ACTA NEUROBIOLOGIAE EXPERIMENTALIS

Acta Neurobiol Exp 2005, 65: 399-407

Maximizing the entropy of histogram bar heights to explore neural activity: A simulation study on auditory and tactile fibers

Burak Güçlü
Biomedical Engineering Institute, Bogaziçi University, Bebek, Istanbul 34342
Turkey; Institute for Sensory Research, 621 Skytop Road, Syracuse, NY
13244 USA, Email: burak.guclu@boun.edu.tr

Abstract. Neurophysiologists often use histograms to explore patterns of activity in neural spike trains. The bin size selected to construct a histogram is crucial: too large bin widths result in coarse histograms, too small bin widths expand unimportant detail. Peri-stimulus time (PST) histograms of simulated nerve fibers were studied in the current article. This class of histograms gives information about neural activity in the temporal domain and is a density estimate for the spike rate. Scott's rule based on modern statistical theory suggests that the optimal bin size is inversely proportional to the cube root of sample size. However, this estimate requires *a priori* knowledge about the density function. Moreover, there are no good algorithms for adaptive-mesh histograms, which have variable bin sizes to minimize estimation errors. Therefore, an unconventional technique is proposed here to help experimenters in practice. This novel method maximizes the entropy of histogram-bar heights to find the unique bin size, which generates the highest disorder in a histogram (i.e., the most complex histogram), and is useful as a starting point for neural data mining. Although the proposed method is *ad hoc* from a density-estimation point of view, it is simple, efficient and more helpful in the experimental setting where no prior statistical information on neural activity is available. The results of simulations based on the entropy method are also discussed in relation to Ellaway's cumulative-sum technique, which can detect subtle changes in neural activity in certain conditions.

Key words: peri-stimulus time histogram, bin size, maximum entropy, auditory nerve, rapidly-adapting fiber

INTRODUCTION

The peri-stimulus time (PST) histogram has been a simple and efficient technique to analyze neural activity in the temporal domain. To construct a classical histogram, the action potentials (spikes) generated at successive (stimulation) trials are grouped in equal-width time bins that are temporally synchronized (usually) with the stimulus onset. Therefore, the PST histogram may be considered to be the initial portion of the cross-correlation between the spike train and an external pulse train that marks the delivery of stimuli (Gerstein and Kiang 1960). In the modern statistical view, PST histogram is a density estimate for the spike rate, which is a function of time (Scott 1992). Many variations of PST histograms exist in the literature e.g., with overlapping time bins, which have *a posteriori* smoothing, or which are generated using continuous kernels (see Romo et al. 1999). Continuous histograms do not add much advantage over the classical discrete histograms, because a resolution parameter analogous to the width of the time bin still needs to be specified. Consequently, each PST histogram is also a function of the time bin as well as underlying neural activity. However, PST histograms do not include complete information on the temporal spike pattern. They are, nevertheless, still commonly used among experimental neurobiologists, because the variation of the number of action potentials with respect to time is usually of great importance. The technique proposed in this article may be especially helpful in experimental studies which explore neural activity, but which have no prior knowledge on the response properties of certain neurons.

What is the reasonable choice for the size of the time bin used in PST histograms? Intuitively, very large time bins will hide the temporal detail in neural activity. Inversely, very small bins will reduce the histogram to overlapping spike trains i.e., to raw data obtained from the successive trials. Time-bin size of the order of the mean spike interval is expected to give a much better result between those two limits. In statistical theory, Sturges' rule have been commonly used to estimate densities using histograms:

$$b = 1 + \log_2 N \tag{1}$$

where N is the number of samples and b is the number of bins. However, this rule is based on a binomial approximation of Gaussian density (Scott 1992) and rather inappropriate for a non-Gaussian spike-rate function. Scott (1992) obtained a more reliable estimate for a density function by minimizing the asymptotic mean-integrated-squared error:

$$h^* = \left[\frac{6}{R(f')}\right]^{1/3} N^{-1/3} \tag{2}$$

where h^* is the optimal bin width and R is a special roughness function that depends on the derivative of the actual density (f). For a Gaussian density with standard deviation of σ, $h^* \approx 3.5\sigma N^{-1/3}$. It is important to note that in an experimental setting, the statistics of the neural response are not known *a priori* (the experiment itself is performed to find out such information). Therefore, it is often difficult to determine the density function in Eq. 2 and its derivative in advance. This is analogous to the chicken-and-egg dilemma. Statistics theory also proposes that the estimation error can be further reduced by varying the bin size at different locations of the density function, but there are no reliable algorithms for constructing such adaptive histogram meshes (Scott 1992). In conclusion, finding the optimal bin size with respect to the actual neural firing rate is theoretically and practically still difficult at this time.

