The Bayesian Approach to Inverse Problems: Hierarchical Bayesian Approaches to EEG/MEG Source Reconstruction

Invited Talk at the University of Cambridge, UK
Outline

EEG/MEG Source Reconstruction: General Demands and Challenges

Depth Localization and Source Separation for Focal Sources

A Sparsity-Promoting Hierarchical Bayesian Model for EEG/MEG

Hierarchical Bayesian Modeling from an Empirical Bayesian Point of View

Take Home Messages & Conclusions
“The human brain undoubtedly constitutes the most complex system in the known universe” (Wolf Singer, Director of the MPI for Brain Research)

Major branches of neuroscience (by Wikipedia):

- Affective neuroscience
- Behavioral neuroscience
- Cellular neuroscience
- Clinical neuroscience
- Cognitive neuroscience
- Computational neuroscience
- Cultural neuroscience
- Developmental neuroscience
- Molecular neuroscience
- Neuroengineering
- Neuroimaging
- Neuroinformatics
- Neurolinguistics
- Neurophysiology
- Paleoneurology
- Social neuroscience
- Systems neuroscience

Needs people from: Biology, chemistry, computer science, engineering, linguistics, mathematics, medicine, philosophy, physics and psychology.

Felix Lucka (felix.lucka@wwu.de)
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Major Modalities for Neuroimaging

X-ray imaging
- Projectional Radiography
- Computed Tomography (CT)

Nuclear imaging
- Planar Scintigraphy
- Positron emission tomography (PET)
- Single photon emission computed tomography (SPECT)

Magnetic resonance imaging (MRI)
- Basic structural scans
- Functional (fMRI)
- Diffusion weighted (DW-MRI)

Bioelectromagnetic imaging:
- Electroencephalography (EEG)
- Magnetoencephalography (MEG)

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Spatio-Temporal Resolution in Neuroimaging


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Source Reconstruction by Electroencephalography (EEG) and Magnetoencephalography (MEG)

Aim: Reconstruction of brain activity by non-invasive measurement of induced electromagnetic fields (bioelectromagnetism) outside of the skull.
Institute for Biomagnetism and Biosignalanalysis

Focus on:
- Affective nsc
- Behavioral nsc
- Cognitive nsc
- Neuroimaging
- Clinical nsc
- Developmental nsc
- Neurolinguistics

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Institute for Biomagnetism and Biosignalanalysis

Focus on:
- Affective nsc
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- Clinical nsc
- Developmental nsc
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Experimental devices used:
- MEG & EEG
- Behavioral laboratory
- MRI (Basic, fMRI, DW-MRI)
- tDCS & TMS

Current fields of research:
- Auditory system: Tinnitus, neuroplasticity;
- Emotion, attention and affection;
- Language & speech: Plasticity, cochlea implantation, aphasia;
- Visual system: Conscious vision;
- Neuromuscular disorders in stroke patients.
- Methodical development

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Aim: Improve quality, applicability and reliability of EEG/MEG based source reconstruction in the presurgical diagnosis of epilepsy patients.
Applications of EEG/MEG

- Diagnostic tool in neurology, e.g., Epilepsy.

- Scientific applications:
  - Examination tool in several fields neuroscience.
  - Validation of therapeutic approaches in clinical neuroscience.
  - Examination tool for neurophysiology.

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Challenges of Source Reconstruction: Mathematical Modeling

Mathematical modeling of bioelectromagnetism:

▶ Understand and model the transformation of the bio-chemical activity of the brain into ionic currents.

▶ Find reasonable simplifications to Maxwell’s equations to formulate forward equations that relate ionic currents to measured signals:

\[ \nabla \cdot (\sigma \nabla \phi) = \nabla \cdot j^{pri} + BC \]

▶ \( \sigma \): volume conductor model

source: Wikimedia Commons

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Challenges of Source Reconstruction: Head Modeling

Development of realistic and individual head models for simulating the forward equations.
Challenges of Source Reconstruction: Inverse Problem

- (Presumably) **under-determined**
- Severely **ill-conditioned**
- Signal is contaminated by a complex spatio-temporal mixture of external and internal noise and nuisance sources.

