving dipoles are not physiologically possible (!)

But maybe movement within a single, functionally homogeneous area makes sense

Use atlases to constrain dynamics

In progress with Valeria Fiori



The dilemma

Our aim:to approximate the posterior distribution

$$p(x|y)$$

with

$$x \in \mathcal{X} := \bigcup_{N=0,1,\dots} \{N\} \times \left(\mathbb{D}^N / \sim\right)$$

and y the electric/magnetic field

But: x and y depend on time! How to treat this?

1. Dynamic dipole:
   Number of dipoles and dipole locations and moment can change every sampled time
2. Static dipole:

   Only dipole moments change in time

Bayesian inference of multiple static dipoles

Assume number N of dipoles and dipole locations $r^{(i)}$ do not change in the analysis window; then the posterior

$$p(x|y) = p(N, \{r^{(i)}\}_{i=1,\dots,N}, \{q_{1:T}^{(i)}\}_{i=1,\dots,N} \mid y_{1:T})$$

splits under Gaussian prior for dipole moments

$$= p(\{q_{1:T}^{(i)}\}_{i=1,\dots,N} \mid N, \{r^{(i)}\}_{i=1,\dots,N}, y_{1:T})p(N, \{r^{(i)}\}_{i=1,\dots,N} \mid y_{1:T})$$

the conditional posterior for dipole moments is analytically tractable; the remainder can be sampled with SESAME

S., Luria, Aramini (2014) **Inverse Problems**, Sommariva and s. (2014) **Inverse Problems**, Viani et al. (2021) **Inverse Problems and Imaging**, Viani et al. (2023) **Statistics and Computing**

SESAME (Sequential Semi Analytic MonteCarlo Estimation)

Sequential Monte Carlo algorithm for estimating dipole locations and moments under static dipole assumptions.

Iterative procedure resembles regularization path

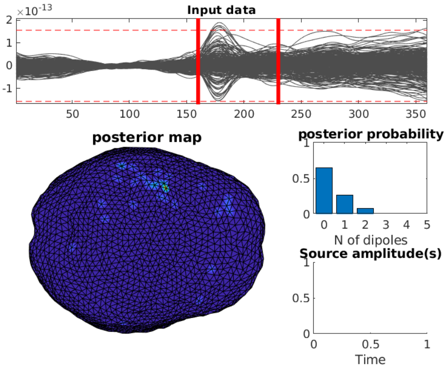
Highly stable against hyper-parameter miss-specification

Python source at
`https://pybees.github.io/sesameeg/`

Matlab source at
`https://github.com/pybees/sesameeg_MATLAB`

Available as Brainstorm plugin!

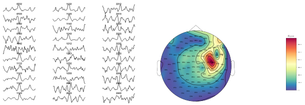
Available in BESA Research 7.0 onwards!

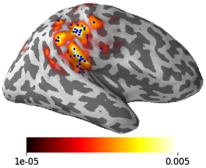


Can it replace manual dipole modelling?

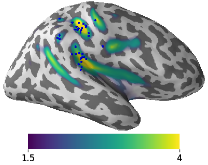
Luria et al. (2020) **Brain Topography**

- retrospective study, collaboration with Istituto Carlo Besta, Milan
- MEG data from 22 epileptic subjects (lesion/non–lesion, SEEG/non–SEEG)
- $>$ 1200 spikes analyzed *individually*
- manual dipole fitting performed by experts, used as *reference location*

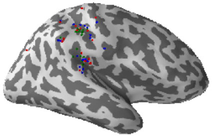




SESAME



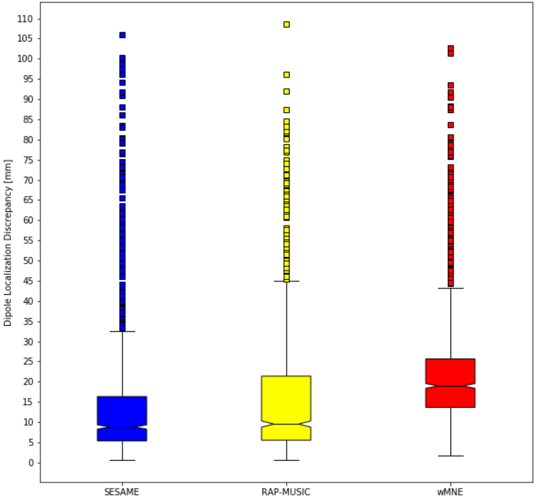
wMNE



RAP–MUSIC

Can it replace manual dipole modelling?

Luria et al. (2020) **Brain Topography**



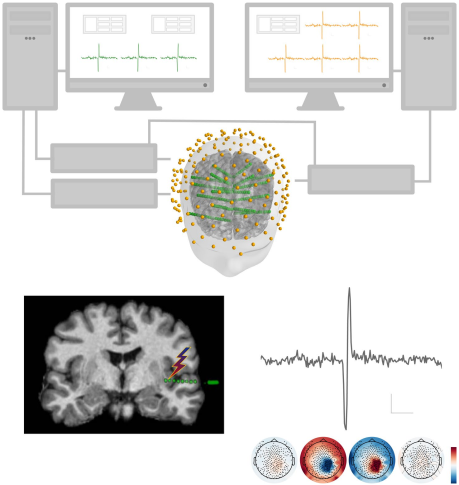
Discrepancy with Equivalent Current Dipole fit location: all spikes (> 1200)

