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Effects of reconstructed magnetic field from sparse noisy boundary measurements on localization of active neural source

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Abstract Localization of active neural source (ANS) from measurements on head surface is vital in magnetoencephalography. As neuron-generated magnetic fields are extremely weak, significant uncertainties caused by stochastic measurement interference complicate its localization. This paper presents a novel computational method based on reconstructed magnetic field from sparse noisy measurements for enhanced ANS localization by suppressing effects of unrelated noise. In this approach, the magnetic flux density (MFD) in the nearby current-free space outside the head is reconstructed from measurements through formulating the infinite series solution of the Laplace's equation, where boundary condition (BC) integrals over the entire measurements provide “smooth” reconstructed MFD with the decrease in unrelated noise. Using a gradient-based method, reconstructed MFDs with good fidelity are selected for enhanced ANS localization. The reconstruction model, spatial interpolation of BC, parametric equivalent current dipole-based inverse estimation algorithm using reconstruction, and gradient-based

selection are detailed and validated. The influences of various source depths and measurement signal-to-noise ratio levels on the estimated ANS location are analyzed numerically and compared with a traditional method (where measurements are directly used), and it was demonstrated that gradient-selected high-fidelity reconstructed data can effectively improve the accuracy of ANS localization.

Keywords Magnetoencephalography · Dipole localization · Reconstruction · Gradient · Spatial interpolation

1 Introduction

Magnetoencephalography (MEG) is a useful noninvasive clinical tool for investigating human neurological functions, in both pathology and applications such as localization of the epileptogenic zone [18], cortex function [5, 9], and brain–machine interface [13]. As MEG is generally free from distortion caused by distinct electric conductivity differences between the brain, skull, and scalp, its measurement is a direct reflection of the primary neuronal currents, from which neural source activities with high temporal and spatial resolution can be detected.

In MEG studies, a common interest is to locate an active neural source (ANS) from the recordings of superconducting quantum interference device (SQUID) on the head surface. This has been widely addressed as an inverse problem that finds a magnetic source from measured data. It has been proven theoretically such a general inverse problem could result an infinite number of solutions [21]. In order to reduce the inverse problem to tractable models from which physically meaningful inverse solutions can be derived, several mathematical simplifications with appropriate

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constraints have been proposed [2–4, 11, 12]. There are two main kinds of ANS models: distributed source [6, 11, 12] and equivalent current dipole (ECD) [11–13, 15]. Under the condition that the active neural region extension is small compared to its distance to sensors, the latter (point-like ECD model) has been widely used as the canonical source model, such as evoked sensory responses for brain function studies and epileptic spikes [12, 15]. Herein, nonlinear parametric models are formulated as an optimization problem (that minimizes the difference between measurements and model predictions) and solved with a least-square (LS) method for the six parameters required to characterize the position vector $\mathbf{L}$ and dipole moment $\mathbf{Q}$ of the ECD [11, 12]. In ANS localization studies, the extremely weak MFD measured outside of the head is several orders smaller than its external interference; for instance, the power ratio of MEG signals to noise equaling 1 is common for clinical event-related measurements [7, 8, 10].

To boost the accuracy of estimated ANS location, various approaches have been focused on improving the robustness of MEG measurements against noise in the last two decades. To detect more information related to neural activities, whole-head SQUID is developed with increased number (300 or more) of sensors. However, it is difficult to increase the number of channels infinitely due to spatial limitation in head-surface area, sensor sizes, and manufacturing technology [12]. Moreover, the cost increases with the numbers of sensors; for example, a 150-channel baby-SQUID system costs around USD 2 million, and for 400 channels, over USD 3 million is required. It has been presented in theory that there is an upper limit to the practical number of sensors and a lower limit to the practical minimum distance between adjacent sensors [1]. Various technologies have been developed to reduce noise from a limited number of sensor measurements, including electromagnetic shielding techniques, reference channels, and signal processing [14]. In theory, data average over epochs can improve signal-to-noise ratio (SNR), but it also introduces several problems, such as limitations of the experimental design, increased burden on subjects, and inability to detect asynchronous brain responses [23]. The noise rejection method by reference channels is based on the assumption that the noise is stable across time and space. Blind-source separation methods, such as independent component analysis, rely on the assumption that the noise is stable across time and can be described with a limited number of spatial components like eye and cardiac artifacts, and requires time-consuming visual inspection [10]. For spatial filtering, such as signal space projection [16, 20] and signal space separation [17, 19], distortion of spatial features representing real MEG signals will be involved [10, 23]. Reduction in unrelated noise (independent, identically distributed under normal distribution, and free from

physiological noises) is important for single-trial or stimulus-absent analysis.

For the above reasons, this paper presents a computational method for enhanced ANS localization, which bases on reconstructed magnetic field from sparsely processed head-surface measurements to minimize unrelated-noise effects realized by gradient-guided selection of high-fidelity reconstructed data. The remainder of this paper offers the followings:

- (1) The biophysically generated MFD in the current-free space outside the head is reconstructed quasi-statically by solving a Laplace's equation with interpolated dense boundary conditions (BCs) from sparse sensor measurements. As will be shown, the reconstructed magnetic field for ANS localization reduces the noise effect by “smoothing” it over the entire hemispherical surface of the modeled head.
- (2) Methods to avoid inclusions of erroneous reconstructed data in ANS localization are discussed. This development leads to a gradient-based method, where high-fidelity reconstructed MFD data that are less sensitive to noise interference are selected for improved ANS localization accuracy.
- (3) The method has been validated numerically by comparing against results obtained from noise-free reconstruction and a traditional method where sparse measurements are directly used in the inverse model. The effects of spatial interpolation on sensor spherical surface, reconstructed MFD, and its gradient distribution on the estimation of the ANS location are numerically analyzed.

2 Methodology

In ANS localization, measurements from SQUID on a head surface are used to solve the inverse problem based on a properly modeled source and head in most clinical and research applications. Simple geometrical models of the head have been extensively investigated. Within the shells (including the brain, skull, and scalp), the different physiological structures in head are almost nonmagnetic with relative permeability $\mu_0 \approx 1$. The magnetic field derived from neural activities (and therefore MEG) is absolutely insensitive to and unaffected by the concentric organization of the tissues; thus, the head has been popularly modeled as a single homogenous sphere with uniform magnetic permeability. As illustrated in Fig. 1, the MFD generated from neural activities at a spatial location (denoted by position vector $\mathbf{L}$) in the spherical head can be modeled as an ECD ($\mathbf{Q}$ of magnitude q and unit vector $\mathbf{q}$). The MFD $\mathbf{B}_c$ of the ECD observed at point p (position vector $\mathbf{r}$) in free space

