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ECoG based cortical function mapping using general linear model

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Abstract—**Electrocorticography (ECoG) is an emerging tool to map brain functions in the context of neurosurgical intervention. Previous mapping methods based on the event related power spectrum are prone to noise. To improve the robustness of cortical function mapping, general linear model (GLM), which has been widely used in the analysis of functional magnetic resonance imaging (fMRI) data, is applied to bandpass filtered ECoG signals from each electrode. For a specific task, electrodes with best fitting parameters of the signal are identified, and the statistical significance of the fitting is mapped on the standard 3D brain model to provide a personalized map of sensorimotor functions. With the analysis of four patients' data, the proposed approach yields consistent results with those obtained by electrical cortical stimulation (ECS), while showing promising performance against noise.**

I. INTRODUCTION

To retain the normal brain function while resecting the epilepsy focus is a challenge in neurosurgery. Electrical cortical stimulation (ECS) is the gold standard for human brain function mapping in the context of neurosurgical intervention [1]. However, the post-surgery ECS sometimes may have false negative results or induce after-discharge. Besides, it also requires the operator to have rich clinical experience and the patients to fully cooperate during the test. Previous reports suggested that during limb movements, the spectral pattern of electrocorticography (ECoG) exhibited event-related desynchronization (ERD) in the alpha band [2] and event-related synchronization (ERS) in the gamma band [3]. The distribution of gamma ERD is more localized than the alpha ERD, hence the power change in the gamma band is more useful for brain function mapping. For example, ECoG high-gamma features have been employed to localize the sensorimotor areas of hand, tongue, foot [4], and the area for language processing [5].

However, due to the recording system noise, the environmental noise and the spike activity from epilepsy focus, the spectrum of ECoG sometimes shows aberrant patterns. As such, the results are unreliable if the mean power in the high-gamma band is simply used for cortical function mapping. To address this issue, the matching pursuit algorithm was employed to investigate the neural correlates of high-gamma oscillations in macaque local field potentials [6]. However, the algorithm was unable to distinguish between the task related brain activity and the activity induced by the environmental noise. Another line of studies used competitive expectation-maximization (EM) algorithm to estimate a gaussian mixture model (GMM) based on resting-state ECoG data [7-8]. Although it could reduce the effects of both the system and environmental noise, a training data set and an additional optimization procedure are required to determine the order of GMM. Moreover, the relationship between the GMM model components and brain activities is ambiguous.

Statistical parametric mapping (SPM) is a statistical framework based on general linear model (GLM), which can be used to detect task-related activations in brain areas. To date, SPM has become the most widely used software for fMRI data analysis [9]. In this study, GLM as the cornerstone of SPM is applied to the ECoG data analysis to find the relationship between a task sequence and the power change in certain frequency bands. By using this method, the statistical parametric maps for hand, tongue, foot movements are obtained from the ECoG data of four epilepsy patients. Compared with ECS, the GLM method shows higher robustness in cortical function mapping.

II. MATERIALS & METHODS

TABLE I
CLINICAL DATA OF THE PATIENTS

Patient	Age	Gender	Handedness	Grid	Electrodes
1	21	Male	R	Rt, Rp	64
2	9	Male	R	Lf, Lp, Lt	96
3	16	Female	R	Rf, Rp, Ro	96
4	14	Female	R	Rf, Rp	80

R=right; L=left; f=frontal; p=parietal; t=temporal; o=occipital

A. Subject

Four subjects with intractable epilepsy underwent temporary placement of a subdural electrode array to localize the epileptic seizure focus before surgical resection. The locations of the electrode arrays were determined according to clinical needs. Table I shows the detailed information of the subjects. All the four subjects had

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electrodes placed over the sensorimotor cortex. The subjects gave informed consent prior to participation and the experiment protocol was approved by the institutional ethics committee. The tests in this study were carried out during stable interictal periods; there were no epileptic seizure within two hours before or after the tests. Each subject's electrode location was projected on an MNI standard 3D brain model by using lateral skull radiographs and a Matlab toolbox LOC [10].

