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A Novel Method for the Characterization of Synchronization and Coupling in Multichannel EEG and ECoG

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***Abstract*—In this paper we introduce a novel method for the characterization of synchronziation and coupling effects in multivariate time series that can be used for the analysis of EEG or ECoG signals recorded during epileptic seizures. The method allows to visualize the spatio-temporal evolution of synchronization and coupling effects that are characteristic for epileptic seizures. Similar to other methods proposed for this purpose our method is based on a regression analysis. However, a more general definition of the regression together with an effective channel selection procedure allows to use the method even for time series that are highly correlated, which is commonly the case in EEG/ECoG recordings with large numbers of electrodes. The method was experimentally tested on ECoG recordings of epileptic seizures from patients with temporal lobe epilepsies. A comparision with the results from a independent visual inspection by clinical experts showed an excellent agreement with the patterns obtained with the proposed method.

***Keywords*—EEG, epilepsy, regression analysis, seizure propagation.

I. Introduction

A. Background

Determination of electroencephalogram (EEG) and electrocorticogram (ECoG) activity propagation is important for the investigation of information processing in the human brain. It can be used for the analysis of epilepsy, a disease that is characterized by a sudded and recurrent malfunction of the brain that is termed seizure. Epileptic seizures reflect an excessive and hypersynchronous activity of neurons in the brain. They originate from a certain region in the brain and may spread out over other regions. Localization of the epileptic focus and brain regions affected by seizures is an important task for the clinical therapy, in particular in the course of presurgical clarification. This is usually done by visual inspection of raw EEG or ECoG. Numerous methods for the analysis of activity propagation have been published that may support clinicians with this task [1]. Important measures hereby are the directed transfer function [2], [3], [4] and modifications of it [5], directed coherence and partial directed coherence [6], [7], and the ordinary coherence of multivariate spectral estimates [8]. These methods are based on autoregressive spectral estimation of multivariate signals [9] and an analysis of the resulting estimated parametric spectra. More precisely, multivariate spectra of the signals are estimated under the assumption of an autoregressive signal model. These are parametric models that are used in order to avoid overfitting, which is an important issue since due to short time stationarity the number of samples for this estimation typically is hardly limited. The measures mentioned above are calculated with regard to the obtained parametric spectra.

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B. Contributions

In this article we introduce a novel approach for the characterization of synchronization and coupling effects in multichannel EEG and ECoG. The method is based on linear spatio-temporal regressions of individual signals that are generated from a specific temporal neighborhood of each sample itself and of a selection of related signals. In contrast to most similar methods based on autoregressive spectral analysis, the temporal neighborhood for the regression may include succeeding samples in addition to preceeding samples. The regression parameters are obtained as the solution of a Wiener-Hopf equation using estimated correlation functions.

For the subsequent analysis a linear decomposition of the regression value into terms related to the individual channels is used. The variance of these terms is derived, revealing measures of interactions and dependencies in the multivariate signal. Employed in a moving window scheme, temporal changes can be observed, and epileptic seizure evolution can be visualized. Based on the detailed spatio-temporal analysis, several measures characterizing synchronization and coupling effects from a more global perspective can be derived. A distinctive characteristic of our approach is the direct statistical analysis of the regression values and their linear terms, i.e., the regressands are linearly decomposed into terms associated to the involved signals. Based on the variances of these terms we introduce *extrinsic-to-intrinsic power ratio* (EIPR) and *total extrinsic-to-intrinsic power ratio* (TEIPR), which are physiologically meaningful and valuable measures. In contrast, numerous methods like directed transfer function, directed coherence, etc., are fundamentally different in that a multichannel autoregressive process is estimated and spectrally analyzed.

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The proposed regression analysis will be used to investigate ECoG signals of epileptic seizures. First results indicate that the proposed analysis allows for fast and reliable detection of interictal periods in the ECoG of epileptic patients and effective examination of seizure propagation.

