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On the number of states of the neuronal sources

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Abstract

In a previous paper (Proceedings of the World Congress on Neuroinformatics (2001)) the authors applied the so-called Lempel–Ziv complexity to study neural discharges (spike trains) from an information-theoretical point of view. Along with other results, it is shown there that this concept of complexity allows to characterize the responses of primary visual cortical neurons to both random and periodic stimuli. To this aim we modeled the neurons as information sources and the spike trains as messages generated by them. In this paper, we study further consequences of this mathematical approach, this time concerning the number of states of such neuronal information sources. In this context, the state of an information source means an internal degree of freedom (or parameter) which allows outputs with more general stochastic properties, since symbol generation probabilities at every time step may additionally depend on the value of the current state of the neuron. Furthermore, if the source is ergodic and Markovian, the number of states is directly related to the stochastic dependence lag of the source and provides a measure of the autocorrelation of its messages. Here, we find that the number of states of the neurons depends on the kind of stimulus and the type of preparation (in vivo versus in vitro recordings), thus providing another way of differentiating neuronal responses. In particular, we observed that (for the encoding methods considered) in vitro sources have a higher lag than in vivo sources for periodic stimuli. This supports the conclusion put forward in the paper mentioned above that, for the same kind of stimulus, in vivo responses are more random (hence, more difficult to compress) than in vitro responses and, consequently, the former transmit more information than the latter.

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1. Introduction

Computational neuroscience is an approach to understanding the content and transmission of information in the nervous system. We consider this process at the level of the information being transmitted from neuron to neuron by trains of action potentials (Rieke et al., 1998). Neurons

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respond to stimuli by changes in their membrane potential. If there is a depolarization of the membrane potential that reaches threshold, 'spikes' or action potentials (sharp peaks of voltage of the same height) are triggered (Hodgkin and Huxley, 1952). Basically all the information that travels without decay along neuronal axons and is transmitted between neurons, does it in the form of individual spikes or trains of spikes. It is still a challenging problem to find out what kind of encoding and decoding mechanisms are used by the neurons and which are the properties of these biological encoders (Borst and Theunissen, 1999). Important for the mathematical modeler is the fact that the relation between stimulus and neuron response is not one-to-one: the same input s can generate different outputs r_k because of noise in the neuron. In the approach we follow in this paper, we will furthermore consider the introduction of *internal states* in the neuron (Gallanger, 1968), analogously to what occurs also in the definition of encoders (Ziv and Lempel, 1978); given s, the actual response r depends additionally on the current state of the neuron. In doing so we will be able to apply the Lempel–Ziv complexity theory and, in particular, our previous results on this subject (Amigó et al., 2001).

An essential role when studying properties of information sources is played by pattern matching (Wyner et al., 1998). In particular, the complexity as defined by Lempel and Ziv (1976) counts the number of new patterns along a discrete sequence, time series or, in more physical terms, digital signal. A related quantity, the normalized complexity, provides a lower bound for the compression ratio of the signal by optimal coding (Ziv and Lempel, 1978), so that the higher the normalized complexity of a discrete signal, the more information it conveys. Moreover, if the source is stationary and has 'good' statistical properties (specifically: ergodicity, which allows to calculate mean values as time averages with respect to some evolution process over this space), the normalized complexity of a single output gives with high probability a very good estimate of the source entropy, which is the average information in bits generated by the source. Observe that, whereas entropy is a property of information sources, complexity is a property of individual sequences which can be calculated independently of the source properties.

Normalized complexity has been extensively applied by the authors in (Amigó et al., 2001) to characterize the responses in vivo and in vitro of single neurons of the primary visual cortex to different kinds of stimuli, including visual stimulation (sinusoidal drifting gratings) and intracellular current injections (sinusoidal and random currents). Our results showed, for example, that the normalized complexity of the outputs in vivo are higher (and hence carry more information) than in vitro for the same kind of stimuli. This paper builds on such results on the complexity of the spike trains and, especially, on the experimental database gathered for this work. Its main goal is to introduce the concept of *neuronal source* and to show that, in general, the number of states of such sources can also be used as an earmark of neural discharges.

