

# Computational Neural Modeling Predicts Cortical Dynamics Underlying MEG Dipole Polarity: Insights Into Human Somatosensory Perception

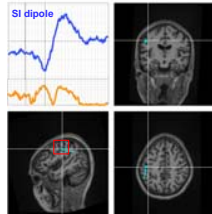
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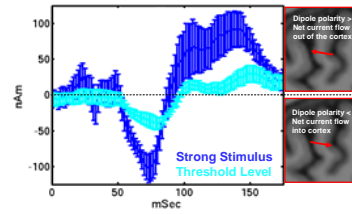
**Abstract:** Sensory processes involve interactions between reciprocally connected "higher" and "lower" cortical areas. Combined MEG and MRI/fMRI studies are exceptional non-invasive techniques to reveal the engagement of these areas during sensory perception in humans. However, the precise neural dynamics regulating these interactions remains unclear. To make a direct link between the measurable macroscopic events, and the underlying cellular level neurodynamics, we have developed a two-fold approach that combines non-invasive human experiments and detailed computational neural modeling. Our primary goal is to understand the neurodynamics of somatosensory perception. To this end, we (1) conducted an MEG study of tactile perception in humans and, (2) developed a laminated biophysical network model simulating activity in somatosensory cortex. Equivalent dipole reconstructions of the MEG data on structural MRI images shows a significant evoked signal in the primary somatosensory cortex (SI), whose magnitude correlates with perception. Model analysis leads to the novel prediction that the polarity of distinct peaks of the measured SI dipole can be explained by the direction of signal flow, feed-forward ("bottom-up") vs. feedback ("top-down"), into that cortex. The validity of this prediction is strengthened with intracranial monkey data. Further, simulating changes in "attentive state" in the model, we were able to reproduce the measured difference in evoked SI response during perceived vs. unperceived trials. Taken together, these findings indicate that signatures of perceptual competence are present in SI, and that, in MEG studies, dipole polarity may be a marker for the influence of feed-forward vs. feedback inputs on local network processes.

## MEG Current Dipole Evoked in SI Correlates with Perception

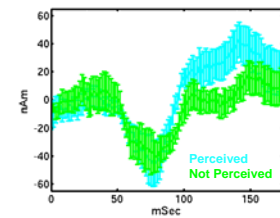
**Experimental Methods:** *Subjects:* 7 neurologically healthy, right handed, 18-45 yrs old. *Stimuli:* A piezo-electric driven device delivers brief 10ms sine wave taps to digit 3 of right hand. Stimulus strength was dynamically maintained at a perceptual threshold level (50% detection) with strong stimuli (100% detection) and null trials randomly interleaved. ISI 3secs. Neural and psychophysical data were integrated with 2-D spatial measures of finger position taken with custom optical sensors. *Data acquisition and analysis:* We recorded 306-channel MEG signals (Elekta NeuroMag VectorView) and extracted somatosensory evoked current dipoles by combining MEG with structural MR images<sup>1</sup>.



**Early activity generated in SI.**  
*Blue curve:* Time course (~50,250) ms of estimated equivalent current dipole (ECD) fit at ~60 ms from strong stimulus (100% detection, step=20ms, Qstep=10nAm). Vertical lines mark 0 and 60ms. The ECD was estimated after spatial filtering of later temporal components in the data. *Orange curve:* % goodness of fit of the ECD to the full data set (steps 10%). *MRI's:* Estimated ECD localization overlaid on structural MRI slices shows precise localization to the contralateral hand area of SI.



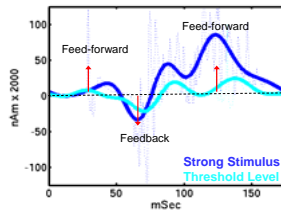
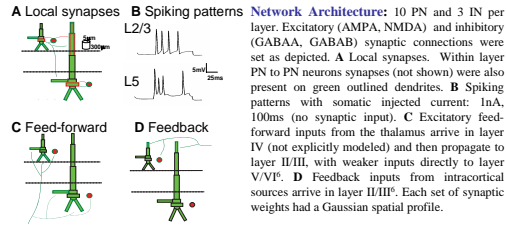
**Dipole polarity reflects direction of net current across cortical layers.**  
SI dipole average (n=7 subj.). Strong stimulus: 100% detection. Threshold level: 50% detection (std. error bars). The early (25ms) and late (100-175ms) positive dipole polarities imply net current flow out of the cortex (infra to supra granular layers), and the (70ms) negative dipole polarity implies a net current flow into the cortex (supra to infra granular layers). Magnitude reflects stimulus strength.



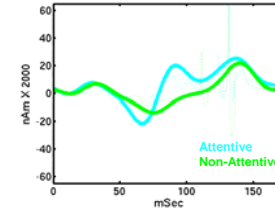
**Magnitude of SI dipole predicts perception.**  
Threshold level stimulus (50% detection) averaged over perceived and unperceived trials (n=7 subj.). A significant difference in magnitude emerges from 80-175ms, such that there is more "outward" current flow during perceived trials.