Instead of finding an optimal bin size in the above sense, this article suggests constructing a histogram such that the bar heights occur with approximately equal chances. This ensures that repetitions in the histogram profile are reduced in order to accentuate changes in the activity pattern. The reason to adopt such a method is that the experimenter usually does not know what to expect in the neural response. The method described herein constructs the most complex histogram with the data on hand, and helps the experimenter to formulate testable hypotheses for further analyses. Some trends in the histogram profile may be overestimated with such a technique as compared to the actual spike rate. However, once the putative activity regions are determined, statistical tests may be performed to test the significances of such regions in specific stimulus conditions. Since the neural data is often quite noisy, initially to err on the positive side may be preferable to false negatives.

In mathematical terms, the technique is based on maximizing the entropy of histogram bars. This is done by assigning empirical probabilities to the bar heights using the available spike data. Two extreme cases may illustrate the idea. For a stationary process, which has theoretically a flat PST histogram, all histogram bars have the same height regardless of the bin width and this results in zero entropy. For special non-stationary processes, which have uniform distributions of bar heights at certain bin widths, the entropy reaches its theoretical maximum: $\log_2$ (number of bins). Typically, the number of different bar heights will not be as many as the number of bins and the distribution of bar heights will not be uniform; therefore, the entropy will be lower than its theoretical maximum. The proposed technique finds the bin width which gets close to that theoretical limiting case as much as possible given the spike train. It is very difficult, in general, to analytically obtain the bin size that maximizes the entropy of histogram bars. However, a short algorithm can be implemented on a computer and the entropy can be calculated as a function of bin width. The desired output is the bin-size estimate which yields the maximum entropy. The computer program is not presented here because of its simplicity, but it will be available on the World-Wide-Web site: *http://web.syr.edu/~bguclu/projects/entropy.*

The new method is illustrated by data from two simulated nerve fibers: an auditory-nerve fiber and a rapidly-adapting tactile fiber. Additionally, histograms with estimates from the statistical theory discussed above are presented. Ellaway (1977) proposed a cumulative-sum technique for detecting change in PST histograms (see also Davey et al. 1986, Ellaway 1978). In this technique, the deviations of bar heights from an overall bar-height average are cumulatively summed over time bins. Therefore, small changes indiscernible in the original histogram accumulate and become visible. The application of this technique to the simulation data is also discussed.

The cumulative-sum technique can easily be explained with the help of the simple example in Fig. 1. The upper plot in Fig. 1 is a standard PST histogram with bar heights (b's) as given. First, the average of bar heights (b') is calculated. The cumulative sums (c's) are derived from the differences between the histogram bar heights and the average. However, to find each bar height in the cumulative-sum plot, the differences are cumulatively summed. Consequently, small, but persistent, differences are emphasized.

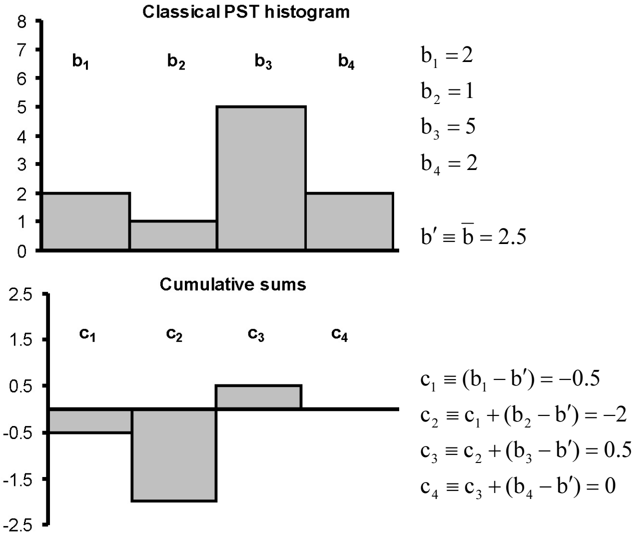

Fig.1. Construction of a cumulative-sum plot from a PST histogram. The bar heights (b's and c's) are given next to the plots; b' is the average of the histogram bar heights.

METHODS

The entropy of bar heights

The complexity of a PST histogram depends on the distribution of bar heights. If only a few bar heights are present, the histogram looks simple and its visual information content is low. Inversely, if many bar heights are present, the visual information conveyed by the histogram is high, because there is more variability in the histogram. The distribution of bar heights changes as a function of bin width (T). Therefore, a bin width should be selected to maximize the entropy. The entropy of histogram bars is defined as:

$$H = -\sum_k P_k \log_2 P_k \qquad (3)$$

where P_k is the probability of bar height k and $k \in \{0,1,2,3,\ldots,N\}$. N is the total number of spikes.