In short, we promote the stimulus, the neuron (eventually, neural network) and the encoding technique of the spike trains (to be explained below) to a finite-state information source generating discrete signals which contain information about the stimulus. In order to quantify the number of states of the neuronal sources, we use a method which is a modification of others already known by Ziv (1990): we compare the entropy estimated by means of the Lempel–Ziv normalized complexity with the entropy of the source, assumed to be ergodic and finite-order Markovian. This procedure is then applied to the same experimental cases studied by Amigó et al. (2001). For convenience we will eventually talk of periodic or random in vivo and in vitro sources, according to the kind of stimulus and to the experimental preparation (in vivo, in vitro). Among other results, we found that the number of states of periodic in vivo sources can differ significantly (depending on the encoding technique) from the number of states of periodic in vitro sources and the same happens with the random in vitro sources as compared with the periodic in vitro sources.

2. Methods

2.1. Codings

Let us consider a single neuron firing a spike train ('output') as response to a stimulus ('input'). Now, in information theory one basically talks of *sources* and *messages* sent by them, where 'message' (or word) stands in this framework for a (finite or infinite) sequence of finitely many symbols or 'letters' (think of a digital signal). Therefore, let us consider for the time being the stimulus together with the neuron as a signal source and the spike train as the would-be message sent by it. In fact, a spike train, far from being digital, is an analog signal which actually comes into the analysis as a table of real numbers generally corresponding to the absolute times of the spike occurrences (Fig. 1). In order to transform them in *bona fide* messages, one needs to translate these sequences of real numbers into sequences of symbols drawn from a finite set called alphabet. This step is called the *codification* of the signal and the procedure, the (*en*)*coding*. Henceforth, always when we talk about spike trains as messages we mean that the signal has been previously codified.

Codification can be made in different ways (Amigó et al., 2001). In this contribution we will restrict, however, to one we call *interval coding* (MacKay and McCulloch, 1952), the reason for this choice being that this coding (out of other we also investigated, like the *interspike time* and *median codings*) delivers the neatest results for our purposes. The recipe to codify a spike train according to this method goes as follows (Fig. 2). Let the first spike of a train occur at time 0 and the last one T time units later. The time interval [0, T] is then split in n bins Δt_i $(1 \leqslant i \leqslant n)$ of the same length. If there are N_k spikes in the bin Δt_k, then assign the number N_k to Δt_k (Dan et al., 1996; Rieke et al., 1998; Zador, 1998). The result is a message of length n with no more than n different letters. If, instead, each bin Δt_i is coded by 0 or 1 according to whether it contains no or at least one spike, respectively, the message will be binary. Whenever necessary, the latter method will be called *binary* interval coding to distinguish it from the former one, the *general* (multi-symbol) interval coding. Notice that, when n is so large (or, equivalently, the length of the bins so small) that

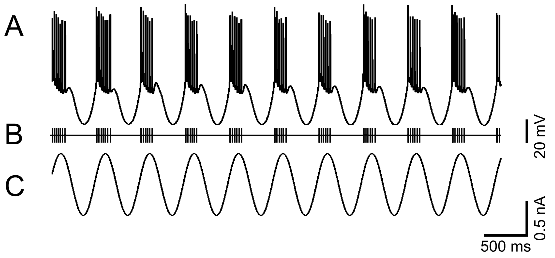

Fig. 1. Intracellular recording from a cortical cell in vitro during sinusoidal current injection. (A) Membrane potential trace showing the trajectory while intracellular sinusoidal current was injected. During the depolarizing phase the membrane potential value reached threshold, inducing a train of spikes or action potentials. (B) Spikes as acquired in a separate channel to be used for the analysis presented here. (C) Sinusoidal current injected into the cell.

