A Framework for Uncertainty Calibration in M/EEG Source Imaging

Physikalisch-Technische Bundesanstalt
Braunschweig und Berlin

Quality in Artificial Intelligence
QAI LABS

Reliable Neural Activity Localization with Calibrated Credible Regions

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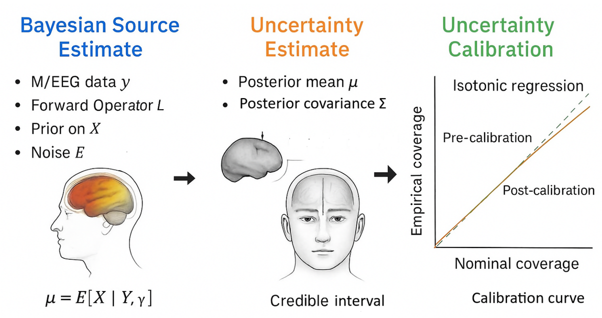
Motivation

- **Clinical & Research Need:** Various applications including **epilepsy surgery, cognitive neuroscience, and brain-computer interfaces** require precise identification of neural sources;
- **Inverse Problem:** **Brain Source Imaging (BSI)** reconstructs neuronal currents from M/EEG sensor measurements;
- **Mathematical Challenge:** Problem is **severely ill-posed and ill-conditioned** ($M \ll N$);
- **Sensitivity:** Small sensor noise propagates into large localization errors in source space;
- **Risk:** Point estimates without **calibrated uncertainty estimation** are **unreliable** for clinical decisions;
- **Solution:** We need **well-calibrated uncertainty measures**.



M/EEG calibration pipeline illustrating the three main stages of the framework: source estimation, uncertainty estimation and uncertainty calibration.

M/EEG Inverse Modeling

- **Forward Model:** A linear regression mapping M **sources** to N **sensors** at T time instants [1]:

$$\mathbf{Y} = \mathbf{L}\mathbf{X} + \mathbf{E}, \quad \mathbf{E} \sim \mathcal{N}(\mathbf{0}, \boldsymbol{\sigma}^2\mathbf{I})$$

  - $\mathbf{Y} \in \mathbb{R}^{M\times T}$: M/EEG sensor recordings over T time points
  - $\mathbf{X} \in \mathbb{R}^{N\times T}$: Unknown neural source activations at N locations
  - $\mathbf{L} \in \mathbb{R}^{M\times N}$: Lead-field matrix from electromagnetic forward modeling
  - $\mathbf{E} \in \mathbb{R}^{M\times T}$: Additive sensor noise, assumed white Gaussian
- **Inverse Model: Bayesian Minimum Norm (BMN) Estimate** [2,3]
  - **Prior:** $\mathbf{x}(t) \sim \mathcal{N}(\mathbf{0}, \boldsymbol{\gamma}\mathbf{I})$
    - Isotropic covariance with scalar hyperparameter $\boldsymbol{\gamma}$
  - **Empirical Bayes:** Learn $\boldsymbol{\gamma}$ from data
  - **Objective:** Negative log marginal likelihood:

$$\mathcal{L}(\boldsymbol{\gamma}) = \log|\boldsymbol{\Sigma}_{\mathbf{y}}| + \frac{1}{T}\sum_{t=1}^{T} \mathbf{y}(t)^\top \boldsymbol{\Sigma}_{\mathbf{y}}^{-1}\mathbf{y}(t)$$

  where $\boldsymbol{\Sigma}_{\mathbf{y}} = \boldsymbol{\gamma}\mathbf{L}\mathbf{L}^\top + \boldsymbol{\sigma}^2\mathbf{I}$ is the **data covariance**.
  - **Posterior Distribution:** Gaussian with analytical form:

$$p(\mathbf{X}\,|\,\mathbf{Y}) = \prod_{t=1}^{T} \mathcal{N}(\mathbf{x}(t)|\boldsymbol{\mu}_{\boldsymbol{x}}(\boldsymbol{t}), \boldsymbol{\Sigma}_{\boldsymbol{x}}), \quad \boldsymbol{\mu}_{\boldsymbol{x}}(\boldsymbol{t}) = \boldsymbol{\gamma}\mathbf{L}^\top\boldsymbol{\Sigma}_{\mathbf{y}}^{-1}\mathbf{y}(t), \quad \boldsymbol{\Sigma}_{\boldsymbol{x}} = \boldsymbol{\gamma} - \boldsymbol{\gamma}^2\mathbf{L}^\top\boldsymbol{\Sigma}_{\mathbf{y}}^{-1}\mathbf{L}$$

Full Posterior & Time-Averaging

- **Full Posterior Distribution:** Product of time-point posteriors is Gaussian:

$$p(\mathbf{X}|\mathbf{Y}) = \mathcal{N}\left(\text{vec}(\boldsymbol{\mu}_X), \boldsymbol{\Sigma}_X\right)$$

  - $\boldsymbol{\mu}_X = [\boldsymbol{\mu}_x(1), \dots, \boldsymbol{\mu}_x(T)]$: concatenated time-varying means
  - $\boldsymbol{\Sigma}_X = \mathbf{blockdiag}(\boldsymbol{\Sigma}_x, \dots, \boldsymbol{\Sigma}_x)$: block-diagonal covariance matrix
- **Key Insight for Time-Averaging:**
  - **Mean is dynamic:** $\boldsymbol{\mu}_x(t)$ varies with time t
  - **Covariance is static:** $\boldsymbol{\Sigma}_x$ is identical for all $t = 1, \dots, T$
  - Due to **i.i.d. temporal assumption in prior and noise** models
- **Time-Averaged Source Estimate:**

$$\bar{\mathbf{x}} = \frac{1}{T}\sum_{t=1}^{T}\mathbf{x}(t), \quad \bar{\mathbf{x}}|\mathbf{Y} \sim \mathcal{N}\left(\bar{\boldsymbol{\mu}}, \bar{\boldsymbol{\Sigma}}\right), \quad \bar{\boldsymbol{\mu}} = \frac{1}{T}\sum_{t=1}^{T}\boldsymbol{\mu}_x(t), \quad \bar{\boldsymbol{\Sigma}} = \frac{1}{T}\boldsymbol{\Sigma}_x$$

- **Key Benefit:** Time-averaging **reduces uncertainty** by factor T

Marginalization & Component-wise Uncertainty

- **Marginalization Principle:** Extract per-source estimate and uncertainty from time-averaged posterior $\bar{\mathbf{x}}|\mathbf{Y} \sim \mathcal{N}\left(\bar{\boldsymbol{\mu}}, \bar{\boldsymbol{\Sigma}}\right)$.
- **Source-wise Posteriors:** Gaussian marginals for each source i:

$$\bar{x}_i|\mathbf{Y} \sim \mathcal{N}\left(\bar{\mu}_i, \bar{\Sigma}_{ii}\right) \quad \bar{\mu}_i = \frac{1}{T}\sum_{t=1}^{T}[\boldsymbol{\mu}_x(t)]_i, \quad \bar{\Sigma}_{ii} = \frac{1}{T}[\boldsymbol{\Sigma}_x]_{ii}$$

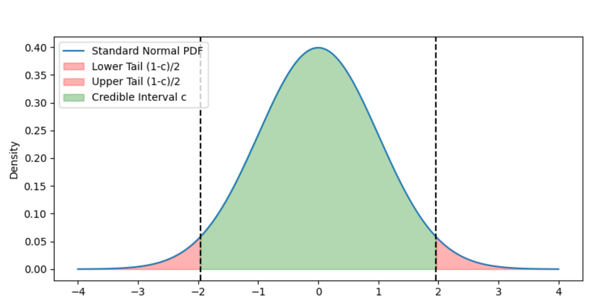
- **Key Advantage:** Critical for clinical decisions about specific brain regions