Unluckily, not just:

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Demands on Source Reconstruction: Spatio-Temporal Aspects

- No principle limit of temporal resolution.
- Sampling rates up to 20000 Hz, i.e., timesteps of 0.05 ms.
- High sampling rates, $> 300$ channels in combined EEG/MEG, long measurement times $\Rightarrow$ Tons of data
- In principle, oversampling a temporal process gives useful additional information.
- However, the lowest temporal scale that contains valuable information is unknown.
- Spatio-temporal inversion can get tricky and computationally demanding.

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Demands on Source Reconstruction: Group Studies

Neuroscientific studies with $n = 1$ subjects: Not really fancy.

Normally,

- Two matched groups $A$ and $B$, each $\sim 30$ subjects.
- Different experimental conditions $C_1$, $C_2$, ...
- Collect data for all subjects and conditions
- Aim: Statistically significant inter-group differences.
- Problem: Large inter- and intra subject differences:
  - Individual head and cortex geometries;
  - Different SNRs;
  - Different cognitive constitution;

$\implies$ A lot of variables and uncertainties.

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Demands on Source Reconstruction: Multimodal Integration

- The brain is a complex **bio-chemical** information processing system.
- EEG/MEG measures only **one correlate** of “brain activity”.
- Other imaging modalities measure other correlates.
- **Multimodal integration** sums up a lot of different approaches to fuse the different information.
- Might lead to big improvements of neuroimaging results
- Many open questions, the relation between the different correlates is subject to active research.
Demands on Source Reconstruction: Subsequent Analysis

- Result of source reconstruction: Temporal evolution of the spatial current distribution.
- Use these results to infer the causal architecture of the brain:
  - Structure of networks that pass and process information
  - Modulation of these networks
- Dynamical causal modeling (DCM): Bayesian model comparison procedure

Source: Andre C. Marreiros et al. (2010), Scholarpedia, 5(7):9568.
The Bayesian Approach in EEG/MEG Source Reconstruction

In summary, not the easiest problem, but a very interesting one!

Depending on the concrete application, we might have

▶ Plenty of variables and various sources of uncertainty
▶ Various sources and types of a-priori information
▶ Demand for statistical results and uncertainty quantification for subsequent processing.

The Bayesian approach seems appealing to deal with these issues!

Bayesian modeling: Determine priors and dependencies for all variables.

▶ Systematic approach due to the number of variables.
▶ Hierarchical Bayesian modeling (HBM): A specific modeling approach that emerged as a promising candidate for this.
A Complex Hierarchical Bayesian Model

HBM for

- Multisubject
- Multimodal (EEG/MEG/fMRI)

Source reconstruction.

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Hierarchical Bayesian Modeling from an Empirical Bayesian Point of View

Take Home Messages & Conclusions
Cooperation with...

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Department of Mathematics
Tampere University of Technology (TUT), Finland

Prof. Dr. Martin Burger
Institute for Computational and Applied Mathematics,
University of Münster, Germany

PD. Dr. Carsten Wolters
Institute for Biomagnetism and Biosignalanalysis,
University of Münster, Germany
Background of the Talk

Felix Lucka., Sampsa Pursiainen, Martin Burger, Carsten H. Wolters.
Hierarchical Bayesian Inference for the EEG Inverse Problem using Realistic FE Head Models: Depth Localization and Source Separation for Focal Primary Currents.
*Neuroimage, 61(4), 2012.*

Felix Lucka.
Hierarchical Bayesian Approaches to the Inverse Problem of EEG/MEG Current Density Reconstruction.
*Diploma thesis in mathematics, University of Münster, March 2011*
Current Density Reconstruction
Discretization of the underlying continuous current distribution by large number of elementary sources with fixed location and orientation.
Notation and Likelihood

