

Mapping and assessment of epileptogenic foci using frequency-entropy templates

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Much effort has been devoted to developing analysis methods of subdural electroencephalogram and depth electrode recordings of epileptic patients being evaluated for surgical resection. The general approach is to investigate the brain activity at different locations as recorded by the different electrodes in an attempt to localize the epileptogenic focus or foci. Currently, most of the methods are based on the notion that epileptogenic brain activity is associated with changes in synchronization and in complexity. Here we present a method that is based on the temporal dynamics combined with the spectral distribution of energy in terms of frequency-entropy (FE) templates. The FE templates are based upon maximum information partitioning into a set of frequency bands. The FE template is calculated by wavelet packet decomposition followed by an application of the best basis algorithm minimizing the entropy cost function. A comparison between two FE templates is performed by a special quantitative similarity measure according to the overlap in the partitioning into frequency bands and weighted by the bands' entropy. For localization of the epileptogenic foci, the templates of each electrode during the interictal period are compared with a representative template evaluated from the ensemble of all electrodes during the ictal period. We suggest associating the locations that reveal high template similarity to the ictal template with the epileptogenic foci. To test the method and the underlying assumptions, we perform retrospective analysis of the recorded brain activity, from both grid and depth electrodes, from 11 patients suffering from medically intractable epilepsy. Application of the ictal-interictal FE template similarity analysis revealed regions in the epileptic brain in which the interictal characteristics are highly similar to those of the ictal period. To assess the foci we compared the interictal templates of the different electrodes to each other, forming interelectrode similarity matrices. Investigation of these similarity matrices revealed the existence of a single distinct subcluster of electrodes with high interelectrode similarity in the brain activity of seven patients (type-I activity), and the existence of multiple high interelectrode similarity subclusters in the activity of four patients (type-II activity). Comparisons of the analysis results to the medical presurgical evaluations and the outcomes of the surgical resections suggest that the method may be helpful in the chronic evaluation of the epileptogenic zone before operation, and in some cases (type-I activity) without the need to wait for seizures to occur.

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I. INTRODUCTION

Epilepsy is a brain disorder characterized by recurrent, unprovoked seizures that affects 1–2 % of the population. In about one-third of patients, medical therapy fails, leaving surgery as the only viable option. When seizures arise from the temporal lobe or a discrete lesion, the success rate with surgery is high (65–85 %). In other cases, the success rate of surgical intervention drops precipitously (to less than 25%) [1–3].

For over 100 years, surgical management of epilepsy has been guided by the tenet that a limited region of the brain—the epileptogenic zone (the focus)—might be responsible for causing seizures. Accordingly, neurosurgical manipulations have been directed toward either its removal or its destruction.

The practical challenge of resective surgery is to remove all relevant brain sites connected with the focus (but no more

than necessary) and at each location to resect the minimum (yet sufficient) volume to prevent seizure events. Hence, the diagnostic tasks before surgery include mapping (localization) of the epileptogenic foci, and assessment of their functional properties and their effect on activity in other parts of the brain.

Localization of the epileptogenic zone has traditionally depended on scalp electroencephalograms (EEGs)—recordings of electrical activity from scalp electrodes. However, these recordings provide partial information, as the electrodes are spatially dispersed, are separated from the brain by bone, muscle, and soft tissue and are subject to inherent high noise (from skin activity). Consequently, the precise location of the epileptogenic zone often remains uncertain after analyzing scalp EEG recordings alone. In these cases further evaluations rely on direct brain recordings [1–9], using arrays of subdural EEG (ECoG) recordings—electrodes placed directly on the surface of the brain (Fig. 1) and/or recordings from depth electrodes that are inserted to record deeper parts of the brain such as the hippocampus.

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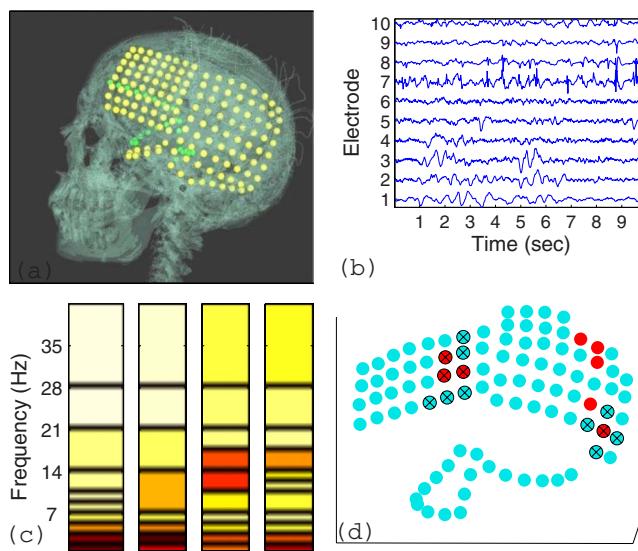