II. Method

A. Multichannel regression.

In the following analysis we consider a set of K real-valued signals $x_k[n]$ with time indices $n \in \mathbb{Z}$ and channel indices $k = 1, ..., K$, representing uniformly sampled multichannel EEG/ECoG recordings. The signals are assumed to be zero-mean and short-time stationary, i.e., stationary within some time windows $n = mT+1, \ldots, mT+N$ used for the analysis. Temporal changes of the signal features can thus be observed from window to window, however, for simplicity and without loss of generality we restrict to the case $m = 0$.

For each signal $x_k[n]$ a regressand is defined as

$$\hat{x}_k[n] \triangleq \mathring{x}_k[n] + \vec{x}_k[n],$$

which is the sum of an *intrinsic regression term* defined as

$$\mathring{x}_k[n] \triangleq \sum_{p\in\mathbb{P}} a_{k,k}[p]\, x_k[n-p]$$

and an *extrinsic regression term* defined as

$$\vec{x}_k[n] \triangleq \sum_{l\in\mathbb{L}_k} \vec{x}_{k,l}[n]. \tag{1}$$

The extrinsic regression term $\vec{x}_k$ is the sum of the *partial extrinsic regression terms,* which are defined as

$$\vec{x}_{k,l} \triangleq \sum_{q\in\mathbb{Q}} a_{k,l}[q]\, x_l[n-q]$$

and reflect the contributions from channels x_l in $\vec{x}_k[n]$. The channels contributing to $\vec{x}_k[n]$ are chosen according to an *extrinsic channel set* $\mathbb{L}_k = \{l_{k,1}, l_{k,2}, \ldots, l_{k,L_k}\}$. This set is separately defined for each regressand $\hat{x}_k$ and contains L_k enumerated values.

The temporal positions of regressors are separately defined for intrinsic and extrinsic terms in the *intrinsic lag index set* $\mathbb{P} = \{p_1, p_2, \ldots, p_P\}$ and the *extrinsic lag index set* $\mathbb{Q} = \{q_1, q_2, \ldots, q_Q\}$ respectively, which are equal for all channels. Note the difference in the definitions of $\mathring{x}_k$ and $\vec{x}_{k,k}$!

B. Wiener estimator.

Given the above definition of the multichannel regression, one question is how to find meaningful regression parameters $a_{k,l}^{(p)}$. Assuming knowledge on the temporal and spatial second order statistics of the signals $x_k[n]$, a common approach therefore is to construct a linear estimator minimizing the mean squared error (MSE)

$$\sigma_{e_k}^2 = \mathrm{E}\left\{|e_k[n]|^2\right\},$$
$$e_k[n] \triangleq x_k[n] - \hat{x}_k[n].$$

These MSE parameters $a_{k,l}[p]$ are obtained by solving a Wiener-Hopf equation $\mathbf{R}_{\mathbf{x}_k}\mathbf{a}_k = \mathbf{r}_{\mathbf{x}_k x_k}$, with regression parameter stacked into the vector [1]

$$\mathbf{a}_k = \Big[a_{k,k}\,[n-p_1] \ldots a_{k,k}\,[n-p_P]$$
$$\vec{\mathbf{a}}_k^T\,[n-q_1] \ldots \vec{\mathbf{a}}_k^T[n-q_Q]\Big]^T,$$
$$\vec{\mathbf{a}}_k[n] = \Big[a_{k,l_{k,1}}\,[n] \ldots a_{k,l_{k,L_k}}\,[n]\Big]^T,$$

and covariance functions $\mathbf{R}_{\mathbf{x_k}}$ and $\mathbf{r}_{\mathbf{x_k}x_k}$ defined as[2]

$$\mathbf{r}_{\mathbf{x}_k x_k} = \mathrm{E}\left(\mathbf{x}_k[n]\, x_k[n]\right), \; \mathbf{R}_{\mathbf{x_k}} = \mathrm{E}\left(\mathbf{x}_k[n]\, \mathbf{x}_k^T[n]\right) \tag{2}$$

