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Publication II

H. Viertiö-Oja, V. Maja, M. Särkelä, P. Talja, N. Tenkanen, H. Tolvanen-Laakso, M. Paloheimo, A. Vakkuri, A. Yli-Hankala, P. Meriläinen. 2004. Description of the Entropy™ algorithm as applied in the Datex-Ohmeda S/5™ Entropy module. Acta Anaesthesiologica Scandinavica 48, no. 2, pages 154-161.

Acta Anaesthesiol Scand 2004; 48: 154–161
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ACTA ANAESTHESIOLOGICA SCANDINAVICA

Description of the Entropy™ algorithm as applied in the Datex-Ohmeda S/5™ Entropy Module

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Concept of entropy

There are a number of concepts and analytical techniques directed to quantifying the irregularity of stochastic signals, such as the EEG. One such concept is entropy. Entropy, when considered as a physical concept, is proportional to the logarithm of the number of microstates available to a thermodynamic system, and is thus related to the amount of 'disorder' in the system. For information theory, entropy was first defined by Shannon and Weaver in 1949 (1), and further applied to a power spectrum of a signal by Johnson and Shore in 1984 (2). In this context, entropy describes the irregularity, complexity, or unpredictability characteristics of a signal. In a simple example, a signal in which sequential values are alternately of one fixed magnitude and then of another fixed magnitude has an entropy value of zero, i.e. the signal is completely regular and totally predictable. A signal in which sequential values are generated by a random number generator has greater complexity and higher entropy.

Entropy is an intuitive parameter in the sense that one can visually distinguish a regular signal from an irregular one. Entropy also has the property that it is independent of absolute scales such as the amplitude or the frequency of the signal: a simple sine wave is perfectly regular whether it is fast or slow. In an EEG application, this is a significant property, as it is well known that there are interindividual variations in the absolute frequencies of the EEG rhythms.

Work performed for Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland, and presented in part at the 27th Congress of the Scandinavian Society of Anesthesiology, and Intensive Care Medicine, Helsinki, Finland, August 16–20, 2003.

There are various ways to compute the entropy of a signal. In time domain, one may consider, for example, the approximate entropy (3, 4) or Shannon entropy (1, 4, 5). In frequency domain, spectral entropy (1, 2, 6, 7) may be computed. In order to optimize the speed at which information is derived from the signal, it is desirable to construct a combination of time and frequency domain approaches. Such an algorithm is implemented in the Datex-Ohmeda Entropy™ Module (Datax-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland). The starting point of the algorithm is the spectral entropy, which has the particular advantage that contributions to entropy from any particular frequency range can be explicitly separated. For optimal response time, the computations can be constructed in such a way that the length of the time window for each particular frequency is individually chosen. This leads to a concept we will call time-frequency balanced spectral entropy.

Spectral entropy

The starting point of the computations is the spectrum of the signal. There are various spectral transformations to obtain the spectrum, of which we consider here the discrete Fourier transformation (8). This provides a transformation from a set of signal values $x(t_i)$ sampled at time moments t_i within a sample of a signal to a set of an equal number of complex values $X(f_i)$ corresponding to a set of frequencies f_i:

$$X(f_i) = \sum_{t_i} x(t_i) e^{-i2\Pi f_i t_i} \quad [1]$$

The spectral components $X(f_i)$ can be evaluated using an effective computational technique called the fast Fourier transform (FFT) (8).

The concept of spectral entropy originates from a measure of information called Shannon entropy (1). When applied to the power spectrum of a signal, spectral entropy is obtained (2). The following steps are required to compute the spectral entropy for a particular epoch of the signal within a particular frequency range [f_1, f_2] (6, 7).

From the Fourier transform $X(f_i)$ of the signal $x(t_i)$, the power spectrum $P(f_i)$ is calculated by squaring the amplitudes of each element $X(f_i)$ of the Fourier transform:

$$P(f_i) = X(f_i) * X^\wedge(f_i), \quad [2]$$

where $X^\wedge(f_i)$ is the complex conjugate of the Fourier component $X(f_i)$ and '*' denotes multiplication.

