Prediction of epileptic seizures from two-channel EEG

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Abstract—*Multivariate spectral estimation based on parametric modelling has been applied to epileptic surface EEG in order to detect EEG changes that occur prior to the clinical outbreak of the seizure. A better time/frequency resolution has been achieved using residual energy ratios (Dickinson's method). Prediction of oncoming seizures was based on detection of increased preictal synchronisation by calculation of coherence and pole trajectories. The method has been tested on simulated EEG data and on real EEG data from patients with primary generalised epilepsy. Prediction times of 1-6 s have been found in several seizures from five patients.*

Keywords—*Epileptic EEG, Seizure prediction, Spectral estimation*

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1 Introduction

MOST PATIENTS with epilepsy, whether of focal origin or generalised, benefit from medical treatment and can, with the help of proper medication, lead a normal life. There is, however, a smaller subgroup of these patients where seizure frequency and severity cannot be properly controlled by medication and/or where the combinations and dosage of the various anti-epileptic drugs cause intolerable side effects. If the presence of a clear ictal focus cannot be confirmed and surgical treatment is thus excluded, these patients might be candidates for an alternative treatment, such as biofeedback (KAPLAN, 1975; KUHLMAN and ALLISON, 1977) or electrical stimulation (ISHIJIMA *et al.*, 1975; VELASCO *et al.*, 1987; PENRY and DEAN, 1990; GEORGE and MICHAEL, 1991) in order to reduce the frequency of the seizures.

Stimulation of intracerebral structures (VELASCO *et al.*, 1987) as a form of anti-epileptic treatment has been carried out in a continuous mode, and the average reduction in seizure frequency assessed statistically. Similarly, the mode of stimulation used by PENRY and DEAN (1990) and GEORGE and MICHAEL (1991) is continuous, with several seconds of stimulation of the vagal nerve every few minutes. However, a better mode of operation would be the detection of the EEG changes that occur *prior* to the clinical outbreak of the seizure, and prophylactic stimulation time-locked to these EEG changes. Hence, prediction of the occurrence of seizures from the preictal scalp EEG should be the first step in seizure reduction carried out either by conditioning (biofeedback) or by electrical stimulation.

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Single channel scalp EEG processing, using AR modelling, in order to predict the occurrence of convulsive episodes has been carried out in a small number of patients with absences (ROGOWSKI *et al.*, 1981). Prediction time in the range of 0.6–6 s was confirmed in 10 out of 12 patients. In five patients with absence seizures, SIEGEL *et al.* (1982) compared the power spectra (using the Fast Fourier transform (FFT)) of 20 s preictal EEG epochs with those of EEG epochs 1 min remote from the spike-wave bursts, and found correct classification in 64% of the cases.

One of the major traits of epileptic EEG is its tendency to have 'over synchronisation' of the signal from various channels. GATH *et al.* (1992) found that synchronisation between depth EEG signals, recorded from the amygdala and hippocampus on both sides, increased during the seizure and reached a peak value greater than 0.9. Thus, multivariate (multichannel) processing of the preictal EEG, instead of processing of a single channel, might increase the chances for prediction of an oncoming seizure.

Spectral analysis of the EEG, whether univariate or multivariate, has been most often carried out using the FFT (BRAZIER, 1973; SIEGEL *et al.*, 1982; GOTMAN, 1983, 1987). However, calculation of power spectra using the FFT requires averaging of several signal segments, a process which leads to smearing of the changes that occur prior to, and at the onset of the epileptic seizure (GATH *et al.*, 1992). A better time/frequency resolution of the events around the onset of the electrical seizure could be obtained by multivariate AR (autoregressive) modelling of the EEG (GERSCH, 1987; GATH *et al.*, 1992). Thus, the aim of the present study is to investigate a method for high time/frequency resolution of seizure EEG, based on multichannel parametric modelling of the signal, in order to devise means for the prediction of seizure episodes.

The second section of the paper outlines the method of high resolution multivariate parametric modelling of the epileptic EEG, and the method of prediction of oncoming seizures using calculations of pole trajectories and coherence. Results of the processing of multichannel EEG from several patients with absence seizures (primary generalised) are given in section 3, and are discussed in section 4.

2 Material and methods

2.1 *Patient material*

Five patients 8–38 years old with absence seizures participated in the study. These patients were selected from a large group of epileptic patients screened by long-time scalp and depth EEG monitoring for surgical treatment, and in whom no signs of focal origin could be confirmed. Fourteen channels of scalp EEG (26 in patient E) were recorded by radio telemetry using silver–silver chloride cup electrodes. Eight sections of seizure EEG were identified in the five patients, four seizures in patient A and one seizure in each of the other four patients. Each section, 30 s long and of which 20 s consisted of the preictal period was sampled at 128 Hz for further processing. In patient E the EEG section was 475 s long of which 326 s were preictal.

2.2 *Multichannel parametric modelling of the EEG signal*

A method of multichannel autoregressive modelling was applied for estimation of the EEG power spectra. The non-stationary seizure EEG signal can be divided into quasi-stationary signal segments 1–2 s long. Computation of power spectra through multichannel autoregressive modelling was based on using a sliding window of 1.6 s length with about 90% overlapping.

Let $y(l)$ be the vector representing the observed m-channelled process and denote the forward prediction of $y(l)$ by

$$\hat{y}_k^f(l) = -\sum_{j=1}^{k} A_{k,j}^f y(l-j) \tag{1}$$

where $A_{k,j}^f$ are the forward autoregressive coefficient matrices of the kth order model. The prediction error is given by

$$e(l) = e_k^f(l) = y(l) - \hat{y}_k^f(l) \tag{2}$$

This equation could be written in the frequency domain as

$$\left(I + \sum_{j=1}^{k} A_{k,j}^f z^{-j}\right) Y(z) = E(z) \tag{3}$$

where $Y(z)$ and $E(z)$ are the z transform of $y(l)$ and $e(l)$ respectively. The expression $(I + \sum_{j=1}^{k} A_{k,j}^f z^{-j})^{-1}$ is the transfer function $H(z)$ between the innovation and $y(l)$.