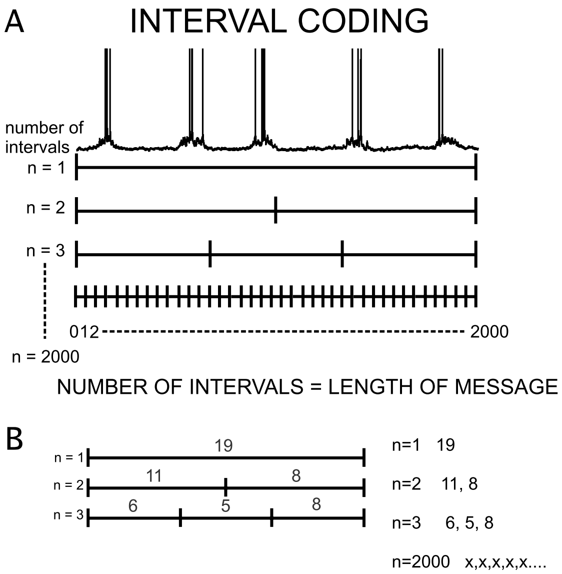

Fig. 2. (A) Illustration of the interval coding with $n = 1,2,3,\ldots,2000$ subintervals. Divide the time duration T of the given spike train in n subintervals Δt_k $(1 \leqslant k \leqslant n)$ of the same length $L = T/n$. If N_k spikes occur in the subinterval Δt_k then assign the 'letter' N_k to the subinterval Δt_k. The length of the ensuing (in general, multi-symbol) message is n. A binary message results instead if Δt_k is coded by 0 or 1 according to $N_\mathrm{k} = 0$ or $N_\mathrm{k} > 0$, respectively. (B) A spike train of, say, 19 spikes is encoded with $n = 1,2,3$ subintervals. The corresponding multi-symbol messages are shown on the right column.

only one spike at most occurs in each Δt_i, both interval codings coincide. This happens for $n \geqslant T/\tau_{\min}$ where $\tau_{\min}$ denotes the shortest interspike time.

The information-theoretic properties of the spike trains depend, in general, on the encoding method used (Amigó et al., 2001; Panzeri and Schultz, 2001; Rieke et al., 1998). This must be kept in mind when studying and comparing such properties.

2.2. SNE sources

Once a spike train has been codified into a message, this can be viewed as emitted by an information source, the source comprising everything preceding the message, namely, the stimulus (S), the neuron or neuronal network (N) and, last but not least, the encoding technique (E). This formal counterpart of the neuron considered as an information source will be called sometimes a SNE source to highlight the dependence of the encoded neural responses on both stimulus and codification. Any source property applied to a neuron or neuron network makes only sense if referred to the corresponding SNE source. By the same token, source properties evaluated from neural outputs should only be compared if codified with the same technique; the numerical differences can then be traced back to differences in the stimuli.

To be more specific, by an information source we mean a so-called finite-state source. Before defining this information-theoretical concept, we need to dwell in the next two subsections on a few technical details. We start with the complexity.

2.3. Lempel–Ziv complexity

Suppose that the source S generates words $x_1^n := x_1 x_2 \ldots x_n$ of length n whose letters x_i $(1 \leqslant i \leqslant n)$ belong to a set $\mathscr{A} = \{a_1, \ldots, a_\alpha\}$ of size $|\mathscr{A}| = \alpha < \infty$, called the source alphabet. Given the word x_1^n, a block of length l $(1 \leqslant l \leqslant n)$ is just a segment of x_1^n of length l, i.e. a subsequence of l consecutive letters, say $x_{i+1}^{i+l} := x_{i+1} x_{i+2} \ldots x_{i+l}$ $(0 \leqslant i \leqslant n-l)$. In particular, letters are blocks of length 1 and blocks of higher length are obtained by juxtaposition of blocks of lower length. Set $B_1 = x_1^1 = x_1$. If $x_2 \neq x_1$, set $B_2 = x_2^2 = x_2$; otherwise, consider blocks of increasing length $x_2^3 = x_2 x_3, \ldots$ until a block $x_2^{n_2}$ is found such that it does not occur previously. Define then $B_2 = x_2^{n_2}$. Suppose recursively that, after k steps,

$$B_1 B_2 \ldots B_k = x_1^{n_k}$$

where $B_1 B_2 \ldots B_k$ denotes the juxtaposition of the blocks $B_1 = x_1^1,\ B_2 = x_2^{n_2}, \ldots,\ B_k = x_{n_{k-1}+1}^{n_k}$ and $n_{k-1} + 1 \leqslant n_k < n$ (with $n_0 = 0$ and $n_1 = 1$). Define

$$B_{k+1} := x_{n_k+1}^{n_{k+1}} \quad (n_k + 1 \leq n_{k+1} \leq n),$$

to be the block of minimal length such that it does not occur in the sequence $x_1^{n_{k+1}-1}$. Proceeding in this way, we obtain a *decomposition* of x_1^n in 'minimal' blocks, say

$$x_1^n = B_1 B_2 \ldots B_p \tag{1}$$

in which only the last block B_p can occasionally coincide with one of the foregoing blocks. The Lempel–Ziv *complexity* $C_\alpha(x_1^n)$ of x_1^n is then defined as the number of blocks in the (clearly unique) decomposition (Eq. (1)):

$$C_\alpha(x_1^n) := p = p(\alpha)$$

The reader must be reminded at this point that there are different definitions and measures of complexity in the literature (Chaitin, 1982; Ebeling and Jiménez-Montaño, 1980; Gonzalez Andino et al., 2000; Rapp et al., 1994). In this paper, complexity is always meant in the sense of Lempel–Ziv. Intuitively speaking, the complexity of a word counts the number of different patterns appearing during its generation process. As explained above formally, the first symbol on the left of the word defines the first block. From there one moves rightward letter by letter, until the string of symbols beginning just after the previous block and ending at the current position happens not to have appeared before. At this point, a new block is defined. The procedure is illustrated by the following example. The decomposition of the binary word $x_1^{19} = 0101101000110111001 0$ into minimal blocks of new patterns is

$$0|1|011|0100|011011|1001|0$$

where the vertical lines separate the blocks. Therefore, the complexity of x_1^{19} is 7.

