Best Practice & Research Clinical Anaesthesiology
Vol. 20, No. 1, pp. 31–48, 2006
doi:10.1016/j.bpa.2005.09.001
available online at http://www.sciencedirect.com

3

Concepts of EEG processing: from power spectrum to bispectrum, fractals, entropies and all that

Helmut Schwilden* MD
Professor of Experimental Anaesthesiology
Anaesthesiology Clinic, University of Erlangen-Nürnberg, Erlangen, Germany

Over the past two decades, methods of processing the EEG for monitoring anaesthesia have greatly expanded. Whereas power spectral analysis was once the most important tool for extracting EEG monitoring variables, higher-order spectra, wavelet decomposition and especially methods used in the analysis of complex dynamical systems such as non-linear dissipative systems are nowadays attracting much attention. This chapter reviews some of these methods in brief. However, a comparison of some of the newer approaches with the more traditional ones with respect to clinical end-points by association measures and to the signal-to-noise ratio raises some doubt over whether the newer EEG-processing techniques really do better than the more traditional ones.

Key words: higher-order spectral analysis; entropy; correlation dimension; state-space; attractor; association measures; signal-to-noise ratio.

INTRODUCTION

The processing of the electroencephalogram (EEG) to a single numerical trend indicator (EEG parameter or EEG variable) for monitoring anaesthesia may be divided into three steps:

1. amplification and filtering of the electrical biosignal received by at least two electrodes mounted on the scalp or other parts of the head;
2. digitisation of the amplified signal, generating a discrete numerical time series;

* Tel.: +49 9131 85 39150; fax: +49 9131 85 39161.
E-mail address: schwilden@kfa.imed.uni-erlangen.de.

3. partitioning of the numerical time series into segments by grouping adjacent numbers and, using an algorithm, projecting each of these on to a number (the value of the EEG parameter as defined by the algorithm for that time segment).

This article will deal primarily with the third point but will also draw attention to aspects of the first two steps that might affect the final outcome of step 3.

As with all measurements, the process of measuring an object will modify the object itself. This becomes more important the smaller the object is (e.g. the uncertainty relationship of quantum mechanics) and also applies to the EEG. Measuring the EEG means measuring small electrical potential differences between two locations on the scalp by amplifying the current along the internal resistor of the amplifier. The different potentials are caused by an electromagnetic field that is generated by moving electrical charges inside the brain. These electrical charges are moving ions through the cell membrane of the brain cells. As the electromagnetic field of moving charges declines with distance according to some power law, the electrodes placed on the surface of the scalp register only very superficial currents. Thus, the EEG is a time- and space-averaged electrical potential difference. The amplification of the EEG signal by a real amplifier adds noise to the signal, filters the signal and affects the phase relationship between the diverse frequency components contained in the signal. Whenever one records an EEG in clinical practice, one thus records not the 'true EEG' but some electrical brain activity modified by the recording process. EEG recording has, however, become more reliable over the past few decades as technology has advanced.

EEG PREPROCESSING

The analogue signal is converted to a discrete time series by an analogue-to-digital converter whose main parameters are amplitude resolution and rate of digitisation (sampling frequency). The amplitude resolution is given in bits with typical values of 12 or 16 bits AD-conversion, meaning that a given voltage range, for example -2 V to $+2$ V, is divided into 2^{12} or 2^{16} intervals, giving a resolution of 976 μV or 60 μV of the amplified signal.

More crucial for the AD conversion process is the sampling frequency, f_s, the inverse of which is the equidistant spacing, dt, of the digitised amplitude. As shown in Figure 1, it is quite obvious that the smaller the dt, the more samples will be available and the better the original signal can be reconstructed. However, the higher the sampling frequency f_s, the higher will be the associated costs in terms of computer memory, processing power and AD-conversion hardware. If the sampling frequency is too low, there will be too few data to reconstruct the signal. An approximate solution for finding the appropriate sampling rate is given by the Nyquist theorem, which states that, for a correct discrete representation of an analogue signal, one needs a sampling rate f_s at least twice as high as the highest frequency, f_{high}, contained in the signal, such that $f_s \geq 2 \times f_{high}$.[1]

As it is difficult to shield the EEG from interference from electrical fields originating in the electrical power supply, which has a frequency of 50 Hz in Europe or 60 Hz in the USA, a sampling frequency of more than 100 Hz or 120 Hz is advisable. Most EEG recording machines have inbuilt analogue filters. There are three types of filter: low-pass filters, high-pass filters and notch filters. These let through signal components with a frequency smaller than the frequency f_L defined by the low-pass filter and higher than the frequency f_H for the high-pass filter, and filter out a small frequency band around a

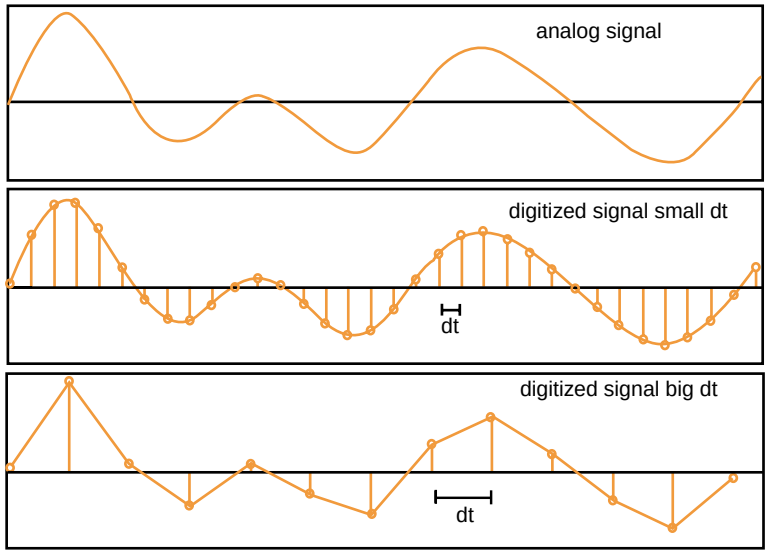

Figure 1. The sampling rate has to be twice as high as the highest frequency contained in the signal.

frequency f_N for the notch filter. Typical values for EEG machines and monitoring devices are $f_L = 30$ Hz, $f_H = 0.5$ Hz and $f_N = 50$ or 60 Hz. The high-pass filter setting in particular is of crucial importance for monitoring the trend in the EEG during anaesthesia. An incorrect setting of the high-pass filter could dramatically change the interpretation of EEG changes during anaesthesia.