Similarly to the forward prediction (eqn. 1), the backward prediction is given by:

$$\hat{y}_k^b(l-k-1) = -\sum_{j=1}^{k} A_{k,j}^b y(l+j) \tag{4}$$

where $A_{k,j}^b$ are the backward AR coefficient matrices of the kth order model. The backward prediction error is given by

$$e_k^b(l) = y(l-k-1) - \hat{y}_k^b(l-k-1) \tag{5}$$

The commonly used covariance method, applying the vectorial version of the Levinson algorithm to solve the Yule–Walker equations (WHITTLE, 1963; WIGGINS and ROBINSON, 1965) is based on the the forward and backward prediction. However, owing to the limitation of short signal segments and the need for a high resolution estimator, the performance of these algorithms is not good enough (PHAM and TONG, 1990). The Dickinson method (DICKINSON, 1978, 1979) based on residual energy ratios was shown to provide better results when used for the spectral estimation of epileptic EEG (GATH *et al.*, 1992). The method estimates directly the partial correlation matrices and then uses the vectorial version of the Levinson algorithm to compute the autoregressive parameters.

The normalised partial correlation matrix of order k is given by (DICKINSON, 1979):

$$P_k = U_{k-1}^{-1/2} E[e_{k-1}^f(l) e_{k-1}^b(l)^T](V_{k-1}^{-1/2})^T \tag{6}$$

where $U_k^{-1/2}$ and $V_k^{-1/2}$ are the inverted Cholesky factors of the covariance matrices U_k and V_k of $e_k^f(l)$ and $e_k^b(l)$, respectively.

The predictor coefficients can be derived from eqn. 6 given the recursive relations detailed in MORF *et al.* (1978).

Let L_p be the Cholesky factor of the mp by mp matrix $Y_p Y_p^T$, where

$$Y_p = \begin{bmatrix} y(p) & \cdots & y(n-1) \\ \vdots & & \\ y(1) & \cdots & y(n-p) \end{bmatrix} \tag{7}$$

p is the model order and n is the length of the time series.

The least square normal equations can be written as

$$(q_1, \ldots, q_p) L_p^T = -(y(p+1), \ldots, y(n)) Y_p^T \tag{8}$$

where $q_k = A_{p,k} L_p$.

It can be shown (DICKINSON, 1979) that the estimators for U_k and P_k can be written as

$$\hat{U}_k = \hat{U}_{k-1} - q_k q_k^T \qquad k = 1, \ldots, p \tag{9}$$

with

$$\hat{U}_0 = \sum_{l=p+1}^{n} y(l) y(l)^T \tag{10}$$

and

$$\hat{P}_k = \hat{U}_{k-1}^{-1/2} q_k \qquad k = 1, \ldots, p \tag{11}$$

From the above estimated partial correlation matrices, the forward and backward autoregressive coefficient matrices can be computed using the vectorial version of the Levinson algorithm. Estimating the forward autoregressive coefficient matrix and the covariance matrix of $e_p^f(l)$ provides the estimation of the power spectral density:

$$\hat{S}_{yy}(f) = \hat{H}(f) \hat{U} \hat{H}^H(f) \tag{12}$$

where $H^H(f)$ is the Hermitian of $H(f)$.

2.3 *Prediction of epileptic seizures*

The EEG signal is considered piecewise stationary and the time varying character of the model emulates changes occurring in the signal generating system, the brain. The AR parameters are estimated using a short sliding window with high overlapping. The high overlapping results in a gradual change of the estimated parameters over two consecutive time slots, and thus, enables better tracking of the changes that occur in the model parameters.

Two methods were tested in order to predict an oncoming epileptic seizure:

(1) The movement of the poles of the transfer function H(z), eqn. 3, towards the unit circle, indicating a tendency towards instability.
(2) Tracking of changes in the coherence function. A sharp rise in coherence indicates increased synchronisation.

Prediction using pole trajectories. The transfer function $H(z)$ is given by $(I + \sum_{j=1}^{p} A_{p,j}^{f} z^{-j})^{-1}$. The poles of this transfer function are determined by the roots of the determinant:

$$\det\left(I + \sum_{j=1}^{p} A_{p,j}^{f} z^{-j}\right) \tag{13}$$

The autoregressive coefficient matrices are estimated using the Dickinson method, and provide us with a set of $(m * p)$ poles at each iteration. After moving the time window another set of poles is recalculated. Owing to the gradual change that occurs in the location of the poles at each time step, it is possible to relate each pole from a current set of poles to an adjacent pole in the consecutive set. In this way a plot of the movement of the poles of the transfer function in the z plane as a function of time is achieved.

The criterion for matching two poles was as follows

$$(\hat{P}_i^l, \hat{P}_j^{l+1}) = \arg\left(\min_i \min_j d(P_i^l, P_j^{l+1})\right) \tag{14}$$

where

P_i^l $\quad 1 \leqslant i \leqslant (m * p)$ is a group of $(m * p)$ poles calculated for the window at time l;

P_j^{l+1} $\quad 1 \leqslant j \leqslant (m * p)$ is a group of $(m * p)$ poles calculated for the window at time l+1;

$d(P_i^l, P_j^{l+1})$ is the distance between the pole P_i^l of the first set and the pole P_j^{l+1} of the next set, and arg gives the indices of the two closest poles from the two sets of poles (current and previous windows).