The generation rate of new patterns along x_1^n, a word of length n with letters from an alphabet of size α, is measured by the *normalized complexity* $c_\alpha(x_1^n)$, which is defined by

$$c_\alpha(x_1^n) = \frac{C_\alpha(x_1^n)}{n/\log_\alpha n} = \frac{p(\alpha)}{n}\log_\alpha n$$

Sequences with a repetitive or poor pattern structure (e.g. periodic or quasi-periodic) have a very small normalized complexity. On the opposite end stand the random sequences, which unfold a rich pattern diversity as time goes on. Although the normalized complexity can take values higher than 1, its value for completely random sequences is about 1 with very high probability.

The normalized complexity is closely related to the source entropy (Amigó et al., 2001), compression ratio for information of lossless sources (Ziv and Lempel, 1978), optimal encoding (Ziv and Lempel, 1978) and randomness (Leung and Tavares, 1985). Other applications of the normalized complexity will be addressed below.

2.4. Finite-state sources

Let $X_1^n = X_1X_2\ldots X_n$ be a sequence of observable random variables taking on values in the alphabet $\mathcal{A} = \{a_1, \ldots, a_\alpha\}$. Similarly, let $Z_1^n = Z_1Z_2\ldots Z_n$ be a sequence of observable random variables (*states*) corresponding to X_1^n, which take on values in another finite set $\mathcal{Z}$ of size $|\mathcal{Z}| = \sigma$. One can think of the realization $x_1^n = x_1x_2\ldots x_n$ as being a message generated by a source with a set of internal states $\mathcal{Z}$, the letter x_i occurring at time i, when the source is in the state z_i. An information source is said to be *finite-state* (with σ states) if the joint probability of x_1^n and z_1^n is given by (Gallanger, 1968; Ziv, 1990)

$$P(x_1^n, z_1^n) = \prod_{i=1}^{n} p(x_i, z_i|z_{i-1})$$

where the initial state $z_0 \in Z$ is assumed fixed and known, and $p(x_i, z_i|z_{i-1})$ denotes the joint probability of a letter x_i and a state z_i at time instant i, given the previous state z_{i-1} at time instant $i-1$.

Furthermore, a source is said to be *stationary* and/or *ergodic* if the stochastic process $(X_i)_{i=0}^{\infty}$ is stationary and/or ergodic, respectively. In simple terms, a source is stationary if the statistical properties of the (in principle, arbitrarily long) messages do not change if the origin of time is shifted. On the other hand, a stationary source is *ergodic* if sample averages and time averages coincide almost surely in the long run, i.e. one can calculate expected values over the word ensemble using the relative frequencies of the letters in a 'typical', sufficiently long word. In particular, all the sequences produced by an ergodic source (except maybe a set of probability zero) have the same statistical properties.

As a rule, stationarity is an assumption which cannot be taken for granted in biological systems and should be checked on a case-by-case basis. Indeed, phenomena such as adaptability, fatigue, etc. amounts to a non-negligeable time variability in the statistical properties of the performances. With regard to ergodicity, it can be tested in practical cases by sampling typical trajectories; every such trajectory should produce the same average. Ergodicity is a kind of efficiency principle which is very often encountered in nature for stationary processes.

Because of its practical importance, we focus henceforth on the subclass of the finite-state sources defined by the ergodic *Markovian* sources of finite order. That is, if $x_{-\infty}^n := \ldots\ x_{n-1}x_n$, then

$$p(x_i|x_{-\infty}^{i-1}) = p(x_i|x_{i-k}^{i-1}), \quad i = 1, 2, \ldots, n \tag{2}$$

for some integer $k \geqslant 1$ called the *order* of the source. Eq. (2) reads that the probability for the letter x_i at instant i depends directly only on the previous k outcomes: $x_{i-1}, \ldots, x_{i-k}$. For this reason, k is also called the *lag* of the source. In this case, the set of states can in-principle be identified with the set of all k-tuples of the form

$$x_{i-k}^{i-1} = (x_{i-k}, \ldots, x_{i-2}, x_{i-1}) =: z_{i-1}$$

Therefore, if all substrings of length k are feasible, the number of states N of such a source is $N = \alpha^k$. But, in general,

$$N \leqslant \alpha^k \tag{3}$$

because not all states need to be occupied. Non-feasible states have formally probability zero and will be dispensed for in the sequel. We conclude that to estimate the number of states of an ergodic finite-state Markovian source, only its order k is needed.