FIG. 1. (Color online) The analysis approach. (a) Example of subdural grid of electrodes that are used for epilepsy evaluation. Electrodes are 3.4 mm in diameter and are spaced by 10 mm. Each electrode records the voltage (local field potential) at a sampling frequency of 400 Hz, digitally resampled to 112 Hz, and low-pass filtered at 40 Hz. (b) Voltage traces of ten electrodes (taken from a recording of a set of 96 electrodes) showing a time window of 10 s of interictal activity. (c) Examples of the frequency-entropy (FE) templates for four different electrodes. The \hat{y} axis is for the range 0–42 Hz and it is divided according to the frequency bands selected by the wavelet packet decomposition (for simplicity, only five levels of decomposition are shown here) and best basis algorithms for maximum information representation of the signal (see text). Each color indicates the corresponding entropy M_n of each band (n). (d) Illustration of the analysis results for patient 04: The method predicted that the epileptogenic focus resided under the red (darker) electrodes. During surgery, resection of the area under the crossed circle electrodes was performed. Surgery in this example was only partially successful (see text).

The electrodes are spatially distributed over the suspected focal regions (as determined from conventional scalp EEG recordings and other imaging techniques such as magnetic resonance imaging and positron emission tomography), and are kept in place for a long period of time (1–3 weeks) so that the focus or foci can be localized by analyzing recorded signals that include several seizure episodes.

The common procedure for localization of epileptogenic foci is visual inspection and interpretation of the intracranially recorded signals by experienced clinicians. It should be noted that the visual inspection is accompanied by complementary anatomical information using various imaging techniques and evaluations of brain functions by neuropsychological and cognitive testing. This procedure is a reliable clinical procedure for temporal lobe epilepsy, but is less successful for other neocortical epilepsies.

Several advanced analysis methods of the recorded activity have been developed over the years [5–22] (including specific use of wavelet packets [9,10]). With the use of spectral analysis, it has been shown that distinct activity at specific frequency bands (such as the delta band [14,15] or gamma band [16,17]) can help in the localization and later-

alization of the epileptogenic zone. Towle *et al.* [18] have shown that some meaningful information on localization can be obtained by coherence, a measure of spectral correlation between two signals. Synchronization has been suggested as a marker of epileptogenicity [19,20], while others have concentrated on additional nonlinear chaos techniques such as measurement of complexity loss [21,22]. However, at present, none of the existing analysis methods is usually implemented as a routine part of the clinical evaluation.

The approach presented here is motivated by the notion that epileptogenic brain activity is also related to global and local changes in the temporal dynamics and spectral characteristics of the brain activity that are reflected in the frequency-entropy (FE) templates at different locations. By FE templates we mean a maximum information (minimum entropy) representation of the temporal dynamics in terms of set of frequency bands and the relative information (entropy) at each band. The FE template is calculated by wavelet packet decomposition (WPD) followed by an application of the best basis algorithm using maximum information cost function [23]. The comparison between two FE templates is performed by a special quantitative similarity measure according to the overlap in the partitioning into frequency bands and weighted by the bands' entropy. For localization of the epileptogenic foci, the templates of each electrode during the interictal period are compared with a representative template evaluated from the ensemble of all electrodes during the ictal period. We suggest associating the locations that reveal high template similarity to the ictal template with the epileptogenic foci. To assess the foci we compared the interictal templates of the different electrodes to each other. More specifically, we constructed similarity matrices that represent the template similarity between each pair of electrodes and investigated these matrices using clustering algorithms. The idea was to check whether there is a FE template that is unique to an epileptogenic focus during the interictal period. Thus, the focal electrodes would be concentrated in a cluster of high interelectrode similarity.

To test the method we performed a retrospective analysis of ECoG and depth electrode recordings from 11 patients (five from the University of Chicago and six from the University of Michigan) who subsequently underwent surgical resection of presumed epileptogenic foci. The location of resection, clinical outcome (in terms of Engel's classes) and activity type (I single focus and II multi foci) are summarized in Table I. Seven patients had a successful operation (Engel's class I or II [24]), for two patients the operation was partially successful (Engel's class III), and in the case of two other patients the operation failed (Engel's class IV). We found that for all the successful cases (patients 01, 02, 03, 07, 08, 09, and 10) the foci predicted by our method matched the resected ones. In the partially successful (patients 04 and 05) or failed (patients 06 and 11) cases, our method identified additional foci that had not been resected.

We identified two types of brain activity: seven patients were identified as having type I, simple activity, and four patients were identified as having type II, complex activity. In the cases of type-I activity we found distinct locations where the FE template during the interictal period bore significant resemblance to the ensemble FE template during sei-

ture. The same locations also showed high interelectrode similarity during the interictal period and matched the locations that were determined as focal by the clinicians.

