

Prospects for routine detection of dementia using the fractal dimension of the human electroencephalogram

G.T.Henderson, E.C.Ifeachor, H.S.K.Wimalaratna, E.M.Allen and N.R.Hudson

Abstract: The paper details research which aims to improve the contribution made by electroencephalogram (EEG) analysis to the diagnosis and care of patients with brain disease; dementia in particular. Previous attempts to automate EEG analysis have concentrated on separating patient groups from control groups, often on the basis of a single neurophysiological index derived from a short, isolated segment of EEG. The authors seek to develop, and test, a novel technique for the analysis of changes in serial EEG recordings on individuals (subject-specific analysis) which may serve as a basis for routine early detection of dementia. The objectives of the reported study were to examine the feasibility of applying appropriate fractal dimension (FD) (complexity) measures to the human EEG, and to examine whether methods using the subject specific variability of these measures are likely to be useful for detecting patients who develop dementia. The reason for undertaking the study was to establish a 'proof of concept' and determine whether research should concentrate in this area. Existing EEG analysis methods were reviewed and four FD measures suitable for EEG analysis were developed. These four measures were applied to a total of 21 EEG recordings (from seven subjects with various dementias, eight age matched controls and two young subjects who gave three recordings each). The results were analysed and the following conclusions were drawn: it is possible to measure the complexity of the human EEG using the FD, and the subject specific variability of the FD is an important candidate method for identifying patients with dementia. Therefore, further work in this area is justified.

1 Early diagnosis of dementia

Advances in nutrition, living conditions and healthcare in the developed world have led to an improved life expectancy [1]. Unfortunately, this brings with it an increase in the number of people who will develop Alzheimer's disease and other dementias because the number of people in the high risk age groups is now increasing [2]. To offset this, efforts are being made to develop treatments such as the Acetylcholinesterase inhibitors (Tacrine, Donepezil and Exelon), which are claimed to slow the progress of the diseases [3]. However, unless a sufferer is diagnosed in the early stages, the treatments cannot give the maximum benefit [4].

Current techniques such as positron emission tomography (PET), that are used to diagnose and assess neurological disorders, require specialist equipment, and expert clinicians to interpret results. Such techniques, which are valuable in the diagnosis of dementia, or assess the nature of a neurological disorder, are inappropriate as a method of detecting individual subjects with early dementia within

the large at-risk population, because everyone within the at-risk group would need to be tested regularly and this would carry a high cost. Therefore, it is desirable to develop a low cost method of assessment which can be carried out quickly by a nonspecialist clinician.

To assess the required sensitivity and specificity of the new system it is necessary to look at the effects of misdiagnosis. Low sensitivity leading to large false negative diagnosis would be undesirable, but would not make the situation any worse than at present. Low specificity leading to false positive diagnoses would be undesirable because of the distress caused to patients and relatives and, perhaps, unnecessary use of expensive drugs.

Potentially, analysis of the electrical activity of the brain (the electroencephalogram or EEG), could provide the basis of an acceptable and affordable method for early detection of dementia [5]. The EEG has long been used for the diagnosis of neurological disorders but always had the disadvantage of subjectivity on reporting. If it were possible to automate the process of interpretation this would add objectivity and provide the desired first line of screening.

It is well known that disorders of the brain are accompanied by changes in the EEG. The difficulty is that such changes in the EEG may be nonspecific. The challenge is to automate EEG analysis such that early EEG changes in dementia can be detected before the development of clinically significant mental decline. The ultimate aim should be that a system based on such an approach may be used by a GP during routine health checks of older patients, e.g. for driving licence renewal.

The purpose of this paper is to report our initial study to demonstrate that subject specific variability of the FD of

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G.T. Henderson and E.C. Ifeachor are with the School of Electronic, Communication and Electrical Engineering, University of Plymouth, Plymouth, Devon, PL4 8AA, UK

H.S.K. Wimalaratna is with the Department of Neurology, Radcliffe Infirmary, Woodstock Road, Oxford, OX2 6HE, UK

E.M. Allen and N.R. Hudson are with the Department of Neurophysiology, Deriford Hospital, Plymouth, PL6 8DH, UK

the human EEG is an important candidate method for the early detection of dementia [6].