Let $z_{i-1} = x_{i-k}^{i-1} \in A \times \cdots \times A =: A^k$ $(1 \leqslant i \leqslant n)$ denote the state of a k-order Markovian source at time i. We denote by $\delta(x_i, a, z_{i-1}, z)$ the indicator function for $x_i = a$ and $z_{i-1} = z (a \in A, z \in A^k)$, i.e.

$$\delta(x_i, a; z_{i-1}, z) = \begin{cases} 1 & \text{if } x_i = a \quad \text{and } z_{i-1} = z \\ 0 & \text{otherwise} \end{cases}$$

Now write for notational convenience $\mathbf{x} = x_1^n$ and let define

$$q_{\mathbf{x}}^k(a, z) = \frac{1}{n} \sum_{i=1}^{n} \delta(x_i, a; z_{i-1}, z)$$

$$q_{\mathbf{x}}^k(z) = \sum_{a \in A} q_{\mathbf{x}}^k(a, z)$$

$$q_{\mathbf{x}}^k(a|z) = \begin{cases} q_{\mathbf{x}}^k(a, z)/q_{\mathbf{x}}^k(z) & \text{if } q_{\mathbf{x}}^k(z) > 0 \\ 0 & \text{if } q_{\mathbf{x}}^k(z) = 0 \end{cases}$$

The $\alpha^k \times \alpha$ matrix whose entries are $q_{\mathbf{x}}^k(a, z)$ will be referred to as the kth order Markov-type of $\mathbf{x}$ and will be denoted by $q_{\mathbf{x}}^k$. It can be proved that $q_{\mathbf{x}}^k$ can be viewed as a kth order Markovian probability measure P_k for any $\mathbf{x}$.

Define next the kth order empirical entropy as

$$H(q_{\mathbf{x}}^k) = -\sum_{z \in A^k} q_{\mathbf{x}}^k(z) \sum_{a \in A} q_{\mathbf{x}}^k(a|z) \log_2 q_{\mathbf{x}}^k(a|z)$$

An *order estimator* is then given by (Ziv, 1990)

$$k^* = \min\left\{ k : H(q_{\mathbf{x}}^k) - \frac{1}{n} \Lambda_{\mathrm{LZ}}(\mathbf{x}) \leq \lambda \right\}, \tag{4}$$

where $\Lambda_{\mathrm{LZ}}(\mathbf{x})$ is the Lempel–Ziv codeword length of $\mathbf{x}$ (Ziv and Lempel, 1978). This estimator has the following intuitive interpretation. We seek the smallest model order k for encoding $\mathbf{x}$, such that the empirical entropy will be sufficiently close (difference less than λn) to the codeword length associated with the Lempel–Ziv algorithm, which in turn serves as an estimate of the source entropy. Then, for any positive integer k,

$$P_k(k^* \geq k) \leq \frac{1}{2^{\lambda n}}$$

i.e. the kth order Markovian probability that k^* overestimates k vanishes exponentially with λn.

On the other hand, our numerical experiments with 2-state Markov processes with transition matrix

$$M = \begin{pmatrix} 1-p & p \\ p & 1-p \end{pmatrix}$$

and different transition probabilities p (in particular, for $p = 1/2$ one gets a completely random process) suggest that the normalized complexity of $\mathbf{x}$ converges faster than $\Lambda_{\mathrm{LZ}}(\mathbf{x})/n$ (with increasing n) to the source entropy $H(S)$ $(= -p\log_2 p - (1-p)\log_2(1-p)$ for the above Markov process), so that we propose to use

$$k^* = \min\{k : H(q_{\mathbf{x}}^k) - c_\alpha(\mathbf{x})\log_2 \alpha \leq \lambda\} \tag{5}$$

as the order estimator instead of Eq. (4). In the calculations we set $\lambda = 0.02$.