Our interpretation of these results is twofold. The strong resemblance to the ensemble FE template during seizure and the high interelectrode similarity of the focal locations suggest the existence of a unique FE template that can be found in the focal locations during the interictal period. The same FE template then becomes dominant during the seizure. The fact that the rest of the locations (even adjacent locations) show very low interelectrode similarity during the interictal period, as well as very low resemblance to the ensemble FE template during the seizure, suggests that the high interelectrode similarity by itself could be considered as a marker of abnormal activity.

In the cases of type-II activity, we found high interelectrode similarities throughout the recorded regions, which could be understood as markers of diffused abnormal activity in the form of multifocal epilepsy or epileptogenic network. Thus, tracking the origin of the epileptic activity in these cases is more complex.

II. EXPERIMENTAL SETUP

The signals analyzed here consist of ECoG grids and depth electrode signals recorded from 11 medically intractable epilepsy patients at the hospitals of the University of Chicago (five patients) and the University of Michigan (six patients) during the presurgical evaluation. The grid electrodes were spatially distributed over (and the depth electrodes were inserted to record from) the suspected focal region (see Fig. 1), so that the focus or foci could be localized by analyzing the ensemble of signals. The amplitude of the signals records the electrical voltage at each electrode (arguably recording local field potentials [25]). The voltage signals were initially recorded at 400 Hz, simultaneously digitized at 112 Hz, and low-pass filtered up to 40 Hz. The recordings were first screened to exclude artifacts. Two seizures per patient were analyzed. The time segments of the interictal activity that were analyzed vary between minutes and hours depending on the data available for each patient. This study was conducted in accordance with established standards on the ethical treatment of human research subjects and was approved by the institutional review boards at the University of Michigan and the University of Chicago.

III. ANALYSIS METHODS

A. The frequency-entropy templates

The ECoG signals were first analyzed by means of WPD to calculate all the possible wavelet packet basis representations. Then, using the best basis algorithm, a minimum entropy (maximum information) basis (frequency partitioning) was assigned to each electrode for each short time segment (see below). This analysis was developed in Ref. [23] and was used to show that, by ensemble and temporal averaging of the spectral profiles of all the electrodes and above an essential time window of about 2 min, the interictal brain activity (between seizures) can be partitioned into patient-

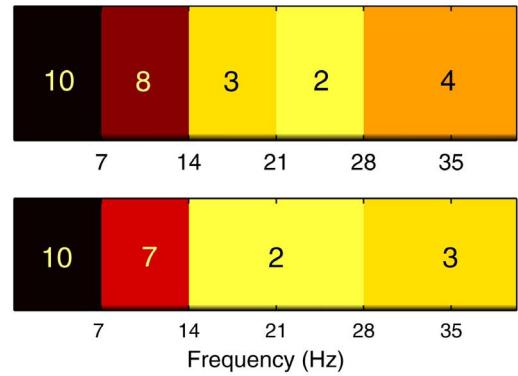


FIG. 2. (Color online) *Similarity measure example*. We show a simplified example of a calculation of the similarity between two frequency-entropy (F-E) templates. The colors and numbers represent the information cost of the template subbands. Only the two left (low frequencies) and right (high frequencies) subbands participate in this calculation, as they are common to both templates. Therefore, the similarity measure between these two templates [see Eq. (2)] is

$$S = \frac{1}{6} \cdot \frac{10/27}{10/22} + \frac{1}{6} \cdot \frac{8/27}{7/22} + \frac{1}{3} \cdot \frac{3/22}{4/27} \approx 0.6.$$

and state-specific frequency-entropy (FE) templates.

The WPD is computed by iterating a set of low- and high-pass filters. The functions underlying the expansions of the filters are “wavelets” (“mother”) and “scaling” (“father”) functions [26]. Here the WPD was utilized using the “Coi-flet” of order 1 as a mother wavelet [26]. The WPD generates an overcomplete representation of the signal. Thus, the best basis algorithm was used to select the minimum entropy partitioning, i.e., a single set of nonoverlapping frequency subbands that spans the frequency spectrum [23,27,28]. In this algorithm, each wavelet packet function (k) is assigned an information cost value

$$M_k(q) = -q \log_2(q), \quad (1)$$

where q is the normalized energy of the (k) wavelet packet. The total information cost M_n (entropy) of a frequency band (n) is obtained by summing over all the packets in the band. The algorithm is designed to select the set of subbands $\{n\}$ with the lowest possible information cost. This set of bands defines the best basis of the specific analyzed time window of the specific electrode. The FE template $\{(n^i, M_n^i)\}$ of an electrode signal (i) recorded during a certain time window is composed of the frequency subbands $\{n^i\}$ as determined by the best basis algorithm and their corresponding entropies $\{M_n^i\}$ [see examples in Figs. 1(c) and 2]. The FE template of an ensemble of signals $\{(n^{i_l}, M_n^{i_l})\}$ is computed by averaging the information costs of every possible WPD subband over the ensemble, i.e., $M_n^{i_l} = \overline{M_n^i}$, followed by the best basis algorithm, as described in [23].