When a match between two poles is obtained, the criterion is retested on two other poles from the remaining poles, and so on, until complete matching between two consecutive sets of poles is achieved, and a complete pole trajectory is obtained.

The Dickinson algorithm provides a stable filter. Movement of the poles towards the unit circle, in particular at an angle corresponding to the seizure frequency, indicates a tendency towards instability. The pole pair whose trajectory exhibits the most significant shift towards the unit circle (and usually at an angle equivalent to the seizure frequency) is termed 'the dominant pole'.

Prediction using the coherence function. Synchronised activity between channels is typical for epileptic seizures. The coherence function provides us with a measure of the correlation between two channels in the frequency domain; a sharp rise in coherence indicates increased synchronisation. The squared magnitude coherence function is given by

$$\gamma^2(f) = \frac{S_{12}^2(f)}{S_{11}(f)S_{22}(f)} \tag{15}$$

where $S_{11}(f)$ and $S_{22}(f)$ are the respective autospectra, and $S_{12}(f)$ the cross-spectrum.

For seizure prediction the following criterion was tested:

A sharp rise in coherence values after a period of low values of coherencies might indicate an oncoming epileptic seizure.

During normal EEG activity the correlation between distant channels is less pronounced than between close channels, while during a typical absence seizure all channels are fully synchronised. Thus, testing pairs of distant channels is more meaningful for the detection of increasing coherence. In the scalar case, the use of AR modelling for the estimation of the coherence function has been shown (ROGOWSKI *et al.*, 1981; GATH *et al.*, 1992) to give better results than when using FFT methods. The number of degrees of freedom of the AR model is given by N/P where N is the number of signal samples and P is the model order. The asymptotic variance of the AR spectral estimate is similar to that of the smoothed periodogram with the same number of degrees of freedom (BERK, 1974).

3 Results

3.1 *Simulations*

A simulation experiment demonstrating the performance of the Dickinson estimator was held on a two channel autoregressive signal, produced artificially. A model order of 6 was selected. The six autoregressive coefficient matrices were chosen to produce filter poles at typical locations of the epileptic EEG signal. Two poles were located close to the unit circle at an angle corresponding to a typical seizure frequency. The estimator's bias and variance were estimated by Monte Carlo simulations using short signal segments. A dual channel Gaussian white noise (uncorrelated) with zero mean and variance = 1 was used as input. The number of samples in each segment was $N = 200$. The selected coefficient matrices were:

$$\begin{array}{ccc} A_{6,1} & A_{6,2} & A_{6,3} \\ \begin{bmatrix} -1.60 & -0.67 \\ -0.67 & -0.83 \end{bmatrix} & \begin{bmatrix} 0.49 & -0.64 \\ -0.64 & 1.23 \end{bmatrix} & \begin{bmatrix} 1.27 & 1.16 \\ 1.16 & -0.07 \end{bmatrix} \end{array}$$

$$\begin{array}{ccc} A_{6,4} & A_{6,5} & A_{6,6} \\ \begin{bmatrix} -0.35 & -0.87 \\ -0.87 & 0.65 \end{bmatrix} & \begin{bmatrix} -0.44 & -0.11 \\ -0.11 & -0.30 \end{bmatrix} & \begin{bmatrix} 0.33 & -0.03 \\ -0.03 & 0.37 \end{bmatrix} \end{array}$$

The corresponding filter poles were: $0.89 \pm 0.31i$, $0.82 \pm 0.27i$, $0.54 \pm 0.66i$, $-0.10 \pm 0.87i$, $-0.71 \pm 0.10i$, $-0.21 \pm 0.80i$.

Table 1 shows the estimated normalised bias error and coefficient of variation of the first three coefficient matrices elements, using a Monte Carlo method on 1000 independent segments of autoregressive signal. The coefficient of variation of elements greater than one was bounded by a value of the order of magnitude 0.1, and their maximum normalised bias error was approximately 1.5%. Fig. 1 shows the normalised bias error and coefficient of variation of the two largest elements $A_{6,1}(1, 1) = -1.60$, $A_{6,3}(1, 1) = 1.27$, calculated for increasing number of averages.

Table 1. Estimated normalised bias error and coefficient of variation for the first three coefficient matrices

	Normalized bias error	Coef. of variation
$A_{6,1}[1, 1] = -1.60$	0.0092	0.04
$A_{6,1}[1, 2] = -0.67$	0.0074	0.10
$A_{6,1}[2, 1] = -0.67$	−0.0057	0.10
$A_{6,1}[2, 2] = -0.83$	0.0134	0.08
$A_{6,2}[1, 1] = 0.49$	0.0433	0.28
$A_{6,2}[1, 2] = -0.64$	−0.0166	0.15
$A_{6,2}[2, 1] = -0.64$	0.0043	0.22
$A_{6,2}[2, 2] = 1.23$	0.0020	0.08
$A_{6,3}[1, 1] = 1.27$	−0.0004	0.10
$A_{6,3}[1, 2] = 1.16$	0.0082	0.10
$A_{6,3}[2, 1] = 1.16$	0.0152	0.11
$A_{6,3}[2, 2] = 0.07$	0.1754	1.69

