

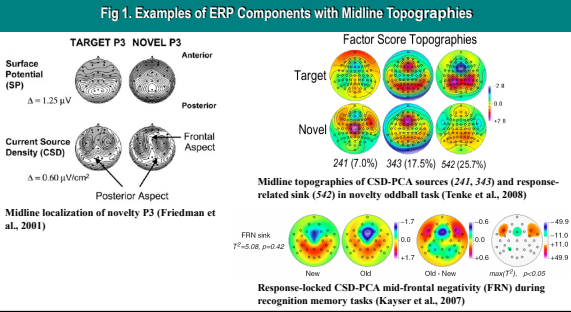
### Abstract

Novelty P3 and frontal response negativity (FRN) are among many EEG/ERP processes (e.g., theta; nogo P3; error-related negativity ERN) that have been attributed to generators within the longitudinal fissure using semi-automatic programs (e.g., BESA) to localize equivalent current dipoles (ECD). These ECDs typically have a radial orientation with a location in the anterior cingulate cortex (ACC) on or near the midline, which is in accordance with results using a less rigid, low resolution inverse method (LORETA). Imaging methods have also been used to determine ECD locations and to validate low resolution findings. Such task- and process-specific findings accord well with the growing literature on the functional significance of midline and basal frontal cortex, and ACC in particular. However, despite what appears to be a parsimonious convergence of findings across methodologies, there is a pervasive problem that is generally unrecognized: inverse models are not intended to account for field potential irregularities caused by local cancellation or field closure. Moreover, the dominant activity expected for a bilateral midline generator should be largely cancelled, and oriented normal to the cortical surface (i.e., tangential to the midline scalp). In contrast to inverse models, the use of more descriptive current source density analysis (CSD; surface Laplacian) methods does not limit field potential irregularities associated with field closure. Using Dipole Simulator, we simulated scalp potentials produced by dipolar generators (unilateral, bilateral, asymmetric) positioned at different depths within the longitudinal fissure (deep: ACC; shallow: supplementary motor area; superficial: bank of sissure), and evaluated LORETA, BESA and CSD solutions. Results for bilateral generators yielded CSD sources that were sharply confined to the frontocentral midline, with the corresponding sinks displaced to the lateral frontal surface, a pattern consistent with previously published CSD maps of novelty P3, and with statistical CSD evidence for FRN. However, sources corresponding to superficial generators yielded sharper topographies, while deep generators were markedly attenuated. Radially-oriented dipoles were also simulated for the medial orbital surface, and for the depths of the cingulate sulcus, resulting in a medial current source that decreased with distance from the midline, but without an abrupt inversion to a current sink. Results indicate that the frontocentral novelty P3 source and FRN sink are generated within the longitudinal fissure, but emphasize the need for additional intracranial CSD evidence. (Supported by NIH grant MH36295)

### Introduction

The time course and topography of the scalp-recorded field potential produced by an electrophysiological process are the result of volume-conduction from the underlying neuronal substrate. However, the identifiability of a component (i.e., its morphology, sign, topography, and overlap with other components or noise) may be profoundly affected by the choice of a recording reference.

Novelty P3 (Friedman et al., 2001; Tenke et al., 2008), frontal response negativity (FRN; Kayser et al., 2007), error-related negativity (ERN) and EEG theta are all examples of phenomena characterized by midline topographies using stronger, reference-free criteria (e.g., midline CSD topographies; Fig. 1). Using semi-automatic programs (e.g., BESA, LORETA), a number of reports have identified their putative generators in cortical regions within the longitudinal fissure (e.g., anterior cingulate cortex (ACC)). Using BESA, equivalent current dipoles have been localized at or near the midline, and are typically oriented radially toward the scalp. Functional imaging measures have provided independent support for some of these generators.



For an inverse solution to be plausible, it must simplify the volume-conducted topography by identifying a generator that is directly interpretable based on neuroanatomical knowledge. We have argued that it is difficult to infer a pattern of activation in the ACC based on an equivalent dipole that has an approximately radial orientation (cf. Tenke & Kayser, 2005; Kayser & Tenke, 2006). In analogy with the laminar properties of cortical ERP generators (Fig. 2A; Tenke et al., 1993), the bilateral activation of midline cortical fields within the longitudinal fissure will yield a predominantly closed field (Fig. 2B), the generators of which may be difficult or impossible to localize using dipole inverse methods. However, the same generator configuration may yield a residual surface potential capable of producing a stable midline CSD topography, identifiable as a restricted source or sink (i.e., the cumulative, uncanceled portion of the midline positivities [negativities] of the cortical dipoles in Fig. 2B), coupled to a distributed lateral frontal sink or source (the cumulative negative underside of the dipoles from each hemisphere). To date, it has not been systematically shown whether the closed field generators underlying such scalp topographies are resolvable by BESA or LORETA.