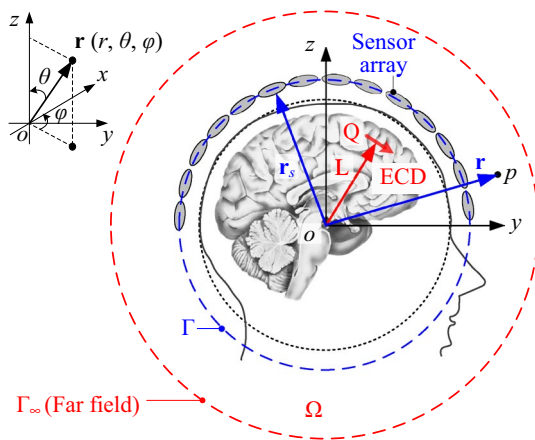


Fig. 1 Illustration of an ECD in spherical coordinates (r, θ, φ), where the x -axis points from *left to right* pre-auricular points, y -axis passes through nasion point, and z -axis meets right-handed coordinate system

(magnetic permeability μ_0) can be derived from the Biot-Savart law in (1a,b,c):

$$\mathbf{B}_c = \frac{\mu_0 q}{4\pi d^2} (\mathbf{q} \times \mathbf{d}) \quad \text{where } d = |\mathbf{r} - \mathbf{L}| \quad \text{and } \mathbf{d} = \frac{\mathbf{r} - \mathbf{L}}{d}. \quad (1a,b,c)$$

A common method to locate the ANS is to recast Eq. (1a) as an inverse problem such that $\mathbf{L}$ and $\mathbf{Q}$ are solved from a discrete set of measurements from a sensor array. As schematically shown in Fig. 1, an array of MFD measurements (B_{si} at $\mathbf{r}_{si}$) on the hemispherical envelop Γ is acquired by a SQUID biomagnetometer that measures only a scalar component of the 3D field. With the inverse problem formulated as a nonlinear optimization problem, the unknown ECD parameters are estimated by minimizing the objective function $f_s(\mathbf{L}, \mathbf{Q})$ where measurements B_{si} are directly used:

$$\text{Minimize } f_s(\mathbf{L}, \mathbf{Q}) = \sum_{i=1}^I \|B_{Si} - B_{Ci}(\mathbf{L}, \mathbf{Q})|_{\mathbf{r}=\mathbf{r}_{Si}}\|^2 \quad (2)$$

$$\text{where } \mathbf{B}_{ci} = \mathbf{B}_{ci} \cdot \mathbf{s}_i = \frac{\mu_0 q}{4\pi d_i^2} (\mathbf{d}_i \times \mathbf{s}_i) \cdot \mathbf{q}. \quad (3a,b)$$

where $\mathbf{s}_i$ is the unit orientation of the i th sensor and I is the total number of measurements used for localization. Theoretically, six or more independent measured data are sufficient to solve for the components of $\mathbf{L}$ and $\mathbf{Q}$ parameters. However, a large number of sensors, which are often sparsely located, are needed in order to cover the entire hemispherical surface of the head.

A practical implementation issue commonly encountered when using (2) with sparsely measured data is the low SNR level of SQUID measurements, which significantly

limits the estimation accuracy for ANS. An alternative method to improve the estimation accuracy for ANS is to use the reconstruction data in the vicinity Ω bounded between the two spherical surfaces Γ and Γ_∞ (denoted by blue and red dashed lines in Fig. 1, respectively) reconstructed from measurements. Unlike traditional methods where nonlinear optimization (2) is directly based on sparsely processed measurements, the reconstructed MFD offers an effective means to improve ANS localization accuracy by allowing a continuous 3D magnetic field distribution $B_r(r \geq r_s, \theta, \varphi)$ in Ω outside the head to be used in formulating the nonlinear optimization:

$$\text{Minimize } f_R(\mathbf{L}, \mathbf{Q}) = \iint \|B_r - B_c(\mathbf{L}, \mathbf{Q})\|_{\mathbf{r}=\mathbf{r}_s+\delta\mathbf{r}}^2 d\theta d\varphi$$

Numerically, the surface integral in the above objective function is evaluated over the reconstructed hemispherical surface at $r = r_s + \Delta r$, which leads to the discrete form in (4) where M_θ is the number of divisions along θ , M_φ is the number of divisions along φ , and r_h is the spherical head radius:

$$\text{Minimize } f_R(\mathbf{L}, \mathbf{Q}) = \sum_{m=1}^{M_\theta} \sum_{n=1}^{M_\varphi} \|B_r(\theta_m, \varphi_n) - B_c(\mathbf{L}, \mathbf{Q}; \theta_m, \varphi_n)\|_{\mathbf{r}=\mathbf{r}_s+\Delta\mathbf{r}}^2 \quad (4a)$$

$$\text{subjected to constraint: } |\mathbf{L}| < r_h \quad \text{and } \mathbf{q} = \mathbf{I}. \quad (4b,c)$$

In (4a), B_c (observed by a sensor located at $\mathbf{r}$ with measurement axis pointing in the $\mathbf{s}$ direction) can be derived from the Biot–Savart law in (1a). In spherical coordinates,

$$B_c(\mathbf{L}, \mathbf{Q}) = \left[\frac{\mu_0}{4\pi |\mathbf{r} - \mathbf{L}|^3} \mathbf{Q} \times (\mathbf{r} - \mathbf{L}) \right] \mathbf{s},$$

where $\frac{\mathbf{r}_i}{r} = [\sin \theta_i \cos \varphi_i \quad \sin \theta_i \sin \varphi_i \quad \cos \theta_i]$. (5)

In (4b,c), $\mathbf{L}$ is constrained within the spherical head and $\mathbf{q}$ is a unit vector. The reconstruction of the BC surface integral B_r at $r = r_s + \Delta r$ and the solutions to (4) are discussed in the following subsections.

2.1 Formulation of reconstructed magnetic field

As illustrated in Fig. 1, the space inside a magnetically shielded room can be treated as a spherical region Ω with far field boundary Γ_∞ . While MEG signals are time varying, their variations are relatively slow such that induction effects can be neglected. Besides, the container of sensors (called Dewar) in a MEG signal measuring system (such as SQUID) is strictly nonferromagnetic to avoid introducing distortion to the neuromagnetic field being measured [12]. The neuromagnetic field in the current-free space between Γ and Γ_∞

can be treated as quasi-static and satisfying Eq. (6a) and is governed by the static Maxwell's equations [11]. Thus, the MFD at any position can be reconstructed from measured BCs. Defined by Eq. (6b), the MFD $\mathbf{B}$ can be represented by a magnetic scalar potential ψ obeying Laplace's Eq. (6c):

$$\nabla \times \mathbf{B} = 0 \quad \text{and} \quad \mathbf{B} = -\mu_0 \nabla \psi \quad (6a,b)$$

$$\nabla^2 \psi = 0 \quad (6c)$$

The BCs in spherical coordinates are given in (7a–d) for solving Laplace's Eq. (6c), where (7c) is periodic BC; (7d) is natural BC; and $B_s(\theta_s, \varphi_s)$ are measured BC on upper surface of Γ ,

$$\psi|_{r \rightarrow \infty} = 0; \quad \frac{\partial \psi}{\partial r} \Big|_{r=r_s} = \begin{cases} -B_s(\theta_s, \varphi_s)/\mu_0 & 0 \leq \theta_s \leq \pi/2 \\ 0 & \pi/2 < \theta_s \leq \pi \end{cases} \quad (7a,b)$$

$$\psi|_{\varphi_s=0} = \psi|_{\varphi_s=2\pi}; \quad \psi|_{\theta_s=0, \pi} = \text{limited} \quad (7c,d)$$