The probability of a bar height is empirically found by dividing the frequency of that bar height by the total number of bins. It is important to note that the existence of a histogram-bar entropy maximum, independent of the underlying neural process, is guaranteed in the interval (0, T) because there are a finite number of bins. If the bin width decreases considerably, most of the bins are unoccupied and the probability of zero bar height (k=0) increases drastically. In this case, the entropy tends to zero. On the other hand, if the bin width increases too much, there will be only a few bins, and eventually one bin which represents a single bar height; hence, zero entropy.

Simulated auditory-nerve fiber

The model presented by Zhang and coauthors (2001) was used to simulate the response of an auditory nerve fiber which had characteristic frequency of 1000 Hz and spontaneous activity of 10 spikes/s. This model has been helpful for calculating psychophysical performance limits (Heinz et al. 2001a, b). The computer code for the model was obtained from the World-Wide-Web site: *http://earlab.bu.edu/models/download/Cfortran.aspx.* The sound stimulus used in the simulations was a rhesus-macaque vocalization, called a harmonic arch, obtained from the Primate Cognitive Neuroscience Laboratory at Harvard University (World-Wide-Web site: *http://www.wjh.harvard.edu/~mnkylab/media/rhesuscalls.html).* This call is typically given by monkeys in the presence of high quality, rare food items. The sound waveform was recorded at 25 kHz sampling rate with 16-bit resolution. The waveform, which had duration of 0.231 s, was processed in MATLAB Version 5.3 (MathWorks, Inc., Natick, MA) to set the intensity at 60 dB SPL and the DC offset at zero (see Fig. 2B). Each simulation lasted 0.3 s and spike-time data were generated for 100 trials.

Simulated rapidly-adapting tactile fiber

The model presented by Güçlü and Bolanowski (2003a, 2004) was used to simulate the response of a rapidly-adapting tactile fiber. The computer code for the spike-generation model is available on the World-Wide-Web site: *http://web.syr.edu/~bguclu/projects/markov.* The stimulus was a mechanical displacement of the skin (see Fig. 4B). Its waveform was a burst of a 40–Hz sine wave with a duration of 1 s as measured between the half-power points, and it had burst rise and fall time of 50 ms. The vibration had an amplitude of 78 μm and was superimposed on a 0.5-mm static indentation. It was assumed that the rapidly-adapting fiber responds within the 1:1 firing regime when subject to the above stimulus parameters (see Güçlü and Bolanowski 2003b, c). That is to say, the nominal firing rate was 40 spikes/s. Each simulation lasted 1 s and was repeated for 100 trials. It is important to note that this model can only accept sinusoidal stimuli and the neural response can be simulated during the steady portion of the stimulus. Therefore, the first two and the last two cycles of the stimulus were ignored to eliminate any effects of transients.

RESULTS

For simulated auditory-nerve fibers, the entropy of histogram bars decreases at small bin widths and at large bin widths, while it has a maximum of 5.53 bits at about 2.7-ms bin width (Fig. 2A). The neural response, as measured by the PST histogram, roughly follows the amplitude envelope of the sound waveform. Using a smaller bin width than the size which maximizes the