Basic forward equation:

$$b = L s$$

- Up to now: Single time slice inversion;
- \(b \in \mathbb{R}^m\): EEG/MEG measurements;
- \(s \in \mathbb{R}^n\): Coefficients of the \(d \in \{1, 3\}\) basic current sources at \(k\) different source locations; \(n = d \cdot k\);
- \(L \in \mathbb{R}^{m \times n}\): Lead-field matrix;

Likelihood:

$$p_{\text{like}}(b|s) \propto \exp \left( -\frac{1}{2} \| \Sigma^{-1/2} (b - L s) \|^2 \right)$$

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Tasks and Problems for EEG/MEG in Presurgical Epilepsy Diagnosis

EEG/MEG in epileptic focus localization:
- Focal epilepsy is believed to originate from networks of focal sources.
- Active in inter-ictal spikes.
- **Task 1**: Determine number of focal sources (*multi focal epilepsy?*).
- **Task 2**: Determine location and extend of sources.

Problems of established CDR methods:
- **Depth-Bias**: Reconstruction of deeper sources too close to the surface.
- **Masking**: Near-surface sources “mask“ deep-lying ones.
Depth Bias: Illustration

One deep-lying reference source (blue cone) and minimum norm estimate:

\[ s_{\text{MNE}} = \text{argmin} \{ \| \Sigma^{-1/2}_e (b - Ls) \|_2^2 + \lambda \| s \|_2^2 \} \]
Depth Bias: Illustration

One deep-lying reference source (blue cone) and sLORETA result (Pascual-Marqui, 2002).
Masking: Illustration

Reference sources.
Masking: Illustration

MNE result and reference sources (green cones).
Masking: Illustration

sLORETA result and reference sources (green cones).
Problems of Classical Inverse Methods: Depth-Bias

- Using normal $\ell_2$ and $\ell_1$ type priors: MAP estimate has depth-bias.

- Heuristic reason: Deep sources have weaker signal; Signal of single deep source can be generated by extended patch of near-surface sources.

- Theoretical reason in simplified EEG example: $q \in \partial J(s_{\text{MAP}})$ is harmonic function and, thus, fulfills maximum principle:
  - $\ell_2$: $s_{\text{MAP}}$ is harmonic $\Rightarrow$ maximum at boundary.
  - $\ell_1$: sign of $s_{\text{MAP}}$ is harmonic $\Rightarrow$ supported only at boundary.
Problems of Classical Inverse Methods: Depth-Bias

Introducing weighted norms \( \|s\|_2^2 \rightarrow \|Ws\|_2^2 \) to give deep sources an advantage.

- Partly solves depth-bias.
- Other drawbacks, e.g., larger spatial blurring \( \Rightarrow \) worse source separation.
- Critical from the Bayesian point of view: Would mean that deep sources usually have a stronger signal \( \Rightarrow \) unphysiological a-priori information.

Reweighting of the solution (e.g., sLORETA) also leads to problems w.r.t. source separation.

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Starting Point for our Studies


- A specific hierarchical Bayesian model (HBM) aims to recover sparse source configurations.
- Calvetti et al., 2009 found promising first results for CM estimates for deep-lying sources and the separation of multiple (focal) sources.

Limitations of Calvetti et al., 2009:

- (Full-) MAP estimates were not convincing; reason unclear.
- No systematic examination; only two source scenarios.
- Head models insufficient.
Contributions of our Studies

- Implementation of Full-MAP and Full-CM inference for HBM with realistic, high resolution Finite Element (FE) head models.
- Propose own algorithms for Full-MAP estimation.
- Examination of general properties, parameter choices, etc.
- Introduction of suitable performance measures for validation of simulation studies (Wasserstein distances).
- Systematic examination of performance concerning depth-bias and masking in simulation studies.
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Take Home Messages & Conclusions
Gentle Introduction to Sparsity Promoting HBMs