with stacked signal sample vector

$$\mathbf{x}_k[n] = \Big[x_k\,[n-p_1] \ldots x_k\,[n-p_P]$$
$$\vec{\mathbf{x}}_k^T\,[n-q_1] \ldots \vec{\mathbf{x}}_k^T[n-q_Q]\Big]^T,$$
$$\vec{\mathbf{x}}_k[n] = \Big[x_{l_{k,1}}\,[n] \ldots x_{l_{k,L_k}}\,[n]\Big]^T.$$

Note that using this notation the regressand can easily be written as $\hat{x}_k[n] = \mathbf{a}_k^T \mathbf{x}_k[n]$.

In practice, covarinace functions $\mathbf{R}_{\mathbf{x}_k}$ and $\mathbf{r}_{x_k\mathbf{x_k}}$ have to be estimated, e.g., by means of a sample covariance function which requires sufficiently large sample sizes N. On the other hand, large N reduces the temporal resolution of the method and may conflict with the assumption of short-time stationarity.

C. Temporal neighborhood.

The lag index sets $\mathbb{P}$ and $\mathbb{Q}$ define the temporal neighborhood for intrinsic and extrinsic regressors respectively. For classical autoregressive modelling, these are usually chosen equal, i.e., either $\mathbb{P} = \mathbb{Q} = \{1, \ldots, P\}$ for forward predictions, or $\mathbb{P} = \mathbb{Q} = \{-P, \ldots, -1\}$ for backward predictions. Since our aim is not to construct autoregressive process models, these sets can be chosen more generally. E.g., 0 may be included in the extrinsic lag index set $\mathbb{Q}$, i.e., $\mathbb{Q} = \{-Q, \ldots, 0\}$, or $\mathbb{Q} = \{0, \ldots, Q\}$. Note that this does not make sense for $\mathbb{P}$, meaning that $x_k[n]$ would be a regressor for $\hat{x}_k[n]$. Moreover it is possible to define temporally symmetric sets, resulting in $\mathbb{P} = \{-P_{max}, \ldots, -P_{min}, P_{min}, \ldots, P_{max}\}$, $\mathbb{Q} = \{-Q, \ldots, Q\}$. Another interesting option is to use empty intrinsic lag index sets $\mathbb{P} = \{\}$ for pure extrinsic regressions.

D. Spatial neighborhood.

Choosing an extrinsic channel set and thus the spatial neighborhood of the regression is a crucial part of this multichannel regression analysis. This is due to the fact that the signals $x_k[n]$, and in particular those that are spatially close together, often have strong correlations causing the correlation matrix $\mathbf{R}_{\mathbf{x}_i}$ to be ill-conditioned. This problem is morover impaired by the fact, that $\mathbf{R}_{\mathbf{x_i}}$ in practice has to be estimated and therefore is affected by an estimation error. For large numbers of channels K, limiting $\mathbb{L}^{(k)}$ to a smaller subset may then greatly improve stability of the algorithm. However, it is not

[1] $\cdot^T$ denotes transposition.
[2] $\mathrm{E}(\cdot)$ denotes expectation.

Table I
ALGORITHM FOR THE SEARCH OF AN OPTIMUM EXTRINSIC CHANNEL SET.