The solutions to (6c) subjected to BCs (7a–7d) are given in Appendix 1. Using Eq. (16) with the MFD $\mathbf{B}$ in Eq. (6b), the reconstructed MFD $B_r(r \geq r_s, \theta, \varphi)$ can be expressed as

$$B_r(r \geq r_s, \theta, \varphi) = \sum_{l=0}^{\infty} \left\{ \frac{2l+1}{2\pi} \left(\frac{r}{r_s} \right)^{-(l+2)} \sum_{m=0}^l \left[\frac{(l-m)!}{\delta_m(l+m)!} P_l^m(\cos \theta) (C_l^m \cos m\varphi + D_l^m \sin m\varphi) \right] \right\} \quad (8)$$

In Eq. (8), $P_l^m(\cos \theta)$ are Legendre polynomials of degree l and order m , and the coefficients (C_l^m and D_l^m) are derived in Eq. (19). Equation (8) uses the surface integrals that appear in C_l^m and D_l^m to reconstruct B_r from measured data $B_s(\theta, \varphi)$ to minimize the noise effect by “smoothing” it over the hemispherical reconstructed surface. Although a large number of sensors are often used to cover the upper hemispherical head surface, they are often sparsely located. For improving the fidelity of BC surface integrals in Eq. (19), a dense BC surface B_b is obtained by spatial interpolation among measured data using a second-order fitting polynomial function with coefficients optimized by a LS technique as outlined in Appendix 2. Substituting the densely interpolated B_b for sparsely spaced measured B_s , Eq. (19) is rewritten as follows:

$$\begin{bmatrix} C_l^m \\ D_l^m \end{bmatrix} = \int_0^{2\pi} \int_0^\pi B_b(\theta, \varphi) \begin{bmatrix} \cos m\varphi \\ \sin m\varphi \end{bmatrix} P_l^m(\cos \theta) \sin \theta d\theta d\varphi \quad (9)$$

2.2 Computation procedure

To be effective, measurement noise B_{ni} on ANS localization must be accounted for. Thus, the SQUID measurement B_{si} of the i th

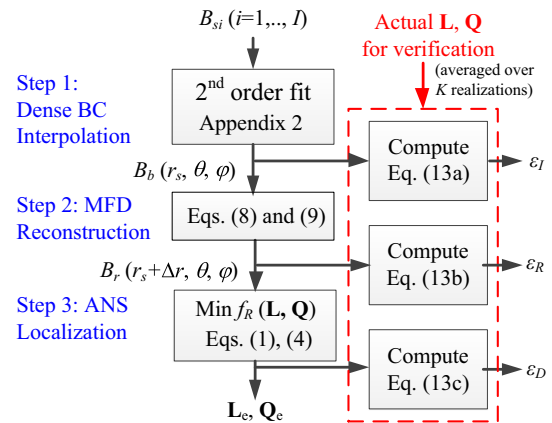


Fig. 2 Flowchart illustrating the ANS localization algorithm

sensor and corresponding SNR is mathematically modeled by Eqs. (10a,b) and (11), respectively, in the following discussion:

$$B_{si}(\theta_{si}, \varphi_{si}) = B_{ci} + B_{ni} \quad \text{where} \quad (10a,b)$$

$$B_{ci} = \mathbf{B}_c|_{\mathbf{r}=\mathbf{r}_{si}} \cdot \mathbf{s}_i \quad \text{and} \quad i = 1, 2, \dots, I$$

and

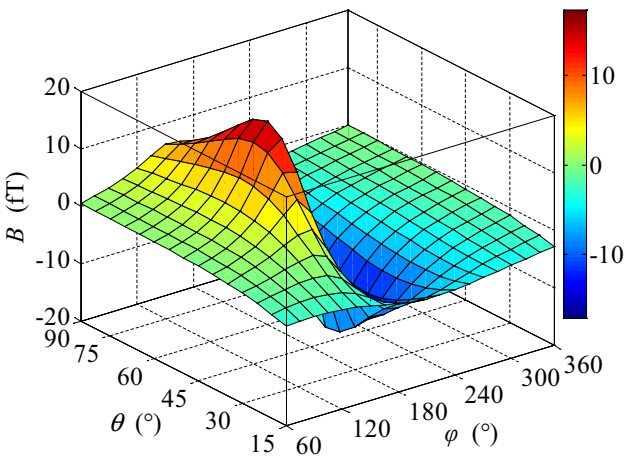
$$\text{SNR} = \left(\sum_{i=1}^I B_{ci}^2 \right) / \left(\sum_{i=1}^I B_{ni}^2 \right) \quad (11)$$

As SNR approaches infinity, the reconstructed MFD in Eq. (8) converges to that computed from the forward model Eq. (1) provided the number of expansion terms M_l for degree l is sufficiently large. Unlike measurement noise B_{ni} which are typically zero-mean Gaussian in nature, biomagnetic signals B_c decay rapidly with distance; thus, $B_r(r \geq r_s, \theta, \varphi)$ near the sensor surface ($r = r_s + \Delta r$) is reconstructed in Eq. (8) for ANS localization.

The flowchart in Fig. 2 illustrates the computation procedure based on reconstructed MFDs to locate an ANS, which consists of three steps.

- Step 1: Given measured data B_{si} , this step interpolates among the measured data using a LS-optimized polynomial fit (Appendix 2) to generate a densely spaced data B_b on the BC (upper hemispherical surface at $r = r_s$).
- Step 2: With the spatially dense BC surface B_b , a continuous MFD surface $B_r(r_s + \Delta r, \theta, \varphi)$ using Eqs. (8) and (9) is reconstructed. Since interpolation and reconstruction introduce errors in the presence of measurement noise, a gradient-based method is developed to establish a rational criterion for selecting high-fidelity reconstructed data to improve ANS localization. This is best illustrated with an example and will be covered in the next section.

Table 1 Nominal parametric values used in simulation

Sensors [22] $r_s = 110\text{mm}$ $I = 65$	
Reconstruction $M_l = 20$ $M_\theta = 15, \Delta\theta = 6^\circ$ $M_\varphi = 20, \Delta\varphi = 18^\circ$ $J = 300, K = 100$	
ECD Q (1nAm, $30^\circ, 30^\circ$) L (75mm, $40^\circ, 160^\circ$)	

Radial MFD components of the specified ECD at $r=115\text{mm}$.