B. Electrical Cortical Stimulation

ECS mapping used the Ojemann cortical stimulator with 1s to 5s trains of 60Hz alternating-polarity square-wave pulses. For each electrode pair the stimulus intensity started from 1mA and increased in a 1mA interval until one of the following requirements was fulfilled: (1) the subject reported any unpleasant sensations (2) the stimulus intensity increment reached 15mA (3) disruption of motor function was observed on the subject during voluntary movements (4) after-discharge was induced.

C. Experiment Protocol & Data Collection

There were nine blocks in the experiment, each lasting 30s. The subject was instructed to relax for 10s at the beginning of each block, and then to execute a voluntary

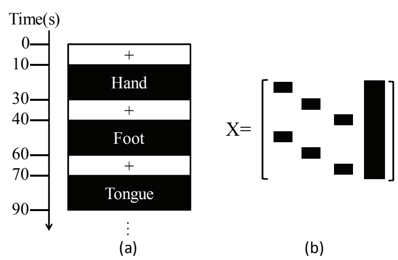

Fig. 1. (a) Scheme diagram of the experiment (b) Design matrix (black and white represent 1 and 0, respectively)

movement task of the contralateral fingers, tongue or bilateral toes for 20s. The three types of movement task repeated three times in an alternated fashion. Fig. 1a shows the scheme diagram of the task sequence. The ECoG data were recorded by a long-term monitoring EEG system (Bio-Logic®, San Carlos, USA) sampled at 1024Hz, along with two digital cameras recording subjects' behavior from different angles simultaneously. The ground and reference electrodes were placed on the scalp. During the test, the subjects followed the instruction presented on the screen to do a designated motor task or to relax. The trigger signal for each screen instruction was delivered to one channel of the amplifier through a photocoupler to synchronize the recording.

D. Analysis

$$Y = X\beta + \epsilon \qquad (1)$$

The general linear model (GLM), which has been widely used in fMRI studies, is employed to analyze the ECoG data. Eqn.1 gives the basic equation of GLM. In fMRI data analysis, Y is the response variable (BOLD signal) of each scan. X, which has one row per observation and one column per stimulus type, is the design matrix. In this study, Y is the power envelope of one ECoG electrode in a certain frequency band at the sample point J. The envelope is defined as the square of the band-pass filtered data. X is formed similarly as in fMRI studies. X has three columns indicating the timetable of the three types of voluntary movement, and a constant column(Fig. 1b). β is the vector of the model parameters that need to be estimated. The error term ϵ consists of independent and identically distributed normal random variables with zero mean and variance σ^2 [11]. Consequently, the GLM in our study can be written in the following matrix form:

$$\begin{pmatrix} Y_1 \\ \vdots \\ Y_j \\ \vdots \\ Y_J \end{pmatrix} = \begin{pmatrix} x_{11} & x_{12} & x_{13} & 1 \\ \vdots & \vdots & \vdots & \vdots \\ x_{j1} & x_{j2} & x_{j3} & 1 \\ \vdots & \vdots & \vdots & \vdots \\ x_{J1} & x_{J2} & x_{J3} & 1 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \vdots \\ \epsilon_j \\ \vdots \\ \epsilon_J \end{pmatrix} \qquad (2)$$

β can be estimated by using ordinary least squares method [11]. The t-statistic and p-value of each electrodes' β can then be computed using the t-test for β. For each electrode, we obtain t_{hand}, t_{foot} and t_{tongue} for β_1, β_2, β_3, respectively. The corresponding p-values are also calculated to threshold the t-statistics: if the p value is larger than 0.05, the corresponding t-statistic of that recording electrode is replaced by zero. Finally, for the same task, the t-statistics are normalized among all the electrodes to yield more prominent patterns:

$$\tilde{t}_{handi} = \frac{t_{handi}}{\max\,(t_{hand})} \qquad (3)$$

where $t_{hand} = [t_{hand\,1}, t_{hand\,2} \cdots t_{handn}]$, n denotes the number of electrodes, $\tilde{t}_{foot}$ and $\tilde{t}_{tongue}$ were calculated in a similar way.