**Wanted:** A prior promoting sparse (focal) source activity.

**First try:**
- Take Gaussian prior with zero mean and covariance $\Sigma_s = \gamma \cdot \text{Id}$, $\gamma > 0$ (Minimum norm estimation).
- Compute MAP or CM estimate (equal)!

\[
\hat{s}_{\text{MAP}} : = \arg\max_{s \in \mathbb{R}^n} \left\{ \exp \left( -\frac{1}{2 \sigma^2} \| b - L s \|_2^2 - \frac{1}{2 \gamma} \| s \|_2^2 \right) \right\} 
= \arg\min_{s \in \mathbb{R}^n} \left\{ \| b - L s \|_2^2 + \frac{\sigma^2}{\gamma} \| s \|_2^2 \right\}
\]
Gentle Introduction to Sparsity Promoting HBMs

First try: NOT a focal reconstruction.
Gentle Introduction to Sparsity Promoting HBMs

What went wrong?

- Gaussian variables = characteristic scale given by variance. (not scale invariant)
- All sources have variance $\gamma \implies$ Similar amplitudes are likely.
- $\implies$ Focal activity is very unlikely.

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Gentle Introduction to Sparsity Promoting HBMs

Idea:

- Let sources at single locations $i, i = 1, \ldots, k$ have different variances $\gamma_i$.
- Let the data determine $\gamma_i \Rightarrow$ New level of inference!

- $\gamma = (\gamma_i)_{i=1,\ldots,k}$ are called hyperparameters.
- Bayesian inference: $\gamma$ are random variables as well.
- Their prior distribution $p_{\text{hyper}}(\gamma)$ is called hyperprior.
Gentle Introduction to Sparsity Promoting HBMs

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- Encode focality assumption into hyperprior:
  - Focality: Nearby sources should a-priori not be mutually dependent.
  - Focality: Most sources silent, few with large amplitude;
  - No location preference for activity should be given a priori.
Gentle Introduction to Sparsity Promoting HBMs

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- Encode focality assumption into hyperprior:
  
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- Encode focality assumption into hyperprior:
  - $\gamma_i$ should be stochastically independent.
  - Sparsity inducing hyperprior, e.g., inverse gamma distribution.
  - No location preference for activity should be given a priori.

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Gentle Introduction to Sparsity Promoting HBMs

Idea:

▶ Let sources at single locations $i, i = 1, \ldots, k$ have different variances $\gamma_i$.
▶ Let the data determine $\gamma_i \implies$ New level of inference!

- $\gamma = (\gamma_i)_{i=1,\ldots,k}$ are called hyperparameters.
- Bayesian inference: $\gamma$ are random variables as well.
- Their prior distribution $p_{\text{hyper}}(\gamma)$ is called hyperprior.

▶ Encode focality assumption into hyperprior:

- $\gamma_i$ should be stochastically independent.
- Sparsity inducing hyperprior, e.g., inverse gamma distribution.
- $\gamma_i$ should be equally distributed.

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Gentle Introduction to Sparsity Promoting HBM\textsc{s}

In formulas:

\[ p_{\text{\text{prior}}}(s|\gamma) \sim \mathcal{N}(0, \Sigma_s(\gamma)), \text{ where } \Sigma_s(\gamma) = \text{diag}(\gamma_i \cdot \text{Id}_3, i = 1, \ldots, k) \]

\[ p_{\text{\text{hyper}}} (\gamma) = \prod_{i=1}^{k} p_{\text{\text{hyper}}} (\gamma_i) = \prod_{i=1}^{k} p_{\text{\text{hyper}}} (\gamma_i) = \prod_{i=1}^{k} \frac{\beta^\alpha}{\Gamma(\alpha)} \gamma_i^{-\alpha-1} \exp \left( -\frac{\beta}{\gamma_i} \right) \]

\( \alpha > 0 \text{ and } \beta > 0 \) determine \textit{shape} and \textit{scale}, \( \Gamma(x) \) denotes the Gamma function.