The power spectrum is then normalized. The normalized power spectrum $P_n(f_i)$ is computed by setting a normalization constant C_n so that the sum of the normalized power spectrum over the selected frequency region [f_1, f_2] is equal to one:

$$\sum_{f_i=f_1}^{f_2} P_n(f_i) = C_n \sum_{f_i=f_1}^{f_2} P(f_i) = 1 \quad [3]$$

In the summation step, the spectral entropy corresponding to the frequency range [f_1,f_2] is computed as a sum:

$$S[f_i, f_2] = \sum_{f_i=f_1}^{f_2} P_n(f_i) \log\left(\frac{1}{P_n(f_i)}\right) \quad [4]$$

Thereafter, the entropy value is normalized to range between 1 (maximum irregularity) and 0 (complete regularity). The value is divided by the factor log ($N[f_1,f_2]$) where $N[f_1,f_2]$ is equal to the total number of frequency components in the range [f_1,f_2]:

$$S_N[f_1, f_2] = \frac{S[f_1, f_2]}{\log(N[f_1, f_2])} \quad [5]$$

Figures 1–3 illustrate these steps. In Fig. 1(A), 2(A), and 3(A), three pieces of signals corresponding to different entropy values are shown. In this simple example, we consider pieces of signal with eight spectral components, of which the 0-frequency component is omitted (taken to be equal to zero) so that $n = 7$ frequency components are analyzed. Figure 1(A) shows a perfect sine wave, Fig. 2(A) a sine wave superposed with white noise, and Fig. 3(A) a perfectly random white noise signal. The discrete Fourier spectra of these signals, normalized according to Eq. 3, are plotted in Fig. 1(B), 2(B), and 3(B), respectively. The normalized spectral components $P_n(f_i)$ are next mapped using the Shannon function in Fig. 1(C), 2(C), and 3(C) to obtain the contributions

$$\frac{1}{\log(N[f_1, f_2])} P_n(f_i) \log\left(\frac{1}{P_n(f_i)}\right) \quad [6]$$

Time-frequency balanced spectral entropy

In real time signal analysis, the signal values $x(t_i)$ are sampled within a finite time window (epoch) of a selected length with a particular sampling frequency. This time window is moved step by step to provide updated estimates of the spectrum. The choice of the epoch length is linked to the choice of the frequency range under consideration, as the time window has to be sufficiently long to allow for the estimation of the slowest (lowest frequency) variations in the signal.

An EEG signal consists of a wide selection of frequencies, ranging from slow delta (from 0.5 Hz) up to frequencies in the order of 50 Hz. At a frequency of 0.5 Hz, a time window as long as 30 s would be required to obtain 15 full cycles of the 0.5 Hz variation. For a frequency of 50 Hz, the same number of full cycles could be obtained with only 0.3 s of data.

A single time window of fixed length is obviously not the optimal choice to acquire information as fast and as reliably as possible. In order to optimize between time and frequency resolution, the Entropy Module utilizes a set of window lengths chosen in such a way that each frequency component is obtained from a time window that is optimal for that particular frequency. In this way, information is extracted from the signal as fast as possible. The approach is closely related to the idea of the wavelet transformation, with wavelets being wave packets with finite variable widths containing an approximately constant number of variations to optimize between time and frequency resolution. The selected technique, however, combines this advantage of wavelet analysis with those of fast Fourier analysis, such as the possibility to explicitly consider the contribution from any particular frequency range, and efficient implementation in software. The basic idea is illustrated in Fig. 4.

In the entropy module, a sampling frequency of 400 Hz is used. The shortest time window is equal to 1.92 s = 768 sample values, and the longest is equal to 60.16 s = 24064 sample values. The shortest time window is used for the frequency range between 32 Hz and 47 Hz. The longest time window is used only for frequencies below 2 Hz. For frequencies between 2 Hz and 32 Hz, window lengths between these two