For each regressand $\hat{x}_k[n]$, $k = 1, ..., K$:
Extrinsic channel set: $\mathbb{L} = \{\}$
Extension pool: $\mathbb{K} = \{1, ..., K\}$
Caluclate cost function σ_e^2
$\forall k \in \mathbb{K}$: calculate cost function $\sigma_e^2(k)$ with extrinsic channel set $\mathbb{L}_k = \mathbb{L} \cup k$
Optimum extension: $k_{\text{opt}} = \arg\min_k \sigma_e^2(k)$
Extend extrinsic channel set: $\mathbb{L} \leftarrow \mathbb{L} \cup k_{\text{opt}}$
Reduce extension pool: $\mathbb{K} \leftarrow \mathbb{K} \backslash k_{\text{opt}}$
Update cost function: $\sigma_e^2 = \sigma_e^2(k_{\text{opt}})$
while $\sigma_e^2 - \sigma_e^2(k_{\text{opt}}) > \theta$
Extrinsic channel set for channel k: $\mathbb{L}_k = \mathbb{L}$

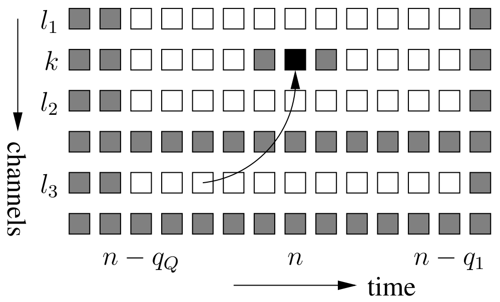

Fig. 1. Example for the illustration of temporal and spatial distribution of regressors: $k = 2$, $\mathbb{L}^{(k)} = \{1, 3, 5\}$, $\mathbb{P} = \{-5, ..., -2, 2, ..., 5\}$, $\mathbb{Q} = \{-5, ..., 5\}$.

obvious how to choose this subset to improve stability without removing strongly coupled channels that could indicate important connections. One obvious method would be to choose the channels of a number of spatially nearest electrodes. Note that this subset is constant over time and requires information about spatial positions of the electrodes. If these positions are not known one can calculate ordinary correlation coefficients and choose a number of signals with the highest correlation coefficients. Here, $\mathbb{L}^{(k)}$ can be recalculated for each window separately. Due to the high correlation of the signals chosen with these methods, the problem of potentially ill-conditioned correletion matrices may arise. Therefore, we propose an iterative procedure for determinig $\mathbb{L}^{(k)}$ and $\hat{x}_k[n]$ for each channel k according to table I. This algorithm is initialized with an empty extrinsic channel set $\mathbb{L}$, which is then iteratively extended according to an optimality criterium. In our case, this optimality criterium is the best reduction of the MSE of the residual $\sigma_k^2 = \mathrm{E}\left(|x_k - \hat{x}_k|^2\right)$. Alternatively the Akaike Information criterion (AIC) [10] or any of its numerous variants, like e.g. corrected AIC [11] could be used in this algorithm for the search of an extrinsic channel set. Although this might be a more elegant criterion it has not yet been tested in practice.

Fig. 1 illustrates an example for temporal and spatial distributions of the regressors $x_l[n-q]$ (white squares) in the regressand $\hat{x}_k[n]$ for $x_l[k]$ (black square). The gray squares indicate the positions of samples not used in the regression.

E. Definitions

The aim of the method described here is the identification of mutual dependencies of multivariate signals, indicating synchronization and coupling effects of brain regions during epileptic seizures. A number of methods using autoregressive modeling have been proposed, analyzing cross correlations and cross spectra of an multichannel autoregressive models for the signals. In contrast to these approaches, we perform a direct analysis of the linear terms of the regressand, which are associated to the respective channels. The variance of the intrinsic regression term can be written as

$$\sigma_{\mathring{x}_k}^2 = \mathbb{E}\left\{|\mathring{x}_k[n]|^2\right\} = \sum_{p=p_1}^{p_P} \sum_{r=p_1}^{p_P} a_{k,k}[p] r_{x_k}[p-r] a_{k,k}[r]$$

with the auto-correlation function $r_{x_k}[p] = \mathbb{E}\left(x_k[n]\, x_k[n-p]\right)$. Similarly, the variance of the partial extrinsic regression term is