PROPERTIES OF TIME SERIES

In essence, the analysis of the EEG is the analysis of time series. Figure 2 gives an example of the awake EEG (the first trace being an alpha rhythm with closed eyes) and its modification by increasing concentrations of ether.

There are many different methods of time series analysis, ranging from simple descriptive statistical measures such as Hjorth's parameters to sophisticated transforms like Wigner transformation or wavelet decomposition, and topological properties of certain sets (trajectories) in state-spaces such as, for example, fractal correlation dimensions. The application of these methods to a given time series depends on the nature of the time series. In general, one may classify time series by the following properties: random versus deterministic, stationary versus non-stationary and linear versus non-linear.

Consider some physical process generating a time series $x(t_1), x(t_2), x(t_3) \ldots x(t_n)$, $n = 1 \ldots$ infinity, such as a spring with a weight generating a trace on a strip chart according to some force applied to the weight (Figure 3). If the force is a random force, the developing time series is a random one, whereas if the force is deterministic, the time series will be deterministic. If the statistical properties of the force over time will not vary, the resulting time series is said to be stationary. Given a string obeying Hooke's law, the time series will be linear, but if the elongation of the spring and the driving force are related by some power law, the time series will become non-linear.

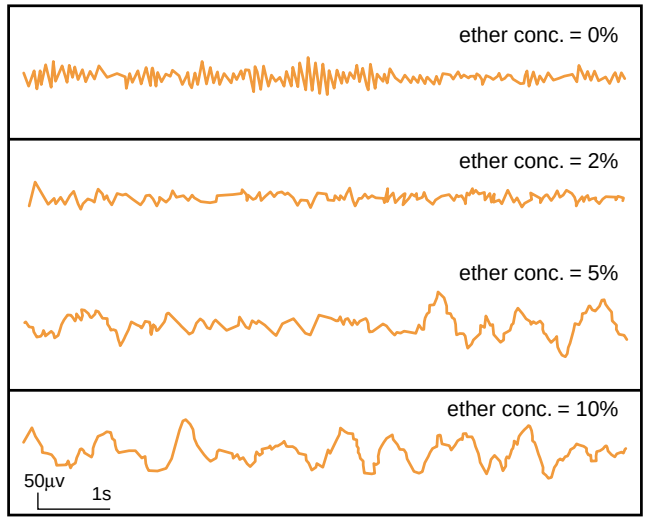

Figure 2. As anaesthesia deepens, the amplitude of the EEG increases and the frequency slows down until a burst-suppression pattern occurs.

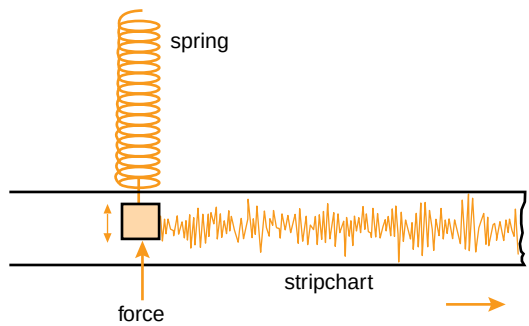

Figure 3. A possible underlying physical process to generate a time series.

There are methods to define these properties in mathematical terms given the digitised values $x(t_i)$, $i = 1 \ldots$ and to prove or reject them, but this will sometimes be too elaborate or even nearly impossible. Given three quantities, each with two different properties, there will $2^3 = 8$ possible combinations of the three properties. These are depicted in Figure 4 with the typical types of analysis applied to such time series.

SPECTRAL ANALYSIS

The basis of spectral analysis is a theorem stating that any function in time can be thought of as a superposition of sinus waves of different frequencies. Let $A_{fi}\sin(2\pi f_i t + \delta_i)$ denote the sinus wave at time t of frequency f_i with amplitude A_{fi} and phase δ_i; then, given any function of time denoted by, for example, eeg(t), eeg(t) can be written as:

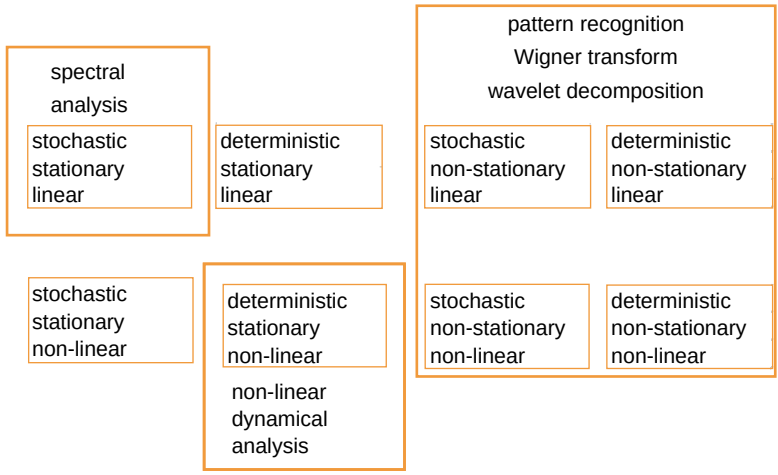

Figure 4. Classification of signals and typical methods for their analysis.

$$\mathrm{eeg}(t) = \sum_{\text{all frequencies } fi} A_{fi}\sin(2\pi f_i t + \delta_i)$$

with suitable coefficients (amplitudes) A_{fi} and phases δ_i. If one considers the square of the amplitudes A_{fi}^2 as a function of the frequency f_i, this function is usually said to be the (power) spectrum of eeg(t) because it gives a measure of how strongly a certain frequency f_i contributes to the signal. That is, instead of representing the signal eeg(t) by N data points eeg(t_1),…,eeg(t_N), it is now represented by the amplitudes A_{fi} and phases δ_i at exactly $N/2$ frequency i_i. Hence N original numbers (the signal data) are transformed into N transformed numbers (A_{fi}, δ_i). This transformation is called Fourier transformation. The upper panel of Figure 5 shows an EEG time segment of 8 seconds, with the lower panel showing the power spectrum, which peaks at around 10 Hz (alpha-type EEG), and the phases, which show no clear pattern but look like random noise.