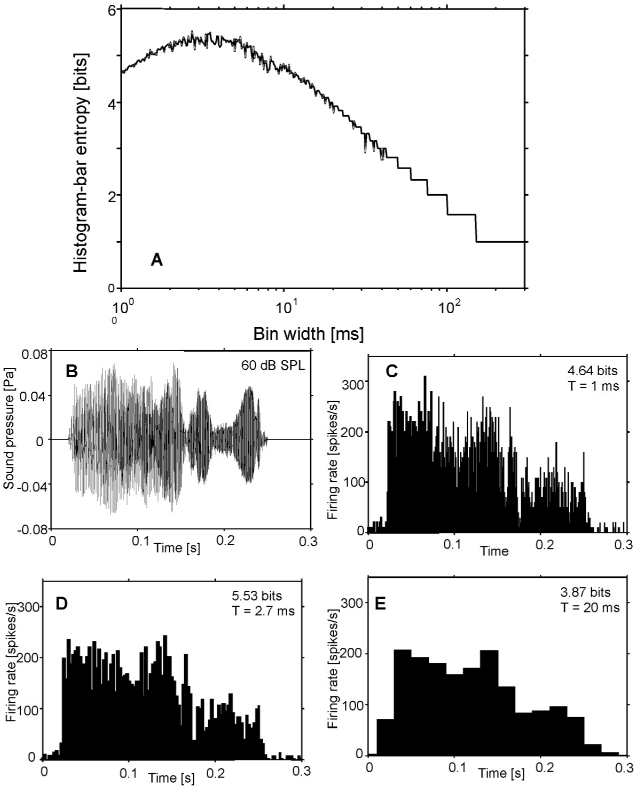

Fig. 2. A model auditory-nerve fiber (characteristic frequency: 1000 Hz, spontaneous activity: 10 spikes/s) was excited by a monkey call. The neural spike trains from 100 simulation trials were analyzed; (A) The variation of histogram bar-height entropy as a function of bin width. The maximum entropy is 5.53 bits; (B) A harmonic arch exemplar vocalized by a rhesus monkey. The stimulus intensity is 60 dB SPL; (C) A redundant PST histogram is produced by using a bin size smaller than the size that maximizes the bar-height entropy; (D) The most complex PST histogram with the highest entropy of bar heights is obtained with 2.7-ms wide bins; (E) A coarse PST histogram is produced by using a bin size greater than the size that maximizes the bar-height entropy.

entropy results in a redundant PST histogram (Fig. 2C). Although there is high temporal detail in Fig. 2C, some bar heights are unnecessarily repeated and this decreases the entropy. In other words, the detail shown in Fig. 2C does not add useful information to the variation of the response in the histogram, as opposed to the detail in the histogram with maximized bar-height entropy (Fig. 2D). For example, the histogram peak at about 0.165 s has fluctuations in Fig. 2C, but the same peak in Fig. 2D is more pronounced without the spurious detail. Additionally, some bar heights are relatively large in Fig. 2C, because the spike count is normalized with a very small bin size. Fig. 2D does not contain that artifact and the bin heights are in good proportion with the overall activity pattern. If the bin size is too large, however, the generated histogram is coarse (Fig. 2E) and much of the information is lost. The peak at 0.165 s is totally absent in Fig. 2E.

The same spike data are analyzed by using the previous techniques in the literature (Fig. 3). The total spike count (*N*) is 3403, which yields approximately 13 bins according to the Sturges' rule. The histogram constructed using the Sturges' rule (Fig. 3A), however, is coarse and the details mentioned above are lost. Applying the Scott's rule requires *a priori* information about the response. A simple assumption is that the response somewhat increases and then decreases during the stimulus period. Hence, the Gaussian estimate mentioned in Introduction may be used. The sample standard deviation of the data is 0.0640 seconds. This yields the optimal bin width as 14.9 ms according to the Scott's rule. The histogram constructed using this bin size (Fig. 3B) is better than the histogram constructed using the Sturges' rule. However, it still lacks the information given in Fig. 2D (e.g., the peak at about 0.165 s). It is important to note that the details in the histogram obtained using the maximum entropy method may be statistically insignificant, but it is safer to run more statistical tests than to omit some because of a coarse histogram. Ellaway's cumulative-sum technique was also tested on the simulated auditory-fiber data, by using the bin size which maximizes the entropy of the bars (Fig. 3C) and the optimal bin size according to Scott's rule (Fig. 3D). The average reference activity (which is subtracted from each bin height in Ellaway's method) was found from the response between 0 and 20 ms, during which the stimulus was inactive. Note that both plots (Fig. 3C,D) are difficult to interpret in relation to the histograms. Ellaway's method sums up the bins cumulatively, so the change of slope signals change in activity. For example, in Fig. 3C, the slope at 0.1 s is larger than the slope at 0.2 s. This signals that there was an activity change between those time markers i.e., the activity decreased with time. Furthermore, the cumulative-sum plot of Fig. 3C has zero slope after 0.25 s; that is to say, the activity level is at the average reference level. Although, some overall change in neural activity can be detected as such in Fig. 3C,D, the details regarding the stimulus envelope are not clear.

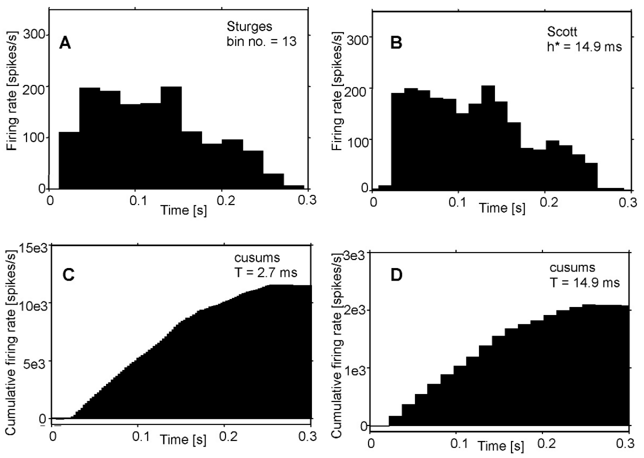

Fig. 3. The simulated spike data from the model auditory-nerve fiber are analyzed using previous methods; (A) Number of bins is determined by Sturges' rule. The PST histogram based on this rule is coarse; (B) The statistically optimal bin width (h^*) is determined by Scott's rule. The PST histogram based on this rule lacks the detail present in Fig. 1D; (C) Cumulative-sum plot based on the bin size which maximizes the entropy of bar heights; (D) Cumulative-sum plot based on the optimal bin size determined by Scott's rule.