2 Subject specific EEG analysis

A great deal of effort has been expended in the pursuit of automated EEG analysis, but there are few successful automated methods that are widely and routinely used in clinical practice. A notable exception is perhaps bispectral analysis in anaesthesia [7]. We believe that one reason why automatic EEG analysis has not brought more success is that research has concentrated on group comparisons, i.e. attempting to separate individuals into normal and diseased groups (Alzheimer's, Parkinson's, etc.), using indexes derived from isolated (snapshot) EEGs. An alternative is subject-specific analysis: comparing serial EEGs from the same subject and looking for trends in indexes developing over time, rather than comparing an EEG to that which is regarded as normal within the population.

When an EEG is analysed, one may extract indexes such as the alpha wave magnitude, FD and bispectrum index. Each of these indexes is subject to short-, medium- and long-term variability. For subject-specific analysis, we require a distinguishable change that implies the onset of disease, and a continuing change that gives a measure of disease progression or effect of treatment.

As an illustration, Fig. 1 shows changes in a hypothetical index from a subject who is initially normal and then enters a notable decline at the onset of disease. The index only becomes 'abnormal' some time after the onset of the disease, when it falls outside the normal spread. This illustrates why a subject-specific method that compares an EEG to those taken previously from the same subject has the potential to provide earlier detection of a disease than a method that compares an EEG to what is generally normal within the population.

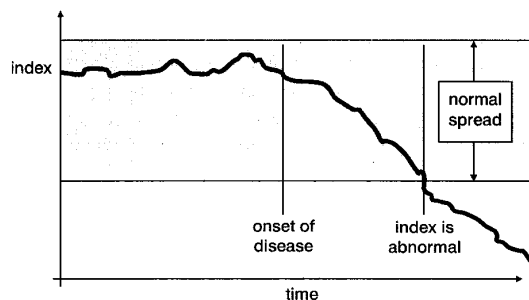


Fig. 1 Conceptual index progression with time

3 EEG complexity

As the brain is constructed of synapses and neurones which have nonlinear behaviours, it has been suggested that the brain could, in a mathematical sense, be chaotic. A tutorial review of nonlinear dynamical analysis of EEGs is given in [8].

Research in EEG dimensional complexity has evolved from an early work which suggests that the human EEG, under some conditions, may represent deterministic chaos of relatively low dimension [9], through studies measuring the dimension of the strange attractor [10], through to a recent work that has questioned whether the EEG represents a chaotic signal [11]. It was reported that surrogate-data testing suggests normal EEG is high-dimensional, and does not represent low-dimensional chaos.

There is an alternative to dimensional complexity measures which rely strongly on the assumption that low dimen-

sional chaos is present. The alternative is the FD, which may be used as a practical measure of signal complexity even if chaos is not present. This study demonstrates that the FD may provide useful results, although it is accepted that the theoretical framework is somewhat weakened.

4 Fractal dimension of the EEG

4.1 Introduction to fractals

The FD index was used and developed in this paper as a vehicle to explore subject specificity. The reason for choosing the FD was that it had been reported to be successful in group comparison trials [12, 13]. To introduce fractals, it is convenient to begin with an example that was conceived by Helge von Koch [14]. The so called Koch curve may be constructed by taking an equilateral triangle and then on each side add another equilateral triangle to cover the middle third of the line. This is then repeated with smaller and smaller triangles (see Fig. 2).

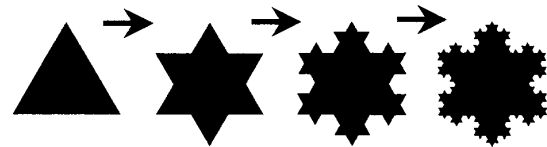


Fig. 2 Development of the Koch curve

The Koch curve reveals an interesting paradox: each time new triangles are added the total length of the outline becomes larger by a factor of $4/3$. Therefore the total length of the outline tends to infinity, even though the area of the curve remains less than the area of a circle drawn around the original triangle, and is therefore finite. A mathematical framework was invented to describe shapes such as the Koch curve. In this framework these shapes are assigned a non-integer or fractal dimension (which for the Koch curve is approximately 1.26). Interestingly, one magnification of the Koch curve shows the same structure as any other magnification of the Koch curve. This is self-similarity, which all fractals exhibit.

4.2 Definition of dimension

In common parlance, the number of dimensions that an object exists within is equal to the number of numbers that would be necessary to describe any point within the object. So, for example a line exists in one-dimensional space because one number is needed to uniquely identify a point on the line, and a square exists in two-dimensional space because two numbers are needed to describe any point within the square. The generally accepted, mathematically rigorous, inductive definition is:

'If the boundaries of arbitrarily small neighbourhoods of all points in a space are $(n - 1)$ -dimensional, then the space is n -dimensional. The empty set, and only the empty set, has a dimension of -1 '.