These phase data are often discarded because they seem to contain no information. The theoretical concept of the power spectrum is founded on theoretical signals extending from minus infinity to plus infinity in time. In practice, one has only a small sample, namely a finite segment of a few seconds, to determine the spectrum. Hence one has to extrapolate the finite time period to a signal extending to infinity. There are many different ways to extrapolate the signal, the two most common techniques for estimating the power spectrum being FFT and maximum entropy. The FFT technique repeats the segment identically to infinity, whereas the maximum entropy method uses a way of extrapolation that maximises the entropy of the total signal.

Each method is associated with a certain error of estimation, just as the mean value in a population is estimated with a certain error if only a portion of the population is sampled. Typically, the error of estimation is in the order of 100% for the power value in a single-frequency bin. To reduce the error of estimation, two averaging procedures are available, averaging over adjacent frequency bins or averaging over adjacent power spectra. To parametrise the change in power spectrum associated with anaesthesia and

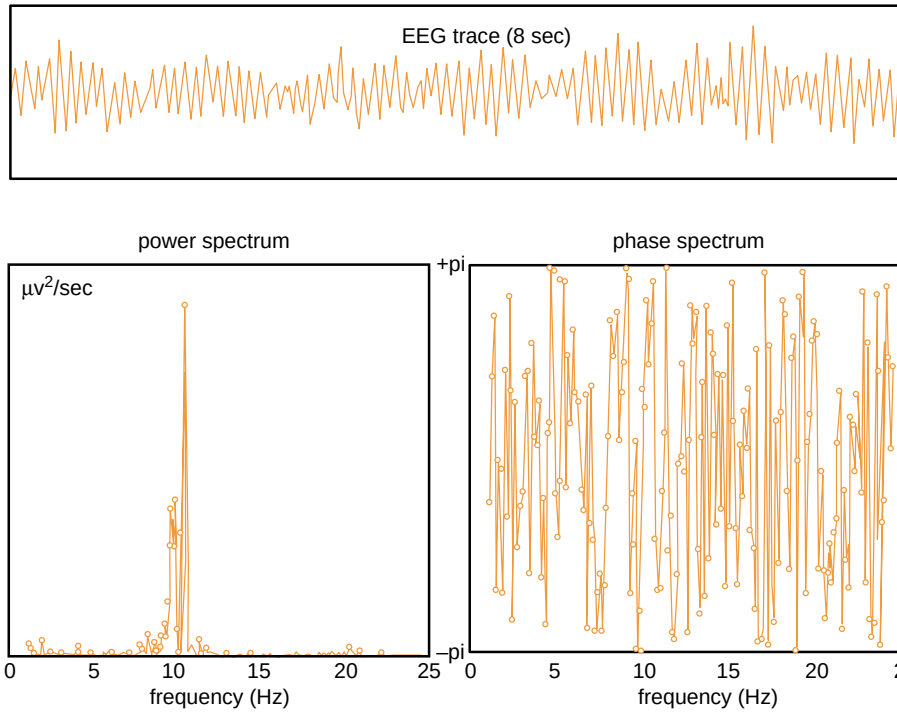

Figure 5. Decomposition of an EEG trace into a power spectrum and phases by Fourier transformation.

anaesthetic drug delivery, single descriptors of the power spectrum have been used, among which are:

total power = area under the power spectrum;
absolute power and relative power = absolute power / total power in diverse frequency bands.

The definition of the boundaries of the bands is somewhat arbitrary. A choice used by the present author, for example, is subdelta =]0.5–2] Hz, delta =]2–5] Hz, theta =]5–8] Hz, alpha =]8–13] Hz and beta > [13 Hz. The gamma band is sometimes defined as activity above 20 Hz or as activity between 35 and 45 Hz. Another set of parameters are diverse percentiles of the normalised power spectrum (area under the curve = 1), regarded as distribution density. The longest used of these has been the 50% percentile, also called the median EEG frequency. Spectral edge frequency is somewhat of a hybrid as it is the mixture of, for example, a 90% percentile with some additional significance rules. Various percentiles have been used to define spectral edge frequency, among which are the 80%, 90% and 95% percentiles.

Figure 6 depicts, as an example, the time course of power spectra during an infusion regimen of thiopental in volunteers with a TCI—infusion scheme for three times linear increasing plasma concentrations. The upper panel depicts the median EEG frequency, which shows a pronounced beta activation at low anaesthetic levels.

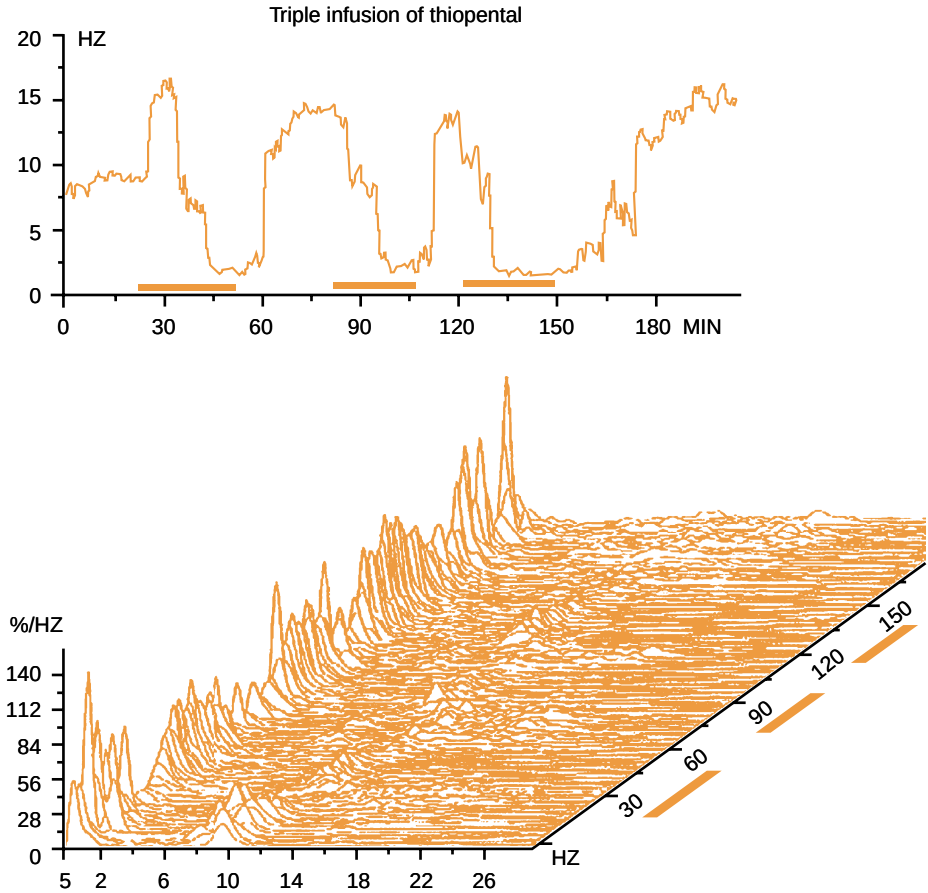

Figure 6. EEG power spectra and the time course of median EEG frequency during a triple-slope infusion of thiopental.