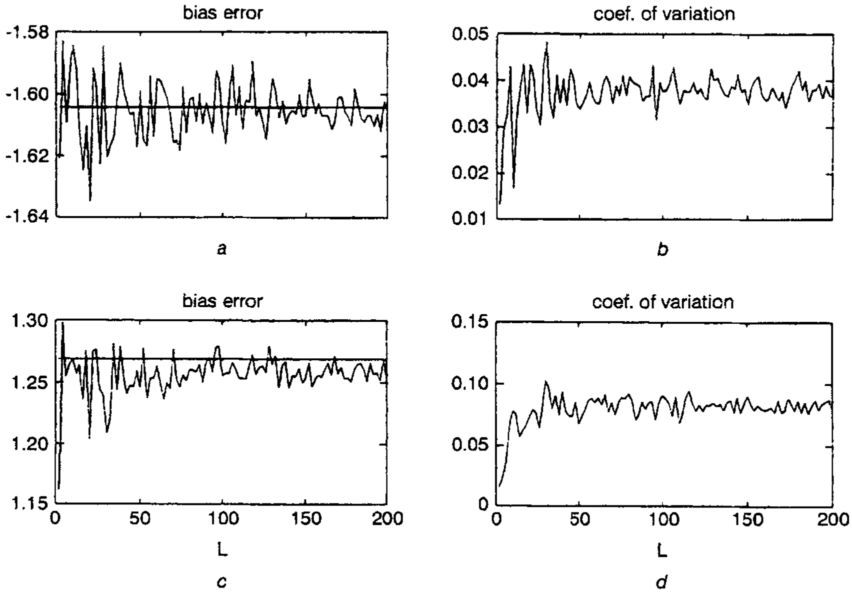

Fig. 1 *Estimation of bias error and coefficient of variation for the two largest elements of the coefficient matrices, $A_{6,1}[1, 1] = -1.60$ (a, b) and $A_{6,3}[1, 1] = 1.27$ (c, d). Simulation experiment, for further details see text. L-number of averages*

3.2 *Epileptic EEG*

The EEG signals of patients A,C,D and E were recorded using a monopolar electrode configuration, and the EEG signal of patient B was recorded using a bipolar configuration. In all cases except for patient B two channels relatively distant from each other (F3 and O2 or F4 and O1) were selected for calculation of the coherence and pole trajectories. The relatively low correlation between two distant channels during inter-ictal periods enables better detection of increasing synchronisation, which characterizes an oncoming seizure. In Patient B the combination P4–O2 and O2–T6 (bipolar) was examined. Although both derivations contain the electrode O2 this had little bearing on the significance of the coherence findings. The reason is that prediction was based on a preictal increase in coherence value compared to its background level.

A highpass filter with a cutoff frequency of 1.5 Hz was applied to the recorded EEG to remove low frequency noise. The sliding time window length was $N = 200$ samples (1.6 s approximately). A model order $P = 8$ was chosen, using Akaike criterion. The model order was determined from multiple preictal EEG segments.

Prediction time was estimated using the two methods described above for tracking changes in the coherence function and pole trajectory. The sliding time window was shifted with high overlapping of more than 90% . Pole trajectories were smoothed using weighted running average:

$$\hat{P}_i = 0.25 * P_{i+1} + 0.5 * P_i + 0.25 * P_{i-1} \qquad (16)$$

where P_i is the location of a pole at the discrete time i.

The smoothed coherence was calculated from

$$\hat{\gamma}_i^2(f) = \frac{1}{5}\sum_{j=-2}^{2} | \gamma_{i-j}(f) |^2 \qquad (17)$$

where $\gamma_i^2(f)$ is the squared magnitude coherence function at the discrete time i and frequency f.

A sharp rise in coherence in the preictal EEG was empirically defined as a change in the magnitude squared coherence from a background level not exceeding 0.5 to a level of at least 0.7. Movement of the poles towards the unit circle has been defined empirically as traversing the circle with a radius of 0.95 by the 'dominant pole'. Table 2 shows prediction times for the various patients and seizures. In patient A a prediction time of 4-6 s was determined by both methods. In patients B and E prediction times of 1 and 1.6 s, respectively, were calculated by both methods. In patients C and D prediction times of 1 s were computed but only by the method of pole trajectory.

3.2.1 *Detailed description of the major results*

Patient A: Two channels (F3 and O2), with the longest inter-electrode distance were selected in all four seizures of this patient. Similar prediction patterns were discerned in all four seizures. A sharp rise in the coherence function was detected 4–6 s prior to the seizure outburst, in parallel with a movement of one of the pole pairs towards the unit circle at an angle corresponding to the seizure frequency. In Figs. 2 and 3 the rise in coherence before the outbreak of the seizures can be seen in two different seizures of this patient. The seizure frequency was about 3.5 Hz. A coherence contour map of the first seizure is demonstrated in Fig. 4. The dominant frequency of maximal coherence reduces from a value of 10 Hz until it reaches the seizure frequency of 3.5 Hz, 6 s before the seizure erupts. Fig. 5 shows pole trajectories for the first seizure. Pole movement towards the unit circle at an angle corresponding to the seizure frequency was traced as early as 6 s before clear seizure activity was present.

Table 2. Seizure prediction time for the five patients. Magnitude squared coherence (MSC)

	Prediction by pole trajectory (s)	Prediction by MSC (s)
patient A, seizure no.1	4.5	4.5
seizure no.2	6	6
seizure no.3	4	4
seizure no.4	6	6
patient B	1	1
patient C	1	–
patient D	1	–
patient E	1.6	1.6