B. The similarity measure

The similarity between two FE templates $\{(n^i, M_n^i)\}$ and $\{(n^j, M_n^j)\}$ is quantified by calculating the entropy-weighted similarity measure $S(i, j)$, defined as

$$S(i,j) = \sum_{n_{ij}} \frac{\min(P_n^i, P_n^j)}{\max(P_n^i, P_n^j)} W_n, \quad P_n^i = \frac{M_n^i}{\sum_{n_i} M_n^i}, \quad (2)$$

where $n_{ij} \in (\{n^i\} \cap \{n^j\})$ and $n_i \in \{n^i\}$. In this definition, every joint frequency band (a band that exists in both templates) contributes its frequency width W_n , i.e., the number of basis coefficients in band (n) divided by the total number of basis coefficients, and is weighted by the ratio of its relative information content P_n . Note that the similarity measure defined in this way assumes values between 0 (no similar frequency bands) and 1 (identical templates). See the example in Fig. 2.

C. The similarity bars: Localization of the epileptogenic foci

The FE templates of each electrode during the interictal activity were compared with the representative ensemble FE template during seizure (Fig. 3).

The representative ensemble FE template is a template that is calculated over the whole ensemble of signals in the following manner. First, all the possible WPDs of every signal are calculated—the entropies of all the possible frequency subbands of every signal. Next, for every frequency subband, a new mean entropy is calculated by averaging the entropies of this subband over all the signals. Then, using the best basis algorithm and minimizing the new mean entropies, a single basis representation is chosen. Thus, the ensemble FE template consists of the chosen frequency subbands together with their corresponding mean entropies.

For each electrode, the similarity between its FE template at each time window (typically 1024 samples long, about 9 s) and the ictal ensemble FE template was calculated. Then the similarities over several minutes (many time windows) were averaged and the results are presented in terms of a similarity bar, as is also shown in Fig. 3. From this figure it is evident that the interictal activity of a specific set of electrodes exhibits high similarity to the ictal ensemble FE template. From a different angle, the results show that the FE template of the brain activity during seizure becomes similar to the interictal template of these special (or significant) electrodes.

We propose to associate the epileptogenic foci with the significant electrodes identified in the similarity bars—the electrodes with higher similarity as explained in Fig. 3. The results shown in Fig. 3 reveal that there are two types of similarity bars: simple bars (type-I activity) with one pronounced cluster of significant electrodes [Figs. 3(b)–3(d)], and more complex bars (type-II activity), with several groups of significant electrodes [Figs. 3(e) and 3(f)]. The similarity bars of six out of the seven patients whose operation was successful were found to be of type-I activity (patients 01, 02, 03, 07, 09, and 10) and their clusters of significant electrodes matched the resected foci. Strictly quantitatively speaking, the clusters of significant electrodes of type-I activity were contained in the resected locations during surgery. The operations of three out of the four patients with type-II brain activity (patients 04, 05, and 06) were only partially successful or failed (Engel's classes III and IV). The