$$\sigma_{\vec{x}_{k,l}}^2 = \mathbb{E}\left\{|\vec{x}_{k,l}[n]|^2\right\} = \sum_{q=q_1}^{q_Q} \sum_{r=q_1}^{q_Q} a_{k,l}[q] r_{x_l}[q-r] a_{k,l}[r],$$

and the variance of the extrinsic regression term is

$$\begin{aligned}\sigma_{\vec{x}_k}^2 &= \mathbb{E}\left\{\left|\vec{x}_k[n]^2\right|\right\} \\ &= \sum_{q=q_1}^{q_Q} \sum_{r=q_1}^{q_Q} \vec{\mathbf{a}}_k^T[q] \mathbf{R}_{\vec{\mathbf{x}}_k}[q-r] \vec{\mathbf{a}}_k[r]\end{aligned}$$

with the cross correlation function $r_{x_k,x_l}[q] = \mathbb{E}\left(x_k[n]\, x_l[n-q]\right)$. Note that $\sigma_{\vec{x}_k}^2$ can not be written as a sum of $\sigma_{\vec{x}_{k,l}}^2$, unless spatial correlations are zero (cf. (1)). Using the correlation matrices in (2) these expressions can alternatively be written in matrix notation as[3]

$$\sigma_{\vec{x}_{k,l}}^2 = \mathbf{r}_{\mathbf{x}_k x_k}^T \mathbf{R}_{\mathbf{x}_k}^{-1} \left[\begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{S}_l \end{bmatrix} \odot \mathbf{R}_{\mathbf{x}_k}\right] \mathbf{R}_{\mathbf{x}_k}^{-1} \mathbf{r}_{\mathbf{x}_k x_k}$$

with the $QL_k \times QL_k$ selection matrix $\mathbf{S}_l$ that masks the elements corresponding to $r_{x_l}[q]$ in $\mathbf{R}_{\mathbf{x}_k}$. Similarly, the variance of the intrinsic regression term can be written as

$$\sigma_{\mathring{x}_k}^2 = \mathbf{r}_{\mathbf{x}_k x_k}^T \mathbf{R}_{\mathbf{x}_k}^{-1} \left[\begin{bmatrix} \mathbf{1}_P & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{bmatrix} \odot \mathbf{R}_{\mathbf{x}_k}\right] \mathbf{R}_{\mathbf{x}_k}^{-1} \mathbf{r}_{\mathbf{x}_k x_k},$$

and the variance of the extrinsic regression term as

$$\sigma_{\vec{x}_k}^2 = \mathbf{r}_{\mathbf{x}_k x_k}^T \mathbf{R}_{\mathbf{x}_k}^{-1} \left[\begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{1}_{QL_k} \end{bmatrix} \odot \mathbf{R}_{\mathbf{x}_k}\right] \mathbf{R}_{\mathbf{x}_k}^{-1} \mathbf{r}_{\mathbf{x}_k x_k}.$$

F. Synchronization measures

Based on the expressions introduced in the previous section we introduce two novel measures for the synchronization of EEG or ECoG. First we introduce the *extrinsic-to-intrinsic power ratio* (EIPR) as

$$\eta_{k,l} \triangleq \frac{\sigma_{\vec{x}_{k,l}}^2}{\sigma_{\mathring{x}_k}^2},$$

[3]An all-zero matrix is denoted by $\mathbf{0}$, a $P \times P$ all-one matrix is denoted by $\mathbf{1}_P$, and $\odot$ stands for element-wise multiplication.

which quantifies coupling or synchronization effects of specific signal pairs. It is high for large partial extrinsic regression variance and small intrinsic regression variance, i.e., when the signal x_l yields significant information about x_k.

The second measure introduced here is the *total extrinsic-to-intrinsic power ratio* (TEIPR) defined as

$$\vec{\eta}_k \triangleq \frac{\sigma^2_{\vec{x}_k}}{\sigma^2_{\hat{x}_k}},$$

which relates the power of the total extrinsic regression terms to the power of the intrinsic regression terms. In contrast to the pair-wise EIPR, this is a global quantity defined for each signal separately. TEIPR is a measure for the total synchronization of one signal with neighboring brain regions and can be utilized for temporal allocation of epileptic seizures and spatial determination of epileptic foci.