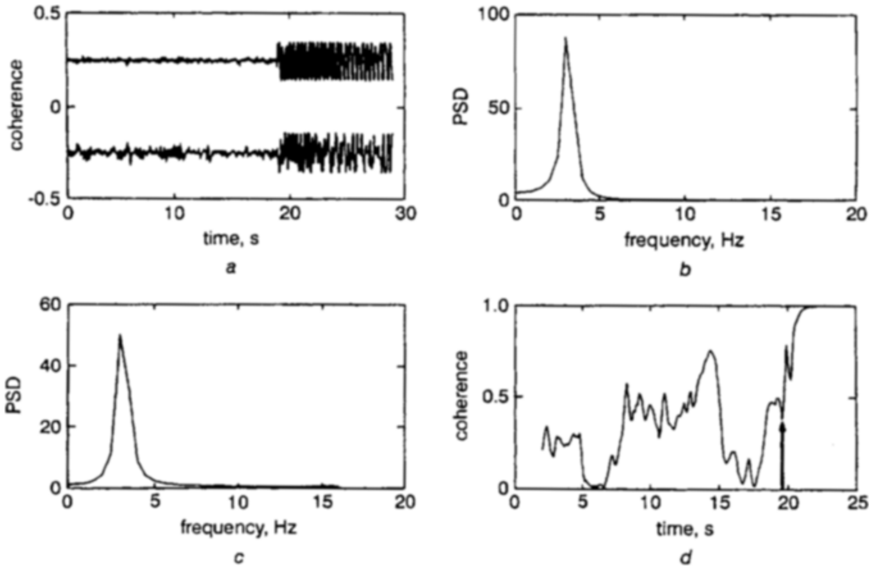

Fig. 2 *Seizure prediction by magnitude squared coherence (MSC). Patient A, seizure No. 1. (a) EEG channels F3 and O2. (b, c) Power spectral density of the two channels during seizure. The magnitude is in arbitrary units. (d) MSC for 3.5 Hz. The arrow depicts the beginning of the seizure*

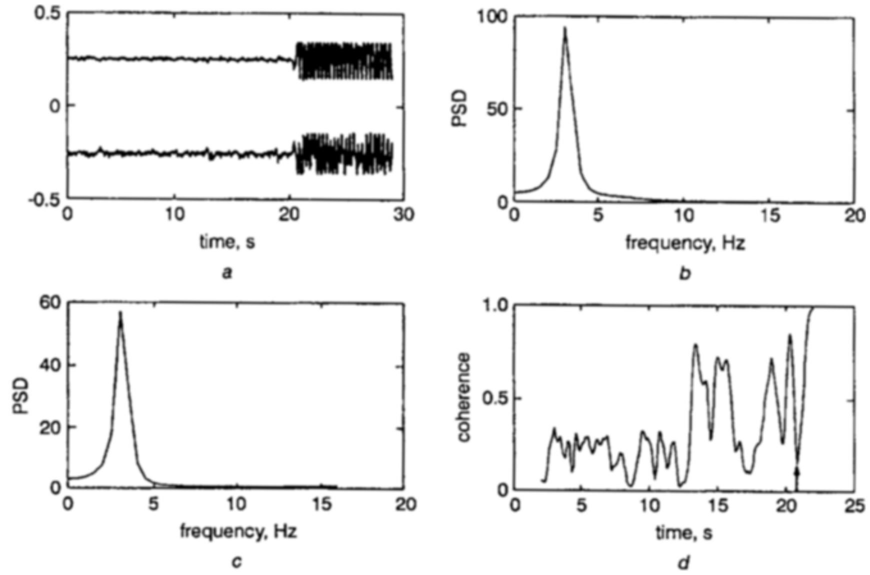

Fig. 3 *Seizure prediction by MSC. Patient A, seizure No. 2. All other details are as in Fig. 2*

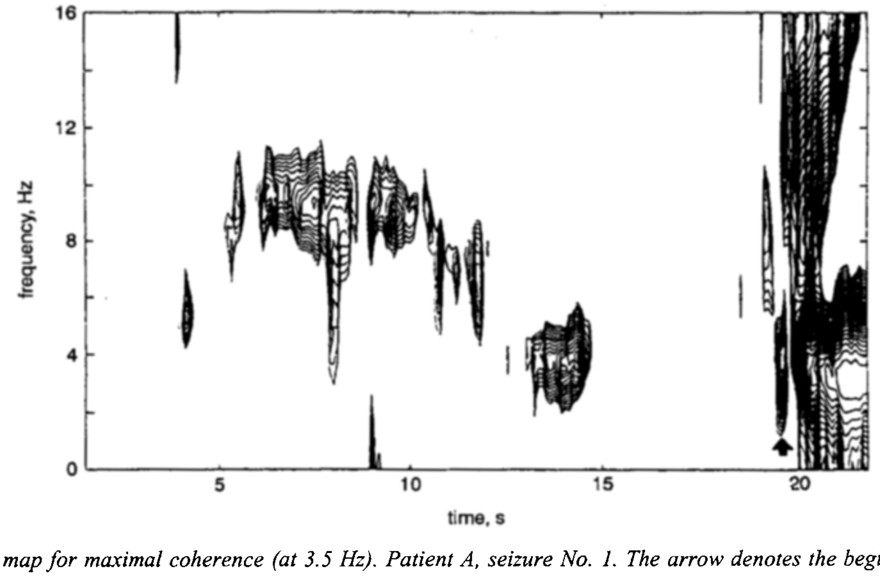

Fig. 4 *Coherence contour map for maximal coherence (at 3.5 Hz). Patient A, seizure No. 1. The arrow denotes the beginning of the seizure*

