INFORMATION CONTENT OF CORTICAL SPIKE TRAINS DURING DIFFERENT BRAIN STATES

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The information carried by spike trains is the basis of neural coding. Each spike has an energy cost (Lennie, Curr Biol *13:* 493, 2003) and therefore its existence must be relevant to the system. During sleep and awake states, even in the absence of stimuli, there is ongoing activity in the cortex as a result of the recurrent connectivity in the cortical and thalamocortical loop. **Here we have determined how much information is carried by spontaneous spike trains of neurons in the cerebral cortex of a chronically implanted animal under different state of vigilance, with an emphasis in the changes of information during transitions between states.** In order to estimate *information content* in the spike trains we have used Lempel-Ziv complexity, a method that has the advantage of estimating entropy with short (non-infinite) recording times (Amigo, J. M., Szczepanski, J., Wajnryb, E., and Sanchez-Vives, M. V. (2004). Neural Comput *16,* 717; Szczepanski, J., Amigo, J. M., Wajnryb, E., and Sanchez-Vives, M. V. (2003) Network *14*: 335).

METHODOLOGY

There are 3 different aspects of the Methodology that we will report here:

1) The realization of single cell recordings in chronically implanted behaving rats: surgery, recordings and cluster cutting.
2) The determination of the brain state of vigilance based on the EEG analysis.
3) The estimation of the information content in the spike trains.

1) Single cell recordings in chronically implanted behaving rats

We recorded from Lister Hooded rats chronically implanted with tetrodes in primary visual cortex (AP: -6, ML: -4 from bregma) during awake, drowsy and sleep periods. Each tetrode was made from four twisted strands of 17 or 25µm diameter HM-L-coated platinum-iridium wire and the four tetrodes were held by a cannula which was attached to a microdrive(Fig.2).

Figure 1. Implanted rat.

After one week of post-operative recovery we started the recording. The electrodes were advanced by up to 50-75µm daily in 25-50µm steps.

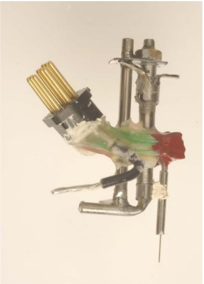

Figure 2. Microdrive mounted with two tetrodes.

Multiple single units recordings and data processing

Electrical spontaneous activity was recorded during sleep, drowsy and awake states while the animal was in its home cage. All the activity included in the analysis was spontaneous and recorded from the visual cortex in the absence of visual stimuli.The recordings were done in darkness and we supervised the animal´s behavior with an infrared camera. Single and multi unit recording were made with a 16 channel data acquisition system from Axona Ltd (London, UK). After amplification (1000x) and filtering, EEG field potentials (sampled at 250Hz, low-pass filtered at 500Hz) and extracellular action potentials (spikes, sampled at 48 KHz, high-pass filtered at 360 Hz) were recorded from supragranullar layers. Recording sessions lasted 30 minutes. After each recording session, the data were transferred to a Pentium IV personal computer and were analyzed off-line.

Spike Sorting

Cluster cutting was done using the Offline Sorter software (Plexon Inc). The waveforms are sorted into units by selecting an automatic method: the valley - seeking algorithm (Fukunaga, 1972, *Introduction to Statistical Pattern Recognition, Chapter 11, Ac. Press.*). The 3D cluster view option was used, with Principal Component (PC) 1, PC2, PC3 as X, Y, and Z axis. (Fig.3)

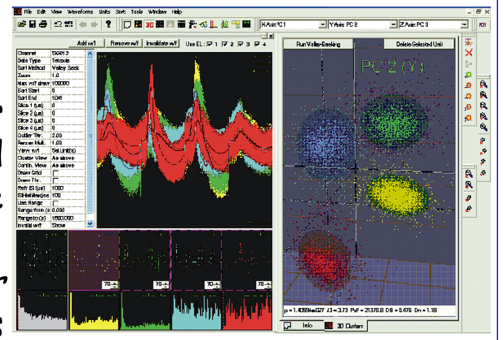

Figure 3. Offline Sorter software showing the isolation of 4 cleared different single units.

2) EEG analysis to determine brain state of vigilance.

