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Letter to editor

Dr. G. Otte

Concerns :

I. Abatzoglou, P. Anninos, A. Adamopoulos and M. Koukourakis. Nonlinear analysis of brain magnetoencephalographic activity in Alzheimer disease patients.

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Since the seminal publication of Babloyanz (1985), research and studies on the non linear analysis of EEG signals have clearly taken off, empowered by progress in methodology of non linear dynamics, fractals, complexity and deterministic chaos and fuelled by the hope -and sometimes optimistic "belief" - that this approach could outperform linear methods in diagnosis of conditions such as Alzheimer's disease, epileptic fits et al.

Whereas in linear modeling one considers the EEG as the realization of a linear stochastic process (fi autoregressive) with superimposed Gaussian noise (fi moving average) in the non linear view the signal is the projection of a trajectory of a dynamical process in state space governed by a function that can settle as a fixed point, a limit cycle or an attractor. In case of deterministic chaos this attractor is often a complex geometrical and sometimes esthetically pleasing object, with non integer (fractal) dimension.

As Chiappa points out, spectral analysis is not very useful in the discrimination of those models for as sharp peaks in the spectrum clearly denote oscillatory behavior in both models, the broad band contributions to the power spectrum can not distinguish the extern noise from the linear model from the intrinsic system dynamics of the non linear generators.

In their article Abatzoglou et al have described in great detail the methods and tools (Grassberger Procaccia, Takens theorem ...) that have been developed to tackle this problem and have applied them skillfully to MEG data. They were able to demonstrate clinical useful results in cases of normals versus patients suffering from Alzheimer disease.

One could be tempted to apply these methods also to EEG signals as they are likely to be more widely available then MEG. Yet this port might not be without some problem and pitfalls. A blind application of the methodology should never be tempted without a firm theoretical knowledge on non linear signal analysis techniques.

He who wants to travel down the road of non linear analysis will be facing a bewildering array of methods and toolkits ranging from all kind of correlation dimension calculations, Hurst dimension, Lyapunov exponents, fractal dimensions both in time as in phase space domain, several types of entropy and complexity measurements and algorithms/methods to estimate the state space embedding dimension ("embedology") and time delay (false nearest neighbors, autocorrelation, mutual information). Less then critical "out of the box" application of these powerful tools can easily lead to incorrect conclusions as many pitfalls await the naive traveler through fractal landscape.

It is estimated that for Grassbergers and Procacia correlation dimension a long enough data segment is necessary of N so that D2<2logN. Such long segments will probably contain artifacts and non stationarities that could jeopardize the whole analysis. And while Takens Theorem states that **If** there is deterministic chaos, **Then** the fractal attractor can be reconstructed in a time delay space of appropriate dimension constructed from only the one dimensional realization (the signal at hand), this does not imply the reverse. Calculating some non integer dimensionality is evidently no sure proof of existence of deterministic chaos.

It has also been proven that linear noise filtering of true random series can generate non integer correlation dimension suggesting deterministic chaos where in fact none is present. This cast doubt on the value of some former results. Theiler and Rapp reexamined previously published EEG data and concluded that due to the autocorrelation effect of over sampling, wrong conclusions were reached.

This is not to say that these techniques are not useful but only to warn that rigueur in the application and signal conditions, as the authors have shown here, is imperative to prevent false "positive" conclusions. There is evidence that long range correlations are present in some EEG signals but as many of the phase space techniques are sensitive to noise (and real world EEG has lots of noise to deal with) models and reality will always be in for difficult reconciliation.

Working with recurrence analysis I was often surprised to see that in contrast to synthetic signals, in real life EEG no clear attractors could be identified, embedding dimension tended more towards high dimensionality (even stochastic) and no clear or "nice" esthetically pleasing fractal like attractor patterns "emerged". Maybe this is different in pathology and further research will be mandatory to define and detect transition zones as the authors have successfully done on their MEG data. Maybe in the future we will eventually focus more on model free approaches and try to demonstrate alternation in signal complexity using time domain fractal dimension (fi Sevcik, Katz, Higuchi, and Sample entropy methods). Multiscale entropy analysis (MSE) is such a technique that is robust, less model dependent (can be applied to deterministic chaos, stochastic and periodic signals), can be used on relative short signal segments and is less noise sensitive. It has also been shown by Escudero et al to be of clinical value in detecting early Alzheimer disease. Maybe we will even move to small world network graph theory to clear out normal from pathological communication patterns in larger neuronal cell assemblies. After all, in the clinical situation the performance of a method is not always evaluated on how it best approaches a theoretical mathematical model benchmark (fi artificially generated time series with known fractal dimensions) but how well it performs in delineating normality from early pathology or in predicting clinically important events (fi epileptic fit, cardiac arrest from hart beat series). There is still a lot of room for innovation and appropriate clinical studies.

Anyhow, the authors are to be congratulated for showing how new mathematical approaches to signal analysis are opening a novel and promising window on the brain that for us clinicians will offer a new and refreshing look on brain dynamics both in normality and pathology. EEG and MEG outperform imaging in their excellent time resolution and now come equipped with even more powerful methods (Source localisation swLoreta, MSE, ICA filtering, ERP) that could sparkle the revival process of these techniques in the field of neurology as well as cognitive neuropsychiatry. This is a fascinating perspective that certainly would not have displeased Dr. Hans Berger.

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