The same procedures were applied to spike data from the simulated rapidly-adapting tactile fiber. The change of histogram-bar entropy as a function of bin width is shown in Fig. 4A. The entropies for this data set are lower than the entropies found from the auditory-fiber data, because the model tactile fiber was excited by a simple periodic stimulus and the fiber generated stereotypical phase-locked responses (see Fig. 4C,D). However, the general trend of decreasing histogram entropy for very small and very large bin sizes is consistently present. The plot in Fig. 4A is rougher than the one in Fig. 2A and it contains sharp peaks and troughs. Although some of those fluctuations may be smoothed out by increasing the number of trials, some of them are due to significant features of the neural response. For example, the large dip observed between bin widths of 15 and 35 ms in Fig. 4A is because of the spikes accumulating at integer multiples of the stimulus period. Therefore, if the PST histogram were constructed using a 25-ms bin width (the exact stimulus period), the entropy would drop sharply (see Fig. 4A) and a flat histogram would be obtained (not shown). The histogram-bar heights that maximize the entropy are obtained when the bin width is about 10 ms. Fig. 4A has a peak of 4.48 bits at this bin size. The histogram constructed using that bin size (Fig. 4D) contains important features that other histograms (Fig. 4C,E) do not. There is a specific trend in that histogram: a longer peak is always preceded by a shorter peak. This information is not apparent in a histogram with a smaller bin size, though phase-locking peaks are still present (Figure 4C). On the other hand, a coarse histogram generated using a large bin size does not show any phase-locking response and is only useful to display the firing rate averaged over the stimulus duration (most of the bar heights are about 40 spikes/s in Fig. 4E). Since the statistical behavior of rapidly-adapting fibers excited by sinusoidal stimulation is fairly well known (see Güçlü and Bolanowski, 2003a, b, c, 2004), one can ask the critical question: is the trend mentioned above relevant? The stimulus half-period is 12.5 ms and we have prior information from the model that the spikes most probably occur during certain intervals within the half-periods of the stimulus (see Güçlü and Bolanowski 2004). Therefore, the most logical bin size to select is 12.5 ms and that removes the trend in Fig. 4D (not shown). The actual significant pattern is one peak and one trough, which correspond to a spike during the positive phase of the stimulus and no spikes during the negative phase. In this example, the entropy method overestimated an irrelevant trend. However, note that the selected bin width lies on a sharp peak in the entropy diagram (Fig. 4A). This makes the histogram constructed with that bin size unstable; slightly changing the bin size to 9.9 ms or 10.1 ms removes the artificial trend. Therefore, it is a good idea to perturb the bin size slightly to avoid sharp peaks or troughs of the entropy diagram.

The tactile-fiber data are analyzed using the previous techniques in the literature (Fig. 5). The total spike count (N) is 3595, which yields approximately 13 bins according to the Sturges' rule. The histogram constructed using the Sturges' rule (Fig. 5A), however, is coarse. The sample standard deviation of the spike data is 0.2604 seconds. This yields the optimal bin width as 59.5 ms according to the Scott's rule with Gaussian *a priori* assumption. The histogram constructed using this bin size (Fig. 5B) is somewhat better than the histogram constructed using the Sturges' rule. However, it does not highlight the phase-locking present in the response (there should be about 36 peaks in the histogram). Ellaway's cumulative-sum