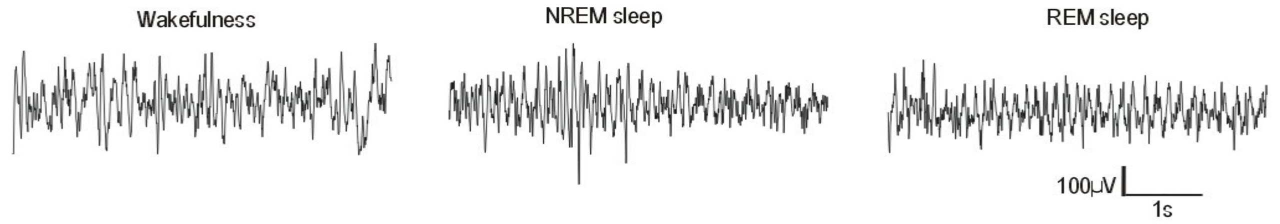

Figure 4. Examples of EEG recording showing different brain states.

Delta	0.5-4.0 Hz
Theta	4.5-8.5 Hz
Sigma	9.0-14 Hz
Beta1	14.5-18.5 Hz
Beta2	19-30 Hz
Gamma	30.5-48 Hz

The method applied consisted in a quantification of each state taking into account the value of the following parameters:

•P1= delta / theta

•P2= theta/(beta2+ gamma)

The representation of the parameters' value in a space of phases showed three different clusters corresponding to the different brain states. P1 served to distinguise between REM and N-REM sleep and P2 served to distinguised between REM and AWAKE state (Maloney,K. et al. 1997; *Neuroscience 76 (2): 541* ; Veasey,SC. et al. 2000, *Sleep 23 (8):1*). In this study we have concentrated on N-REM *versus* WAKE state.

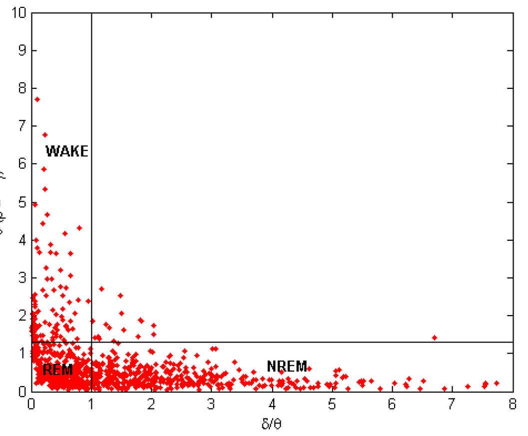

Figure 5. Phase's space showing the three clusters corresponding to REM, N-REM and AWAKE state.

3) Analysis of the information content in the spike trains

Encoding Procedure

Each second is divided into *f* (encoding frequency) bins (each bin=12.5 ms). **With each bin we associate 1 or 0 depending on whether or not there has been at least one spike in this bin** (Fig. 5).

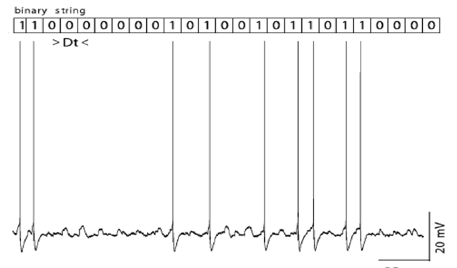

Figure 5. Illustration of the encoding procedure (from Amigo et al, 2004).

Lempel-Ziv Complexity (1976)

For a given sequence S_n of bins Lempel-Ziv76 complexity ***denotes the number of new patterns that appear when we go along the sequence.* Normalized complexity is defined as** $c_2(S_n)=\frac{C_2(S_n)}{n/\log_2 n}$

Entropy Estimation

In the case of stochastic processes, ***entropy*** *H* can be expressed as entropy per symbol (***average information carried by symbol,*** *the symbol being 0 or 1).* Assuming ergodicity of stochastic processes (generating sequences) **it was proven that** $C_{norm}(S_n)\to H$

Information carried by a spike-train

Information carried by event *A* in Shannon sense is $I(A)=-\log_2 P(A)$ where *P(A)* is probability of *A*; we see that less probable events carry more information. For ergodic sources we have $\frac{I(S_n)}{n}\to H$

Thus, for sufficiently long sequences, information carried by single spike-trains is close to **entropy**. Consequently, normalized complexity for sufficiently long **(in time)** sequences approximate the information carried by single encoded spike-train.

Moving Window Assumptions

We consider normalized complexity within sliding windows along encoded spike-trains with the length to be 5 sec. This is due to trade off between:

- keeping conditions like ergodicity of the process (thus we assume also local stationarity) for which normalized complexity works from one side, and
- considering sufficiently long window (sequences) to get good approximation of information via normalized complexity.

RESULTS

1. We recorded from a total of 44 neurons. An average value of information for the spike trains of each neuron was obtained for the periods of slow wave sleep and awake. The following figures show the distribution of slow wave sleep and awake average information values.