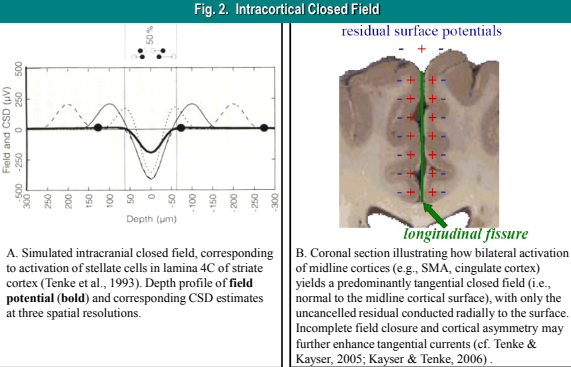
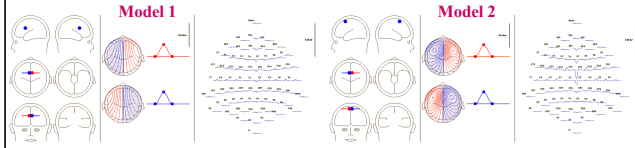
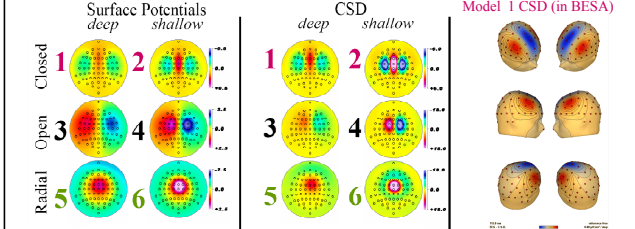


Fig. 3. Closed Field Models at Deep and Shallow Depths in the Longitudinal Fissure



Scalp potentials (67-channel montage) were simulated from dipoles (Berg, 2006) in order to correspond to closed fields produced by opposed generators at deep (Model 1; left) and shallow (Model 2; right) depths within the longitudinal fissure. These topographies ('reference-free' waveforms shown) reproduced properties expected for the scalp-recorded residuals of intracranial closed fields, including narrowly aligned, midline frontocentral positivities, with corresponding negativities at lateral sites.

Fig. 4. Six Generator Models: Surface Potentials and Corresponding CSD Topographies

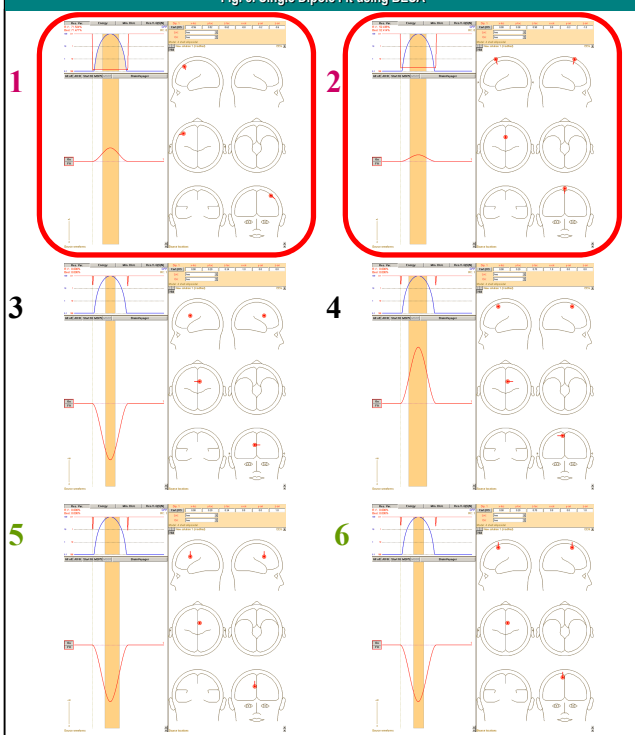


**Closed Field (top row):** Surface Potential (left) and CSD (middle) topographies corresponding to the Deep (Model 1) and Shallow (Model 2) closed fields described in Fig. 3. CSD for Model 1 (right) is also shown using the 3-dimensional head model of BESA.

**Open Field (middle row):** The open fields produced by single deep (Model 3) and shallow (Model 4) right hemisphere dipole are also shown (i.e., left pole eliminated).

**Radial Open Field (bottom row):** Radially oriented deep (Model 5) and shallow (Model 6) dipoles at the same right hemisphere sites (cf. Models 3 and 4) were also simulated.

Fig. 5. Single Dipole Fit using BESA



Although open field generators were adequately localized and oriented using BESA (Models 3-6), closed field generators were not easily identified. Single dipole solutions (Models 1 & 2) were uninformative, and two-dipole solutions (not shown) were unstable. All of these noise-free generators were best localized with no regularization.