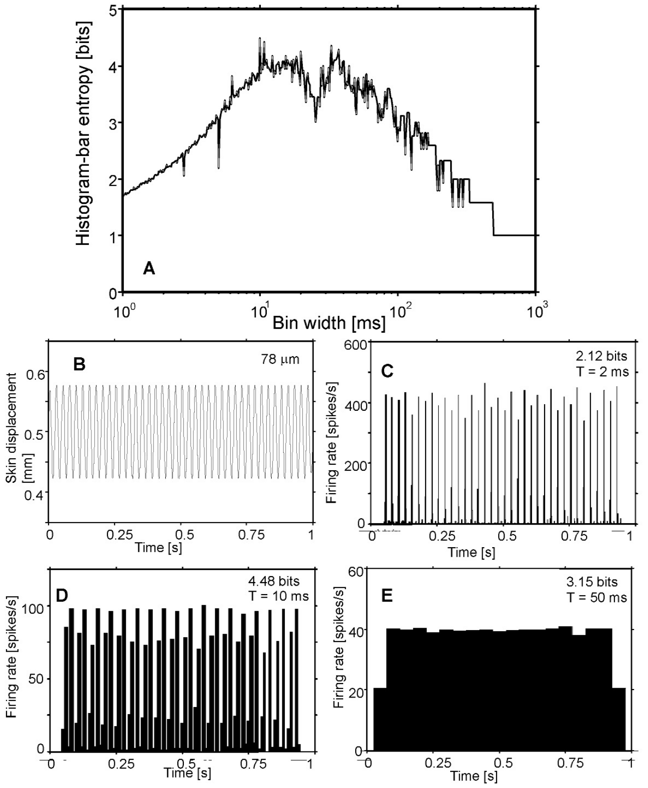

Fig. 4. A model rapidly-adapting tactile fiber was excited by a vibratory stimulus at the 1:1 firing regime. The neural spike trains from 100 simulation trials were analyzed; (A) The variation of histogram bar-height entropy as a function of bin width. The maximum entropy is 4.48 bits; (B) The stimulus is a sinusoidal burst with amplitude of 78 µm and a frequency of 40 Hz. The rise and fall times are 50 ms. Only the stimulus duration of 1 s between the half-power points is shown; (C) A redundant PST histogram is produced by using a bin size smaller than the size that maximizes the bar-height entropy; (D) The most complex PST histogram with the highest entropy of bar heights is obtained with 10-ms wide bins. However, the trend in the histogram peaks is irrelevant (see text); (E) A coarse PST histogram is produced by using a bin size greater than the size that maximizes the bar-height entropy.

technique was also tested on the simulated tactile-fiber data, by using the bin size which maximizes the entropy of the bars (Fig. 5C) and the optimal bin size according to Scott's rule (Fig. 5D). The average reference activity (which is subtracted from each bin height in Ellaway's method) was set to zero, because rapidly-adapting tactile fibers do not have spontaneous activity. Because the evoked activity is regular, the cumulative-sum plots (Fig. 5C,D) may be interpreted in relation to the histograms. The slopes are approximately constant in Fig. 5C and D, which show that the activity profile is quite constant. The upward steps in the plots give information about how the activity changes in detail. For example, a big step after a small step signals a slight increase in activity. Conversely, a big step followed by a little step signals a slight decrease. However, the steps in a cumulative-sum plot are not as efficient as the peaks and troughs of a classical histogram for capturing attention. While there is a big change when the activity decreases from a histogram peak to a trough, the cumulative-sum plot does not signal a change, because the minimum level is equal to the preset average activity level used in this example. As a result, the phase-locking pattern is not clear in the cumulative sums.

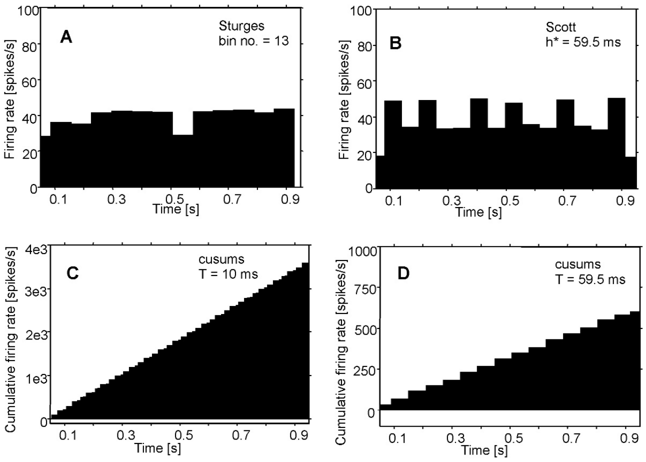

Fig. 5. The simulated spike data from the model rapidly-adapting tactile fiber are analyzed using previous methods; (A) Number of bins is determined by Sturges' rule. The PST histogram based on this rule is coarse; (B) The statistically optimal bin width (h^*) is determined by Scott's rule. The PST histogram based on this rule lacks the phase-locking pattern present in Fig. 2C,D; (C) Cumulative-sum plot based on the bin size which maximizes the entropy of bar heights, (D) Cumulative-sum plot based on the optimal bin size determined by Scott's rule.