Of course, always when one applies concepts involving mathematical limits (like entropy, complexity, etc.) to real time series, the problem of undersampling or good estimation is lurking. As said above, our experience shows that the complexity converges very fast so that it typically saturates from word length 400 on, what covers the samples we use.

2.5. Experimental work

The experimental data was obtained from primary cortex recordings both in vivo and in brain slice preparations (in vitro). Intracellular recordings in vivo were obtained from anesthetized adult cats (see Sanchez-Vives et al., 2000a for details). For the preparation of slices, 2–4 month old ferrets of either sex were used (see Sanchez-Vives et al., 2000b for details). Action potentials were detected with a window discriminator and the time of their occurrence was collected with a 10 μs resolution. The resulting time series were used to analyze the neuronal spiking. Concerning the stimuli, they were of three kinds:

(1) *Periodic current injection.* Intracellular sinusoidal currents were injected in vivo and in vitro. The frequency of the waveform was 2 Hz and the intensity ranged between 0.2 and 1.5 nA.

(2) *Periodic visual stimulation.* The visual stimulus used in vivo consisted of a sinusoidal drifting grating presented in a circular patch of 3°–5° diameter, centered on the receptive field. The preferred spatial frequency, temporal frequency and orientation were previously determined from peristimulus time histograms, in order to use the optimal stimulus during the experiment. Only simple cells (classified as shown by Skottun et al., 1991) were included in this study.

(3) *Random current injection.* Correlated stochastic currents with either $1/f^2$ or $1/f$ statistics were injected during the intracellular recording from cortical brain slices (in vitro).

All in all we have four ensembles of stimuli with well-defined properties. The sample count is as follows:

1) Periodic current injection in vivo: 8 samples (spike train lengths between 15.56 and 47.64 s). The average firing rate of these samples was 13.32 spikes/s.
2) Periodic current injection in vitro: 8 samples (spike train lengths between 15.87 and 23.62 s). The average firing rate of these samples was 15.97 spikes/s.
3) Periodic visual stimulation: 8 samples (spike train lengths between 36.74 and 81.81 s). The average firing rate of these samples was 15.98 spikes/s.
4) Random current injection in vitro: 20 samples (spike train lengths between 16.32 and 35.47 s). The average firing rate of these samples was 22.30 spikes/s.

3. Results

As explained above, in order to apply the methods of the information theory to neuronal responses, it is necessary to codify them. After the codification, the original neuronal output becomes a message $\mathbf{x} = x_1x_2 \ldots x_n$, where both the length n and the number of letters α depend in general on the particular coding. Correspondingly, we identify the source of $\mathbf{x}$ with everything preceding it, namely, the stimulus, the neuron and the encoding method. Out of several codification techniques considered in the literature, we use the sharpest one for our present purposes, which happens to be the (general and binary) interval coding. Then one calculates the normalized complexity $c_\alpha(\mathbf{x})$ and the kth order empirical entropy $H(q_{\mathbf{x}}^k)$ of x and insert them in Eq. (5) to obtain the order estimator k^* for each single spike train. Finally, the different k^* are averaged over each sample.

We have carried out this program on the sample of spike trains listed in the previous subsection. The normalized complexity of the sensory outputs have been taken from Amigó et al. (2001). The tables of results below show the (rounded-off) values taken by k^* within the samples in form of intervals. We got the following estimations for k.

(1) General interval coding (with 5000 intervals)

k^*	In vivo	In vitro
Periodic current injection	2–4	9–11
Visual stimulation	2–4	–
Random current injection	–	1–3

(2) Binary interval coding (with 4048 intervals)

k^*	In vivo	In vitro
Periodic current injection	4–6	9–11
Visual stimulation	3–4	–
Random current injection	–	2–3

Although these numbers are the order estimators of the corresponding SNE sources assumed to be ergodic and finite-order Markovian, we will refer to them with the more neutral term of ‘number of states’. The reason should be clear. Our primary purpose is to use them to distinguish neuronal sources from each other, independently of the concrete meaning of k and the source properties. If the source is actually ergodic and Markovian of finite order, then the number of states N and the source order k are related through Eq. (3) but, since k is smaller, it is more manageable. Otherwise, k is no longer the lag of a Markovian source or process but, nevertheless, it retains its capability to differentiate neuronal sources. Important for us is that k^* is a numerical invariant for SNE sources. In particular, for a given neuron preparation and coding, k^* depends only on the kind of stimulus (i.e. on the experimental subcase considered out of the four experimental cases given in Section 2.5), but not on individual stimuli. This comes as no surprise since the same is true for the normalized complexity (Amigó et al., 2001).