Joint prior: \[ p_{\text{\text{pr}}} (s, \gamma) = p_{\text{\text{prior}}}(s|\gamma) \ p_{\text{\text{hyper}}} (\gamma) \]

Implicit prior: \[ p_{\text{\text{\text{pr}}}} (s) = \int p_{\text{\text{\text{prior}}}} (s|\gamma) \ p_{\text{\text{\text{hyper}}}} (\gamma) d\gamma \]

\[ = \int \mathcal{N}(0, \Sigma_s(\gamma)) \ p_{\text{\text{\text{hyper}}}} (\gamma) d\gamma \quad \sim \text{“Gaussian scale mixture”} \]
Gentle Introduction to Sparsity Promoting HBM:

Posterior, general:

\[ p_{post}(s, \gamma | b) \propto p_{like}(b | s) \, p_{prior}(s | \gamma) \, p_{hyper}(\gamma) \]

Comparison: \[ p_{post}(s | b) \propto p_{like}(b | s) \, p_{prior}(s) \]

Posterior, concrete:

\[ p_{post}(s, \gamma | b) \propto \exp \left( -\frac{1}{2\sigma^2} \| b - Ls \|_2^2 - \sum_{i=1}^{k} \left( \frac{\| s_i^* \|_2^2 + \beta}{\gamma_i} + (\alpha + \frac{5}{2}) \ln \gamma_i \right) \right) \]

Analytical advantages...

- Energy is quadratic with respect to \( s \)
- Factorizes over \( \gamma_i \)'s.

and disadvantages...

- Energy is non-convex w.r.t. \( (s, \gamma) \) (posterior is multimodal)
Excursus: Full-, Semi-, and Approximate Inversion

Two types of parameters → more possible ways of inference.

**Full-MAP:** Maximize $p_{post}(s, \gamma|b)$ w.r.t. $s$ and $\gamma$.

**Full-CM:** Integrate $p_{post}(s, \gamma|b)$ w.r.t. $s$ and $\gamma$.

**$\gamma$-MAP:** Integrate $p_{post}(s, \gamma|b)$ w.r.t. $s$, and maximize over $\gamma$, first. Then use $p_{post}(s, \hat{\gamma}(b)|b)$ to infer $s$. (*Hyperparameter MAP/Empirical Bayes*)

**S-MAP:** Integrate $p_{post}(s, \gamma|b)$ w.r.t. $\gamma$, and maximize over $s$.

**VB:** Assume approximative factorization $p_{post}(s, \gamma|b) \approx \hat{p}_{post}(s|b) \hat{p}_{post}(\gamma|b)$; Approximate both with distributions that are analytically tractable.

Focus of our work: **Fully Bayesian inference.**
Gentle Introduction to Sparsity Promoting HBMs

Full-MAP estimate
Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-CM result.
Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-MAP result proposed by Calvetti et al., 2009.
Results Depth Bias: Illustration

One deep-lying reference source (blue cone) and Full-MAP result proposed by us.
Results Masking: Illustration

Full-CM result and reference sources (green cones).
Results Masking: Illustration

Full-MAP result (by our algorithm) and reference sources (green cones).
Sparsity-Promoting HBM: Implicit Prior

Implicit prior on $s$ is a Student’s t-distribution on the (scaled) source amplitudes:

$$p(s) \propto \prod_{i=1}^{k} \left( 1 + \left( \frac{s_{i}^{\text{amp}}}{2\beta} \right)^{2} \right)^{-(\alpha+3/2)} = \prod_{i=1}^{k} \left( 1 + \frac{t_{i}^{2}}{\nu} \right)^{-\frac{1}{2}(\nu+1)}$$

with $t_{i} = s_{i}^{\text{amp}}/\sqrt{\hat{\gamma}}$, $\hat{\gamma} = \beta/(\alpha + 1)$, $\nu = 2(\alpha + 1)$.