HIGHER-ORDER SPECTRA

Spectral analysis is intimately related to the moments of the time series. The first moment of a time series $x(t_i)$, $i = 1 \ldots$ infinity is defined as:

$$m_1 = \lim_{n\to\infty} \frac{1}{n} \sum_{i=1}^{n} x(t_i)$$

which is apparently the mean. It is common to subtract the mean from the time series such that one may assume that the time series now has a mean of zero. The higher moments are then defined by the following formulae, whereby E denotes the expectation operator, which is an abbreviation of $\lim_{n\to\infty} \frac{1}{n} \sum_{i=1}^{n}$:

$m_2(t_k) = E(x(i_i)x(i_i + k))$ second moment

$m_3(t_k, t_l) = E(x(t_i)x(t_i + k)x(t_i + l))$ third moment

$m_4(t_k, t_l, t_m) = E(x(t_i)x(t_{i+k})x(t_{i+l})x(t_{i+m}))$ fourth moment

… *n*th moment

It can be shown that the Fourier transform of $m_2(t)$ is the power spectrum of the signal and vice versa; hence, one may write:

$$m_2(t) = \int df\ e^{2\pi itf} P(f), \quad P(f) \text{ power of the signal } x(t) \text{ at frequency } f$$

Similarly, the Fourier transform of the higher moments will define higher-order spectra:

$m_3(t,t') = \int\int df_1\, df_2 e^{2\pi i(tf_1 + t'f_2)} B(f_1, f_2)$, $B(f_1, f_2)$ denotes the bispectrum of the signal $x(t)$

$m_4(t,t',t'') = \int\int\int df_1\, df_2\, df_3 e^{2\pi i(tf_1 + t'f_2 + t''f_3)} C(f_1, f_2, f_3)$, $C(f_1, f_2, f_3)$ denotes the trispectrum

…

Looking at the higher moments at times $t = t' = t'' = 0$, one gets:

$$m_2(0) = \int df P(f) = E(x(t_i)x(t_i)), \text{ but } E(x(t_i)x(t_i)) = \sigma^2 = \text{variance of the signal } x(t)$$

That is, the integral over the power spectrum is equal to the variance of the time series, or stated another way, the power spectrum represents the spectral decomposition of the variance. In a similar way, one may look at $m_3(0,0)$ and at $m_4(0, 0,0)$:

$$m_3(0,0) = \iint df_1\, df_2\, B(f_1, f_2), m_4(0,0,0) = \iiint df_1\, df_2 df_3 C(f_1, f_2, f_3)$$

If one looks at the definition of the higher moments, one can immediately relate $m_3(0,0)$ and $m_4(0,0,0)$ to the skewness and kurtosis of the histogram of the time series. Thus, in essence, the bispectrum is the spectral decomposition of skewness of the histogram of the time series, and the trispectrum is the spectral decomposition of the kurtosis of the histogram of the time series. Put another way, whenever the histogram of a time series is skewed, the bispectrum must be different from zero. The reverse is not true, but if the time series is generated by a Gaussian process, the bispectrum is zero.

A non-trivial bispectrum different from zero can often be identified taking a look at the EEG trace. This is shown in Figure 7 below. The upper part depicts an artificial graphical element of an EEG that may occur during deep anaesthesia (poli-spikes). One immediately recognises that the amplitude of the histogram has to be skewed because of the arcs on the bottom of the signal and the spikes at high amplitude; thus, the integral over the bispectrum is different from zero and the bispectrum itself is therefore different from zero.

An important property of signals with random phases is that the higher moments are zero and the spectral decomposition of the second moment (power spectrum) contains all the information of the signal.

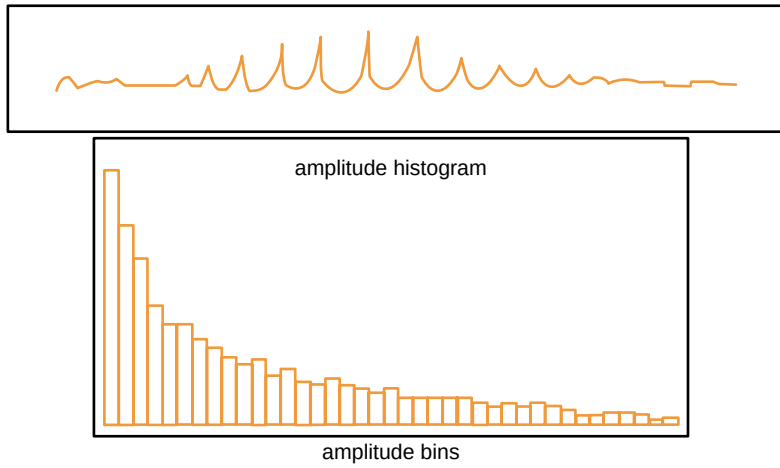

Figure 7. An EEG segment with a sew symmetrical amplitude histogram has a non-trivial bispectrum and can often be identified by taking a look at the EEG trace.

As with the power spectrum, one does not calculate the bispectrum, but one has to *estimate* the bispectrum from a finite EEG time segment. As the power spectrum estimation has an error of estimation of the order of 100%, estimating the bispectrum carries with it an even larger error of estimation.[1] To determine whether a given EEG has a non-trivial bispectrum different from zero, statistical tests have been developed to test whether or not the bispectrum is identical to zero.[2] These tests have become important in non-linear analysis of the EEG because a non-zero bispectrum is considered to be a first hint that the underlying process that generated the time series might be non-linear.[3]

To investigate whether or not a given time series contains information in the phase spectrum, one uses the method of phase-randomisation to generate surrogate time series with exactly the same power spectrum as the original time series but whose phases are made artificially random. This is shown in Figure 8, which depicts two original traces—the gauge pattern with 50 μV steps and an original EEG trace—and their phase-randomised versions. The original trace and its phase-randomised version have an identical power spectrum and differ only in their phases. With the gauge pattern, there is obviously a big impact of the phases on constitution of the signal, whereas the original EEG segment and its phase-randomised version seem not to differ greatly in their statistical properties.