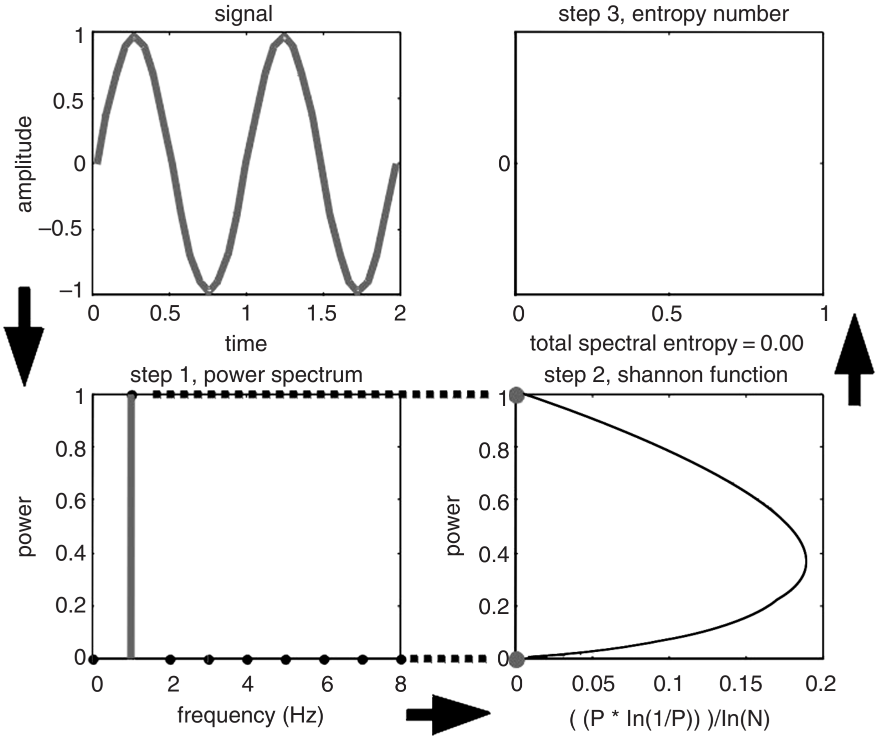

Fig.1. The perfect sine wave in Fig. 1 includes only one nonzero spectral component, which is normalized to 1 in the normalization step (2). In the Shannon mapping, both values 1 and 0 contribute a value of 0, thus corresponding to entropy = 0.

extremes are used. The very short window of less than 2 s for the range of frequencies from 32 Hz to 47 Hz ensures that the entropy value rises readily at arousal. In particular, it provides for immediate indication of EMG activation.

State entropy and response entropy

A biopotential signal measured from the forehead of a patient includes a significant electromyographic (EMG) component, which is created by muscle activity. The EMG signal has a wide noise-like spectrum