4. Discussion

The mathematical model we use to study the transmission of information among neurons via spike trains is a finite-state information source. The neurons, which in our case belong to the primary visual cortex in vivo or in vitro, are exposed to several external stimuli (sinusoidal modulation of luminosity, injection of sinusoidal and random currents). The properties of these stimuli (periodicity, randomness, etc.) go into the model as subsets of the parameter space, each stimulus being determined by fixed values of the parameters (e.g. frequency or correlation length). By observing different properties of the stimuli (what effectively amounts to exploring distinct domains of the parameter space), we can have different distribution functions on the same ensemble of stimuli. In the sense of Shannon (1948), this means that the same subset of stimuli can contain different amounts of information depending on the properties we are interested in. The question arises as to (i) what is (are) the encoding(s) neurons use and (ii) whether the same encoding method is actually employed to transmit different groups of properties of the stimuli. To gain some insight into these interesting and difficult problems we study information sources consisting of the neuron together with the stimulus and the encoding method. In our approach we further assume such sources to be ergodic and Markovian of order k and estimate k.

The results of the calculations show:

1) For periodic stimuli, the number of states in vivo are smaller than the number of states in vitro in all encoding methods used. The restriction to periodic stimuli is due, of course, to the fact that output records both in vivo and in vitro were available only for this kind of stimuli.
2) The number of states in vivo is similar for periodic current injection and periodic visual stimulation within the same encoding method.
3) The number of states in vitro is significantly larger for periodic stimuli than for random stimuli if (binary or general) interval coding is used.

Multiplicity of coding methods poses the following question: if quantitative results depend on the coding used, are they meaningful in some sense? From a formal point of view there is no objection since, in our approach, the coding is part of the source being analyzed: quantities gained with different codings refer rather to different sources.

Another important issue concerns the choice of the coding. First of all, information tools are sometimes used only to discriminate neural signals produced under different conditions. In this case, one should choose, of course, those codings which lead to different behaviors or numerical values of the properties in question (entropy, complexity,...)—the coding becomes part of the tag which characterizes the signal. So to say, two codings are equivalent as far as any of them can be used for this purpose, but the best will be the one providing the broadest or sharpest gaps so that the neural responses to different stimuli classes can be unambiguously differentiated.

But many times one seeks quantitative rather than qualitative results. In these cases, the choice of the coding depends, generally speaking, on the information one wants to get. In principle, different codings target different properties, although in a concrete situation it can be difficult to find an appropriate coding. One could even try to tailor codings to differentiate specific features of the neural behavior! As it was already said in the Section 1, the ultimate problem in this context is to unveil the 'natural' code employed by the neurons.

Finally, the question about the choice of the coding can be also reversed: for a given coding of the spike trains, what kind of information can be obtained about the stimuli as a whole (e.g. distribution function of quantities characterizing stimuli) or about the individual stimuli that caused the spike train under consideration (Borst and

Theunissen, 1999)? This is something that, in general, can only be answered out of experience, although the very definition of the coding might help to figure out the relevant aspects involved.

5. Conclusions

A first general conclusion is that the number of states of the neuronal sources can be used to characterize neural discharges according to the experimental conditions (four in our study) they come from. To be more specific, we have actually estimated the order of ergodic SNE sources, additionally assumed to be Markovian. In principle, the estimators obtained form a set of invariants which tell some neuronal sources from others, independently of their real meaning (stochastic lag) and whether ergodicity is fulfilled. For example, the cases ‘periodic current injection’ in vivo and in vitro can be easily distinguished from each other if either interval coding is employed. In the ideal case that the hypotheses on the source are fulfilled, these invariants can eventually tell about other interesting properties too. So, if the source happens to be Markovian, we conclude that in vitro responses are more correlated than in vivo responses.

The estimation of the number of states of a given neuronal source requires the codification of a typical discharge and the calculation of its normalized complexity. We already mentioned that the choice of coding affects the results, what translates in different SNE sources having different number of states. As a consequence, the information obtained from a neuronal source depends on the coding used and, eventually, several codings may be necessary to discriminate them. We think that this interplay between properties and codings is something more than a mathematical artifact of our model and somehow reflects what actually happens at the neuronal level. We conjecture that different properties are transmitted by means of different codes.

In conclusion, we have shown in this paper how neural responses can be singled-out via the number of states of neuronal sources. In doing so we have modelled the neuron as an information source and discussed our results according to this approach. Eventual practical applications thereof include the assessment of the spike trains entropy in an alternative way and the study of epilepsy (Rapp et al., 1994) as well as the decorrelation effects of neurons. Further applications are the subject of current investigation.