Step 3: With the reconstructed B_r at $r = r_s + \Delta r$ and Eq. (5), the third step estimates the unknown parameters (**L** and **Q**) of ECD by solving the LS problem Eq. (4). In this work, the MATLAB nonlinear optimization toolbox has been used; specifically, Eq. (4a–c) is solved as a constrained optimization with the command *fmincon*. Guided by the automated search algorithm of sequential quadratic programming (SQP), the set of **L_e** and **Q_e** that minimizes the squares of the differences between the observations $B_r(r_s + \Delta r, \theta, \varphi)$ and the predictions $B_c(r_s + \Delta r, \theta, \varphi)$ computed from the ECD model is determined.

2.3 Parameters used for model verification

For the purpose of model verification, the reconstruction is evaluated numerically in terms of error e_R defined by Eq. (12a):

$$e_R = \frac{1}{J} \sum_{j=1}^J \left| \frac{B_{rj}}{B_{cj}} - 1 \right|_{\mathbf{r}=\mathbf{r}_s+\delta\mathbf{r}} \times 100 \% \quad (12a)$$

where $j = M_\varphi(m-1) + n$; $m = 1, 2, \dots, M_\theta$; The indexes $n = 1, 2, \dots, M_\varphi$; and $J = M_\varphi M_\theta$. (m and n) have been defined in (4). Similarly, the estimated ANS localization **L_e** is evaluated numerically in terms of error e_D defined by Eq. (12b):

$$e_D = \frac{1}{|\mathbf{L}|} |\mathbf{L}_e - \mathbf{L}| \times 100 \% \quad (12b)$$

To statistically evaluate the accuracy of interpolation and the effects of SNR on the reconstruction and ANS

localization, the average errors are computed over K realizations:

$$\varepsilon_I = \frac{1}{K} \sum_{k=1}^K e_{Ik}, \quad \varepsilon_R = \frac{1}{K} \sum_{k=1}^K e_{Rk} \quad \text{and} \quad \varepsilon_D = \frac{1}{K} \sum_{k=1}^K e_{Dk} \quad (13a,b,c)$$

where e_l is the interpolation error averaged over the hemispherical surface at $\mathbf{r} = \mathbf{r}_s$.

3 Numerical analysis and discussion

The ANS localization based on reconstructed magnetic field with BC surface integrals and the effects of inverse model under the influence of independent measurement noise on its accuracy are numerically investigated, as shown in Fig. 2. The effects of SNRs on the reconstructed MFD and ECD localization accuracy were analyzed by adding a zero-mean Gaussian white noise to MFD at the sensor locations computed from forward model (representing sensor measurements). As a basis for comparison, the simulated results using the ANS localization algorithm are compared with the conventional method that directly uses measurements for ECD estimation by minimizing the objective function (2). Sequential quadratic programming (SQP) method is used to search for the unknown source parameters.

The parametric values used in the simulations are summarized in Table 1 for a 90-mm-radius spherical head ($r_h = 90\text{ mm}$, taking into account the thickness of scalp, skull, and brain tissues) with an ECD that models a typical ANS. The right column of Table 1 shows the spherical

surface distribution of the radial MFD component (B_c in fT or 10^{-15} Tesla) computed from the dipole model Eq. (1) at $r = (r_s + \Delta r) = 115$ mm for a specified dipole $\mathbf{Q}$ (with magnitude $q = 1$ nAm) located at $\mathbf{L}$, which provides the true values for verification. Sixty-five radial sensors are mutually independent and uniformly distributed on a 110-mm-radius spherical surface (20 mm from the head surface as illustrated in Fig. 1); their specific placements can be found in [22]. Numerical results summarized in Sects. 3.1 and 3.2 are discussed in Sect. 3.3.

3.1 Verification of noise-free reconstruction

$$B_r(r \geq r_s, \theta, \varphi)$$

For illustration and as a basis for comparison, the MFDs reconstructed with exact BCs in the curl-free region (Step 2 of the algorithm in Fig. 2) were verified with respect to that of a specified ECD. For verifying the reconstructed MFDs, the dense BC surface integrals were numerically computed using Eq. (1) that serves as the forward model with an $(\theta \times \varphi)$ array of 30×90 $\mathbf{B}_b$ data grids. Based on parametric values in Table 1, the computed B_{rj} results at reconstructed location from Eq. (1) are compared in Fig. 3a where the index j ($=1, \dots, 300$) has been defined in Eq. (12a). For clarity, the reconstruction errors e_R along φ (in step of $\Delta\varphi = 18^\circ$ from 18° to 360° in Table 1) are plotted in Fig. 3b at specified $\theta = 48^\circ$. As shown in Fig. 3b, the relative % errors have a mean value of 0.84 %, and except in regions where $B_{rj} \approx 0$, the errors are smaller than 1 %. The numerical analyses in Fig. 3c, d provide a basis to analyze the effects of reconstruction surface ($r = r_s + \delta_r$) and source depth (below head surface with $r = r_1 - \delta_s$) on the number of expansion terms in Eq. (8) and on reconstruction errors in Eq. (12a, b).

The following conclusions can be drawn from Fig. 3:

- The reconstruction errors e_R decrease rapidly with $M_l < 12$ and in all cases gradually approach to a constant value after 12 expansion terms.
- In Fig. 3c, further away from the head surface, fewer the number of expansion terms are needed for the reconstruction to converge but at the expense of reconstruction errors e_R ; this is because the magnetic field rapidly decays with increasing radial distance in the equation of multi-pole expansions. As compared in Fig. 3c, the converged e_R (with $M_l = 30$) on the $(r_s + 5$ mm)-radius spherical surface is only 1/10 of that on the $(r_s + 45$ mm)-radius surface. Thus, the reconstructed MFD at the nearest sensor surface ($\delta_r = 5$ mm) is used in this paper for ANS localization.
- Unlike Fig. 3c, where the errors converge to a set of constant values, Fig. 3d shows that the errors e_R defined in Eq. (12a) in the reconstruction for different source

depths along degree l converge to a value of 1.5 %. Thus, $M_l = 20$ is used in the simulations related to reconstruction.

3.2 Effects of SNRs on reconstructed MFD and ANS localization

To investigate the effect of measurement noise levels on the accuracy of reconstructed MFD and subsequent ECD localization, zero-mean Gaussian white noise was added to each B_{ci} ($i = 1, \dots, 65$) computed from Eq. (1) at the radial sensor locations ($r = r_s$) to model the 65 measurements B_{si} ($i = 1, \dots, 65$); 5 noise levels (SNR = 0.25, 0.5, 1.0, 2.0, and 4.0) were tested. For each SNR level, the averages of 100 independent simulations of B_{rj} ($j = 1, \dots, 300$) and $\mathbf{L}_{ek}$ ($k = 1, \dots, 100$) are numerically computed using the algorithm as illustrated in Fig. 2.