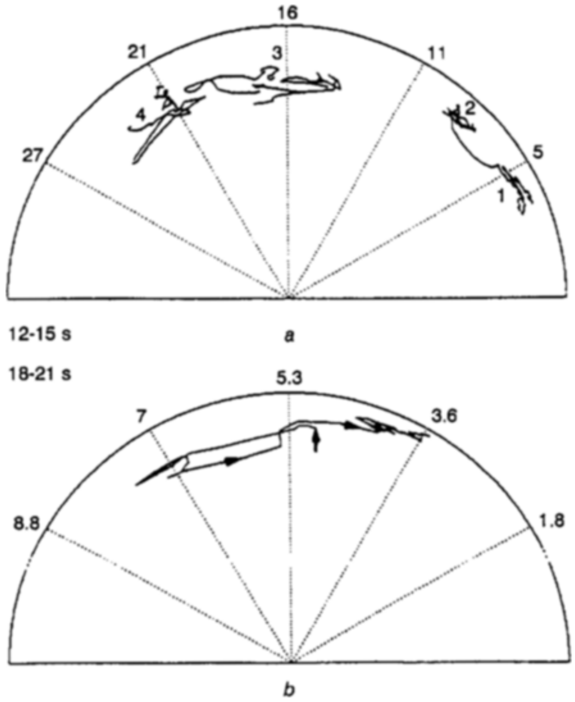

Fig. 5 *Seizure prediction using pole trajectory. Patient A, seizure 1. (a) Movement of four poles in the upper right quadrant of the unit circle, stretched into half circle, during the time 12–15 s of the EEG signal in Fig. 2. (b) magnification of the movement of pole No. 1 during the time 18–21 s of the EEG signal in Fig. 2. Instead of degrees the corresponding frequencies are denoted. Seizure starts at 19 s. The arrows denote progression in time*

Fig. 6 demonstrates the disadvantage of choosing two neighbouring channels. Coherence between the two channels is typically higher than for two distant channels, which limits the ability to detect any further preictal rise in coherence.

Patient B: The EEG signal was recorded using a bipolar electrode derivation. The channels selected were P4–O2 and O2–T6. A prediction time of 1 s was produced by both methods. Fig. 7 shows the movement of the dominant pole pair for a signal stretch of 6 s, starting at a time point 4 s prior to the seizure outburst (and including 2 s of seizure activity).

Patients C and D: In both patients a prediction time of 1 s was calculated by the method of pole trajectory only. In patient C it is possible that a pole pair located close to the unit circle at an angle corresponding to 8–10 Hz had a screening effect on the tracking of the dominant pole relative to the seizure. Fig. 8 shows the movement of the dominant pole towards the unit circle as the epileptic seizure comes nearer.

Patient E: Prediction times of 1.6 s were calculated using both pole trajectory and coherence methods. Fluctuations in the value of the coherence function during 324 s of preictal EEG could be discerned (Fig. 9a–c), but coherence never exceeded the value 0.45. A sharp rise in coherence was detected (Fig. 9d) approximately 1.6 s prior to the seizure outbreak.

4 Conclusions

Electrical stimulation of intracerebral structures in order to reduce the frequency of epileptic seizures was conducted by VELASKO *et al.* (1987) in a continuous random mode (pulse trains of 1 min every 5 min for 2 hours each day) with no direct time relation to seizure build up. This alternative approach to seizure suppression is invasive and carries some risk of operative complications, bleeding and infection (OJEMANN and ENGEL, 1987). Vagal nerve stimulation in a continuous mode has also been carried out for the purpose of reducing seizure frequency (PENRY and DEAN, 1990; GEORGE and MICHAEL, 1991). Other potential forms of non-medical non-invasive anti-epileptic treatment include conditioning and biofeedback (KAPLAN, 1975; KUHLMAN and ALLISON, 1977).

A necessary prerequisite for any rational form of alternative treatment of epilepsy such as biofeedback and electrical stimulation, is prediction of the EEG changes that occur *prior* to the outburst of the clinical seizure, and *time locking* of the therapeutic manoeuvre to these seizure warning signs.

Prediction of oncoming seizures should be based on scalp EEG recordings if complications due to intracerebral recordings and invasive modes of treatment are to be avoided. However, scalp EEG changes that might announce an oncoming primary generalised seizure are usually not obvious during visual interpretation of the EEG recording, and signal processing is needed to recover such warning signs. Processing of the EEG traces using FFT methods (SIEGEL *et al.*, 1982; GOTMAN, 1987) suffers from the fact that long signal traces (relative to

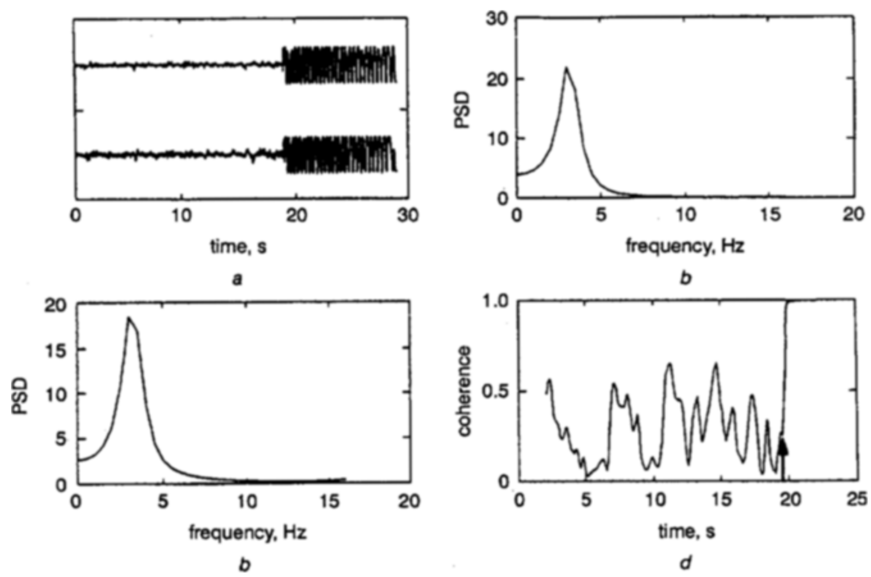

Fig. 6 *Seizure prediction by MSC. Patient A, seizure No. 1, EEG channels F3 and F4. All the other details are as in Fig. 2*