The z-component of the so-called Lorenz attractor is often used as an example of a signal with a bispectrum that is known to be non-zero (upper left panel of Figure 9). To the right of this signal is an original EEG trace, and below each signal is a phase-randomised version of the signal above. Below each signal, there is an estimation of the bicoherence (normalised version of the bispectrum). One can see that the bicoherence for the Lorenz signal is up to more than 100 times larger than that for the original EEG trace and for the corresponding phase-randomised surrogate data. We found that, for approximately 90% or more of all stationary EEG time segments, the bicoherence was no different from zero or another constant.

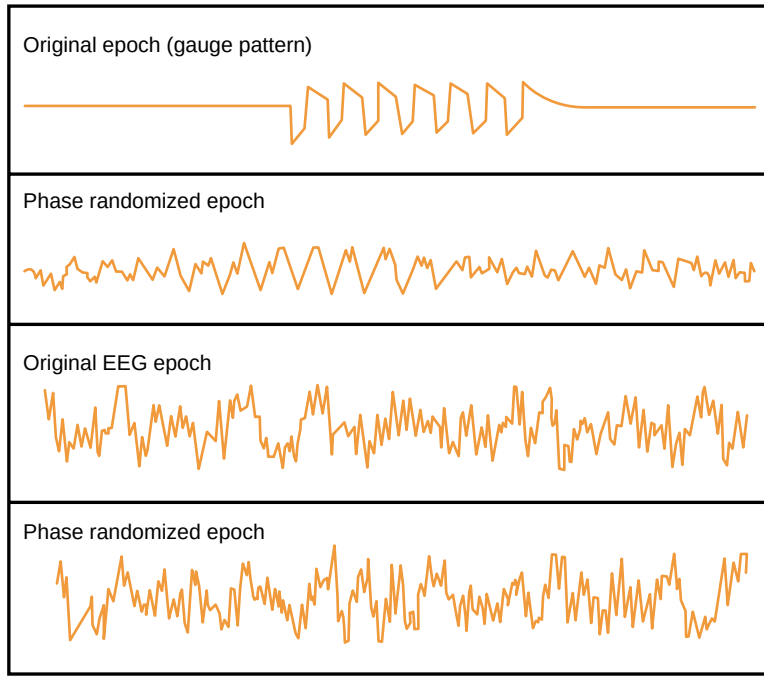

Figure 8. The method of phase randomisation is used to generate surrogate data with an identical power spectrum and reveals the impact of possible phase relationships.

ANALYSIS OF NON-LINEAR DYNAMICAL SYSTEMS

The principle of so-called 'chaos analysis' is to transform the properties of a time series into the topological properties of a geometrical object constructed out of the time series, which is embedded in a so-called state-space.[4]

The concept of state-space originates from theoretical mechanics. The laws of motion, as given by Newtonian laws, are differential equations of the second order (which is equivalent to two first-order differential equations) that have a unique solution if two initial conditions for the mass point are given: its position and its velocity or impulse. Given these two values, the trajectory of the mass point in space and time is uniquely defined by the laws of motion. To each point in state-space belongs one unique trajectory, being the set of all points in state-space that the mass point will occupy during time.

The differential equation system in pharmacokinetics may also be associated with a state-space. Given, for example, the three differential equations of first order (being equivalent to one third-order differential equation), describing for instance the pharmacokinetics of propofol as a three-compartment model, one needs three initial conditions for a unique solution. This could be, for example, the amount of drug in the central compartment and its first and second derivative at a specific moment in time, or equivalently it could be the amounts of drug in the three compartments at that specific moment in time. Given a point in state-space, in this case a triplet of amounts of drugs in compartments 1, 2 and 3, which can be visualised as a point in three-dimensional space, there is a unique trajectory in state-space that is the solution of the differential equations describing the three-compartment model. Figure 10 illustrates an example