The noise effects on the computing convergence of the MFD reconstruction can be analyzed by rewriting Eq. (8) as follows:

$$B_r(r, \theta, \varphi) = B_r|_{l=0} + \sum_{l=1}^{M_l} \Delta B_{rl} + \text{neglected terms} \quad (14a)$$

where $\Delta B_{rl} = B_{rl} - B_{r(l-1)}$

$$\text{and } B_{rl}(r, \theta, \varphi) = B_{cl}(r, \theta, \varphi) + B_{nl}(r, \theta, \varphi) \quad (14b,c)$$

The incremental ΔB_{rl} in (14a, b) represents the contribution of the l th expansion term in Eq. (8). At any specified location, the reconstructed B_r can be viewed to consist of two parts, B_c and B_n , as shown in (14c), corresponding to noise-free and only noise measurements B_{si} , respectively. As an illustration, the incremental ΔB_{cl} and ΔB_{nl} at the observation point (115 mm, 54° , 180°) with $M_l = 20$ are compared in Fig. 3e where $\Delta B_{cl} + \Delta B_{nl}$ computed by linearly summing ΔB_{cl} and ΔB_{nl} is identical to ΔB_{rl} directly computed Eq. (8) with measurements of SNR = 1. Unlike ΔB_{cl} that converges smoothly to 0 after $l > 12$, small ΔB_{nl} variations persistently stay throughout l . The influences of different noise levels (SNR = 4, 1, $\frac{1}{4}$) are illustrated in Fig. 3f. The BC integrals over the entire sensor spherical surface for constructing the magnetic field using (9) provide an opportunity to “abandon” some B_n effects by properly truncating expansion terms; for example, $l > 12$ as illustrated in Fig. 3e, f for source at S_1 .

The noise effects on the BC interpolation and MFD reconstruction are illustrated in Fig. 4a, b, respectively, by comparing simulated results against exact solutions of Eq. (1) for the case of measured BCs with SNR = 1. In Fig. 4a, the interpolated MFDs (observed at $\theta = 48^\circ$ over $\varphi = [0, 2\pi]$) of polynomial fitting (20) are compared with that computed by nearest neighbor interpolation function using Comsol, a commercial

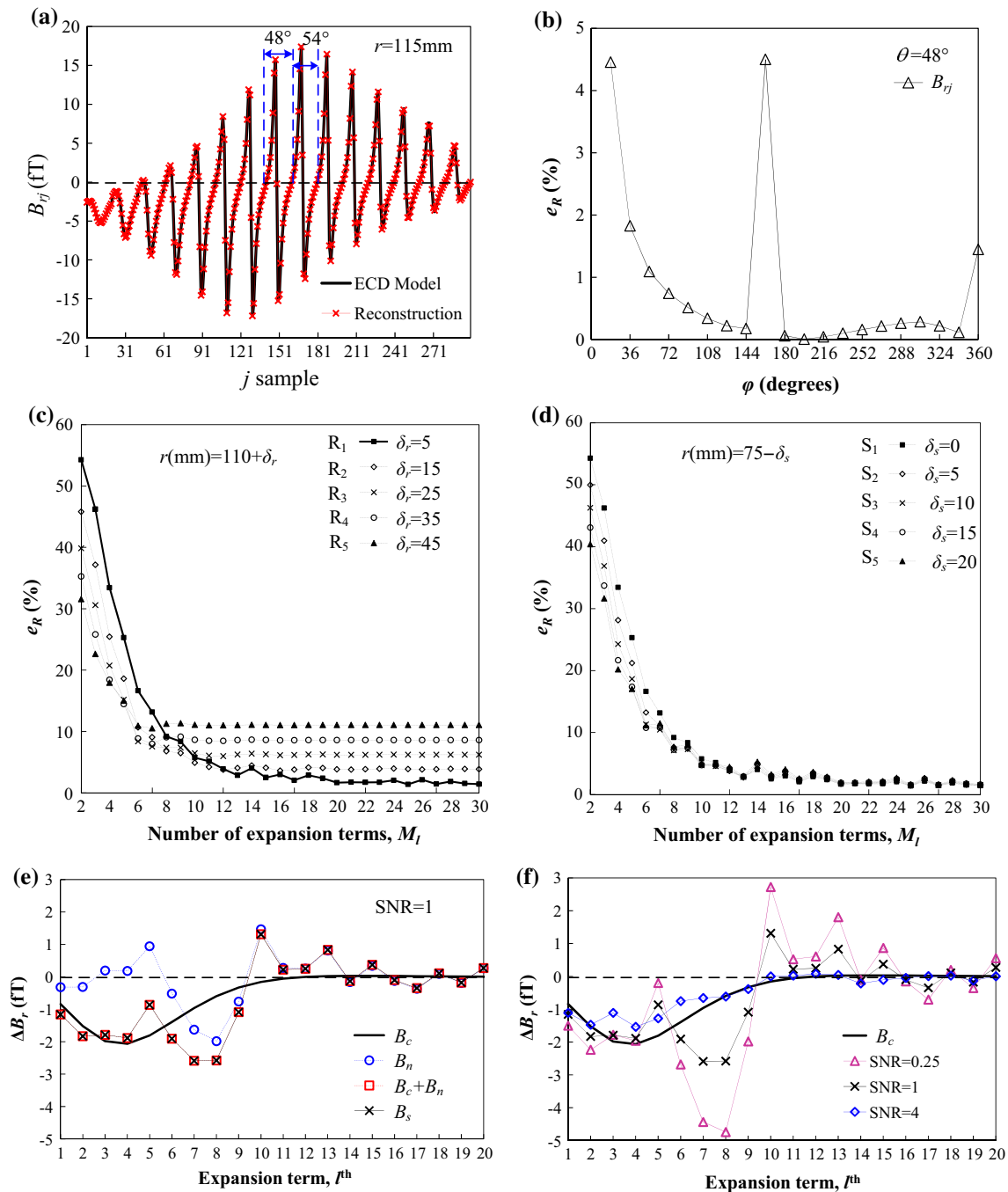


Fig. 3 Verification of reconstructed MFDs with exact BCs and illustrations of parametric effects of the number of expansion terms and SNR levels on reconstructed MFDs. **a** Reconstructed MFD with exact BCs (S_1). **b** Reconstruction errors with exact BCs (S_1). **c** Reconstructed errors with different numbers of expansion terms and recon-

struction surfaces (S_1). **d** Reconstructed errors with different numbers of expansion terms and source depths. **e** Effect of noise on reconstruction on position (115 mm, 54° , 180°) (S_1). **f** Effect of different noise levels on position (115 mm, 54° , 180°) (S_1)

finite-element analysis (FEA) software. The interpolation and reconstruction errors are further analyzed in Fig. 4c. Some observations can be made from these results:

- Although the two interpolation methods yielded similar results, the MFDs interpolated by (B.1) are smoother and exhibit smaller errors than Comsol results. The reconstructed MFDs (at R_1 or