SESAME
RAP–MUSIC
wMNE

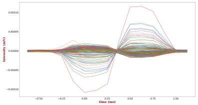
$>$ 75% within 1.5 cm from ECD
RAP–MUSIC second best (with one dipole)

An in vivo validation of source localization methods

A. Pascarella et al. (2023) **NeuroImage**



- Epileptic patients with implanted SEEG
- Single Pulse Electrical Stimulation
- HD EEG registration
- true location known exactly!
- 7 subjects
- open dataset Mikulan et al. (2020) **Scientific Data**

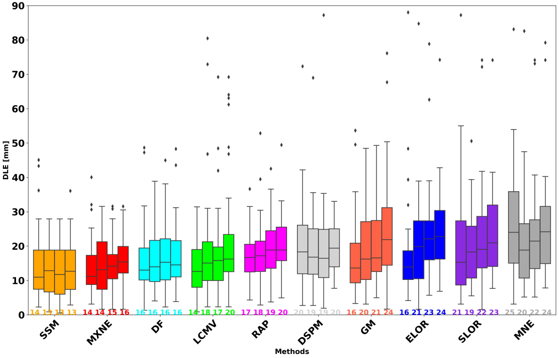


An in vivo validation of source localization methods

A. Pascarella et al. (2023) **NeuroImage**

- 10 source localization methods: wMNE, dSPM, sLORETA, eLORETA, MxNE, Gamma Map, RAP-MUSIC, LCMV beamformer, dipole fitting, SESAME
- various subsampling from 32 to 256 channels
- methods tested with different parameters in comparable ranges
- peak activity selected for each method automatically (automated pipeline)

An in vivo validation of source localization methods



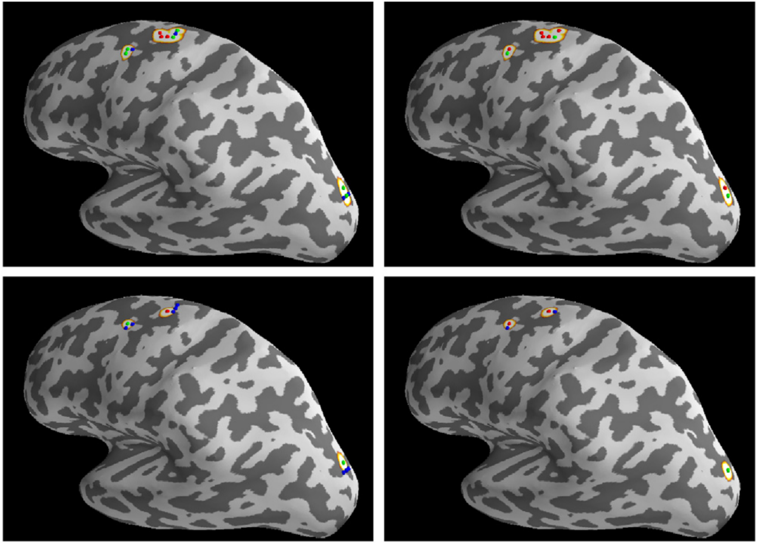
- focal methods much better
- older methods less accurate (mathematics matters!)
- little impact of number of channels
- SESAME $\sim$ MxNE

Luria et al. (2019) Journal of Neuroscience Methods

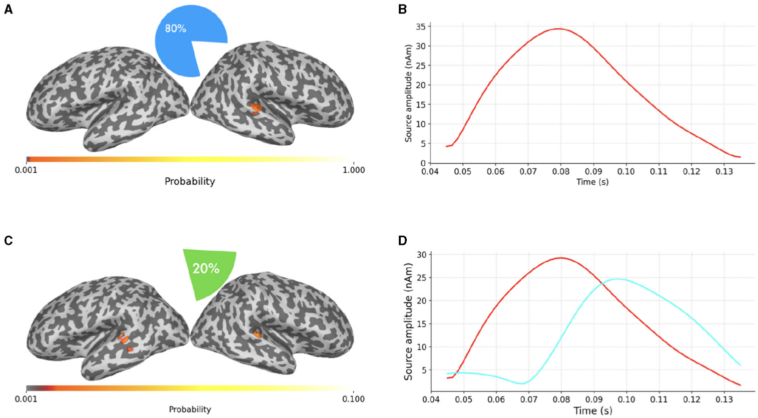
- Applied SESAME to estimate dipoles in frequency bands (instead of time windows)
- Applied SESAME in a *dipolar* (small N, large q) vs *distributed* (large N, small q) settings

Luria et al. (2019) Journal of Neuroscience Methods

Left column: true sources are dipole clusters; right column: true sources are single dipoles. Top row: SESAME with distributed setting; bottom row: SESAME with dipolar settings.



Showcasing multiple alternative solutions



Bayesian Estimation for Engineering Solutions s.r.l.

- growing need for sound statistical models
- desire to transfer developed methods to the real world
- startup, born June 2021 as a spinoff of UNIGE
- explore commercial potential of Bayesian models and Monte Carlo algorithms
- EEG/MEG data analysis on demand (for hospitals, etc)
- happy to participate to EU projects
- nothing to do with actual bees...

More at `www.bees.srl`

BEES

Spin off
Università degli Studi di Genova

Further developments

Can we...

- Go beyond dipoles to include source extent?
- Distinguish static sources from moving sources?
- Provide Bayesian One-step Connectivity estimates?

Thanks

Joint work with (among others):

Riccardo Aramini
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Michele Piana
Sara Sommariva
Elisabetta Vallarino
Alessandro Viani

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