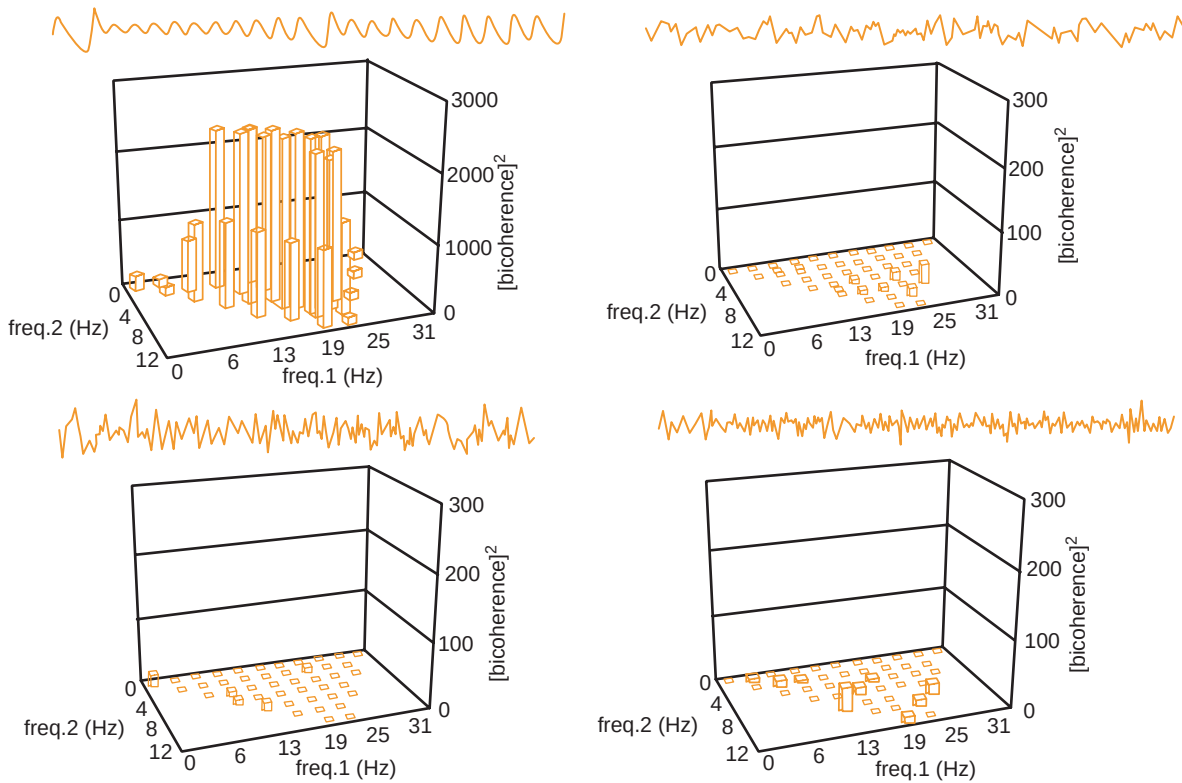

Figure 9. Bispectra of the Lorenz attractor (z-component) and an EEG trace, along with their phase-randomised versions.

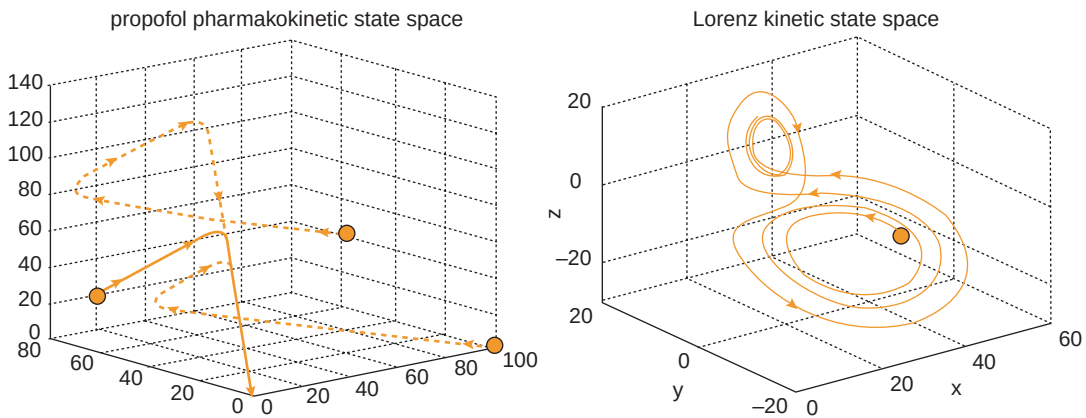

Figure 10. The concept of state-space and trajectories in state-phase for the propofol three-compartment model and Lorenz attractor.

of three trajectories belonging to initial values (m_1,m_2,m_3) of (100,0,0), (100,60,40) and (20,80,20) mg propofol. It can be seen that all trajectories converge towards the point (0,0,0) because the drug is eliminated and eventually all three compartments are cleared of propofol. This point, as a zero-dimensional geometric object, is in this case the (trivial) attractor of the system.

This is quite different from the Lorenz attractor, a system that is also described by three first-order differential equations, but has two inbuilt non-linear terms.

Here, the attractor is a geometric object (a set of data points x_i in three-dimensional space) that looks like a somewhat distorted '8' in three dimensions. Given a discrete version of the attractor as given by the series x_i,i = 1… infinity, one may define a cumulative correlation function $C(r)$ that just counts the number of data points within a neighbourhood of radius r. One can show that this function behaves in the following way:

$$C(r) \sim r^d \text{ as } r -> 0.$$

The number d is called correlation dimension of the object. This relates to the number of neighbours on a lattice scale with the dimension of the space; for example, in one dimension on a line there are $2 = 2^1$ neighbours, in two dimensions there are $4 = 2^2$ neighbours, in three dimensions there are $8 = 2^3$ neighbours, etc. If one determines the number d, which is also called the D2 dimension of the Lorenz attractor, computationally one gets 2.055 ± 0.004. Thus, this is a broken or fractal dimension.

Ruelle and Takens have shown that one can reconstruct the topological properties of the state-space trajectories of dynamical systems from observations of a single one-dimensional variable by the method of delays.[5,6] Figure 11 exemplifies this method by constructing a two-dimensional and three-dimensional state-space delay vector. As this vector moves along the time series, a trajectory is generated in the embedding space. There are many papers dealing with this kind of analysis of the EEG for certain diseases, epilepsy in particular,[7] but there are only a very few papers in which this analysis has been applied to the EEG during anaesthesia.

Much more applied to the EEG during anaesthesia are so-called entropy measures. Entropy is a quantity defined in thermodynamics. The second law of thermodynamics was formulated by Clausius, who stated (1850): 'Es ist unmöglich, Wärme von einem kälteren zu einem wärmeren Körper ohne Compensation zu überführen'. In quantitative terms, this law is formulated as $dS = dQ/T$, whereby dS is the change of the quantity S called entropy, dQ is the change of heat of a physical system (e.g. gas), and T is the temperature. Given this notation, the quantitative form of Clausius' statement is $dS > 0$ for irreversible processes and $dS = 0$ for reversible processes. One can show that the entropy of a system is somehow related to the probability of finding the state of the system in a specified volume of state-space.

In this, there is a connection to the theoretical definition worked out by Kolmogoroff and Shannon in the last century. Given a system that is described by n numbers $p_i \geq 0$, $i = 1 \ldots n$, $\Sigma p_i = 1$, then the quantity $H = -\Sigma p_i \ln(p_i)$ is called entropy. Given any distribution density of an observable quantity O having a range of measured values between [a,b] (the support of the distribution density), one might divide the interval into n bins $[a = x_0 < x_1 < x_2 \ldots < x_n = b]$, and with each bin there is now the probability $p_i = P(x_{i-1} \leq O < x_i)$, $i = 1 \ldots n$, for which the (formal) entropy value can be calculated. How this formal value is related to physical quantities for the process generating the observable quantity can be matter of endless debate.

