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Measuring entropy in continuous and digitally filtered neural signals

Andrew S. French*, Keram Pfeiffer

Department of Physiology and Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada B3H 1X5

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ABSTRACT

Neurons receive, process and transmit information using two distinct types of signaling methods: analog signals, such as graded changes in membrane potential, and binary digital action potentials. Quantitative estimates of information in neural signals have been based either on information capacity, which measures the theoretical maximum information flow through a communication channel, or on entropy, the amount of information that is required to describe or reproduce a signal. Measurement of entropy is straightforward for digital signals, including action potentials, but is more difficult for analog signals. This problem compromises attempts to estimate information in many neural signals, particularly when there is conversion between the two signal formats. We extended an established method for action potential entropy estimation to provide entropy estimation of analog signals. Our approach is based on context-independent data compression of analog signals, which we call analog compression. Although compression of analog signals is computationally intensive, we describe an algorithm that provides practical, efficient and reliable entropy estimation via analog compression. Implementation of the algorithm is demonstrated at two stages of sensory processing by a mechanoreceptor.

1. Introduction

Nerve cells receive and transmit information in two distinct formats that can be broadly characterized by the terms analog and digital. Continuous, or graded variation of physical parameters, including membrane potential, membrane current or transmitter concentration, are analog signals. In addition, sensory neurons can receive analog signals such as light intensity or mechanical displacement, while muscle cells produce analog contraction force or movement. In contrast, many neurons transmit and receive information as action potentials, which are often treated as point events whose only important property is their time of occurrence, creating a binary digital signal.

Therefore, quantitative measurement of information carried or processed by neurons requires methods of measuring information that can be reliably applied to both analog and digital neural signals. One approach to neural information measurement is via signal-to-noise ratio, which provides an estimate of information capacity, the amount of information that could theoretically be carried by a noisy communication channel (Shannon and Weaver, 1949). This has the advantage that some methods of estimating signal-to-noise can be applied to both analog and digital signals (Juusola and French, 1997; Borst and Theunissen, 1999; Pfeiffer and French, 2009), providing valid comparisons.

Information capacity estimates the maximum performance of a neural component but not the actual rate of information transmission. Instead, information content can be estimated from the signal entropy (Rieke et al., 1997; Juusola and French, 1997; Chacron et al., 2003; Juusola and de Polavieja, 2003; French et al., 2003). While entropy can be estimated directly from a binary signal (Rieke et al., 1997), the situation is more complex for analog signals. Extrapolation of the binary approach leads to a measure called differential entropy (Cover and Thomas, 1991) based on the probability density function (PDF) of randomly distributed values arriving at a receiver. This can be extended to the conditional probability between input and output signals to a neuron (Juusola and de Polavieja, 2003). However, a central problem with PDF based methods is their assumption of randomness in time, which is clearly false for many neural signals.

An alternative approach to entropy measurement is data compression (Salomon et al., 2007). The signal is treated as a data set consisting of a series of symbols and the entropy of the data set is calculated from the total number of symbols multiplied by the amount of information required to uniquely identify each symbol. The data set is then compressed by removing any redundancies in the symbolic description to produce the minimum entropy that is required to reproduce the original signal. This approach has been used to estimate entropy in action potential signals of several systems by treating the action potentials as binary values (Rapp et al., 1994; Jiménez-Montano et al., 2000; French et al., 2003). Here, we extend the data compression approach to analog signals, and describe an algorithm that allows the entropy of neural analog signals to be estimated reliably and efficiently.

* Corresponding author. Tel.: +1 902 494 1302; fax: +1 902 494 2050.
E-mail address: andrew.french@dal.ca (A.S. French).

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2. Materials and methods

2.1. Animal preparation and electrophysiology

Details of the preparation for recording receptor potential and action potentials from spider mechanoreceptors have been described in detail before (Pfeiffer and French, 2009) and will only be briefly summarized here. Legs of adult spiders, *Cupiennius salei*, were autotomized following a protocol approved by the Dalhousie University Committee on Laboratory Animals. Patella cuticle containing the intact VS-3 slit-sense organ was cut from the leg and waxed to a Plexiglas holder that permitted access to both the outer and the inner surfaces of the organ (Juusola et al., 1994). The preparation was continuously superfused with spider saline (in mM: NaCl, 223; KCl, 6.8; $CaCl_2$, 8; $MgCl_2$, 5.1; HEPES, 10; Glucose, 17; pH 7.8). Tetrodotoxin (1 μM in spider saline) was applied during measurements of receptor potential. Chemicals were purchased from Sigma (Oakville, ON, Canada).