DISCUSSION

A systematic and repeatable strategy for obtaining objective PST histograms has been presented. This technique is based on finding the bin size that maximizes the entropy of histogram-bar heights. This approach may at first seem counterintuitive, as if similar to maximizing noise. However, it may be better interpreted as maximizing the visually apparent change in the bar heights, which is actually desired in order to highlight details. In practical terms, this special histogram may be an ideal starting point for data mining and statistical analyses of response properties, because the bar heights are mathematically arranged according to greatest disorder (i.e., complexity). The reason for adopting such a technique may largely be attributed to the lack of an accurate estimate for the optimal bin size in the statistical sense. The statistical theory offers many methods to minimize the error when estimating the actual firing rate, but they often have *a priori* assumptions on the original probability density (e.g., Sturges' rule, Scott's rule). The examples given in this article show that the entropy method yields more relevant histograms compared to the statistical estimates. Sturges' rule was found to be particularly inappropriate, because it generated coarse histograms with no regard to underlying neural activity. This could be expected, because it is based solely on the number of samples. On the other hand, overestimating the trends in the histogram is possible with the entropy method. The example on the tactile fiber illustrated a special type of such error. The calculated bin size was based on an entropy value located at a sharp peak in the entropy diagram. This departure from the overall entropy curve can be avoided by perturbing the resultant bin size slightly.

The calculated entropy estimate is expected to improve as the number of trials is increased to a certain extent. The estimate may also be improved with the help of correction factors (Treves and Panzeri 1995, Victor 2000). However, since the bar-height distribution somewhat changes with the number of trials, it is beneficial to consider extreme cases when there are too few or too many trials. When the average firing rate is very low, and there are only a few trials, most of the bins will be unoccupied and the entropy will tend to zero. If the average rate is high with just a few trials, the entropy is hard to predict; however, for a Poisson process with a monotonic intensity function, more bar heights will be represented in the PST histogram. This will result in higher entropy than the condition with low activity. For many trials, one can refer to the limit theorem for pooled point processes (Snyder 1975). Pooling the points of independent and sparse self-exciting processes (like some neural activity) converges under weak conditions to a Poisson process. The sparseness implies that each trial contributes only a few spikes to the pooled process i.e., the activity is low. Therefore, when the average firing rate is very low, but there are many trials, the result is approximately a Poisson process with many spikes. If one assumes a monotonic intensity function again, the entropy is expected to be significantly higher than zero. On the other hand, it is difficult to predict the entropy when both the activity is high and there are many trials, but it is interesting to note a special case with high activity. Although the bar heights are discrete and non-negative, there may be a process with a relatively high mean bar height and with an approximately Gaussian bar-height distribution. This implies a quite high average firing rate and an entropy only dependent on the standard deviation (σ_b) of bar heights i.e., $H = \log_2 \sigma_b \sqrt{2\pi e}$. If small (or very large) bar heights still occur with such high activity (i.e., σ_b is large), the entropy is expected to be quite high, but cannot, of course, exceed the theoretical maximum mentioned in Introduction.

The practical use of histograms with identical or comparable neurons raises an interesting proposition: different data sets may yield PST histograms with different bin widths when the entropy method is used. However, this does not pose a serious problem. PST histograms can be simply viewed as piece-wise functions with steps; different bin widths will result in PST histograms with steps of different widths. This can be easily represented numerically on the computer and analyzed mathematically.

Although PST histograms are commonly used in experimental neurobiology, a PST histogram is not the best strategy to analyze neural data. It has many disadvantages: e.g., it is noisy compared to 'mean individual rate' (Knight et al. 1979), but more importantly, it lacks the temporal information contained in the spike pattern. The original spike train has the complete information; histograms are merely incomplete summaries. However, they are still useful to test certain hypotheses. For example, to test the goodness of fit of Poisson models, PST histogram is often smoothed to obtain the intensity function of the process (e.g., Kass and Ventura 2001). Models based on PST histograms may perform worse than inhomogeneous Markov interval models (Brown et al. 2001), which include some dependence on previous spikes. Markov models are frequently utilized in neurophysiology (e.g., for hearing see Gaumond et al. 1982, for touch see Güçlü and Bolanowski 2004). It is important to note that the technique discussed in this article, and other fixed-bin-width methods, are not very useful for testing stochastic models (Kass et al. 2003, Ventura et al. 2002). Nevertheless, the proposed entropy method is more helpful in the experimental setting where such elaborate algorithms are not practical.

Ellaway's (1977, 1978) cumulative-sum technique was also tested on the simulation data presented in this article. When the neural activity was simple as in the periodically excited tactile fiber, the cumulative-sum plots could be interpreted in relation to the PST histograms. However, it was rather difficult to interpret the cumulative-sum plots for the complex activity of an auditory fiber excited by a natural sound. Cumulative-sum technique was originally devised for detecting subtle changes in ongoing spontaneous activity. The results of this article suggest that it may not be useful for analyzing highly variable neural activity. Therefore, the entropy method can be used instead, to accentuate changes in such neural activity. It is also important to note that cumulative-sum technique does not offer a solution for choosing the best bin size.