This definition is accurate but difficult to understand. Taking a square as an example, any point within the square has a boundary that is a closed (circular) line. Therefore, a square has one more dimension than a line. Furthermore, any point on the line has a boundary that comprises two points and similarly the boundary to the points is the empty set. Thus, working back to the square; the empty set has a dimension of -1 , the set of points has a dimension of 0, the line has a dimension of 1 and the square has a dimension of 2.

The above definition of the dimension of a space always gives an integer. This is the topological dimension D_T . It

will be seen that a fractal set is characterised by a number of dimensions which is greater than the topological dimension and that this dimension need not be integer. To understand the non-integer dimension it is convenient to consider the Koch curve, where a single number is not sufficient to describe a point on the outline because the length is infinite and two numbers would be too much because the outline does not have an area: thus the number of dimensions needed to describe it is between 1 and 2 (in fact the dimension is ~ 1.26).

Returning to a more rigorous argument, consider a smooth curve of length L which has a topological dimension D_T of 1. The length of the curve may be estimated by covering it with N small line segments of length δ , where N would be a function of δ . Now L would be given by:

$$L = \lim_{\delta \rightarrow 0} (N(\delta)\delta) \quad (1)$$

Similarly, consider a shape with a topological dimension of 2, such as a circle or square, where the area may be estimated by covering it with small squares of side δ :

$$A = \lim_{\delta \rightarrow 0} (N(\delta)\delta^2) \quad (2)$$

Thus, the measured quantity (length, area etc.) may be found by covering the shape with small objects which have the same topological dimension. If these objects are covered by small objects of an inappropriate dimension then the result is either zero or infinite. For example, if we use vanishingly small squares to cover a smooth curve, then in the limit the 'area' will be zero. Also, if we cover a circle with small line segments, then in the limit the 'length' will be infinite. We may write a generalised expression for the measured quantity M_d :

$$M_d = \lim_{\delta \rightarrow 0} (N(\delta)\delta^d) = \begin{cases} \infty & d < D \\ M_{d0} & d = D \\ 0 & d > D \end{cases} \quad (3)$$

The value of M_{d0} is not important in this context, but the Hausdorff-Besicovitch dimension D is of great significance [15]. For a fractal set, this dimension (the FD) obeys the inequality $D_T < D \leq D_T + 1$ and is not normally an integer. For the Koch curve the apparent length of the outline continues to increase indefinitely as the step-size decreases in accordance with the rule set out in eqn. 3.

4.3 Measuring the fractal dimension

A coastline is an example of a natural approximation to a fractal; if one steps around a land-sea boundary using N steps of length δ , then N would be found to be a function of the step length, approximately given by:

$$L(\delta) = \delta N(\delta) = L_0 \delta^{D-1} \quad (4)$$

Here L is the apparent length of the coast, L_0 is a constant and D is the FD. Using a range of values for δ , and measuring the corresponding values for length $L(\delta)$ it is possible to use a least squares (or similar) method to estimate D ; e.g. for Norway the FD $D \sim 1.5$. This technique of using line segments to cover a fractal with a topological dimension of 1 is known as the divider dimension (DD).

An alternative to the DD is to cover the coastline with squares; this is the box dimension where the total area A is found to be related to the length of the squares side δ by:

$$A(\delta) = \delta^2 N(\delta) = A_0 \delta^{D-2} \quad (5)$$

Using a range of values for δ , and measuring the corresponding values for area $A(\delta)$, it is possible to use a least squares (or similar) method to estimate D .

The FD applied to the EEG is a good candidate to be an indicator of possible dementia because it is a measure of signal complexity, and it has been shown that the complexity of the EEG is less in demented subjects [12].

4.4 Fractal dimension in affine space

There is a complication when one considers computing the FD of the EEG which exists in an affine space. In an affine space the axes have incompatible units, and there is no natural scaling between them (distance along the time axis cannot be compared with distance along the voltage axis) and as such δ and computed D may not be meaningful [16].