Credible Intervals

- **Time-Averaged Credible Intervals:** For each source component i at nominal level $\boldsymbol{\alpha} \in (0, 1)$:

$$\mathrm{CI}_i^{(\boldsymbol{\alpha})} = \bar{\mu}_i \pm z_{(1+\boldsymbol{\alpha})/2}\sqrt{\bar{\Sigma}_{ii}}, \quad z_{(1+\boldsymbol{\alpha})/2} = \Phi^{-1}\big((1+\boldsymbol{\alpha})/2\big)$$

where Φ is the standard normal CDF.
- **Interpretation:** True time-averaged source amplitude lies in $\mathrm{CI}_i^{(\boldsymbol{\alpha})}$ with probability $\boldsymbol{\alpha}$.



Two-sided equal-tailed credible interval with central mass $\boldsymbol{\alpha}$.

Uncertainty Calibration

- **Definition:** A model is **perfectly calibrated** if for all confidence levels $\boldsymbol{\alpha} \in [0, 1]$:

$$\mathbb{P}\left(x^{\text{true}} \in \mathrm{CI}^{(\boldsymbol{\alpha})}\right) = \boldsymbol{\alpha}.$$

- **Empirical Coverage:** Given N sources, the empirical coverage at confidence level $\boldsymbol{\alpha}$ is:

$$\hat{\boldsymbol{\alpha}} = \frac{1}{N}\sum_{i=1}^{N}\mathbb{I}\left[x_i^{\text{true}} \in \mathrm{CI}_i^{(\boldsymbol{\alpha})}\right]$$

- **Calibration Condition:** $\hat{\boldsymbol{\alpha}} = \boldsymbol{\alpha}$ for all confidence levels $\boldsymbol{\alpha}$
- **Calibration Curve:** Plot $\hat{\boldsymbol{\alpha}}$ vs $\boldsymbol{\alpha}$ across multiple confidence levels

Critical Observation

Bayesian models are often **mis-calibrated** in practice!

Isotonic Regression Calibration

- **Problem Statement:**
  - **Given:** Miscalibrated intervals where $\hat{\boldsymbol{\alpha}} \neq \boldsymbol{\alpha}$
  - **Goal:** Learn mapping f such that $f(\hat{\boldsymbol{\alpha}}) = \boldsymbol{\alpha}$
- **Learning the Calibration Function:** We learn a monotonic function $f : [0, 1] \to [0, 1]$ such that:

$$\boldsymbol{\alpha} \approx f(\hat{\boldsymbol{\alpha}})$$

  using **isotonic regression**:

$$\hat{f} = \arg\min_{f\ \text{monotonic}}\sum_{k=1}^{K}(\boldsymbol{\alpha}_k - f(\hat{\boldsymbol{\alpha}}_k))^2$$

- **Calibration Process:**
  1. **Input:** Miscalibrated empirical coverages $\hat{\boldsymbol{\alpha}}$ from inverse solvers
  2. **Learn:** Monotonic mapping $f : \hat{\boldsymbol{\alpha}} \to \boldsymbol{\alpha}$ via isotonic regression
  3. **Apply:** Transform new empirical coverages $\hat{\boldsymbol{\alpha}}_{\text{new}} \to f(\hat{\boldsymbol{\alpha}}_{\text{new}})$
  4. **Output:** Calibrated confidence levels

Robust Calibration

Cross-validation prevents overfitting by learning f on training data and validating on held-out sets.