CONCLUSIONS

A novel technique for constructing peri-stimulus time histograms is presented. This method maximizes the entropy of histogram-bar heights and thus generates the most complex histogram as a starting point for neural data mining. The method finds trends in data better than statistical optimization estimates when there is no prior information available on neural activity. The entropy method is particularly useful for highlighting change in neural activity and therefore, promising as a helpful tool for experimental neurobiologists.

ACKNOWLEDGMENTS

This article is dedicated to the memory of Dr. Stanley J. Bolanowski who introduced me to neuroscience. I greatly appreciate Dr. Ronald Verrillo's helpful comments on the manuscript. This work was supported by Bogaziçi University Research Fund grant no.: 04HX101 and by TÜBITAK grant no.: 104S228.

REFERENCES

Brown EN, Barbieri R, Ventura V, Kass RE, Frank LM (2001) The time-rescaling theorem and its application to neural spike train data analysis. Neural Comput 14: 325–346.

Davey NJ, Ellaway PH, Stein RB (1986) Statistical limits for detecting change in the cumulative sum derivative of the peristimulus time histogram. J Neurosci Methods 17: 153–166.

Ellaway PH (1977) An application of cumulative sum technique (cumsums) to neurophysiology. J Physiol 265: 1P–2P.

Ellaway PH (1978) Cumulative sum technique and its application to the analysis of peristimulus time histograms. Electroencephalogr Clin Neurophysiol 45: 302–304.

Gaumond RP, Molnar CE, Kim DO (1982) Stimulus and recovery dependence of cat cochlear nerve fiber spike discharge probability. J Neurophysiol 48: 856–873.

Gerstein GL, Kiang NY-S (1960) An approach to the quantitative analysis of electrophysiological data from single neurons. Biophys J 1: 15–28.

Güçlü B, Bolanowski SJ (2003a) Time-dependent Markov model for the sinusoidal steady-state response of rapidly-adapting fibers. Soc Neurosci Abstr 29: Program No: 172.16.

Güçlü B, Bolanowski SJ (2003b) Distribution of intensity-characteristic parameters of cat rapidly adapting mechanoreceptive fibers. Somatosens Mot Res 20: 149–155.

Güçlü B, Bolanowski SJ (2003c) Frequency response of cat rapidly adapting mechanoreceptive fibers. Somatosens Mot Res 20: 249–263.

Güçlü B, Bolanowski SJ (2004) Tristate Markov model for the firing statistics of rapidly-adapting mechanoreceptive fibers. J Comput Neurosci 17: 107–126.

Heinz MG, Colburn HS, Carney LH (2001a) Evaluating auditory performance limits: I. One-parameter discrimination using a computational model for the auditory nerve. Neural Comput 13: 2273–2316.

Heinz MG, Colburn HS, Carney LH (2001b) Evaluating auditory performance limits: II. One-parameter discrimination with random-level variation. Neural Comput 13: 2317–2338.

Kass RE, Ventura V (2001) A spike-train probability model. Neural Comput 13: 1713–1720.

Kass RE, Ventura V, Cai C (2003) Statistical smoothing of neural data. Network: 14: 5–15.

Knight BW, Brodie SE, Sirovich L (1979) Treatment of nerve impulse data for comparison with theory. Proc Natl Acad Sci U S A 76: 6026–6029.

Romo R, Brody CD, Hernández A, Lemus L (1999) Neuronal correlates of parametric working memory in the prefrontal cortex. Nature 399: 470–473.

Scott DW (1992) Multivariate Density Estimation: Theory, Practice, and Visualization. John Wiley & Sons.

Snyder DL (1975) Random Point Processes. John Wiley & Sons.

Treves A, Panzeri S (1995) The upward bias in measures of information derived from limited data samples. Neural Comput 7: 399–407.

Ventura V, Carta R, Kass RE, Gettner SN, Olson CR (2002) Statistical analysis of temporal evolution in single-neuron firing rates. Biostatistics 3: 1–20.

Victor JD (2000) Asymptotic bias in information estimates and the exponential (Bell) polynomials. Neural Comput 12: 2797–2804.

Zhang X, Heinz MG, Bruce IC, Carney LH (2001) A phenomenological model for the responses of auditory-nerve fibers: I. Nonlinear tuning with compression and suppression. J Acoust Soc Am 109: 648–670.

Received 22 August 2005, accepted 21 December 2005