In an early study [12], the DD of the EEG was used to separate subjects with Alzheimer's Disease from a group of normal subjects. When this method was repeated on a single Alzheimer's subject and a single normal subject it was found that the arbitrary voltage/time scaling affected the results; a scaling of 0.6 nV/s for example, gave FDs similar to those reported (1.66 for a normal subject and 1.28 for an Alzheimer's subject); but a higher scaling of 2.5 nV/s gave very different results, where the normal subject had a lower FD (1.21) than the Alzheimer's subject (1.61). This problem is a direct consequence of applying the divider dimension to an EEG, which exists in an affine space.

A number of methods have been reported in the literature which are suitable for estimating the FD of shapes in an affine space [17]. The adapted box dimension and the dimension of the zero-set were chosen for this study. The adapted box dimension was chosen because it is similar to the box dimension often used in non-affine space, and the dimension of the zero-set was used because it is computationally efficient.

To compute the adapted box dimension we divide the record of duration T into slices of length Δt , and note the difference between the maximum and minimum during each slice (the extent). The mean extent $\varepsilon(\Delta t)$ is computed for a range of Δt , and the dimension is computed by finding a best fit to the equation:

$$A(\Delta t) = T\varepsilon(\Delta t) = A_0 \Delta t^{2-D} \quad (6)$$

To compute the dimension of the zero-set we form the set of instances when the record intersects with a suitable straight line (we have used the line formed by linear regression). The topological dimension of this set is zero. The FD of this zero-set is computed by covering it with N line segments of length Δt , and finding the best fit to the equation:

$$L(\Delta t) = \Delta t N(\Delta t) = L_0 \Delta t^{1-D} \quad (7)$$

4.5 Combining estimates of fractal dimension

In this analysis the raw EEG data are divided into 1s segments, and the estimated FD from each segment through the entire duration of the recording and across all 21 channels was plotted on a histogram. Then, the highest point on the histogram (the mode) was taken as the composite measure of fractal dimension for that recording. This use of a histogram is intended to reduce the effects of artefacts and unusual activity on the final result. However, it is conceivable that artefacts of long duration may have an effect and this will be addressed in future work.

The choice of segment length can have a detrimental effect on the results. However, the results obtained are almost invariant for segment lengths between 0.5 and 2s. Below 0.5s the results become erratic because of the number of samples becoming too small compared to the

sampling rate employed, 256Hz. With segment lengths greater than 2s the results are affected by the nonstationary nature of the EEG [5]. Thus, 1s is seen to be a reasonable choice for segment length.

The adapted box and zero-set dimension of the EEG were estimated in this way. A further two measures were produced by applying adapted box and zero-set dimension estimating techniques to the auto-correlation of the data; that is replacing the data segments with the discrete time analogue of the auto-correlation function:

$$R_S(t) = \int_{s \cdot \Delta t}^{(s+1) \cdot \Delta t} x(\tau)x(\tau+t)d\tau \quad 0 \leq t < \Delta t \quad (8)$$

where s is the segment number and Δt is the segment duration (1s).

5 Data

Data for this study were obtained using the traditional 10-20 system in conjunction with a strict protocol [18]. The common average montage (using the average of all channels as the reference) was used in all recordings, and the sampling rate was 256Hz.

EEGs were collected from seven patients (three Alzheimer's patients, three mixed type (Alzheimer's and multi-infarct dementia) patients and one multi-infarct dementia patient), eight age-matched controls (over 65 years of age), one young male and one young female. All of the age matched controls and the two young volunteers had normal EEGs (confirmed by a Consultant Clinical Neurophysiologist). One age-matched control (known as 'vol1') has subsequently developed Alzheimer's disease; this record is of particular interest because it is potentially of a subject early in transition from 'normal' to Alzheimer's diseased. The young male (denoted by 'X') and the young female (denoted by 'Y') had their EEG recorded three times at intervals between 7 and 14 days. These recordings give an indication of the variability of a single subject's FD, which may be compared with the variability between members of the set of normals.

The EEG recordings encompass various states: awake, hyperventilation, drowsy and alert with periods of eyes closed and open. The analysis described in this paper takes the whole recording including artefacts and has no *a priori* selection of elements 'suitable for analysis'. This approach leads to a prediction of the usefulness of the techniques as they would most conveniently be used in practice.

6 Results

It was found that the variation in FD over areas of the head was too irregular to give significant results, but there is an indication that the front of the head tends to have lower but more variable FD than the rear of the head. The authors suspect that this is because the effects of artefacts are more pronounced, and the abundance of slow waves is greater, at the front of the head. It may be necessary to investigate these variations over the scalp in future work. The data presented below are the FD aggregated from all channels over the scalp.