The high gamma band is typically defined as the frequency band above 60Hz [3]. In case of possible influence of line power harmonics (100Hz, etc.), we use the power between 60Hz and 90Hz for high gamma GLM mapping. After bandpass filtering and the envelop extraction of the ECoG raw signals, the t-statistics of the three tasks (hand movement, tongue movement and foot movement) are computed in conjunction from GLM model. The larger the absolute value of a t-statistic, the more significant change is present at the corresponding electrode.

There have been several studies using power spectral density (PSD) method for functional mapping based on high gamma ECoG signal [12-14]. In these studies, functional areas are distinguished based on the difference between the average PSD during tasks execution and during relaxation. For comparison, power spectral density (PSD) method were also applied to our ECoG data. All data analysis programs used in this study were developed in MATLAB (Mathworks, MA, USA).

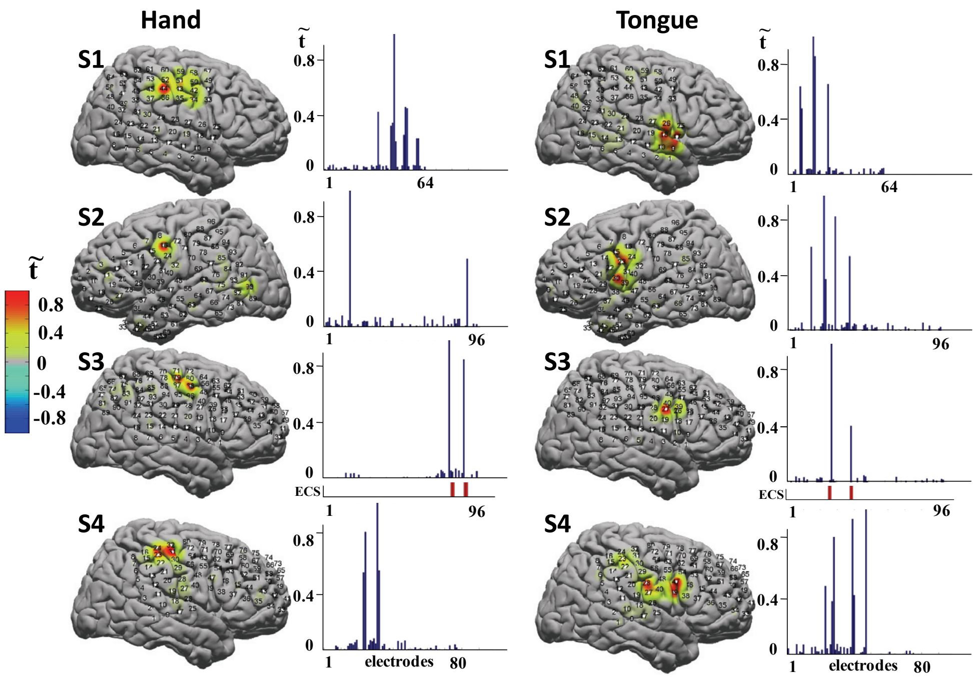

Fig. 2. GLM mapping results of the functional areas for hand (left column) and tongue (right column). Comparison between normalized t-statistics from GLM Mapping results (blue) and ECS Mapping results (red) is also shown for Subject 3

III. Results

A. Sensorimotor Cortex Mapping

GLM mapping results of the four subjects are shown in Fig. 2. The brain topographies are obtained by superimposing the normalized t-statistics on the MNI standard brain model. The bar graphs next to each topography indicate the normalized t-statistic of each electrode in the order of the electrode number.