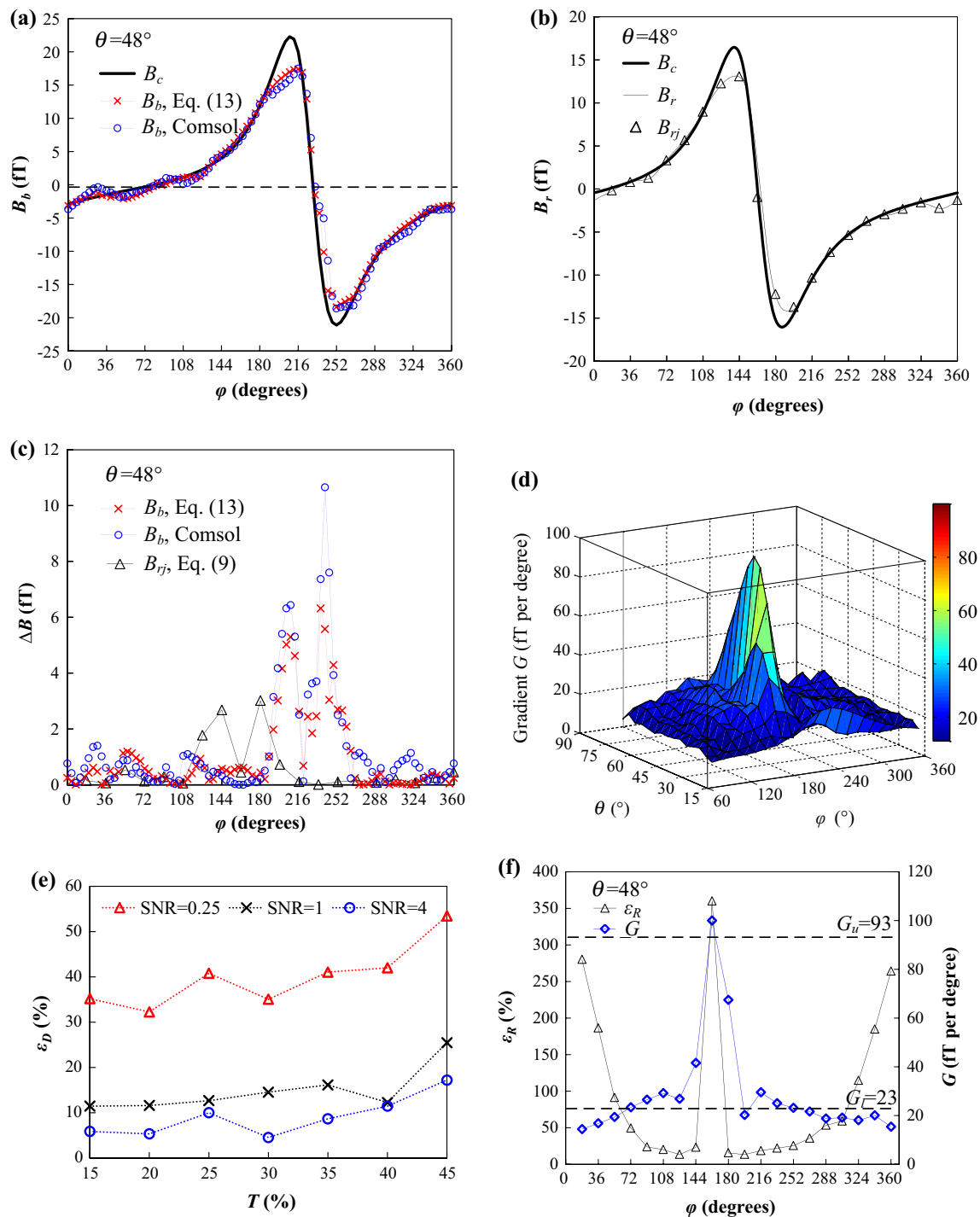


Fig. 4 Comparisons of interpolated MFDs using polynomial fitting in (13) and Comsol and reconstructed MFDs against exact solutions (SNR = 1); illustrations of relation between reconstruction errors and gradient (average of 100 realizations, S_1). **a** Interpolated MFDs

(SNR = 1). **b** Reconstructed MFDs (SNR = 1). **c** Interpolation and reconstruction errors (SNR = 1). **d** Gradient of reconstructed MFDs (SNR = 1). **e** ε_D using selected B_r with different gradient thresholds. **f** Relation between reconstruction errors and gradients (SNR = 1)

$r = 115$ mm) fit well with exact solutions of Eq. (1) with errors significantly smaller than interpolated MFDs (at $r_s = 110$ mm), confirming the contributions from the reconstruction.

- Most of the interpolation errors occur in regions where the MFD gradient experiences a sign change (corresponding to a local maximal or minimal) and $B_{rj} \approx 0$, and most of the reconstruction errors occur in regions

