

Modified excerpt from

## **Cross-Approximate Entropy of cortical local field potentials quantifies effects of anesthesia – a pilot study in rats**

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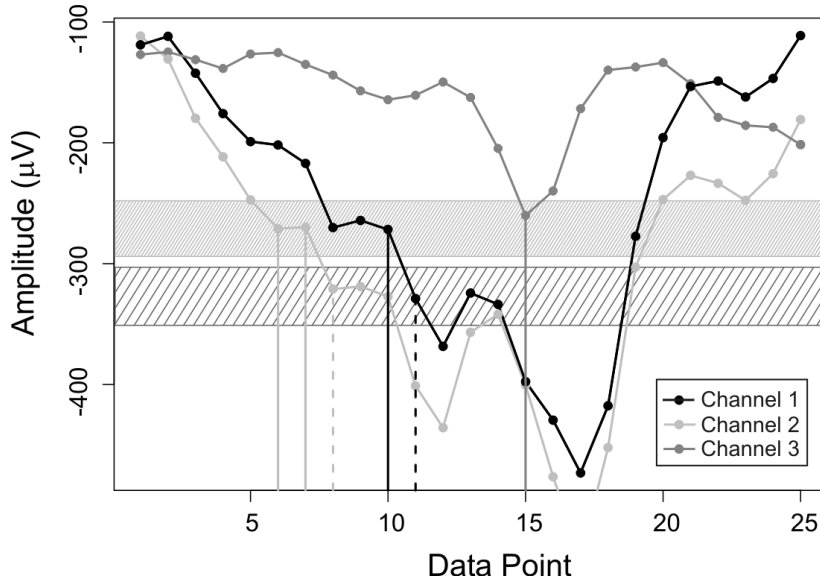
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### **Data analysis: Pearson's correlation and Cross Approximate Entropy**

Cross-approximate entropy (XApEn) was introduced by Pincus for the analysis of hormone secretion processes (Pincus et al. 1996). It is an extension of approximate entropy which has been widely used in the analysis of biosignals such as EEG, electrocardiogram and, recently, local field potentials (Bruhn et al. 2000; Pincus 1991; Beckers et al. 2001; Silva et al. 2010). XApEn quantifies the predictability of the appearance of common patterns in two time series, not heeding the order in which they appear. Higher values of XApEn indicate higher degrees of independence or dissimilarity of the signals. As pointed out by Hudetz et al (Hudetz 2002), XApEn is sensitive to changes in signal independence over a wide frequency spectrum and does not require stationarity of signals; thus it is very well suited to the analysis of local field potentials. In a preprocessing step, the selected data sequences were low pass filtered by a MATLAB 6.5 (The MathWorks, Inc., Natick, MA, USA) double reverse butterworth filtering routine (-3dB frequency of 200 Hz), which allows filtering with zero phase shift, and subsequently downsampled to 500 Hz. Next, data from each channel were normalized by subtracting the mean, followed by a division by the standard deviation. XApEn was calculated according to Pincus et al. (Pincus et al. 1996):

$$XApEn(m, r, N)(x \parallel y) = \Phi^m(r)(x \parallel y) - \Phi^{m+1}(r)(x \parallel y)$$

$\Phi^m(r)(x \parallel y)$  is the average of  $\ln(C_i^m(x \parallel y))$ .  $C_i^m(x \parallel y)$  is the number of times which a sequence of defined length  $m$  in signal  $x$  starting at data point  $i$  has a similar counterpart anywhere in signal  $y$ , divided by  $N-m+1$  (the number of comparisons possible). Two sequences are defined as similar if none of their scalar component differences  $(x_i - y_i)$  exceeds tolerance  $r$  (see Figure 2 for a detailed illustration of the computations). For analysis of the presented data, length  $m$  was set to 1 and tolerance  $r$  was 20% of the standard deviation of the signal in the channel combination with the lower channel number, i.e. if the channel combination was [1,4], SD was calculated for the signal recorded from channel 1. These settings are in accordance with the settings recommended by Pincus (Pincus et al. 1996). XApEn calculation was performed with MATLAB 6.5.



**Figure 2. Calculation of XApEn**

Short excerpt of raw data from three channels shown to illustrate the computation of XApEn. Parameters were set to  $r=23 \mu V$  (tolerance) and  $m=1$  (sequence length). Thus, the 'sequence' length is one data point. For illustration purposes we choose data point  $i=10$  of Channel 1. Similar sequences (data points of similar amplitude) of Channels 2 and 3 are found within the upper rectangle representing tolerance  $r$ , i.e. data points 6 and 7 of Channel 2 and data point 15 of Channel 3. This leads to coefficients

$$C_{10}^1(r)(Channel1 \parallel Channel2) = \frac{2}{25 - 1 + 1} = \frac{2}{25} \text{ and } C_{10}^1(r)(Channel1 \parallel Channel3) = \frac{1}{25}. \text{ In}$$

the second pass, sequence length is extended to  $m+1=2$  points so that now the two point-sequence Channel 1 (10,11) is under consideration. For all previously identified data points in channels 2 and 3 (namely, those similar to Channel 1 (10)) the algorithm checks if the consecutive data point is similar to Channel 1 (11) and hence a pattern similar to Channel 1 (10, 11) exists. Graphically this means that two consecutive data points of channels 2 and 3 have to reside within the upper and lower rectangle, respectively. Only Channel 2 (7, 8)

fulfils this requirement. This leads to coefficients  $C_{10}^{1+1}(r)(Channel1 \parallel Channel2) = \frac{1}{25}$  and

$$C_{10}^{1+1}(r)(Channel1 \parallel Channel3) = \frac{0}{25}. \text{ This pattern matching procedure is performed for all}$$

possible sequences so that:

$$XApEn(Channel1 \parallel Channel2) = \frac{\sum_i \ln C_i^m(Channel1 \parallel Channel2)}{N - m + 1} - \frac{\sum_i \ln C_i^{m+1}(Channel1 \parallel Channel2)}{N - m}$$

If a specific pattern in one channel can not be detected in the other, as in the example above, the corresponding  $\ln C_i^m(x \parallel y)$  is undefined. In the analyzed data sets and with the parameters chosen, this case did not occur.

## Reference List

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