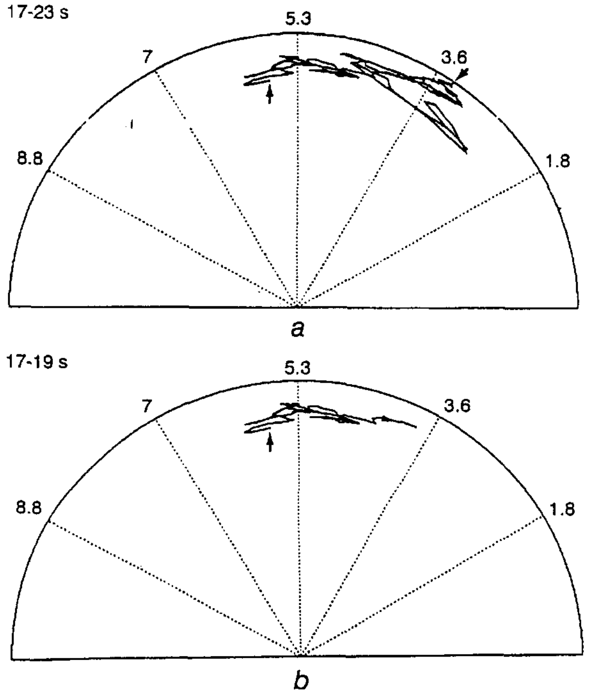

Fig. 7 *Seizure prediction using pole trajectory. Patient B, EEG channels P4–O2 and O2–T6. (a) Movement of the dominant pole in the upper right quadrant of the unit circle, stretched into half circle, during the time 17–23 s. The seizures onset is at 21 s. Instead of degrees the corresponding frequencies are denoted. (b) Portion of the upper trace, movement of the pole during the time 17–19 (preictal). The arrows denote progression in time*

the non-stationary character of the EEG signal) are needed for the analysis because of the averaging inherent in the FFT technique (GATH *et al.*, 1992). To reveal such immediate preictal changes high time/frequency methods have to be employed, and processing based on multivariate parametric modelling of the EEG is the method of choice (GATH *et al.*, 1992).

The method outlined in the present study is aimed at detecting two strongly linked phenomena which might indicate convulsive EEG changes, namely the tendency to oversynchronisation, and that towards instability. Thus, tracking of pole trajectories and calculation of coherence have been carried out, using the method of residual energy ratios (DICKINSON, 1978; DICKINSON, 1979) in order to obtain the necessary high time/frequency resolution (HARRIS *et al.*, 1994).

Numerical experiments on a two-channel autoregressive signal simulating the epileptic EEG signal have shown that precise estimation of the coefficient matrices elements can be obtained from short record lengths.

Prediction of an oncoming seizure was carried out on several epileptic signal segments with various forms of seizure activities. Movement of a dominant pole-pair towards the unit circle was found in all cases examined and was interpreted as a tendency towards instability, allowing a prediction time in the range 1-6 s. Early oversynchronisation has been detected by increased magnitude squared coherence (MSC) in six out of eight seizure outbursts, and can also be used for seizure prediction. Although prediction by MSC is based on a preictal increase in the value of the coherence compared to its background level and thus should not be significantly influenced by the mode of electrode derivation, the use of monopolar electrode derivation is recommended. This is in order to prevent calculation of MSC from two EEG channels having a common electrode (as in the bipolar case) and to avoid any

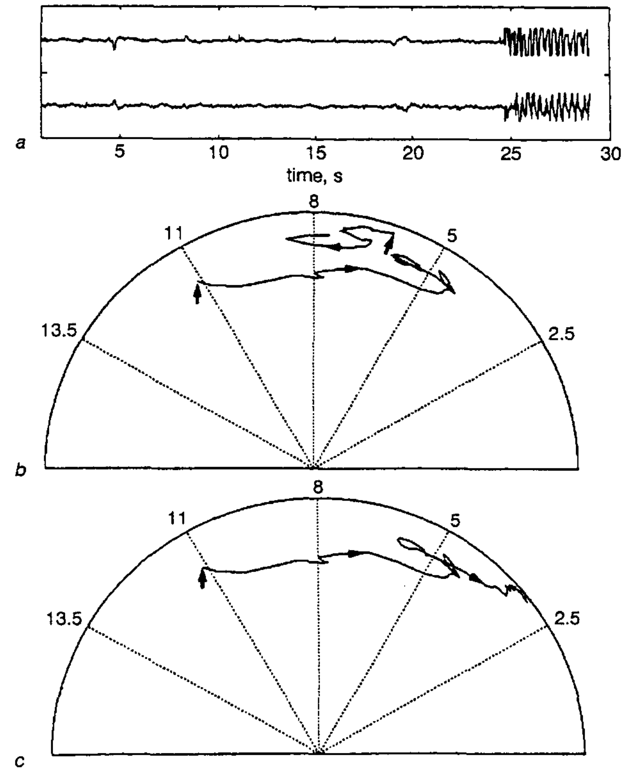

Fig. 8 *Seizure prediction using pole trajectory. Patient C. (a) The two EEG channels, F4 and O1. (b) Movement of two poles in the upper right quadrant of the unit circle, stretched into half circle, during the time 22–24 s of the EEG signal in (a) (preictal). Instead of degrees the corresponding frequencies are denoted. (c) As (b), but for the time 22–26 s (preictal and ictal). The arrows denote progression in time. The pole at around 7–8 Hz has been discarded*

doubt as to the reliability of the results. Likewise, it is preferred that two EEG channels with the longest possible inter-electrode distance be chosen thus obtaining relatively low values of MSC during the inter-ictal periods. It is concluded that calculation of preictal coherence and pole trajectories, using multivariate parametric modelling of scalp