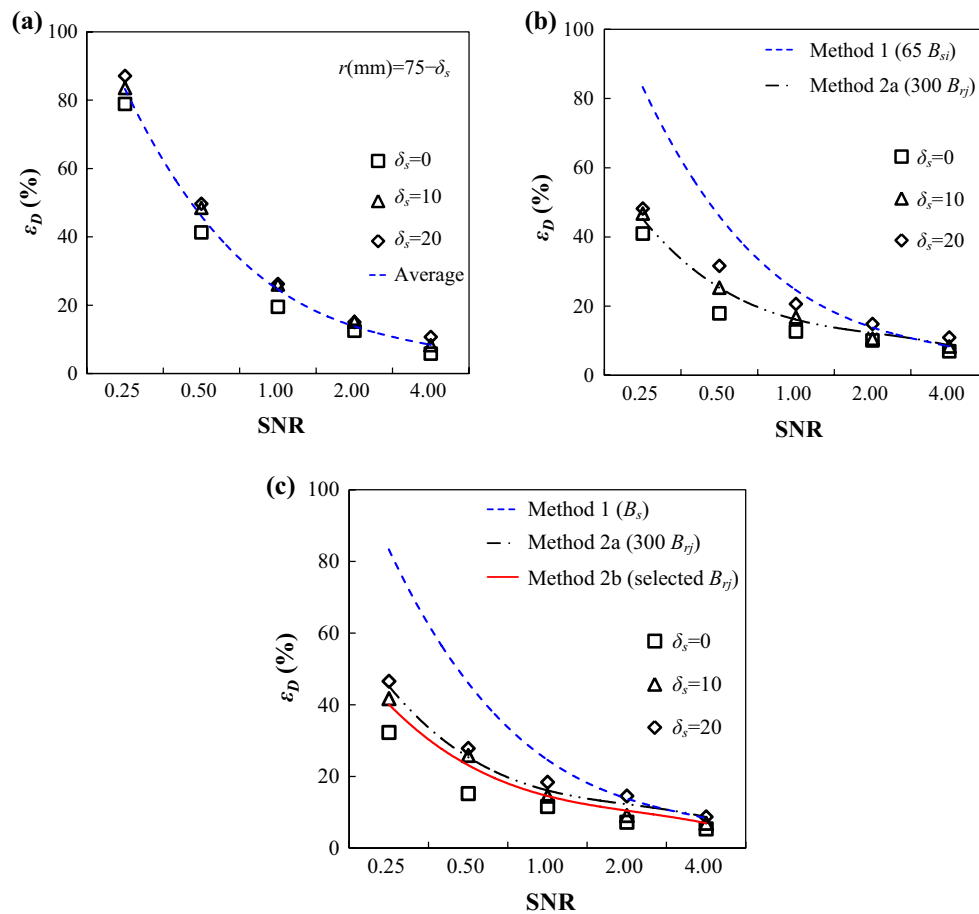


Fig. 5 Comparisons of ANS localization under influences of sensor noise (average of 100 realizations). **a** Based directly on 65 MEG measurements B_s . **b** Based on 300 reconstructed B_r at $r = 115$ mm. **c** Based on selected reconstructed B_r at $r = 115$ mm with $T = 20\%$

around high gradients and $B_{rj} \approx 0$ as illustrated in Fig. 4(c). Thus, a pair of gradient-based lower bound G_l and upper bound G_u are defined in Eq. (15) in terms of threshold T ($0 \leq T \leq 1$) to avoid erroneous data in locating ANS, where G_j is the gradient B_{rj} :

$$[G_l \ G_u]^T = [T \ 1 - T]^T \text{Max}\{G_1, \dots, G_J\} \quad (15)$$

Equation (15) is best illustrated with an example. For this, Fig. 4d shows a typical 2D gradient distribution obtained by Sobel operators (for reconstructed MFDs of S_1 with SNR = 1). The effects of different gradient threshold T values on the estimated error in ANS localization are plotted for three different SNRs (based on $K = 100$ realizations) in Fig. 4e, which leads to the selection of $T = 20\%$ with errors minimized over the five SNR levels simulated. As illustrated in Fig. 4f which relates the B_{rj} gradients and reconstruction errors at $\theta = 48^\circ$, high reconstruction errors are avoided when selecting B_{rj} within the bounds between $G_l = 23$ and $G_u = 93$ (corresponding to $T = 20\%$).

The ANS localization is estimated using two different methods:

- Method 1 (Fig. 5a): Inverse model based on the 65 directly measured B_s .
- Method 2a (Fig. 5b): ANS localization based on reconstructed B_{rj} (300 uniformly distributed B_r data as shown in Table 1).
- Method 2b (Fig. 5c): ANS localization based on selected B_r using a gradient threshold T .

Results of Methods 1, 2a, and 2b are summarized in Fig. 5a–c where the accuracy of three dipole locations (S_1 , S_3 , and S_5) is evaluated statistically in terms of the average error ϵ_D defined in (13c) based on $K = 100$ realizations. As shown in Fig. 5a, the location estimated by Method 1 deteriorates rapidly as the SNR drops lower than 2. The location errors using reconstructed magnetic fields in Methods 2a and 2b are half of that by Method 1 for cases when $\text{SNR} < 2$ as demonstrated in Fig. 5b, c. The location errors appear to be somewhat sensitive to the source depths.

Table 2 Estimation of source locations. Real $\mathbf{L} = (-49.8, 18.1, 53.0)$ mm (S_1)

SNR	Estimated location $\mathbf{L}_e$: average (x, y, z); standard deviation (x, y, z); error (ε_{Dx} , ε_{Dy} , ε_{Dz})		
	Method 1 (65 B_{si})	Method 2a (300 B_{ij})	Method 2b (selected B_{ij} , $T = 20$ %)
4	(-49.7, 18.0, 53.2) mm; (3.0, 2.1, 3.2) mm; (4.6, 9.4, 4.8) %	(-46.9, 17.1, 51.2) mm; (3.2, 1.6, 3.0) mm; (6.9, 8.6, 5.0) %	(-47.6, 18.0, 53.8) mm; (2.6, 1.5, 2.0) mm; (5.6, 7.0, 3.5) %
2	(-49.5, 20.0, 50.9) mm; (5.1, 11.1, 10.8) mm; (8.5, 25.0, 10.4) %	(-46.4, 17.0, 50.9) mm; (5.3, 2.8, 4.5) mm; (9.9, 13.5, 7.3) %	(-47.5, 17.6, 53.1) mm; (3.6, 2.8, 2.9) mm; (6.9, 12.2, 4.1) %
1	(-46.8, 18.6, 51.6) mm; (14.8, 15.1, 15.3) mm; (15.8, 36.4, 15.9) %	(-45.7, 15.4, 52.4) mm; (6.1, 3.2, 6.4) mm; (11.7, 17.9, 9.1) %	(-46.9, 15.9, 53.9) mm; (6.1, 3.5, 5.3) mm; (11.3, 18.4, 7.8) %
0.5	(-41.6, 17.1, 42.9) mm; (32.9, 26.3, 26.9) mm; (35.7, 73.5, 29.5) %	(-45.3, 16.2, 51.9) mm; (12.8, 5.0, 7.3) mm; (20.1, 22.5, 10.4) %	(-48.2, 16.8, 52.7) mm; (9.5, 5.5, 6.7) mm; (15.0, 24.8, 9.6) %
0.25	(-19.2, 6.7, 34.6) mm; (50.7, 36.4, 29.9) mm; (77.7, 133.2, 48.4) %	(-39.0, 7.7, 49.0) mm; (18.9, 19.3, 18.9) mm; (31.0, 70.2, 26.5) %	(-39.6, 10.5, 51.6) mm; (19.7, 16.1, 15.5) mm; (30.5, 54.8, 21.3) %

Table 3 Interpolation, reconstruction, and ANS localization error analysis (S_1)

Errors (%)	Noise-free BC			Measured BC with different SNR levels		
	Exact dense BC	Interpolated BC		SNR = 4	1	1/4
		Eq. (20)	Comsol			
Method 1						
ε_D	3×10^{-5}	–	–	5.81	19.53	78.93
Method 2						
Step 1, ε_I	0	5.99	7.44	18.26	34.17	62.25
Step 2, ε_R	3.01	6.63	9.23	19.65	26.84	47.36
Method 2a						
Step 3, ε_D	0.79	–	–	6.93	12.67	40.96
Method 2b						
Step 3, ε_D	0.1	–	–	5.33	11.60	32.27

3.3 Error analysis and discussion of results

The BC interpolation, MFD reconstruction, and ANS localization errors are summarized in Tables 2 and 3. Table 2 details the simulated estimations of ECD locations showing the average and standard deviation of the dipole location and average % errors in Cartesian coordinates. Table 3 shows the computed errors for two different conditions, noise-free and measured BCs, and compared against that computed with exact dense BC using (1) which serves as a basis for evaluation.