Table 1 shows the results from three recordings of each of the two young subjects (subjects X and Y). The variation from recording to recording of the same subject is the short term variability of the FD. The estimated population standard deviation (SD) for a single subject for each measure is given in Table 2.

Table 1: Comparison of fractal dimension from two young subjects (three readings from each)

Record	Raw EEG		Auto-correlation of EEG	
	Adapted box	Zero-set	Adapted box	Zero-set
X1	1.564	0.563	1.350	0.536
X2	1.574	0.608	1.385	0.559
X3	1.559	0.564	1.223	0.555
Y1	1.521	0.577	1.273	0.411
Y2	1.519	0.561	1.284	0.425
Y3	1.513	0.558	1.269	0.423

Table 2: Variability of fractal dimension measures from two young subjects

	Raw EEG		Auto-correlation of EEG	
	Adapted box	Zero-set	Adapted box	Zero-set
SD	0.006	0.020	0.060	0.010

Table 3 shows the results for the age-matched controls, and the mean result for each of the young normals. It may be seen that for all the measures, except the zero-set dimension of raw data, the SD of the results from the group of normals is larger than the variation for a single subject (Table 2).

Table 3: Fractal dimension measures from controls and young normals

Record	Raw EEG		Auto-correlation of EEG	
	Adapted box	Zero-set	Adapted box	Zero-set
vol2	1.596	0.562	1.434	0.590
vol3	1.572	0.560	1.452	0.648
vol4	1.551	0.561	1.496	0.662
vol5	1.592	0.562	1.587	0.562
vol6	1.591	0.561	1.638	0.627
vol7	1.538	0.564	1.391	0.539
vol8	1.596	0.616	1.500	0.670
X	1.566	0.578	1.319	0.550
Y	1.518	0.559	1.275	0.420
Mean	1.569	0.569	1.475	0.585
SD	0.028	0.018	0.117	0.079

Table 4: Fractal dimension measures from demented subjects

Record	Raw EEG		Auto-correlation of EEG	
	Adapted box	Zero-set	Adapted box	Zero-set
AD1	1.560	0.565	1.134	0.323
AD2	1.520	0.560	1.181	0.368
AD3	1.512	0.554	1.183	0.331
MID1	1.483	0.496	1.219	0.384
MIX1	1.533	0.562	1.148	0.324
MIX2	1.442	0.497	1.118	0.270
MIX3	1.608	0.669	1.265	0.438

The results for the demented subjects are shown in Table 4. The results show that the adapted box dimension and zero-set dimension of the auto-correlation function are generally lower than normal when dementia is present. For these data there is no overlap in the adapted box dimension

of the auto-correlation function for normal subjects and for demented subjects (100% specificity). However, the separation between the two groups of subjects is small, and there would undoubtedly be an overlap if more recordings were taken.

Finally we consider the results from the age-matched control 'vol1' who was at the time of recording confirmed by a clinician to be 'normal', but went on to develop Alzheimer's disease. The results from 'vol1' show that the adapted box dimension of the auto-correlation function and the dimension of the zero-set for the auto-correlation function are suspiciously low, but not outside the range for normal subjects. Unfortunately, in the absence of recordings before or after this recording it is not possible to say whether subject specific analysis would have detected the onset of this dementia.

Table 5: Fractal dimension measures from subject prior to dementia

Record	Raw EEG		Auto-correlation of EEG	
	Adapted box	Zero-set	Adapted box	Zero-set
vol1	1.547	0.564	1.325	0.516

The results in Tables 1–5 are reproduced graphically in Figs. 3–6.