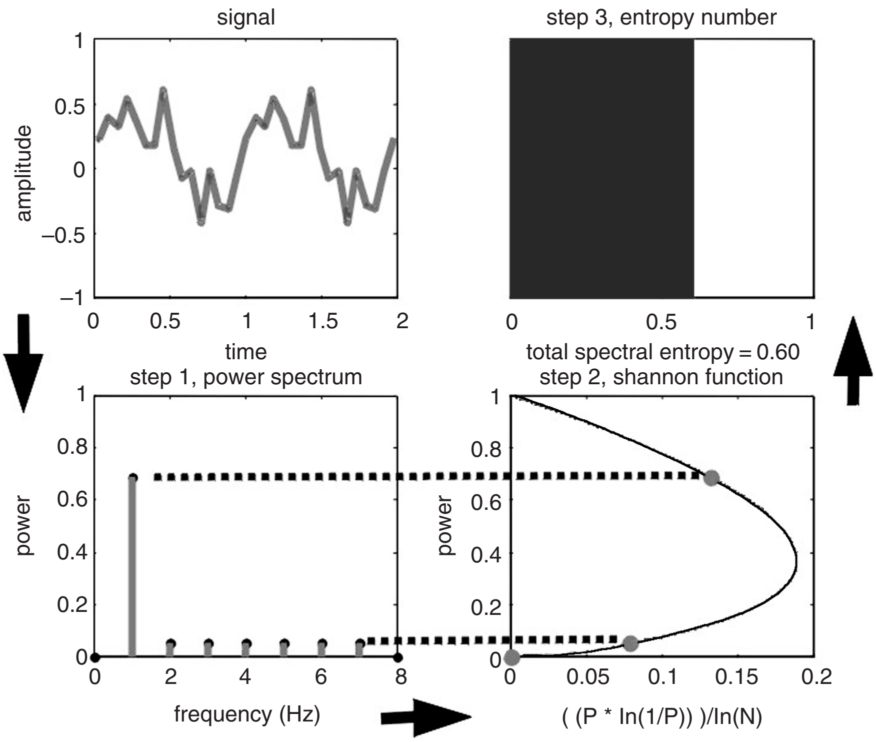

*Fig.2. Some amount of white noise is superimposed on top of the sine wave. After normalization, the spectrum includes one high component corresponding to the frequency of the sine wave, and 6 smaller nonzero components. In the Shannon mapping, both types of components contribute nonzero values to the entropy of the signal, corresponding to a total entropy = 0.12 + 6 * 0.08 = 0.60.*

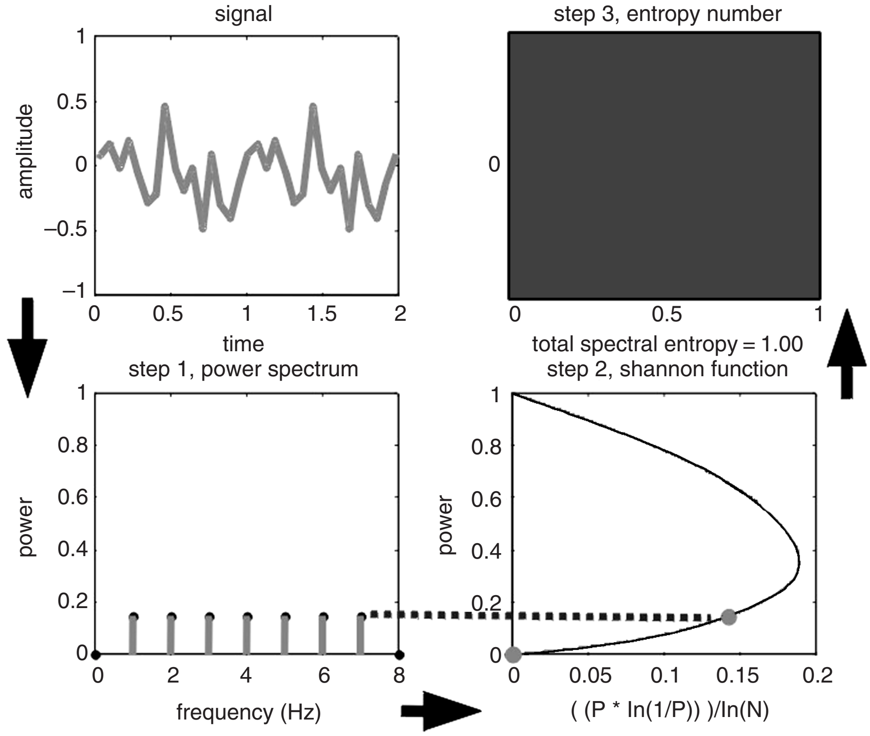

Fig.3. The sine wave has disappeared, and there is only white noise left. After normalization, the noise contributes to $N = 7$ components that are equal to $P_n(f_i) = 1/7$. These are transformed to values (1/7)log(7) by the Shannon mapping. Finally, summation of these components and normalization by 1/log(7) give an entropy value = 7(1/7)log(7)/log(7) = 1. White noise has maximal entropy = 1.*

and during anesthesia typically dominates at frequencies higher than 30 Hz. The EEG signal component dominates the lower frequencies (up to about 30 Hz) contained in the biopotentials existing in the electrodes. At higher frequencies, EEG power decreases exponentially (Fig. 5).