III. Results

In this section we present numerical results from a propagation study of eplileptic seizures. Electrocorticogram (ECoG) recordings analyzed in this study are taken from two patients in the Vienna General Hospital, Department of Neurology, "Patient A" and "Patient B". Both patients had temporal lobe epilepsies and the data were obtained in the course of a pre-surgical clarification, each lasting for approximately one week. For the time of two seizures extrinsic-to-intrinsic power ratios (EIPR) were calculated, whereby the following preprocessing was used. The ECoG signals were referenced to an electrode oustside of the seizure focus, line interference was removed using an appropriate notch filter at 50 Hz, and the signals were were downsampled from 256 Hz to 128 Hz sampling rate. The EIPR was calculated within windows of length 6 s and with temporal neighborhood index sets $\mathbb{P} = \{-5, -4, -3, 3, 4, 5\}$ for the intrinsic and $\mathbb{Q} = \{-5, -4, ..., 5\}$ for the extrinsic regressors. The results obtained are illustrated in Figs. 2 and 3 for a temporally equidistant sequence of the windows, starting 15 s before seizure onsets in steps of 6 s. The times written in each graph quote the end of each window, i.e., the time when a result can be obtained in an online implementation of the algorithm. In each graph the circles represent the spatial layout of the electrodes, and the arrows indicate values of EIPR between two electrodes. Arrows for values below a certain treshold were removed in order to obtain clear pictures. This treshold was manually chosen. Note that thick, dark arrows represent high values and thin, light arrows represent low values of EIPR. Arrows pointing from electrode k to electrode l represent $\eta_{k,l}$.

IV. Discussion

According to clinicians who visually inspected the raw ECoG signals, the seizure onset in the ECoG of Patient A (cf. Fig. 2) was at 12:45:45 in the right hemisphere of the brain (left side in the figure). Then seizure activity spreads out over the left hemisphere (right side) at 12:46:04. Later activity reduces on the left hemisphere, and finally stops at the right hemisphere at 12:47:00. Comparing these results with the EIPR it can clearly be seen that they are in excellent agreement. Although the seizure start is indicated with a slight latency, the propagation of activity from one to the other hemisphere can nicely be visualized. Furthermore, the drop at the end of the seizure is consistent with the clinicians results.

The seizure onset for the data of Patient B was identified by clinicians at 08:06:34 in the right hemisphere (left figure side) and spreads over to the left hemisphere at 08:06:46. The seizure activity first reduces in the left hemisphere and finally the seizure stops at 08:08:30. Here, our visualization indicates synchronization on the focus channels even slightly before the first signs are visible in the raw ECoG. We note that this might be an early synchronization indicator. The seizure start is clearly indicated by strong EIPRs corresponding to the left hemisphere. Also the spread-over to the right hemisphere is nicely visualized. Finally, the end of this seizure is clearly visible, since no activity is indicated after 08:08:31.

Our results suggest that the arrows point to the "source of activity" and start from brain regions that are synchronized to this "source". Looking to a temporal sequence of graphs, the activity propagation can be tracked over time. Our method therefore has the potential to assist clinicians with their diagnoses and thereby serve as an objective measure. This however requires further research in order to investigate properties of EIPR measure in more detail.