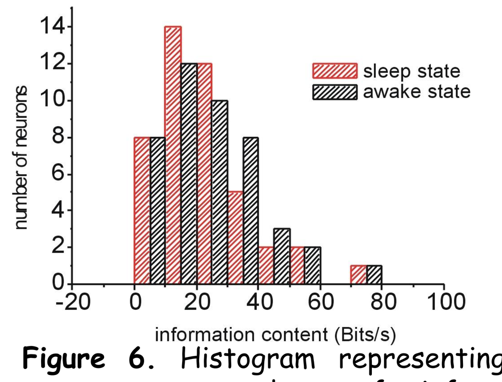

Figure 6. Histogram representing the average raw values of information content across neurons during sleep and awake state.

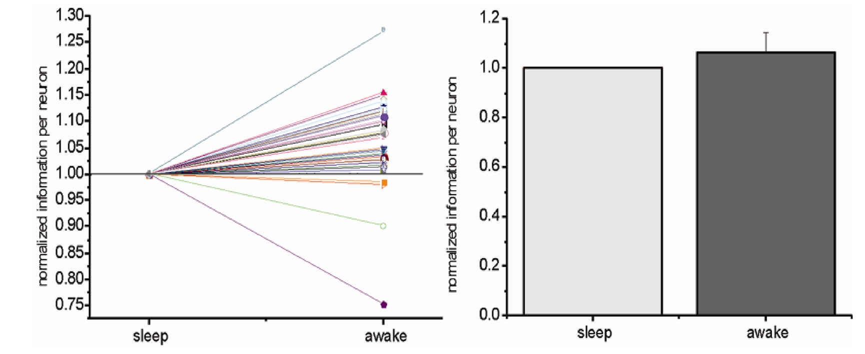

Figure 7. Normalized information content values with respect to the sleep value. The information carried by the spike trains was consistently higher in awake than in sleep state.

For all the neurons, we normalized their information values to the ones during sleep. If we take the a priori null hypothesis as there being an equal probability of an increase or decrease in information rate from sleep to awake then the probability of observing 32 out of 39 cases as increasing in information is extremely small. We would therefore reject the hypothesis of equal probability in favour of the alternative that the probability is greater that there will be an increase (p<0.0001). **Therefore, the average value of information in spike trains was higher in awake with respect to sleep states** (see Fig. 7).

On the other hand, the average raw (non-normalized) values of information between sleep and awake states for the population were not significantly different given the variability of absolute information between neurons (Fig. 6). This **variability between neurons** expanded between 5.4 and 72.5 bits/sec for sleep and between 4.12 and 75.5 bits/sec for the awake states.

2. There was **positive relation between firing rate and information content, however in most of the cells a plateau was reached, such that higher rate did not correlate with higher information content** (Fig.8).

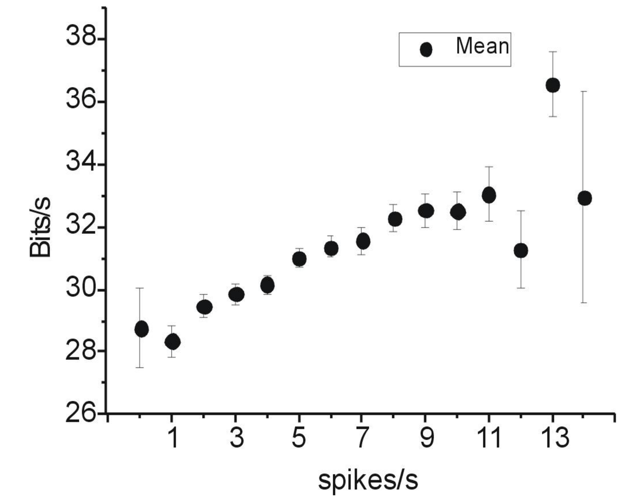

Figure 8. Relationship between firing rate and information content. Its shows a positive relation between then until a plateau is reached.

3. Information rate in the spike trains of neighboring neurons was highly correlated, both during sleep and also during the awake state (Fig. 9). This phenomenon was observed even for neurons that were recorded with different tetrodes and 250-300 microns apart.