This corresponds to the regularization functional:

$$\mathcal{J}(s) = (2\alpha + 3) \sum_{i=1}^{k} \log \left( 1 + \left( \frac{s_{i}^{\text{amp}}}{2\beta} \right)^{2} \right)$$

convex for $|x| < \sqrt{2\beta}$, concave for $|x| > \sqrt{2\beta}$.  

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Sparsity-Promoting HBM: Implicit Prior


Isocontours of Different Priors

(a) $\ell_2$

(b) $\ell_1$

(c) $\ell_{(1/2)}$

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Isocontours of Different Priors

Figure: Students-t, $\nu = 3$
Strategies for Full-MAP Estimation and "Near-Mean" Estimates

- Optimization algorithm converges to the nearest mode $\implies$ initialization is important.
- "Random initialization" (i.e. draw from hyperprior) does not help, it is not sparse enough.
- "Random sparse initialization": Combinatorial complexity.
- MCMC sampling suffers less from multi-modality: Initialization by $\gamma_{CM}$?
  - **Full Near-Mean Estimates** (NM): Initialize by $\gamma_{CM}$.
  - Heuristic for Full-MAP estimates: Initialize by various $\gamma^\text{approx}_{CM}$, pick the result with the highest probability.

Results:

- Initializations by $\gamma^\text{approx}_{CM}$ or $\gamma_{CM}$ give higher posterior probability than uniform initialization.
- The reconstructions perform better.
- Full-NM vs. Full-MAP estimates? Not yet clear. Real data?
- Convert heuristic into proper reasoning? Alternative optimization schemes?

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Empirical Bayesian Inference

Let the same data determine the prior used for the inference based on this data!
Empirical Bayesian Inference

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Sounds like...

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Empirical Bayesian Inference

Let the same data determine the prior used for the inference based on this data!

Sounds like...

...but can be formulated into a consistent, statistical reasoning by adding a new dimension of inference: Hyperparameters and hyperpriors.

→ Parametric Empirical Bayesian inference

Top-down construction scheme → Hierarchical Bayesian modeling (HBM).

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HBM as Empirical Bayesian Inference

\[ p_{\text{prior}}(s|\gamma) \sim \mathcal{N}(0, \Sigma_s(\gamma)), \quad \text{where} \quad \Sigma_s(\gamma) = \text{diag} (\gamma_i \cdot l d_3, i = 1, \ldots, k) \]

- Using the data to determine \( \gamma \): **Learn** the prior from the data.

- Popular in **machine learning**.
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Take Home Messages & Conclusions
Take Home Messages: EEG/MEG Source Reconstruction

- Measures one correlate of "brain activity" with a high temporal resolution.
- Various challenges and demands from the practical application.
- High uncertainty about various variables.
- Intrinsic challenges due to the spatial characteristics of the forward operator.

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Take Home Messages: Hierarchical Bayesian Modeling

- Current trend in all areas of Bayesian inference.
- Extension of the prior model by hyperparameters $\gamma$ and hyperpriors.
- Flexible framework for the construction of complex models with different levels for the embedding of different qualitative and quantitative a-priori information.
- Gaussian w.r.t. $s$, factorization w.r.t. $\gamma$.
- **Motivation 1**: Capture the various variables and their dependencies in EEG/MEG in a systematic way.
- **Motivation 2**: Alternative formulation of sparse Bayesian inversion that has interesting features (no depth-bias, non-convex energy but the possibility to infer the support from CM estimate).
- **Motivation 3**: Use the element of adaptive, data-driven learning emphasized by the empirical Bayesian view.

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Thank you for your attention!

- **D. Calvetti, H. Harri, S. Pursiainen, E. Somersalo, 2009.**
  Conditionally Gaussian hypermodels for cerebral source localization

- **D. Wipf and S. Nagarajan, 2009**
  A unified Bayesian framework for MEG/EEG source imaging.

- **F. L., S. Pursiainen, M. Burger and C.H. Wolters, 2012.**
  Hierarchical Bayesian Inference for the EEG Inverse Problem using Realistic FE Head Models: Depth Localization and Source Separation for Focal Primary Currents.