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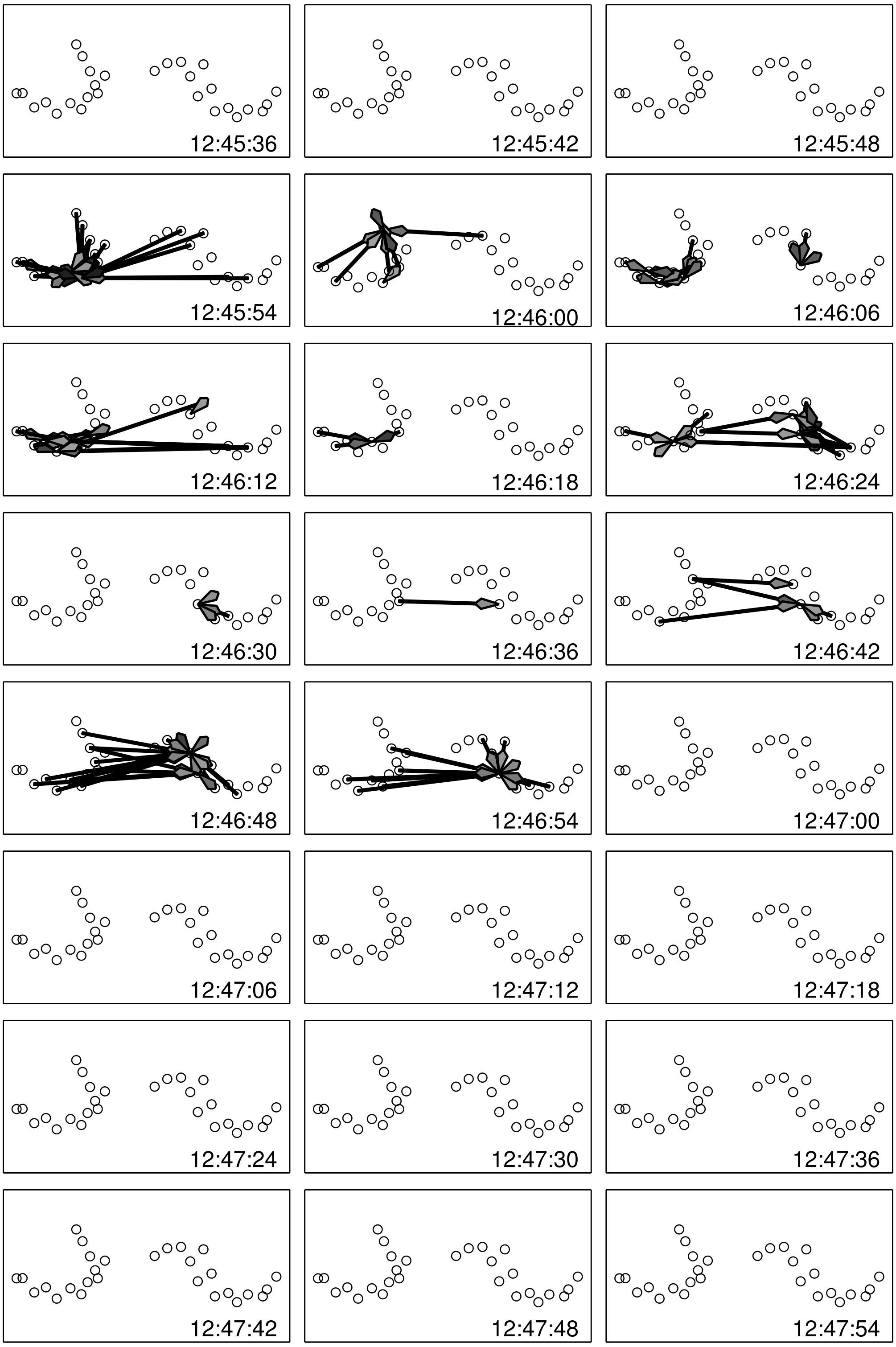

Fig. 2. Partial extrinsic-to-intrinsic power ratio illustrated during an epileptic seizure of Patient A starting at 12:45:51 and ending at 12:47:00.