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References

Amigó, J.M., Szczepański, J., Wajnryb, E., Sanchez-Vives, M.V., 2001. On the number of states of the sources as defined by neuron responses of the primary visual cortex. In: Ratta, F. (Ed.), Proceedings of the World Congress on Neuroinformatics. ARGESIM Report no. 20. Vienna: ARGESIM/ASIM Verlag, (ISBN: 3-901608-20-6).

Borst, A., Theunissen, F.E., 1999. Information theory and neural coding. Nat. Neurosci. 2, 947–957.

Chaitin, G.J., 1982. Algorithmic information theory. In: Encyclopedia of Statistical Sciences I. Wiley, New York.

Dan, Y., Atick, J.J., Reid, R.C., 1996. Efficient coding of natural scenes in the lateral geniculate nucleus: experimental test of a computational theory. J. Neurosci. 16, 3351–3362.

Ebeling, W., Jiménez-Montaño, M.A., 1980. On grammars, complexity and information measures of biological macromolecules. Math. Biosci. 52, 53–71.

Gallanger, R.C., 1968. Information Theory and Reliable Communications. Wiley, New York.

Gonzalez Andino, S.L., Grave de Peralta Menendez, R., Thut, G., Spinelli, L., Blanke, O., Michel, C.M., Seeck, M., Landis, T., 2000. Measuring the complexity of times series: an application to neurophysiological signals. Hum. Brain Mapp. 11, 46–57.

Hodgkin, A.L., Huxley, A.F., 1952. Currents carried by sodium and potassium ions through the membrane of the giant axon of *Loligo*. J. Physiol. 116, 449–472.

Lempel, A., Ziv, J., 1976. On the complexity of an individual sequence. IEEE Trans. Inform. Theory IT-22, 75–88.

Leung, A.K., Tavares, S.E., 1985. Sequence complexity as a test for cryptographic systems. In: Blakley, G.R., Chaum, D. (Eds.), Advances in Cryptology: Proceedings of CRYPTO 84, volume 196 of Lecture Notes in Computer Science, 19–22 August, 1984. Springer-Verlag, pp. 468–474.

MacKay, D., McCulloch, W.S., 1952. The limiting information capacity of a neuronal link. Bull. Math. Biophys. 14, 127–135.

Panzeri, S., Schultz, S.R., 2001. A unified approach to the study of temporal, correlational and rate coding. Neural Comput. 13, 1311–1349.

Rapp, P.E., Zimmerman, I.D., Vining, E.P., Cohen, N., Albano, A.M., Jiménez-Montaño, M.A., 1994. The algorithmic complexity of neural spike trains increases during focal seizures. J. Neurosci. 14, 4731–4739.

Rieke, F., Warland, D., de Ruyter van Steveninck, R., Bialek, W., 1998. Spikes: Exploring the Natural Code. MIT Press, Boston.

Sanchez-Vives, M.V., Nowak, L.G., McCormick, D.A., 2000a. Membrane mechanisms underlying contrast adaptation in cat area 17 in vivo. J. Neurosci. 20, 4267–4285.

Sanchez-Vives, M.V., Nowak, L.G., McCormick, D.A., 2000b. Cellular mechanisms of long-lasting adaptation in visual cortical neurons in vitro. J. Neurosci. 20, 4286–4299.

Shannon, C.E., 1948. A mathematical theory of communication. Bell Sys. Tech. J. 27, 379–423, 623–656.

Skottun, B.C., DeValois, R.L., Grosof, D.H., Movshon, J.A., Albrecht, D.G., Bonds, A.B., 1991. Classifying simple and complex cells in the basis of response modulation. Vision Res. 31, 1079–1086.

Wyner, A.D., Ziv, J., Wyner, A.J., 1998. On the role of pattern matching in information theory. IEEE Trans. Inform. Theory 44, 2045–2056.

Zador, A., 1998. Impact of synaptic unreliability on the information transmitted by spiking neurons. J. Neurophysiol. 79, 1219–1229.

Ziv, J., Lempel, A., 1978. Compression of individual sequences via variable-rate coding. IEEE Trans. Inform. Theory IT-24, 530–536.

Ziv, J., 1990. Compression, tests for randomness and estimating the statistical model of an individual sequence. In: Capocelli, R.M. (Ed.), Sequences. Springer, New York, pp. 366–373.