Sudden appearance of EMG signal data often indicates that the patient is responding to some external stimulus, such as a painful stimulus, i.e. nociception, due to some surgical event. Such a response may result if the level of analgesia is insufficient. If stimulation continues and no additional analgetic drugs are administered, it is highly likely that the level of hypnosis eventually starts to lighten. EMG can thus provide a rapid indication of impending arousal. Importantly, because of the higher frequency of the EMG data signal, the sampling time can be significantly shorter than that required for the lower frequency EEG signal data. This allows the EMG data

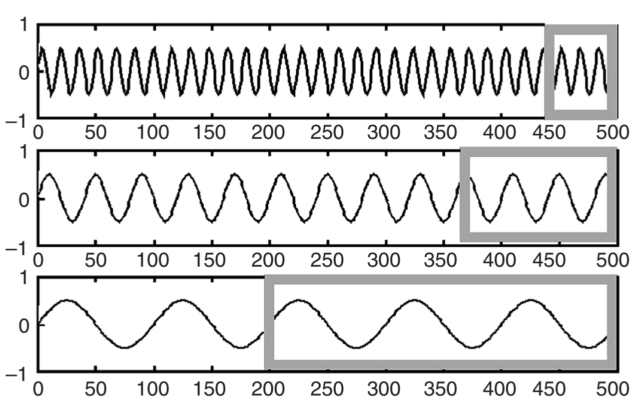

Fig.4. Time windows of various lengths provide optimal balance between time and frequency resolution. Short time windows for highest frequencies ensure rapid response time.

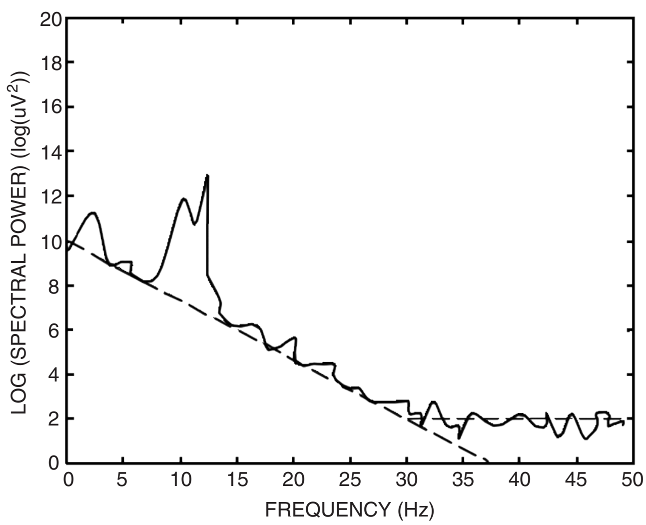

Fig.5. Typical power spectrum of a biopotential signal measured from the forehead of a patient. The EEG signal dominates up to frequencies about 30 Hz, while the EMG signal dominates the higher frequency range. The vertical scale is logarithmic.

to be computed more frequently so that the overall diagnostic indicator can quickly indicate changes in the state of the patient.

It is informative to consider two entropy indicators, one over the EEG dominant frequency range alone and another over the complete range of frequencies, including both EEG and EMG components. State entropy (SE) is computed over the frequency range from 0.8 Hz to 32 Hz. It includes the EEG-dominant part of the spectrum, and therefore primarily reflects the cortical state of the patient. The time windows for SE are chosen optimally for each particular frequency component, and range from 60 s to 15 s according to the explanation given earlier under the heading *Time-Frequency Balanced Spectral Entropy.* Response entropy (RE) is computed over a frequency range from 0.8 Hz to 47 Hz. It includes both the EEG-dominant and EMG-dominant part of the spectrum. The time windows for RE are chosen optimally for each frequency, with the longest time window equal to 15.36 s and the shortest time window, applied for frequencies between 32 Hz and 47 Hz, equal to 1.92 s.

It is advantageous to normalize these two entropy parameters in such a way that RE becomes equal to SE when the EMG power (sum of spectral power between 32 Hz and 47 Hz) is equal to zero, as the RE–SE-difference then serves as an indicator for EMG activation. Let us denote the frequency range from 0.8 Hz to 32 Hz as R_{low} and the frequency range from 32 Hz to 47 Hz as R_{high}; the combined range from 0.8 Hz to 47 Hz is denoted by $R_{low+high}$. It follows from Eqs 2–5 that when spectral components within the range R_{high} are zero, the unnormalized entropy values $S[R_{low}]$ and $S[R_{low} + R_{high}]$ coincide whereas for the normalized entropies one obtains an inequality: $S_N[R_{low}] > S_N[R_{low}+R_{high}]$. The normalization step (5) is therefore redefined for SE in the following way:

$$SE = S_n[R_{low}] = \frac{S[R_{low}]}{\log(N[R_{low+high}])} = \frac{\log(N[R_{low}])}{\log(N[R_{low+high}])} \cdot \frac{S[R_{low}]}{\log(N[R_{low}])} \qquad [7]$$