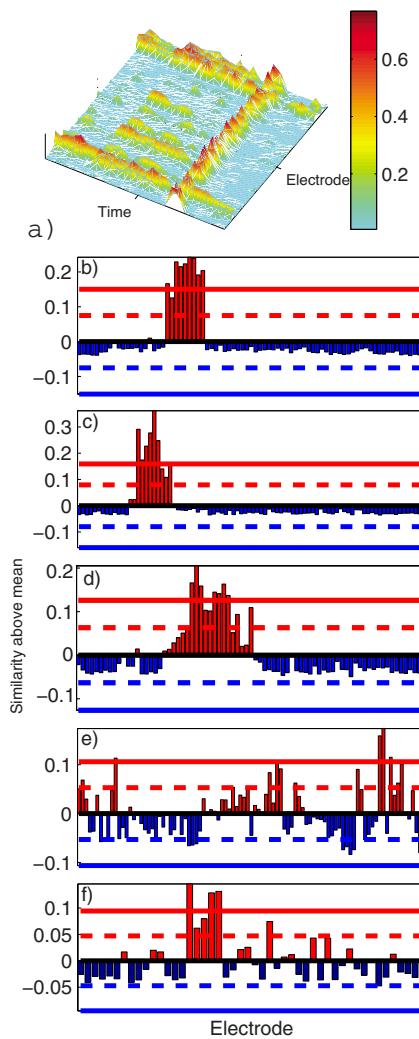


FIG. 3. (Color online) The similarity bars. (a) The similarity between the best bases of each electrode for each time window (9 s) and the ensemble FE template during a seizure. Time is along the \hat{x} axis and the electrodes are located along the \hat{y} axis. The height in the \hat{z} direction is proportional to the computed similarity and is also colored accordingly—cyan (bright) to red (dark) for 0 to 1. The seizure activity is marked by high similarity between the electrodes. To reveal the focal electrodes, we calculate the time-averaged similarity between the FE templates and the ensemble seizure FE template, for every electrode, during the interictal period. The vertical bars indicate the similarity of each electrode relative to the mean similarity. Red (blue) [brighter (darker)] bars are for similarity above (below) the mean. The electrodes are ordered according to the order of the similarity matrices (see text and also Fig. 4). The dashed horizontal lines show ± 1 standard deviation from the mean (STD) and the solid lines are for ± 2 STD. The similarity bars in (b), (c), and (d), of patients 01, 02, and 03, respectively, which exhibit a single, tight cluster of significant electrodes, are identified as type-I. The similarity bars in (e) and (f), of patients 04 [Fig. 1(d)] and 06, are identified as type-II, as they exhibit a very different (complex) structure. The significant electrodes in (b), (c), and (d) match the resected foci. In (e), the significant electrodes form three clusters.

analysis for these patients revealed the existence of significant electrodes that had not been resected during surgery.

D. The interelectrode similarity matrices: Assessment of the epileptogenic foci

For assessment of the epileptogenic foci, we also investigated the averaged interelectrode similarity matrices during the interictal period. The element (i, j) of a similarity matrix for a given time window is the similarity between the FE templates of electrodes (i) and (j) within this time window. To calculate the mean similarity matrices we averaged many successive similarity matrices each for a time window of 1.5–2.5 min according to the data available. Examples of the mean similarity matrices (ordered by the dendrogram algorithm) of six patients during the interictal period are shown in Fig. 4. The matrices of type-I patients exhibit a single cluster that corresponds to the cluster of significant electrodes in the similarity bar and matches the resected focus.

From a dynamical systems perspective, these results imply the existence of a single functional focus that has its own characteristic FE template (during the interictal period) and is significantly different from the FE templates of all other electrodes. From a clinical perspective, these findings also demonstrate that for type-I patients it may be possible to accurately identify the epileptogenic foci by analysis of interictal activity alone. In these cases, the epileptogenic zone will be reflected in the single evident cluster in the interictal interelectrode similarity matrix, and no comparison to ictal activity will be necessary. Usually the functional focus in the similarity matrix also corresponds to a single localized epileptogenic zone (Fig. 5). However, for some patients the electrodes of the functional focus can also be located at more than one epileptogenic zone. In this situation these zones have the same FE template and hence can be viewed as one functional focus.

In contrast, the matrices of type-II brain activity show more complex organizations of several clusters, each characterized by its own FE template [Figs. 4(d)–4(f)]. Thus, the complex organizations of the similarity matrices of this group suggest that there are several functional foci, each having its own characteristic dynamics. Hence, it implies the existence of a multifocal epileptic network.

As pointed out earlier, with one exception (patient 08), surgical resections in patients with type-II activity were either partially successful in treating the epilepsy, or failed altogether. It is known that the identification of the epileptogenic foci of patients with multifocal epilepsy is more challenging [29]. Investigating the similarity matrices for these patients during seizures, we found that they are also composed of several clusters, implying that for type II it is not sufficient to use a single seizure FE template as is done for type I. Instead, one has to identify the electrodes with high similarity to the seizure ensemble FE template of each of the clusters separately. Indeed, we found that, by calculating the similarity bars by comparing separately to the templates of each seizure cluster, we were able to identify additional significant electrodes [e.g., patient 05 in Fig. 6(f)].

IV. COMPARISON TO SURGICAL OUTCOME

Examples of comparison between the prediction of the method and the results of the surgical resections for six pa-