Some observations made from Tables 2 and 3 are discussed as follows:

- As compared in Table 2, Method 2b exhibits smallest (average, standard deviation) location errors for all five SNR levels. For measurements with a high SNR (≥ 2), Method 1 offers a better estimation than Method 2a but rapidly deteriorates when SNR drops below 2. Since

actual SNR is generally unknown in practice, Method 2b that is less sensitive to noise represents a preferred method.

- The near-zero-error solutions solved with exact dense BC in Table 3 verify the inverse model for field reconstruction and ANS localization. Numerical results suggest that when high-fidelity measurements ($\text{SNR} \geq 4$) are available, the ANS can be accurately located and solved from the inverse model (2) with the direct use of the measured data, which is consistent with observations made in Table 2.
- For solutions based on interpolated dense BC from noise-free BC at the sensor locations, both interpolation and reconstruction introduce errors to solutions; however, reconstruction tends to be more tolerant than interpolation. Particularly, when erroneous reconstruction data are carefully avoided using gradient-based thresholds, ANS estimation can be significantly improved. This can be illus-

trated with the case of solutions using exact dense BC in Table 3; the estimated ANS-location errors drop from 0.79 % (Method 2a) to 0.1 % (Method 2b) despite a 3 % reconstruction error. Similar patterns can be seen in the last three columns of Table 3 where field reconstruction and ANS localization errors are much lower than errors contributed by data interpolation.

- For measurements with low SNR, Methods 2a and 2b (that bases on reconstructed data) offer a significantly more accurate localization than Method 1 (where direct measurements were used) despite errors in data interpolation and field reconstruction. This is because the BC integrals over the entire surface (instead of scattered interpolated data) are taken into account in the physics-based model (8) to reconstruct a smooth MFD leading to a more representative set of “reconstructed measurements” for ANS location.

$$\psi(r, \theta, \varphi) = \sum_{l=0}^{\infty} \sum_{m=0}^l \left[r^l (a_l^m \cos m\varphi + b_l^m \sin m\varphi) P_l^m(\cos \theta) + r^{-(l+1)} (c_l^m \cos m\varphi + d_l^m \sin m\varphi) P_l^m(\cos \theta) \right] \quad (16)$$

4 Conclusions

A novel computational method to improve the location estimation of an unknown ANS using reconstructed magnetic field from sparse noisy measurements has been presented. This method requires no additional measurements and no alteration to existing measuring equipment by taking advantages of the fact that biophysically generated magnetic fields outside the head are quasi-static in current-free space.

Numerical investigations have been conducted with various sources and measurement SNR levels. Although both interpolation and reconstruction introduce errors to the solution, reconstruction is more tolerant and robust compared to interpolation. Additionally, simulations show that errors introduced by interpolation and reconstruction can be effectively reduced by means of a gradient-based data selection method which greatly improves the ANS localization accuracy particularly for measurements with poor SNR below 2, an approximately 60 % improvement over traditional methods where direct measurements are directly utilized in solving the inverse problem.

The results presented here demonstrate the potentials of the reconstruction-based ANS localization and gradient-guided selection methods for applications with actual MEG data. While the method has been demonstrated in the context of ANS localization, it can also be applied to other magnetic source tracking applications such as capsule endoscopy localization and magnet-marker tongue movement monitoring.

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Appendix 1: Solutions to magnetic scalar potential in Ω outside the head

Solved by the separation-of-variable method in spherical coordinates, the solutions to Eq. (6c) with BCs (7a–d) are a linear combination of the spherical harmonic functions which are products of trigonometric functions and associated Legendre polynomials $P_l^m(\cos \theta)$ of degree l and order m :

Noting that $\psi|_{r \rightarrow \infty} = 0$, $a_l^m = b_l^m = 0$, and $c_l^m = d_l^m$ are determined from the BCs:

$$\begin{bmatrix} c_l^m \\ d_l^m \end{bmatrix} = \frac{r_s^{(l+2)}}{\mu_0(l+1)} (N_l^m)^{-2} \begin{bmatrix} C_l^m \\ D_l^m \end{bmatrix} \quad (17)$$

where the modulus of spherical harmonics

$$(N_l^m)^{-2} = \left(\frac{2l+1}{2\pi\delta_m} \right) \frac{(l-m)!}{(l+m)!} \quad \text{with } \delta_m = \begin{cases} 2, & m=0 \\ 1, & m \neq 0 \end{cases} \quad (18)$$

and

$$\begin{bmatrix} C_l^m \\ D_l^m \end{bmatrix} = \int_0^{2\pi} \int_0^\pi B_s(\theta, \varphi) \begin{bmatrix} \cos m\varphi \\ \delta_m \sin m\varphi \end{bmatrix} P_l^m(\cos \theta) \sin \theta d\theta d\varphi \quad (19)$$

Appendix 2: H-nearest neighborhood interpolation of measured data on BC surface

The second-order fitting polynomial function in Eq. (20) is used to interpolate among the sparse measured data on a three-dimensional surface:

$$B_b(\theta, \varphi) \approx g_0 + r_s \mathbf{g}^T \mathbf{x} + r_s^2 \mathbf{x}^T \mathbf{G} \mathbf{x} \quad (20)$$

$$\text{where } \mathbf{x} = \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} \sin \theta \cos \varphi \\ \sin \theta \sin \varphi \\ \cos \theta \end{bmatrix}; \quad \mathbf{g} = \begin{bmatrix} g_1 \\ g_2 \\ g_3 \end{bmatrix} \quad \text{and } \mathbf{G} = \begin{bmatrix} g_7 & g_4 & g_5 \\ 0 & g_8 & g_6 \\ 0 & 0 & g_9 \end{bmatrix}.$$

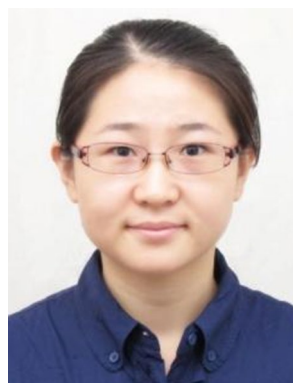
The coefficients (g_0 , $\mathbf{g}$, $\mathbf{G}$) in Eq. (20) are determined by LS technique weighted over the H -nearest neighbor measurements, which minimizes the objective function (21) where w_i is determined by the distance δ_i between the i th nearest neighbor measurement B_{si} and the point being interpolated:

$$\text{Minimize } f_b(g_0, \mathbf{g}, \mathbf{G}) = \sum_{i=1}^H w_i \|B_{bi}(\theta_i, \varphi_i) - B_{si}\|^2 \quad (21)$$

$$\text{where } w_i = 1 - 3t_i^2 + 2t_i^3 \text{ and } t_i = \frac{\delta_i}{\text{Max}\{\delta_1, \delta_2, \dots, \delta_H\}} \quad (22,23)$$

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