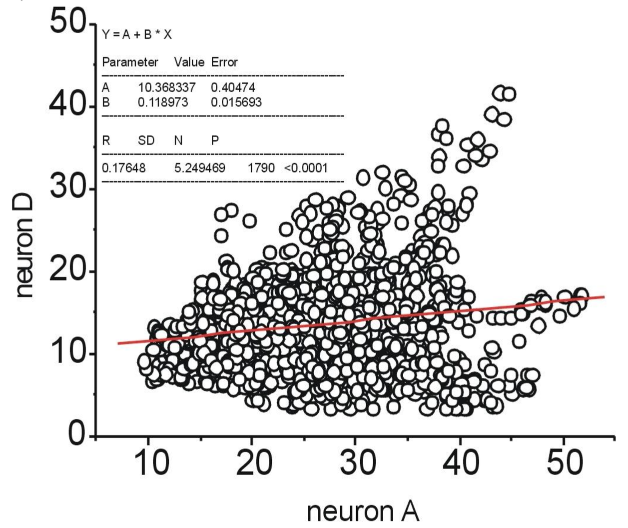

Figure 9. Correlation between the information content (in bits/s) of two different neurons recorded with the same tetrode. Statistical significance is shown in the left inset (p<0.0001).

4. The **transition from sleep to awake** was studied in a total of 15 neurons. Out of them 13 had a detectable increase in the information rate, 1 had a decrease and 1 showed no change.

The average increase in information rate in the transition from sleep to awake was of 10.29 bits/s.

From this we conclude that, *even when during sleep periods there is a rhythmicity in the discharge, there is enough variability in the interspike intervals such that the information conveyed by spike trains is similar to the one during awake states.*

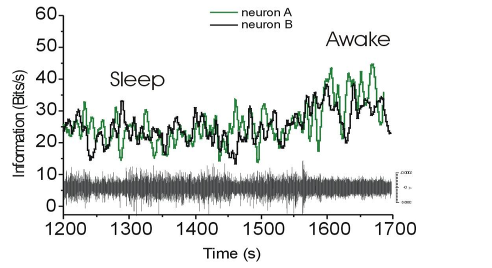

Figure 11. Transition from sleep to awake state. Notice the simultaneous change in the EEG signal at 1580s and the increase in the information content at the transition. Changes in information rate between the spike trains of two different neurons run in parallel.

5. The **transition from awake to sleep** was studied in a total of 24 neurons. Out of them 19 had a detectable decrease in the information rate, 4 had an increase and 1 showed no change.

The average decrease in information rate in the transition from awake to sleep was of 10.94 bits/s.

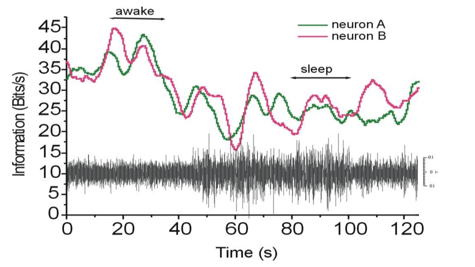

Figure 13. Transition from awake to sleep state. Notice the parallel change in the EEG signal at 40s with the decrease in the information content carried by two neurons. There is a correlation between the information content of the spike trains from two different neurons.

6. The influence of the spike cutting in a more restrictive (1.3SD) or less restrictive (2.0 SD) criteria determined the absolute values of information carried by spike trains but not the relative transitions between states (Fig. 14).

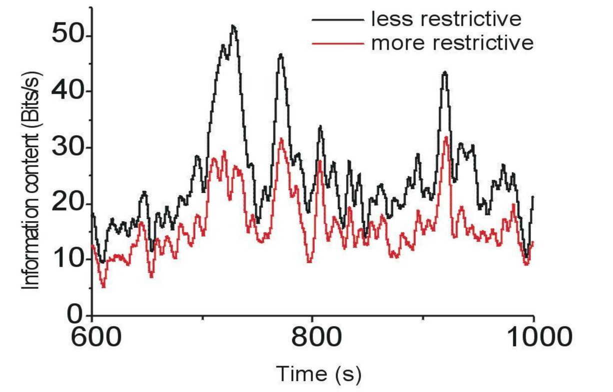

Figure 14. Comparison between the absolute value of the information content and the used of different parameters of cutting.

CONCLUSIONS

• During awake states the average value of information in spike trains was higher than during slow wave sleep states (5.3+/- 0.8%). This is a moderate change and suggests that, even when rhythmic, neuronal activity during slow wave sleep has high information content.

• In most cases we observed a positive relation between firing rate and information content until a plateau was reached.

• Transitions from awake to slow wave sleep and from sleep to awake resulted in similar changes in information content in the spike trains (around 10 bits/s increase/decrease).

•Changes in the parameters of the spike sorting did not influence in the results if we take into account the relative transitions between states.

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