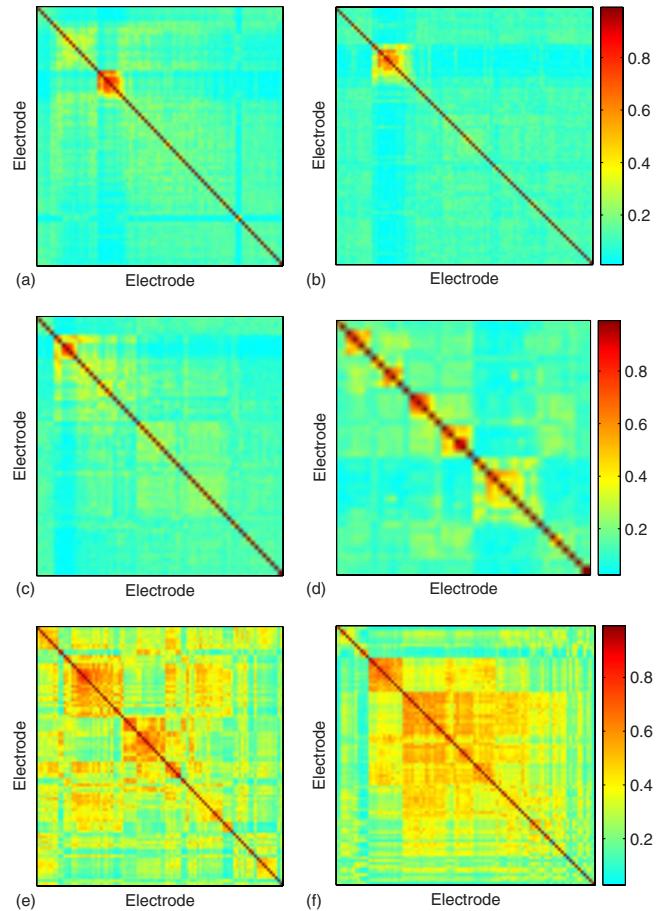


FIG. 4. (Color online) Interelectrode similarity matrices. We show six representative examples of similarity matrices, evaluated for the interictal activity. The matrices were ordered by applying the dendrogram clustering algorithm, which reorders the matrix so that electrodes with higher similarity appear as distinct clusters. The colors correspond to the level of the similarity, from cyan (bright) for 0 to dark red (dark) for 1. The six examples illustrate the existence of the two classes of matrices. The matrices in (a), (b), and (c) (patients 01, 02, and 07, respectively) that exhibit a single distinct cluster belong to type-I [the matrices of patients 01 and 02 correspond to the similarity bars in Figs. 3(b) and 3(c), respectively]. The matrices in (d), (e), and (f) (patients 08, 04, and 05, respectively), which belong to type-II, are characterized by multiple clusters of electrodes. The complex structure of these matrices is concordant with their complex similarity bars [the one for patient 04 is shown in Fig. 3(e)].

tients [patients 01, 02, 05, 09, 10, and 11, in addition to the results for patient 04 shown in Fig. 1(d)] are shown in Fig. 6. For patients 01, 02, 09, and 10, who showed type-I brain activity and whose operation was successful, the predicted electrodes match the resected foci very well. In the case of patient 05, who showed type-II brain activity and whose surgery was partially successful, only a partial match with the resected electrodes was found. More specifically, one resected location was not identified by the analysis as a focus and one identified location was not resected. In the case of patient 11 the epileptologist suspected an epileptogenic zone that matched our method's suspected location, but this region could not be completely removed during surgery. In the case

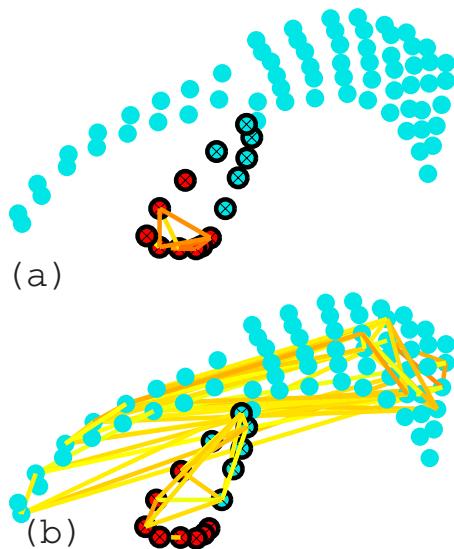


FIG. 5. (Color online) Interictal and ictal interelectrode similarity network. Interelectrode similarities for patient 01 (type-I) are drawn as lines connecting the electrodes' physical locations (for clarity, only similarities above 0.6 are shown), thus projecting the similarity network. The significant electrode locations as depicted by our method are colored in red (darker). Crossed circles represent electrodes located upon subsequently resected brain regions. (a) The interictal similarity network shows high connectivity between the electrodes of the suspected epileptogenic zone and low connectivity elsewhere. The functional focus electrodes, as taken from the similarity bar and matrix, are also located in a single physical area. (b) During the later part of the ictal period, high interelectrode similarities are generated, leading to the formation of an extended network, while the connectivity between the electrodes of the functional focus has decreased significantly.

of patient 04 [Fig. 1(d)], who has type-II brain activity, the analysis identified an additional location suspected to be epileptogenic. In the cases of patients 03 and 07 (type-I activity) our method's suspected electrodes matched the resected locations and the operations were successful. In the cases of patients 06 and 08 (type-II activity), for patient 08 our method's suspected locations were resected and surgery was also successful, but for patient 06 our method's suspected locations were different from those resected and surgery failed. The patients' activity types are summarized in Table I, together with additional clinical information.