For RE, the normalized entropy value is computed according to (5):

$$RE = S_N[R_{low+high}] = \frac{S[R_{low+high}]}{\log(N[R_{low+high}])} \qquad [8]$$

Consequently, RE varies from 0 to 1, whereas SE varies from 0 to $\log(N[R_{low}])/\log(N[R_{low+high}]) < 1$.

The two entropy values coincide when $P(f_i) = 0$ for all f_i within the range $[R_{high}]$. When there is EMG activity, spectral components within the range $[R_{high}]$ differ significantly from zero and RE is larger than SE.

With these definitions, SE and RE both serve their own informative purposes for the anesthesiologists. State entropy is a stable indicator of the effect of hypnotics on the cortex. The time windows for SE are selected in such a way that transient fluctuations are removed from the data. Response entropy, on the other hand, reacts fast to changes. A typical situation in which the different roles of these parameters is demonstrated is during arousal, when RE rises first simultaneously with muscle activation and is some seconds later followed by SE.

Entropy during burst suppression

When burst suppression pattern (Fig. 6) sets in, entropy values RE and SE are in principle computed in the same way as they are calculated at lighter levels of hypnosis. The part of the signal that contains suppressed EEG is treated as a perfectly regular signal with zero entropy, whereas the entropy associated with the bursts is computed as described previously.

It is customary to quantify burst suppression by presenting the relative amount of suppression, called burst suppression ratio (BSR), within 1 min to obtain a sufficiently stable estimate. A 1-min window includes a sufficiently long sample of both bursts and suppression to provide a stable indication of the relative amount of suppressed EEG, whereas much shorter time windows would produce highly fluctuating BSR values. For the same reason, a 1-min window, instead of the set of varying time windows, is applied for all frequency components of the SE and RE values whenever suppressed epochs have been detected during the last minute of data.

Burst suppression is detected by applying the technique described by Särkelä et al. (9). In order to eliminate baseline fluctuations, a local average is

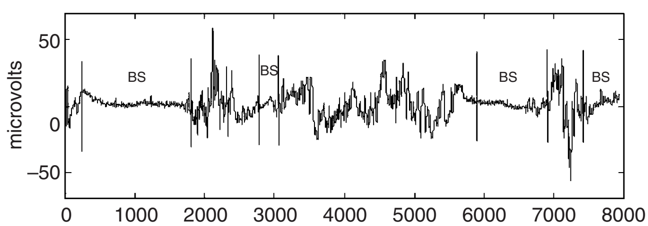

Fig.6. EEG signal containing bursts and suppression. Suppressed periods in EEG are denoted with ''BS''.

subtracted from each signal sample. The signal is then divided into two frequency bands by elliptic filters. Cut-off frequencies of these low-pass and high-pass filters are 20Hz and 75Hz, respectively. At this point the signal sampling frequency is 200Hz. The low-frequency band is used to detect the burst suppression pattern and the high-frequency band to detect artifacts. A non-linear energy operator *(nleo)* is derived in both bands for each 0.05-s epoch (eq. 9). *NLEO* (eq. 10) is applied to estimate the signal power from overlapping 1-s frames offset by 0.05 s:

$$nleo(j) = \sum_{i=j}^{j-10} |x(i-1)x(i-2) - x(i)x(i-3)| \qquad [9]$$

$$NLEO(k) = \sum_{j=k}^{k-20} nleo(j) \qquad [10]$$

During suppression periods, ECG artifacts may corrupt classification and therefore their interference is eliminated in the burst suppression band. This is performed by replacing the current *nleo* by the average *nleo* from the frame of 1 s, if the following rules are fulfillled:

A The squared difference between the current *nleo* from the 0.05 second epoch and the average *nleo* for the 1-s frame is over three times bigger than the mean of all the squared differences in the frame of 1 s, and
B The 1-s frame includes at most four epochs that fulfill condition A.