Numerical Results

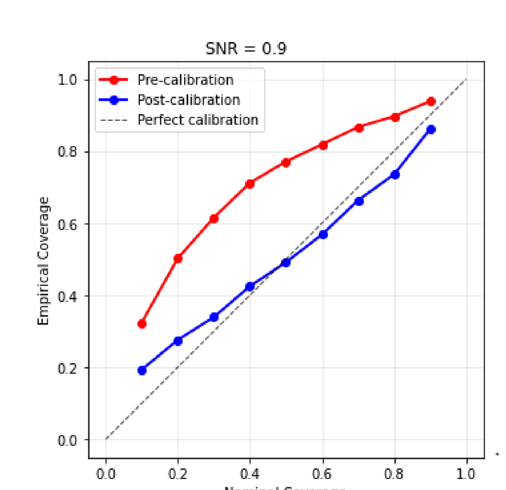
- **Source Model:** Macroscopic neuronal sources in the cortical gray matter of the brain with fixed-orientation dipoles
  - $N = 1284$ candidate dipoles normal to cortical surface
  - $M = 64$ EEG sensors, $T = 1000$ time samples
  - 1000 active sources uniformly distributed
  - Source time courses: i.i.d. zero-mean Gaussian
- **Noise Model:** Controlled SNR via normalized additive noise

$$\mathbf{Y} = \mathbf{Y}^{\text{signal}} + \frac{(1-\alpha)\|\mathbf{Y}^{\text{signal}}\|_F}{\alpha\|\mathbf{E}\|_F}\mathbf{E}, \quad \mathbf{Y}^{\text{signal}} := \mathbf{L}\mathbf{X}$$

  - $\mathbf{E} \sim \mathcal{N}(\mathbf{0}, \sigma^2\mathbf{I})$: sensor noise with oracle value
  - $\text{SNR} = 20\log_{10}\left(\frac{\alpha}{1-\alpha}\right)$
  - SNR range: $\alpha = [0.1, 0.3, 0.5, 0.7, 0.9]$ (13 dB to 40 dB)
- **Key Trends:**
  - $\downarrow \gamma$ with $\uparrow$ SNR
  - $\downarrow$ **Uncertainty** with $\uparrow$ SNR
  - $\downarrow$ **Calibration error** with $\uparrow$ SNR
  - $\downarrow$ **EMD** with $\uparrow$ SNR
- **Performance Insights:**
  - All metrics improve with higher SNR
  - High SNR $\to$ less regularization $\to$ lower γ
  - Uncertainty becomes more precise
- **Evaluation Metrics:**
  - **EMD:** Earth Mover's Distance (source localization error)
  - **Avg Std:** Average posterior standard deviation
  - **AAD:** Average Absolute Deviation

$$\text{AAD} = \frac{1}{K}\sum_{k=1}^{K}|\hat{\boldsymbol{\alpha}}_k - \boldsymbol{\alpha}_k|$$

  - **Pre-/Post-Calibration:** Before **(Pre-AAD)** and after **(Post-AAD)** calibration analysis



Calibration curve

SNR	EMD	Avg Std	γ	Pre-AAD	Post-AAD
0.1	0.0287	0.0456	1.1234	0.1345	0.0456
0.3	0.0234	0.0321	0.8912	0.0987	0.0321
0.5	0.0189	0.0254	0.6789	0.0765	0.0254
0.7	0.0156	0.0187	0.4567	0.0543	0.0187
0.9	0.0123	0.0123	0.2345	0.0321	0.0123

Conclusion

BMN delivers **accurate source localization** and **well-calibrated uncertainty** across SNR conditions. **All metrics improve with higher SNR: EMD decreases, posterior uncertainty reduces, and learned gamma properly decreases**. The method provides **reliable** performance for M/EEG source imaging.

References

[1] Sekihara, K. & Nagarajan, S. S. (2015). **Electromagnetic Brain Imaging: A Bayesian Perspective.** *Springer*.
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[3] Wipf D., Ramírez R., Palmer J., Makeig S., Rao B. D. (2007) . **Analysis of empirical bayesian methods for neuroelectromagnetic source localization.** *Advances in Neural Information Processing Systems* 19, 1505-1512.

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