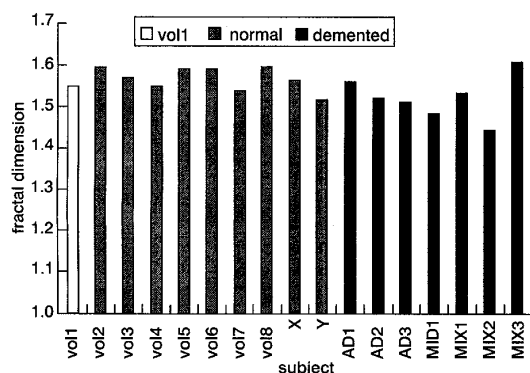


Fig. 3 Adapted box dimension of raw EEG data

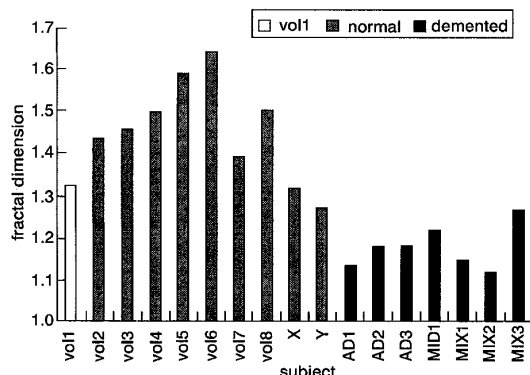


Fig. 4 Adapted box dimension of auto-correlation of EEG data

7 Sensitivity and specificity

The results described so far are reasonably good with some separation of demented from normal subjects, however it is possible to achieve more by using the subject-specific concept. Consider the zero-set dimension of the auto-correlation function for which the results from specific subjects vary over a number of weeks by only 0.01 (SD)

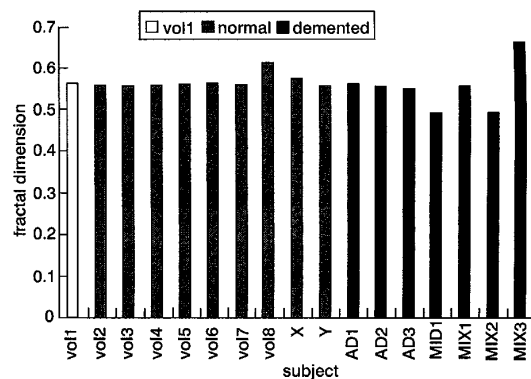


Fig. 5 Zero set dimension of raw EEG data

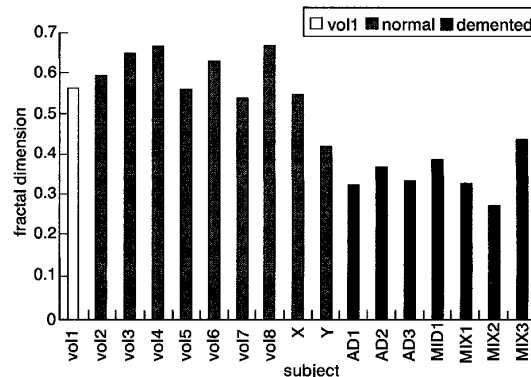


Fig. 6 Zero set dimension of auto-correlation of EEG data

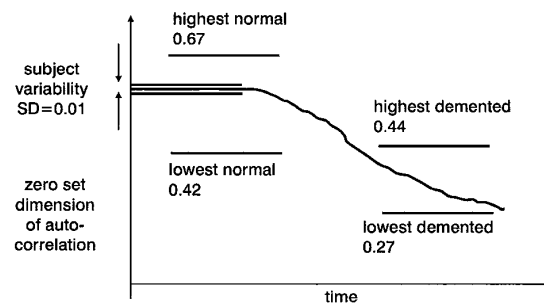


Fig. 7 Subject specific variability

and the range of results from normal subjects (0.42 to 0.67, from Table 3) overlaps with the range from demented subjects (0.27 to 0.44, from Table 4). These results are summarised in Fig. 7. If we were to compare the FD from a subject to one taken from the same subject some time earlier, then we would be able to detect a subtle decrease and possibly the onset of dementia. Clearly this is only indicative, and further work will be required to demonstrate that there is a measurable rate of decline in the early stages of dementia, that the stability of FD among normal subjects exists over longer periods and this stability is common among a substantial proportion of normal subjects.

8 Conclusions and future work

The results in this paper show that two of the FD measures (the adapted box dimension of the auto-correlation function, and the dimension of the zero-set for the auto-correlation function) are good candidates for use in subject-specific detection of dementia. This is because the measured FD of the EEG is generally lower for a demented subject

than for normal subjects, and the variability of a single normal subject's FD is small in comparison to the variability between members of the set of normals.

Having met the objectives of this study by measuring the complexity of the human EEG using the FD, and by demonstrating that the subject-specific variability of the FD is an important candidate method for the routine detection of dementia, we may conclude that further work in this area is justified.

The research will continue with more data being analysed to provide statistical significance (including serial recordings from Alzheimer's subjects who are in decline) and with indexes other than FD, such as bicoherence, being tested.

Further work will also be required to assess whether the use of a histogram to eliminate the effects of artefacts is adequate, because artefacts of long duration may continue to have an effect.

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