Suppression is detected if *NLEO* is below a fixed threshold for at least 0.5 s and artifacts are not present. The BSR is the percentage of 0.05-s epochs in the last 60 s that were considered suppressed.

Modifications for enhanced usability

The parameters RE and SE have been designed to be used in conjunction with a substantial amount of other important information on the same monitor screen. This complicated set of information is interpreted by a professional clinician in an utmost demanding dynamically varying clinical situation. In order to provide the entropy information as effectively as possible, certain modifications to the presentation of these parameters were made to optimize their usability.

A two-digit integer value such as 56 on a monitor screen can be perceived more rapidly than a decimal value such as 0.56 or a three-digit number such as 562. For this reason, the original entropy values that vary continuously between 0 and 1 were transformed to a scale of full integers between 0 and 100.

A relatively large portion of the original mathematical scale of the entropy values is in a range in which the level of hypnosis can be considered too deep, whereas the most interesting range of adequate hypnosis and emergence lies between 0.5 and 1.0. Simple division of the original scale into equidistant integer values from 0 to 100 would therefore result in a somewhat compromised resolution in the interesting range and unnecessarily high resolution in the very deep levels. For this reason, the transformation from the original continuous entropy scale [0 ... 1] to the integer scale [0 ... 100] has been performed by a non-linear transformation. This transformation is defined by a particular monotonous spline function F(S) that maps the scale [0 ... 1] to the scale [0 ... 100].

Any spline function has the property that it is continuous and its derivatives of any order are continuous. Therefore, a transformation operation defined by a monotonous spline function is perfectly smooth with no discontinuities or 'kinks'. The function F(S) employed for the transformation is presented in Fig. 7. As can be seen in Fig. 7, the slope of the function is highest in the range of clinical anesthesia and emergence for optimal resolution in this range. Response entropy ranges from 0 to 100, whereas SE varies between 0 and 91.

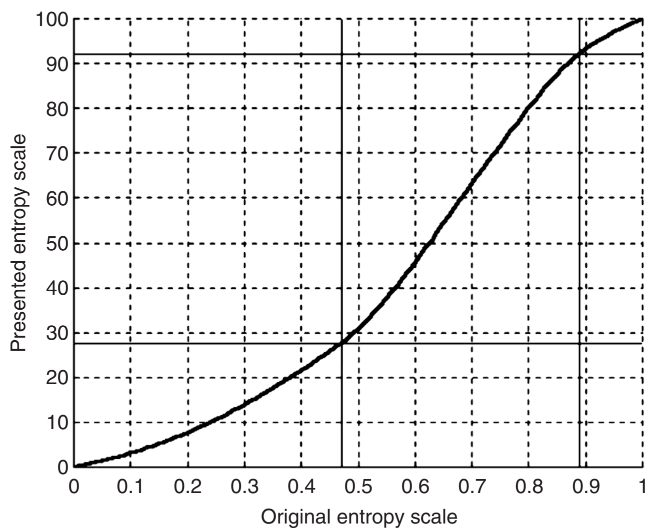

Fig.7. Spline function applied for transformation of original entropy values to RE and SE values presented on the monitor screen. The dashed lines separate the middle range with slope >1 from the high and low ranges with slope <1. The resolution of the measurement is enhanced in the middle region by the transformation.

If the amplitudes of the low-frequency components are particularly high, as may occur in very deep anesthesia, the difference between RE and SE, as they are originally obtained from Eqs 7 and 8, may fall below the integer resolution used on the monitor screen. In order to provide a detectable indication of EMG activity, the treatment of frequency components in the range $[R_{high}]=[32\,Hz,\ 47\,Hz]$ is modified. Instead of applying the normalization constant C_n according to Eq. 3 to all frequency components, a distinct normalization constant C_n^{high} is used for the range $[R_{high}]$ in this situation. As long as C_n has a value below a particular threshold C_n^{limit}, C_n^{high} is taken to be equal to C_n, but if C_n exceeds C_n^{limit}, C_n^{high} is taken to be equal to C_n^{limit}. This modification ensures that active EMG is detectable on the monitor screen in any situation.