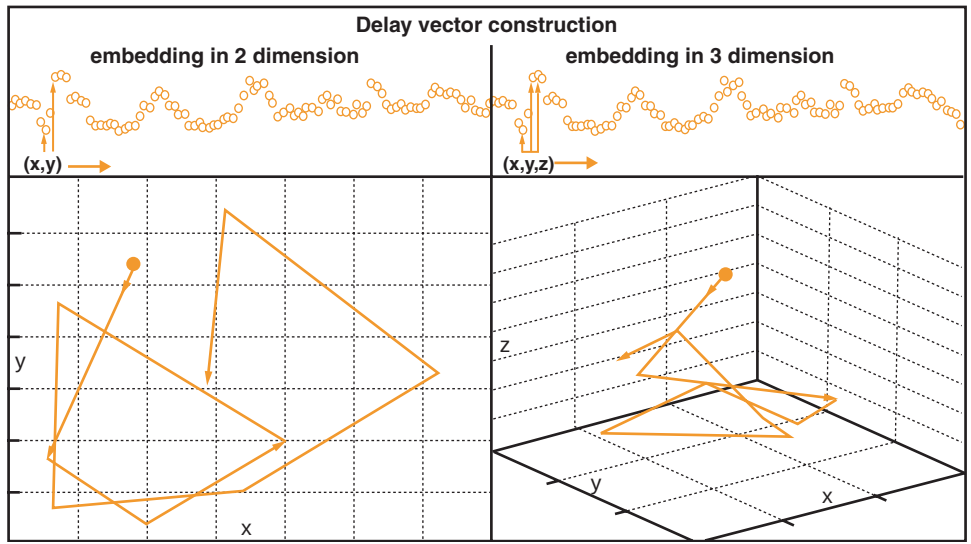

Figure 11. Constructing trajectories in multidimensional embedding spaces. Left: two-dimensional embedding; right: three-dimensional embedding.

If the observable *O* is, for example, the digitally sampled amplitude of the EEG, one gets a histogram and may end up with an EEG parameter that has been called the 'Shannon entropy' of the EEG. It has also been proposed as 'symbolic entropy', taking account of the fact that the metric of the bins is irrelevant to this parameter—put simplistically, if we divided the amplitudes into 'yellow', 'blue', 'red' and so on bins, one would achieve the same entropy value. Furthermore, as the amplitude histogram is invariant with respect to reordering of the signal amplitudes, the two traces shown in Figure 12—an EEG segment and surrogate data (EEG ordered by amplitude)—have an identical symbolic entropy (3.73) because they have identical amplitude histograms.

Spectral entropy is another measure that has been used. If one normalises the area under the power spectrum to 1, the power spectrum can be considered as a distribution density for which one may immediately calculate the corresponding entropy, as detailed above. This is an EEG variable that is based only on the spectrum and does not consider phase information. However, as discussed above, phase information only rarely contributes to the clinical significance of EEG monitoring during anaesthesia.

A third entropy measure used in anaesthesia is Kolmogoroff–Sinai entropy. This is an immediate generalisation of Shannon entropy, described above, for higher-dimensional spaces. If one constructs, out of the signal, a trajectory that is embedded in a *k* (embedding dimension)-dimensional space, one may ask how many states are in a *k*-dimensional voxel of a given *k*-dimensional lattice, or alternatively how often the trajectory passes such a voxel. The calculation of such entropy is rather difficult and time-consuming. Pincus has suggested an approximation to this entropy measure, which he called approximate entropy, that can be assessed with less computation.[8] He applied his algorithm to the analysis of heart beat variations, Bruhn then applied it to the digitised EEG.

Figure 13 depicts traces of three EEG parameters during the administration of propofol to a volunteer, which generated the plasma concentrations depicted in the bottom panel of the figure. Each dot of the figure represents the corresponding value of the EEG parameter for an EEG segment of 8 seconds without any further processing, for example smoothing or artefact rejection. The solid line represents a smoothed version created by median smoothing according to Tuckey's method. Measures of association of EEG parameters with clinical signs of anaesthetic action, such as Kim's Pk value, have become popular in developing criteria for the rational selection of EEG parameters for monitoring. Another important aspect, however, is the signal-to-noise

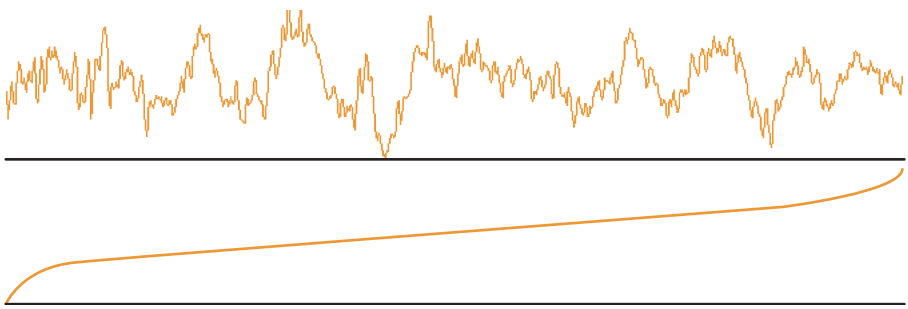

Figure 12. The Shannon or symbolic entropy of a signal depends only on the set of amplitude numbers and not on their ordering.