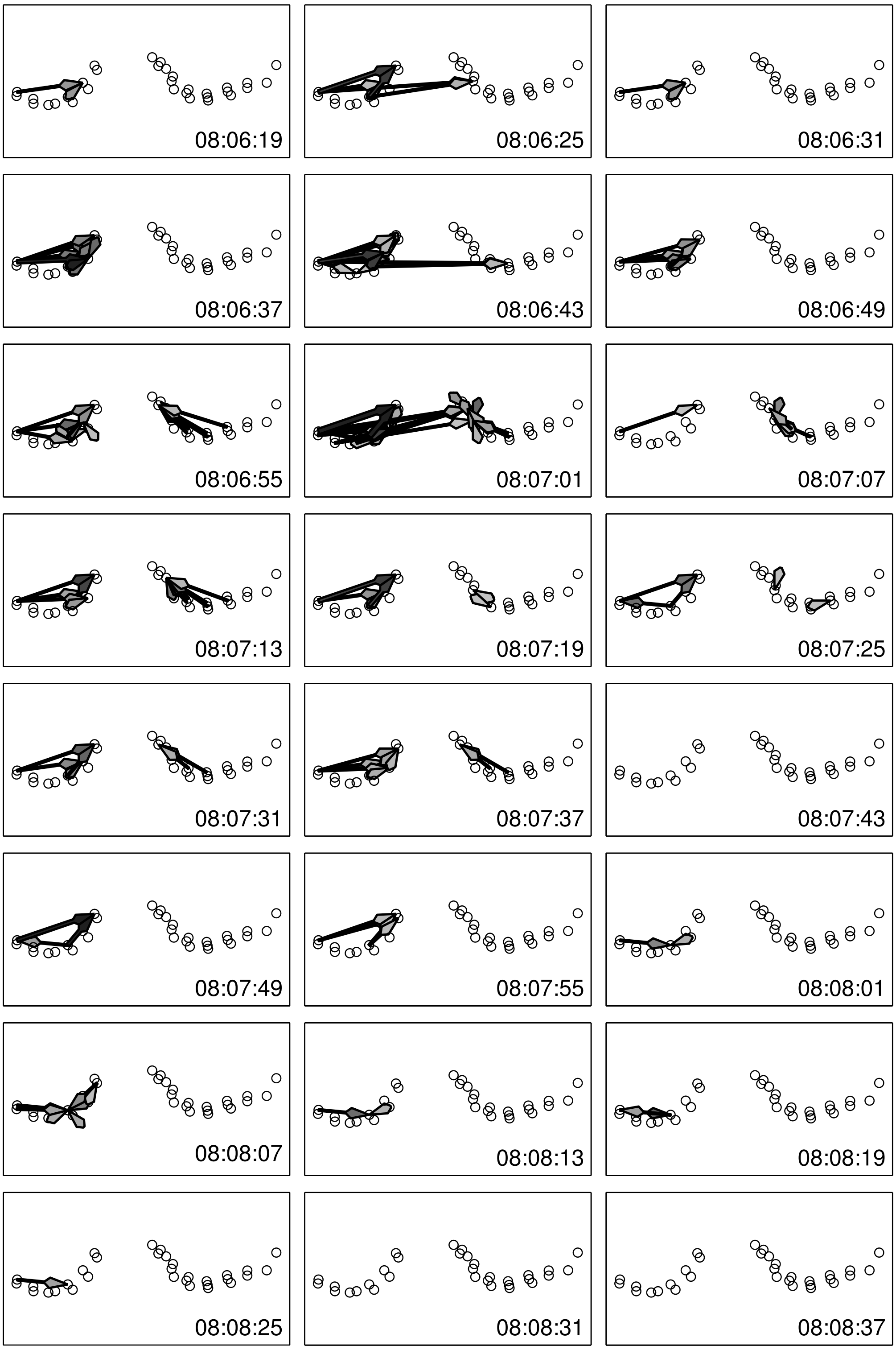

Fig. 3. Partial extrinsic-to-intrinsic power ratio illustrated during an epileptic seizure of Patient B starting at 08:06:34 and ending at 08:08:30