Neurons were visualized by an Axioskop 2 FS Plus upright compound microscope with an Achroplan 40X water immersion objective (Zeiss, Oberkochen, Germany), mounted on a gas-driven vibration isolation table inside a Faraday cage (Technical Manufacturing, Peabody, MA). Sharp borosilicate glass microelectrodes (OD, 1 mm; ID, 0.5 mm; Hilgenberg, Malsfeld, Germany) were pulled using a P-2000 horizontal laser puller (Sutter Instrument, Novato, CA). Electrodes were filled with 2.5 M KCl and had resistances between 40 and 100 MΩ in solution. Neuronal somata were impaled with the microelectrodes using a PatchStar micromanipulator (Scientifica, Uckfield, UK). Recordings were made in discontinuous single-electrode current-clamp mode using a SEC-10LX amplifier (npi electronic, Tamm, Germany). Switching frequencies between 18 and 20 kHz and a duty cycle of 1/4 (current passing/voltage recording) were used. The voltage was low-pass filtered at 33.3 kHz and the current signal was filtered at 3.3 kHz by the amplifier.

Mechanical stimulation was by pseudorandom Gaussian white noise generated by a 33-bit binary sequence algorithm with a time resolution of 0.1 ms, using a P-841.10 piezoelectric stimulator driven by an E-505.00 LVPZT amplifier (Physik Instrumente, Auburn, MA) that pushed a glass probe against the slits from below. Personal computers performed data recording and stimulation using custom-written software. Stimulation was via a 12-bit D/A converter and recordings via a 16-bit A/D converter (National Instruments, Austin, TX).

Action potentials were detected by a threshold-detection algorithm (French et al., 2001) and stored as time of occurrence, then digitally filtered by convolution with a $\sin(x)/x$ function (French and Holden, 1971) and re-sampled at 1 ms intervals (Fig. 1). Continuous signals (mechanical stimulus and receptor potential) were also re-sampled at 1 ms intervals.

2.2. Simulations

Simulated continuous, or analog, signals were generated by a Gaussian random number generator using 10-bit quantization with a nominal sample interval of 1 ms. Action potentials were initially simulated at an operator-selected regular firing rate as values of zero or unity with nominal sample interval of 0.1 ms.

2.3. Entropy estimation by analog compression

Analog signals (mechanical stimulus, receptor potential and digitally filtered action potentials) were normalized and digitized so that the maximum amplitude range was represented by 10-bit numbers, or 1024 different amplitude levels (Fig. 1). Entropy was obtained by context-independent data compression (Jiménez-Montano et al., 2000; French et al., 2003). Each of the 1024 numerical values representing the digitized signal was treated as an independent symbol in a linear sequence, or message. Data compression was performed by repeatedly replacing pairs of symbols that occurred with greatest frequency by new symbols, until no further compression was achieved (Fig. 1). The compression entropy, E_c, was then obtained from:

$$E_c = N \log_2 M \qquad (1)$$

where N = number of symbols in the compressed message, M = number of different symbols in the message (French et al., 2003).

The entropy of a digitized signal increases linearly with the number of bits used in digitization (Cover and Thomas, 1991). Values of E_c were divided by the digitization level (in this case 10) to allow direct comparison with other entropy measures. Note that this method allows complete reconstruction of the original digitized signal from the compressed sequence, and is independent of original signal structure. Therefore, the method gives lossless and context-independent data compression. This method of entropy estimation will be referred to as *Analog compression*.

2.4. Entropy estimation by digital compression

In this method, action potentials were represented as regularly sampled binary values of zero (no action potential) or one (action potential) during each sample in time. The resulting binary sequences were compressed directly by the same process as analog compression, but utilizing only the two initial symbols (Jiménez-Montano et al., 2000; French et al., 2003). This method was used to estimate entropy of action potentials before digital filtering, and will be referred to as *Digital compression*.

2.5. Entropy estimation by probability density function

For some simulations an alternate estimate of analog signal entropy was obtained from the probability density function, $p(x)$, of the different amplitude levels, x, by averaging over time (Fig. 1). Differential entropy, E_p, was then estimated from:

$$E_p = -\int p(x) \log_2 p(x)\, dx \qquad (2)$$

(Cover and Thomas, 1991). Values of E_p were divided by the digitization level (in this case 10) to allow direct comparison with other entropy measures.

2.6. Entropy estimation by serial compression of analog signals

An alternative data compression technique for analog signals was tested. Digitized values (10 bits) were obtained as for analog compression, but instead of assigning a different symbol to each value, they were written in binary format (ones and zeros) and concatenated to produce a stream of bits ten times longer than the original signal. The binary stream was then processed by digital compression, identical to that used for action potentials in Section 2.4 above. This method will be referred to as *Serial compression*.

2.7. Pointer sorting in analog compression

Analog or digital compression requires identification and counting of all paired symbol combinations in the sequence. The time required for these operations grows nonlinearly with the length of the sequence (to be shown in Section 3) and becomes a limiting factor in entropy estimation. The number of possible pair combinations is clearly m^2, where m is the number of different symbols in