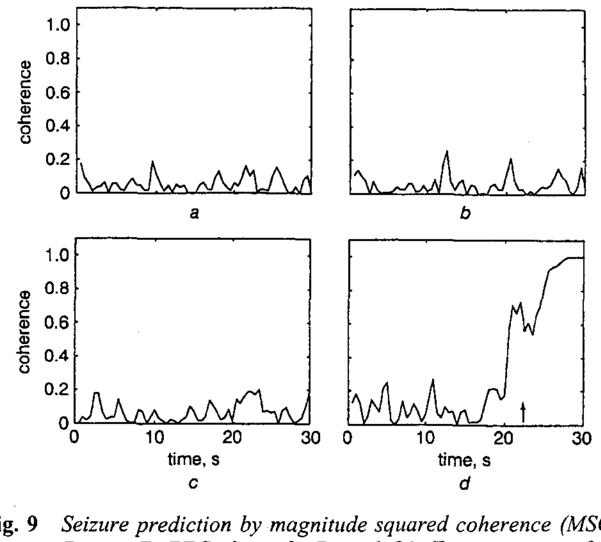

Fig. 9 *Seizure prediction by magnitude squared coherence (MSC). Patient E, EEG channels F4 and O1. Traces a–c are from different sections of the 324 s of interictal EEG. (d) Immediate preictal and ictal EEG. The arrow depicts the beginning of the seizure*

EEG can be an aid in the design of alternative anti-epileptic treatment such as electrical stimulation or conditioning and biofeedback.

References

BERK, K. N. (1974): 'Consistent autoregressive spectral estimates', *Ann. Stat.*, **2**, pp. 489–502.

BRAZIER, M. B. A. (1973): 'Spread of seizure discharge in epilepsy : anatomical and electrophysiological considerations', *Exp. Neurol.*, **36**, pp. 263–272

DICKINSON, B. W. (1978): 'Autoregressive estimation using residual energy ratios', *IEEE Trans. Inform. Theory*, **24**, pp. 503–506

DICKINSON, B. W. (1979): 'Estimation of partial correlation matrices using Cholesky decomposition', *IEEE Trans. Autom. Contr*ol, **24**, pp. 302–305

GATH, I., FEUERSTEIN, C., PHAM, D.T. and RONDOUIN, G. (1992): 'On the tracking of rapid dynamic changes in seizure EEG', *IEEE Trans. Biomed. Eng.*, **39**, pp. 952–958

GEORGE, R. E., and MICHAEL, J. E. (1991): 'Efficacy of vagal nerve stimulation for the treatment of partial seizures', *Epilepsia*, **32**, pp. S3–80

GERSCH, W. (1987): 'Non stationary multichannel time series analysis', in GEVINS, A. S. and REMOND, A. (Eds.): 'EEG handbook revised series' Vol. II, pp. 261–296

GOTMAN, J. (1983): 'Measurement of small time differences between EEG channels: method and application to epileptic seizure propagation', *Electroencephal. Clin. Neurophysiol.*, **56**, pp. 501–514

GOTMAN, J. (1987): 'Interhemispheric interactions in seizures of focal onset: data from human intracranial recordings', *Electroencephal. Clin. Neurophysiol.*, **67**, pp. 120–133

HARRIS, B., GATH, I., RONDOUIN, G. and FEUERSTEIN, C. (1994): 'On time delay estimation of epileptic EEG', *IEEE Trans. Biomed. Eng.*, **41**, pp. 820–829

ISHIJIMA, B., MORI, T. and YOSHIMASU, N. (1975): 'Neuronal activities in human epileptic foci and surrounding areas', *Electroencephal. Clin. Neurophysiol.*, **39**, pp. 643–650

KAPLAN, B.J. (1975): 'Biofeedback in epileptic equivocal relationship of reinforced EEG frequency to seizure reduction', *Epilepsia*, **15**, pp. 477–485

KUHLMAN, W.N. and ALLISON, T. (1977): 'EEG feedback training in the treatment of epilepsy: some questions and some answers', *Pavlovian J. Biol. Sci.*, **12**, pp. 112–122

MORF, M., VIEIRA, A. and KAILATH, T. (1978): 'Covariance characterization by partial autocorrelation matrices', *Ann. Stat.*, **6**, pp. 643–648

OJEMANN, G. A. and ENGEL, J. (1987): 'Acute and chronic intracranial recording and stimulation', in ENGEL, J. (Ed.): 'Surgical treatment of the epilepsies' (Raven Press, New York) pp. 263–288,

PENRY, J. K. and DEAN, J. C. (1990): 'Prevention of intractable partial seizures by intermittent vagal stimulation in humans', *Epilepsia*, **31**, pp. S40–3

PHAM, D. T. and TONG, D. Q. (1990): 'Maximum likelihood estimation for multivariate autoregressive model'. Research report RR 807-M, Laboratoire LMC/IMAG, Université Joseph Fourier, Grenoble

ROGOWSKI, Z., GATH, I. and BENTAL, E. (1981): 'On the prediction of epileptic seizures', *Biol. Cybern.*, **42**, pp. 9–15

SIEGEL, A., GRADY, C.L. and MIRSKY, A.F. (1982): 'Prediction of spike-wave bursts in absence epilepsy by EEG power-spectrum signals', *Epilepsia*, **23** pp. 47–60

VELASCO, F., VELASCO, M. OGARRIO, C. and FANGHANEL, G. (1987): 'Stimulation of the centromedian thalamic nuclei in the treatment of convulsive seizures, a preliminary report', *Epilepsia*, **28**, pp. 421–430

WHITTLE, P. (1963): 'On the fitting of multivariate autoregressions and the approximate canonical factorization of a spectral density matrix', *Biometrika*, **50**, pp. 129–134

WIGGINS, R. A. and ROBINSON, E. A. (1965): 'Recursive solution to the multichannel filtering problem', *J. Geophys. Res.*, **70**, pp. 1885–1891

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