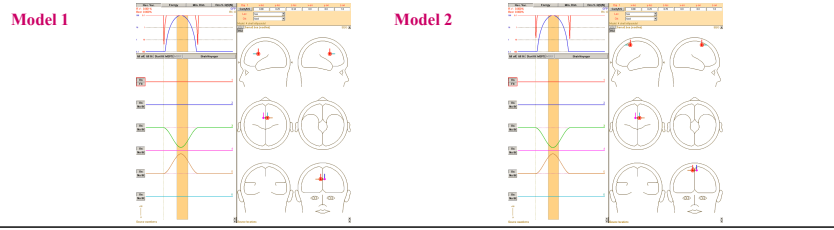
### Methods: Summary of Generator Simulations

Six models constructed of dipoles located *Deep* (#1, #3, #5) or *Shallow* (#2, #4, #6; cf. Fig. 3) using Dipole Simulator (Berg, 2006)

- **Models 1 & 2: CLOSED FIELDS**, composed of symmetric dipoles oriented normal to the midline cortical surface (i.e., tangential to scalp)
- **Models 3 & 4: RIGHT HEMISPHERE, ONLY** (i.e., open fields oriented normal to the midline cortical surface)
- **Models 5 & 6: RADIALLY ORIENTED**, Right Hemisphere dipole (i.e., nonphysiological; tangential to the midline cortical surface)

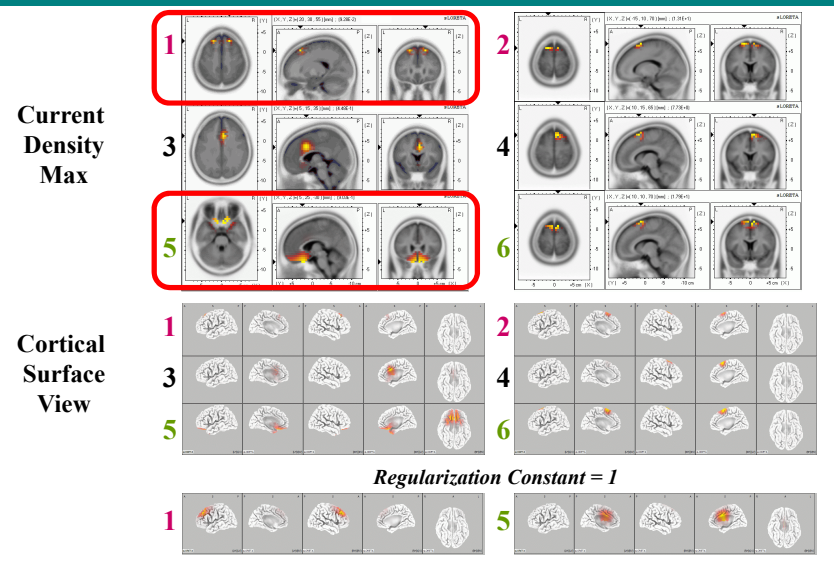
Inverses via BESA (v. 5.1.8.10; Scherg & von Cramon, 1986) and sLORETA (v. 2008-08-23; Pascual-Marqui, 1994), and compared to Current Source Density (CSD; Perrin et al., 1989) topographies

Fig. 6. Improved BESA Solution for Closed Fields



The accuracy of the BESA solution improved markedly for both closed field generators (Models 1 & 2) when regional dipoles were defined having fixed, symmetric component orientations.

Fig. 7. sLORETA solutions



sLORETA solutions (no regularization) consistently placed generators correctly for all three shallow generators (Models 2, 4, 6), identifying dorsal, right hemisphere sites in all models and bilateral generators for the closed field (Model 2). However, the **deep closed field (Model 1) was erroneously identified as a pair of dorsal generators displaced laterally from the midline**. This error was not observed when the field was opened by eliminating the left hemisphere dipole (Model 3). Surprisingly, a **deep, radially-oriented dipole at the same location (Model 5) was mislocalized to the ventral surface**. Solutions using no or a nonzero regularization constant were overall highly comparable, but a nonzero regularization increased the **error for the deep closed field (Model 1)** (more distributed over lateral surface), but **improved localization for the deep radial dipole (Model 5)**.

### Summary and Conclusions

- ✓ Extreme caution must be used when interpreting inverse solutions:
  - Inverse models fail for deep closed fields (e.g., within longitudinal fissure)
  - Inferred generators may not be credible (despite plausibility)
- ✓ In contrast, CSD topographies simplify and summarize essential constraints imposed by scalp potentials on putative generators, and may provide a conservative alternative to inverse solutions

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