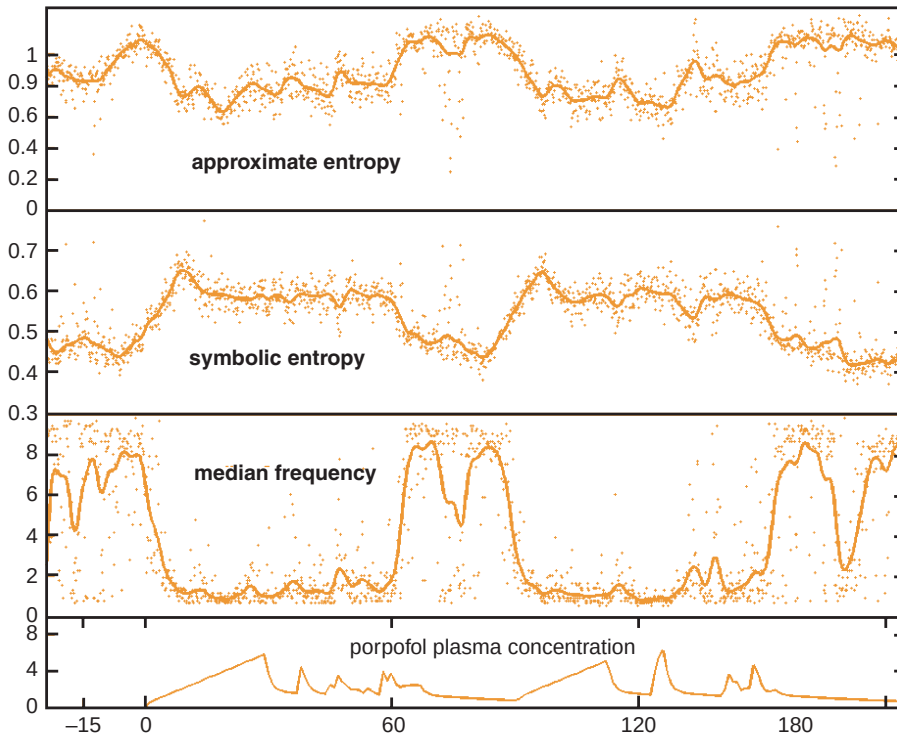

Figure 13. Time course of approximate entropy and symbolic entropy compared with the median EEG frequency during propofol administration in a volunteer.

ratio of the parameter, because the higher this ratio, the less smoothing is necessary for trend detection, the less hysteresis is generated by the smoothing process and the earlier one may recognise trend variations.

Table 1 compares these values for the anaesthetic action of propofol in volunteers for five EEG parameters out of a set of 32 that had the best Pk and signal-to-noise ratio values.[9] In this study, anaesthetic depth was estimated at 17 different times for nine different clinical signs (e.g. falling asleep, no response to verbal command, loss of eyelash

Table 1. The measure of association of EEG parameters to clinical endpoints, Pk, and signal–to–noise ratio for different EEG parameters.

Parameter	Pk value	Signal-to-noise ratio
m95	0.74	5.16
rel20-26	0.74	4.05
ApEn	0.73	4.51
m50	0.71	1.91
Symbent	0.68	4.66

See text, for abbreviations.

reflex, loss of corneal reflex, etc). These clinical criteria were quantitatively associated with the corresponding values of the EEG parameters by means of the Pk value. Astonishingly, simply the 95% quantile of the power spectrum (m95) was the best measure, with approximate entropy (ApEn) calculated according to Bruhn's algorithm as the next best. Median EEG frequency had a reasonable Pk value but a less good signal-to-noise ratio compared to m95 and ApEn.

ApEn seems to be a fairly reasonable EEG parameter for monitoring trends during anesthesia, but one should be cautious with respect to its name. Just as one does not know how much bispectrum is in the BIS,[10] one also does not know how much entropy of an underlying non-linear dissipative dynamical system is in ApEn. This is because, given the suggested parameters for calculating ApEn, one misses the necessary requirements of the statistical independence of the axes of the state-space. I suggest calling this parameter the Bruhn parameter[11] because there is virtually no relationship between (EEG) ApEn and the entropy of an assumed underlying non-linear dissipative dynamic system. The difference in applying the Pincus algorithm to the ECG and to the EEG is that the HRV time series have a sampling frequency of the order of 1 sample per second, whereas two adjacent EEG samples have a spacing of several milliseconds and are definitely not statistically independent, as the location of the first zero of the autocorrelation function shows.

OUTLOOK

Given the many proposed new EEG derivations, there is no need to publish a single paper on the 'new promising approach' and leave it at that. Instead, there is a much stronger requirement to characterise any new derivation in relation to clinically meaningful signs. Correlating the values of an EEG derivation to biophase concentrations is nice, but it is misleading to use such an approach during surgical anaesthesia to characterise the suitability of an EEG derivation for monitoring surgical anaesthesia. The selection of an EEG parameter with respect to the best correlation between concentration and effect selects those parameters which are insensitive to alterations caused by surgical stimuli. In the past, we have constructed sophisticated pharmacokinetic-pharmacodynamic models to relate drug dosing and drug concentrations to EEG effects. In future, we need to develop methods of quantifying the intensity of surgical stimulation and to construct integrated 'pharmacokinetic-pharmacodynamic-surgical-stimulation' models, because both the drug and surgery (as well as a number of other confounding variables) cause the EEG changes encountered during surgical anaesthesia.

CONCLUSION

In the past two decades, quite a few alternatives to power spectrum-derived EEG parameters have been created and investigated, some of which are highly sophisticated and impress by their mathematical complexity. However, it seems to be that simple power spectrum-based parameters show a good correlation with clinical signs and a reasonable signal-to-noise ratio.

REFERENCES

1. Bendat Julius SPAG. *Random Data: Analysis and Measurement Procedures*. London: Wiley; 1971.
2. Rao T & Gabr M. A test for linearity of stationary time series. *Journal of Time Sereies Analysis* 1980; **66:** 479–484.
3. Gantert C, Honerkamp J & Timmer J. Analyzing the dynamics of hand tremor time series. *Biological Cybernatics* 1992; **66:** 479–484.
4. Marek MIS. *Chaotic Behaviour of Deterministic Dissipative Systems*. Cambridge: Cambridge University Press; 1991.
5. Ruelle D. Small random perturbations of dynamical systems and the definition of attractors. *Communications in Mathematical Physics* 1981; **82:** 137.
6. Takens F, *Detecting Strange Attractors in Turbulence. Dynamical Systems and Turbulence. Lecture Notes in Mathematics 898*. Berlin: Springer; 1981.
7. Pijn JP, Velis DN, van der Heyden MJ et al. Nonlinear dynamics of epileptic seizures on basis of intracranial EEG recordings. *Brain Topography* 1997; **9:** 249–270.
8. Pincus SM. Approximate entropy as a measure of system complexity. *Proceedings of the National Academy of Sciences of the United States of America* 1991; **88:** 2297–2301.
9. Jeleazcov Ch, Bremer F, Schwilden H. Identifikation geeigneter EEG-parameter für das narkose-monitoring durch simultane analyse von klinischen endpunkten und signal-rausch-verhältnis. Anaesthesiologie, Intensivmedizin; in press.
10. Jeleazcov C, Fechner J & Schwilden H. Electroencephalogram monitoring during anesthesia with propofol and alfentanil: the impact of second order spectral analysis. *Anesthesia & Analgesia* 2005; **100:** 1365–1369.
11. Bruhn J, Ropcke H & Hoeft A. Approximate entropy as an electroencephalographic measure of anesthetic drug effect during desflurane anesthesia. *Anesthesiology* 2000; **92:** 715–726.