V. DISCUSSION AND CONCLUSIONS

Based on the analysis results, we suggest the following interpretation. For normal brain activity, it is reasonable to expect that the FE templates at different locations will show low similarity, since, in general, each location is associated with the execution of different brain functions. It should be noted that even adjacent locations, which could be assumed to show a bias toward high interelectrode similarity, usually show low interelectrode similarity. Thus, the existence of a subcluster of electrodes (with high interelectrode template similarity) in the interictal similarity matrix that matches the epileptogenic focus (as seen for type I activity) could indi-

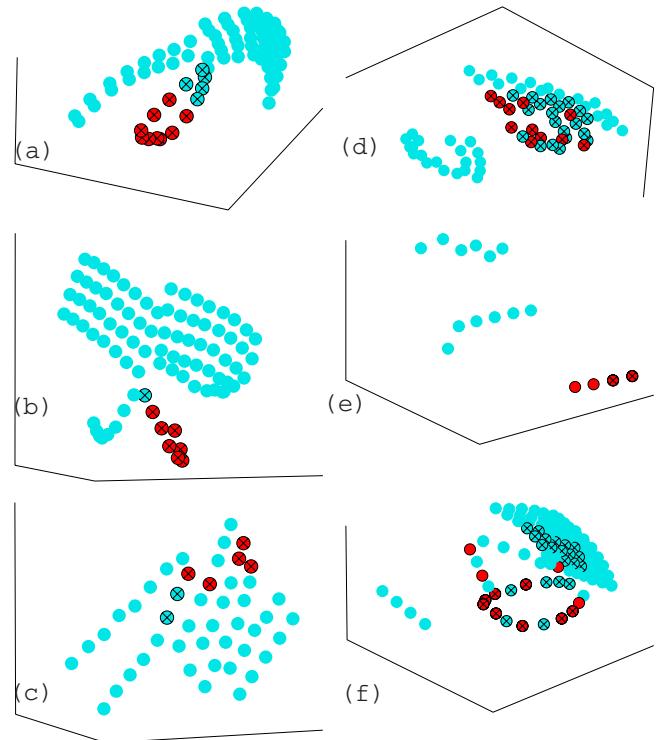


FIG. 6. (Color online) Mapping the identified electrodes on their grid locations on the brain. The red (darker) colored electrodes are the ones identified using our method and the resected electrodes are marked by a crossed circle. The comparison in (a), (b), (c), and (d) (patients 01, 02, 09, and 10, respectively) is for patients that were identified as type-I. As mentioned, the operations of these patients were successful. For these patients the resected foci match the predicted ones. In (e) and (f), we show comparisons for patients 11 and 05, respectively, whose operation failed. In the case of patient 05, a location not predicted by our method was resected while a predicted focus was not resected.

cate abnormal interictal activity of the focus. We also found that the ictal ensemble-averaged FE template is similar to that of the focus during interictal activity. This result indicates that the seizure can be understood as if the brain is slaved by the characteristics of the focus. The results for type-II activity, high average interelectrode template similarity throughout the recorded regions, indicate the existence of multifocal epilepsy or an epileptogenic network, meaning that the epileptogenic activity might not be restricted to well-defined spatial locations or a single functional focus (characterized by a unique FE template). Consequently, these cases are more complex and mapping of the foci is more challenging.

Although some analysis methods have shown that electrodes placed at the epileptogenic zone are characterized by high interelectrode association [18,19], the FE template similarity measure provides additional important information. The FE templates withhold important temporal information depicted in the entropies of each of the frequency subbands. The subbands of each FE template are chosen by the best basis algorithm to obtain maximum temporal information. It is therefore suggested that this method, capturing both temporal and spectral information, may better represent the simi-

TABLE I. Patient clinical data and activity type. TL, temporal lobe; FL, frontal lobe; PL, parietal lobe; OL, occipital lobe; MTL, mesial temporal lobe.

Patient	Suspected focal side	Resection	Surgery outcome	Activity type
01	L	TL	I	I
02	R	TL	II	I
03	R	FL+PL	I	I
04	L	FL+PL	III	II
05	R	TL+PL	III	II
06	L	PL	IV	II
07	R	FL	III ^a	I
08	R	MTL	I	II
09	L	MTL	II	I
10	L	TL	I	I
11	R	OL	IV ^b	I

^aDespite having Engel's class III-outcome, this patient's condition has improved dramatically [24] and the surgery is classified as successful.

^bIn this case the epileptologist predicted an epileptogenic zone that matched our method's suspected location, but this region could not be completely removed during surgery.

larity between two recordings than methods that concentrate on one of these aspects (such as cross correlation in time, or coherence in frequency) only.

We presented an approach to analyze the ECoG and depth electrode recorded brain activity based on comparison between the FE templates of the individual electrodes. The approach was tested by retrospective analysis of 11 patients

that underwent resective surgery and was demonstrated by showing their detailed results. Two types of brain activity were identified: seven of the patients (patients 01, 02, 03, 07, 09, 10, and 11) were identified as having type-I (simple) activity, associated with a single functional focus, and four (patients 04, 05, 06, and 08) were identified as having type-II (complex) activity, associated with multifocal epilepsy. Using the method, it appears to be possible to identify the type of activity based on the interelectrode similarity matrices during interictal intervals alone, i.e., without the need to wait for seizures.