## Cortical Column Model Predicts Contributions of Feed-forward and Feedback Input to MEG Dipole Polarity

**Model Methods:** The primary neural generators of current dipoles estimated from MEG data are the summed post-synaptic activities within dendrites of large spatially extended pyramidal neurons (PNs)<sup>2</sup>. Our modeled SI cortical column included the morphology and physiology of PNs in Layers II/III and V. The PNs (green) were simulated with reduced multi-compartment equivalent cylinder models of somatosensory pyramidal neurons<sup>3</sup>, and included Hodgkin-Huxley type active ionic current kinetics in both the soma and dendrites<sup>4</sup>. Inhibitory interneurons (IN) (red) in the supra and infragranular layers were modeled as single compartment spiking neurons. Simulations performed with NEURON software. *Calculation of the Net Current Dipole:* The net current dipole was calculated as the net sum of the post-synaptic longitudinal current in each compartment of each PN multiplied by its arc length perpendicular to the cortical surface<sup>5</sup>.

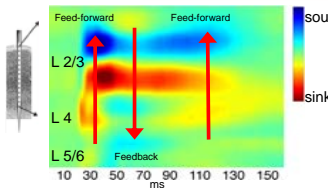


**Timing and location of synaptic inputs sets dipole polarity in the model.** Feed-forward synaptic activity simulated at ~25ms and ~125ms creates a net positive current dipole (infra to supra granular layers), and feedback input at ~70 ms creates a net negative dipole (supra to infra granular). Strong stimuli: ~5x stronger synaptic input than threshold level. Dotted curves: averaged data over trials (n=7); solid curves: low pass filtered average.



**Simulated changes in the level of "attentive state" reproduce the measured perceptual differences in dipole magnitude.**  
In attentive state, PNs have lower potassium current conductances,  $I_{Kp}$ ,  $I_{Kca}$  (an effect of high acetylcholine levels: present during attentive states), and greater feedback ("top-down") input, than in non-attentive state.

## Intracranial Monkey Data Validates Model Predictions



**Intracranial current source density (CSD) profile in monkey from brief finger stimulation.** Extracellular field potential activity recorded from 24 electrodes (125µm spacing) in the hand area (3B) of a Macaque monkey during a 10ms stimulus to the D5 digit. CSD is second spatial derivative of the signal. Current sinks (blue) correspond to net currents flowing into cells, and sources (red) to net currents flowing out of cells. The red arrows depict estimated net intracellular currents flowing within the layer 2/3 and 5 pyramidal neurons. The timing and direction of these intracellular currents is consistent with those creating the net current dipole from feed-forward and feedback inputs in the model. *CSD data generously provided by: M.L. Lipton, N. O'Connell, and C.E. Schroeder, The Nathan S. Kline Institute for Psychiatric Research, Orangeburg, New York.*

### References:

- Hämäläinen M, Hari, R. et al., 1993, *Reviews of Mod. Physics*, 65(2):413-97.
- Ikeda H, Wang Y, Okada YC. 2005, *Clin Neurophysiol.*, 116(4):827-41.
- Bush PC, Sejnowski TJ. 1993, *J. Neurosci. Methods*, 46(2):159-66.
- Mainen ZF, Sejnowski TJ. 1996, *Nature*, 382(6589):363-6.
- Murakami S, Hirose A, Okada YC. 2005, *J. Physiol.* 553(Pt 3):975-85.
- Fellman DJ, VanEssen DC. 1991, *Cerebral Cortex*, 1(1):1-47
- Hasselmo ME. 1995, *Behav. Brain. Res.*, 67(1):1-27.

### Conclusions:

- Combining MEG and structural MRI neuroimaging techniques during a tactile perception task in humans we found:
- An early somatosensory signal from 0-250ms, which localizes to the hand area of the primary somatosensory cortex.
  - Magnitude of peaks in the SI dipole reflect the size of the stimulus, and the polarity reflects current flow out of and into the cortex.
  - Signatures of perceptual competence are present early in SI, and are predicted by the SI dipole magnitude (80-175ms).

Our computational neural model of a laminated somatosensory cortex produces current dipoles with magnitudes and polarities that are realistic to the measured signals. The model results lead to several novel and testable predictions:

- The polarity (positive vs. negative) of the MEG dipole arises from the differential effects of feed-forward ("bottom-up") vs. feedback ("top-down") synaptic inputs on the net current flow within the PN dendrites.
- The greater dipole magnitude during perceived vs. unperceived trials arises from an increase in "attentive state", characterized by an increase in the strength of feedback input and the effects of an increase in the level of the neuromodulator acetylcholine (present during attentive states) on local network dynamics.

Intracranial laminar electrophysiological data from the monkey validates the model predictions.