From the $\tilde{t}$ distribution plot on MNI 3D brain model, it can be seen that the GLM mapping results are consistent with the physiology-anatomy locations corresponding to the tasks. The areas with significantly high $\tilde{t}$ values are concentrated at those plausible functional centers on sensorimotor cortex, which also matches the previous findings in an fMRI study [15]. Moreover, the task related(R) areas and unrelated (NR) areas can be obviously distinguished from GLM mapping. Due to the lack of electrodes placed over foot motor cortex area, no significant function-related results of the foot movement are available based on the GLM model, and thus the distribution of $\tilde{t}$ is not shown.

B. Comparison of GLM Mapping and ECS Mapping

Comparing the ECS mapping with GLM mapping for the tongue/hand functions of Subject 3, the results show good consistency. Electrodes involved in positive responses (tongue being numb or hand being tremble) during ECS matches well with the electrodes with significantly high t-statistics obtained by GLM (see Fig.2).

C. Prominent Frequencies of Different Cortical Functions

To observe frequency response patterns, we obtain the power envelopes in different bands and then fit them with GLM to compute the t-statistic for each band. There are 12 subbands selected in this study, including the theta (4~7Hz), alpha (8~13Hz), beta (15~30Hz), low gamma (30~60Hz) and high gamma (60~120Hz, with 10Hz for each bin) bands.

GLM mapping results shown in Fig. 3 demonstrate distinguishable spectral features. The positive t-statistic indicates significant power increase in the gamma band when executing different tasks. By contrast, the negative t-statistic in the alpha (8Hz~13Hz) and theta (4Hz~7Hz) bands indicate significant power decrease in these two frequency bands during motor tasks, which is consistent with the findings in previous studies on ECoG [2-3].

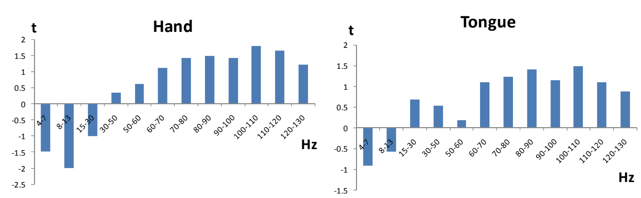

Fig. 3. T-statistic in each frequency band of the two electrodes with max t-statistic in High Gamma band (Subject 2 in Fig. 2) during hand movement task and tongue movement task.

D. Comparison of the GLM and PSD methods

An ECoG data set with 90s duration (there is an abrupt noise around 40s in the signal) was used to investigate the dependency of GLM and PSD on the data length. For this data set the data length is varied from 30s to 90s with a 1s interval, and in each case these two methods was applied to obtain the event-related spectral power and t-statistic, respectively.

Compared with the PSD method, the advantage of GLM model is its better tolerance to noise. Fig. 4 shows that the t-statistic based on GLM algorithm is less influenced by noise than PSD method. As the red dashed line indicates, simply using average PSD in gamma-band might lead to false positives when there is strong noise present, such as the occasional spectral impulse due to the displacement of electrodes, movement of subjects or environmental noise. At the early stage of the task, the strong noise leads to an abrupt change in high-gamma band and increases the average PSD of a task-unrelated electrode, which is even higher than the average PSD of task-related electrode. This type of false positive can hardly be prevented, but it can be smoothed out after averaging with long period of signals with better quality or can be removed manually by careful visual inspection.

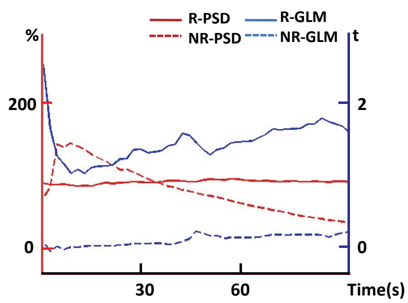

Fig. 4. The effect of strong noise on the PSD method and GLM. (R = task related electrode ; NR = task unrelated electrode)

By contrast, the t-statistic from GLM algorithm, shown as blue curves, is merely slightly affected by the occasional occurrence of large noises. Moreover, the discrimination of the t-statistic between task-related electrodes (blue-solid) and task-unrelated electrodes (blue-dash) is identically good under all the cases.