We suggest that for type-I patients the epileptogenic zones can be mapped based on the interictal recordings: for all of these patients the focal locations predicted by the interelectrode similarity matrix matched the resected locations. Accurate identification of the multiple foci of type-II patients requires template comparison with the ictal activity also. The operations of six (out of seven) type-I patients were successful. (In the failed operation, patient 11, the focus was very deep and could not be completely removed.) Out of the four type-II patients, one also had a successful operation. We note that in all the successful operations the resected locations matched (contained) the focal locations predicted by our method. In all the partially successful or failed operations, some of the focal locations predicted by the method were not removed.

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[1] S. J. Schiff, *Nat. Med.* **4**, 1117 (1998).
[2] V. L. Towle *et al.*, in *Epilepsy as a Dynamic Disease*, edited by P. Jung and J. Milton (Springer, Berlin, 2002).
[3] W. K. Doyle and D. D. Spencer, in *Epilepsy: A Comprehensive Textbook*, edited by J. Engel, Jr. and T. A. Pedley (Lippincott-Raven, Philadelphia, 1998), Vol. 2, pp. 1807–1817.
[4] B. Litt and J. Echauz, *Lancet Neurol.* **1**, 22 (2002).
[5] M. Chavez, M. Le Van Quyen, V. Navarro, M. Baulac, and J. Martinerie, *IEEE Trans. Biomed. Eng.* **50**, 571 (2003).
[6] M. Le Van Quyen, J. Martinerie, V. Navarro, M. Baulac, and F. Varela, *J. Clin. Neurophysiol.* **18**, 191 (2001).
[7] V. L. Towle *et al.*, *Electroencephalogr. Clin. Neurophysiol.* **106**, 30 (1998).
[8] K. Lehnertz and C. E. Elger, *Phys. Rev. Lett.* **80**, 5019 (1998).
[9] J. Gutiérrez, R. Alcántara, and V. Medina, *Med. Eng. Phys.* **23**, 623 (2001).
[10] S. Blanco, A. Figliola, R. Quijan Quiroga, O. A. Rosso, and E. Serrano, *Phys. Rev. E* **57**, 932 (1998).
[11] T. I. Nethoff and S. J. Schiff, *J. Neurosci.* **22**, 7297 (2002).
[12] I. Baruchi, V. L. Towle, and E. Ben-Jacob, *Complexity* **10**, 38 (2005).
[13] I. Baruchi *et al.*, *Chaos* **16**, 015112 (2006).
[14] D. Panet-Raymond and J. Gotman, *Electroencephalogr. Clin. Neurophysiol.* **75**, 474 (1990).
[15] A. Gambardella, J. Gotman, F. Cendes, and F. Andermann, *Epilepsia* **36**, 122 (1995).
[16] G. A. Worrel *et al.*, *Brain* **127**, 1496 (2004).
[17] P. J. Allen, D. R. Fish, and S. J. Smith, *Electroencephalogr. Clin. Neurophysiol.* **82**, 155 (1992).
[18] V. L. Towle, R. K. Carder, L. Khorasani, and D. Lindberg, *J. Clin. Neurophysiol.* **16**, 528 (1999).
[19] C. A. Schevon *et al.*, *Neuroimage* **35**, 140 (2007).
[20] F. Mormann, K. Lehnertz, P. David, and C. E. Elger, *Physica D* **144**, 358 (2000).
[21] K. Lehnertz and C. E. Elger, *Electroencephalogr. Clin. Neurophysiol.* **95**, 108 (1995).
[22] G. Widman, K. Lehnertz, H. Urbach, and C. E. Elger, *Epilepsia* **41**, 811 (2000).
[23] I. Doron, E. Hulata, I. Baruchi, V. L. Towle, and E. Ben-Jacob, *Phys. Rev. Lett.* **96**, 258101 (2006).
[24] Although patient 07 was classified as having Engel's class-III outcome, we included him as a successful case, as his condition has improved immensely following surgery. Before surgery this patient was having daily continual disabling seizures.

After surgery (more than two years) this patient has been having nondisturbing twitches a few times per month.

- [25] J. Ph. Lachaux, D. Rudrauf, and P. Kahane, *J. Physiol. Paris* **97**, 613 (2003).
- [26] *A Wavelet Tour of Signal Processing* (Academic, San Diego, 1999), 2nd Ed.
- [27] R. R. Coifman and M. V. Wickerhauser, *IEEE Trans. Inf. Theory* **38**, 713 (1992).
- [28] E. Hulata, I. Baruchi, R. Segev, Y. Shapira, and E. Ben-Jacob, *Phys. Rev. Lett.* **92**, 198105 (2004).
- [29] *Surgical Treatment of the Epilepsies*, edited by J. Engel, 2nd ed. (Raven Press, New York, 1993).