Treatment of the raw signal for artifact detection and removal

For artifact analysis, the EEG signal is divided into epochs of 0.64 s (including 256 signal values). These epochs are inspected to detect and remove the following artifacts:

Electrocautery artifact

The hardware of the entropy module tolerates substantial electrocautery, so that it rarely occurs that any data needs to be rejected during electrocautery. In order to detect these situations, power in the frequency range from 200 kHz to 1000 kHz is continuously measured. If this power exceeds a set threshold value, the collected EEG data in the frequency range of 66–86 Hz is inspected to check whether electrocautery affects the signal or not. If this is the case, the epoch is rejected from further analysis.

ECG and pacer artifacts

The high sampling frequency of 400 Hz ensures that the sharp peaks associated with ECG and pacer can be readily distinguished from the underlying EEG signal. These artifacts are subsequently removed by subtracting the distortion from the underlying signal, which can be used for entropy calculations.

Electromyography (EMG)

As discussed earlier under the heading *State Entropy and Response Entropy*, EMG is treated as a component signal rather than an artifact.

Eye movements and blinks, movement artifacts

The epoch length of 0.64 s is too short, as such, to reliably detect all epochs that contain these artifacts. Therefore, these artifacts are considered in two steps:

Step 1: A stationarity analysis is performed for the signal within a time window of $24*0.64 = 15.36\,s$ (including 6144 signal values). The signal is classified either stationary or non-stationary depending on the statistical distribution of the signal values among and within these 24 epochs.

Step 2: For each epoch, five signal characteristics in time and frequency domains are computed. These characteristics are considered simultaneously in the corresponding five-dimensional parameter space that has been divided to regions of 'normal signal' and 'artifact contaminated signal'. Each epoch is either accepted or rejected depending on the region in the parameter space that the epoch belongs to. There are two sets of rejection rules: a 'stronger' set of rules, which is applied if the analyzed piece of the signal has been classified as non-stationary in Step 1; and a 'weaker' set of rules if the analyzed piece of the signal has been classified as stationary.

Acknowledgements

Following persons are acknowledged for their valuable contribution in data collection and analysis: Clinical Specialists Minna Kymäläinen, RN, and Reijo Nikula, RN, Datex-Ohmeda Division, Instrumentarium Corp, Helsinki, Finland; and Riitta Drachman-Mertsalmi, RN, Department of Anesthesia, Women's Hospital, Helsinki University Hospital, Helsinki, Finland.

References

1. Shannon CE. A mathematical theory of communication. *Bell System Techn J* 1948; **27** (379–423): 623–56.
2. Johnson RW, Shore JE. Which is the better entropy expression for speech processing: -S log S or log S? *IEEE Trans Acoust* 1984; **ASSP-32**: 129–37.
3. Pincus SM, Gladstone IM, Ehrenkranz RA. A regularity statistic for medical data analysis. *J Clin Monit* 1991; **7**: 335–45.
4. Bruhn J, Ropcke H, Hoeft A. Approximate entropy as an electroencephalographic measure of anesthetic drug effect during desflurane anesthesia. *Anesthesiology* 2000; **92**: 715–26.
5. Bruhn J, Lehmann LE, Ropcke H, Bouillon TW, Hoeft A. Shannon entropy applied to the measurement of the electroencephalographic effects of desflurane. *Anesthesiology* 2001; **95**: 30–5.
6. Rezek IA, Roberts SJ. Stochastic complexity measures for physiological signal analysis. *IEEE Trans Biomed Eng* 1998; **45**: 1186–91.

7. Inouye T, Shinosaki K, Sakamoto H et al. Quantification of EEG irregularity by use of the entropy of the power spectrum. *Electroencephalogr Clin Neurophysiol* 1991; **79**: 204–10.
8. Marple SL. *Digital Spectral Analysis with Applications*. Englewood Cliffs: NJ Prentice Hall, 1987.
9. Särkelä M et al. Automatic analysis and monitoring of burst suppression in anesthesia. *J Clin Monit Comp* 2002; **17**: 125–34.

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