IV. Discussion & Conclusion

GLM is a statistical model with the design matrix constructed by the task sequence. By applying regression analysis on the model, for each electrode we can obtain a t-statistic that represents the significant brain activities under different tasks. As such, the adverse effect of the noise is largely avoided and the result of the cortical function mapping is rendered more stable. In addition, the t-statistic from regression analysis can also be used to assess whether the power in certain frequency band rises or falls significantly along with the task. This may provide a new tool to explore oscillatory networks underlying different cognitive tasks [16]. Moreover, we can obtain the t-contrast map by using GLM to see the ECoG power contrast between different conditions in an experiment, as that has been done in fMRI imaging.

In future studies, it is presumable that the trial-based design would produce even more robust result and lead to higher t-statistics. In this respect, the high temporal resolution of the ECoG offers the possibility of getting a time-frequency featured template of each task from the trial-based design. This template function could play a similar role as hemodynamic response function in fMRI data analysis, which may yield more accurate mapping of cortical functions.

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References

[1] M. M. Haglund, et al., "Cortical localization of temporal lobe language sites in patients with gliomas.," Neurosurgery, vol.34, pp. 567-576, 1994.

[2] N. E. Crone, et al., "Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. I. Alpha and beta event-related desynchronization.," Brain, vol.121, pp. 2271-2299, 1998.

[3] N. E. Crone, et al."Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. II. Event-related synchronization in the gamma band.," Brain, vol.12, pp. 2301-2315, 1998.

[4] E. C. Leuthardt, et al., "Electrocorticographic frequency alteration mapping: a clinical technique for mapping the motor cortex.," Neurosurgery, vol.60, pp. 260-271, 2007.

[5] A. Sinai, et al., "Electrocorticographic high gamma activity versus electrical cortical stimulation mapping of naming." Brain, vol.128, pp. 1556-1570, 2005.

[6] S. Ray, et al., "Neural correlates of high-gamma oscillations (60-200 Hz) in macaque local field potentials and their potential implications in electrocorticography.," J Neurosci, vol. 28, p. 11526-36, 2008.

[7] G. Schalk, et al., "Real-time detection of event-related brain activity.," Neuroimage, vol.43, pp. 245-249, 2008.

[8] P. Brunner, et al., "A practical procedure for real-time functional mapping of eloquent cortex using electrocorticographic signals in humans.," Epilepsy Behav, vol.15, pp. 278-286, 2009.

[9] C. Lueck, et al., The colour centre in the cerebral cortex of man Nature 1989; 340:386-389.

[10] K. J. Miller, et al., "Cortical electrode localization from X-rays and simple mapping for Electrocorticographic research: The "Location on Cortex" (LOC) package for MATLAB.," J Neurosci Methods, vol.162, pp. 303-308, 2007.

[11] K. J. Friston, et al., "Statistical parametric maps in functional imaging: a general linear approach," Human brain mapping, vol.2, pp. 189-210, 1994.

[12] K.J. Miller, et al., Real-time functional brain mapping using electrocorticography. Neuroimage, 2007. 37(2): p. 504-7.

[13] L.J. Miller, et al., Spectral changes in cortical surface potentials during motor movement. J Neurosci, 2007. 27(9): p. 2424-32.

[14] S. Zanos, et al., "Electrocorticographic spectral changes associated with ipsilateral individual finger and whole hand movement.," Conf Proc IEEE Eng Med Biol Soc, vol.2008, pp. 5939-5942, 2008.

[15] C. Stippich, et al., Motor, somatosensory and auditory cortex localization by fMRI and MEG. Neuroreport, 1998. 9(9): p. 1953-7.

[16] C.M. Gaona, et al., Nonuniform High-Gamma (60-500 Hz) Power Changes Dissociate Cognitive Task and Anatomy in Human Cortex. J Neurosci, 2011. 31(6): p. 2091-2100.