3B2v8.06a/w (Dec 5 2003).51c
+model
NEUCOM : 10290
Prod.Type:FTP
pp.1–5(col.fig.:1–3)
ED:BabuB.
PAGN:Raj SCAN:sgeetha

ARTICLE IN PRESS

Available online at www.sciencedirect.com

SCIENCE DIRECT®

ELSEVIER

Neurocomputing ▮ (▮▮▮▮) ▮▮▮–▮▮▮

NEUROCOMPUTING

www.elsevier.com/locate/neucom

Smoothing and thresholding in neuronal spike detection

Nhamoinesu Mtetwa*, Leslie S. Smith

Department of Computing Science and Mathematics, University of Stirling, Scotland, UK

Abstract

We discuss spike detection for noisy neuronal data. Robust spike detection techniques are especially important for probes which have fixed electrode sites that cannot be independently manipulated to isolate signals from specific neurons. Low signal-to-noise ratio (SNR) and similarity of spectral characteristic between the target signal and background noise are obstacles to spike detection. We propose a new technique based on cumulative energy.

Keywords: Smoothing; Cumulative energy; Template matching

1. Introduction

Multiple electrode arrays (MEAs) are now a standard tool in neuroscience research that make it possible to study simultaneous activity of several neurons in a piece of neural tissue. Data from MEA studies presents analysis challenges that must be resolved to answer questions about how the brain works [2]. Extracting useful information from these measurements relies on the ability to correctly detect and sort the recorded neural spikes [4].

Neurophysiologists record using many different techniques. In some (e.g. patch clamping, intracellular recording) the SNR is high so that there is no problem detecting spikes. However, in extracellular recording signal-to-noise ratio (SNR) is much lower so that spike detection is more difficult. In vivo experimenters often move the exposed tip of an electrode so that spikes from a single neuron dominate the signal. However, in vitro experimenters are often restricted to using MEAs fixed to the bottom of the culture dish (e.g. MCS MEA series: see http://www.multichannelsystems.com/). Signal transfer from neuron to electrode may be resistive and/or capacitative, resulting in weak noisy signals whose shape may differ from intracellularly recorded spikes. Extracellularly recorded signals are inevitably corrupted by noise from a number of sources: the recording hardware, electromagnetic interference, the superimposed activity of multiple neurons and the spatially averaged activity of distant neurons [7]. Importantly, the activity of distant neurons appears as noise which is highly correlated with the signal of interest [10]. Further, the shape and amplitude of the signals of interest are highly variable. All these issues complicate the spike detection task. Spike detection techniques which rely primarily on the signal amplitude perform poorly in low SNR, characteristic of MEA recordings. In this paper we compare spike detection techniques, including results from trials of these techniques on real physiological data.

2. Spike detection techniques

Visual spike detection provides a standard of performance against which automated techniques can be judged. However this is impractical for large datasets. There is a need for reliable automatic detection algorithms that are at least as sensitive as visual detection, and whose performance can be characterised under a variety of SNR conditions. Automatic detection algorithms can be separated into two categories: (i) those which compare a fixed template to a recorded signal, and search for accurate matches [12] or local maxima in the cross-correlation and (ii) those that search for an event that crosses an amplitude threshold [1] or whose first derivative [6], energy [3] or

*Corresponding author.
E-mail address: nmt@cs.stir.ac.uk (N. Mtetwa).

0925-2312/$ - see front matter © 2006 Published by Elsevier B.V.
doi:10.1016/j.neucom.2005.12.108

wavelet transform coefficients [7] crosses a threshold. Template-based algorithms require bootstrapping: we used simple thresholding of smoothed data to detect spikes and used these to generate templates which are approximations of actual spikes. We briefly discuss the five implemented techniques.

Convolution-based template matching (*CONV*): Template convolution is a filtering process for spike pre-emphasis. CONV convolves the template with a section of the signal which selectively amplifies the areas of the signal that are correlated to the template (see Fig. 1(a,e)).

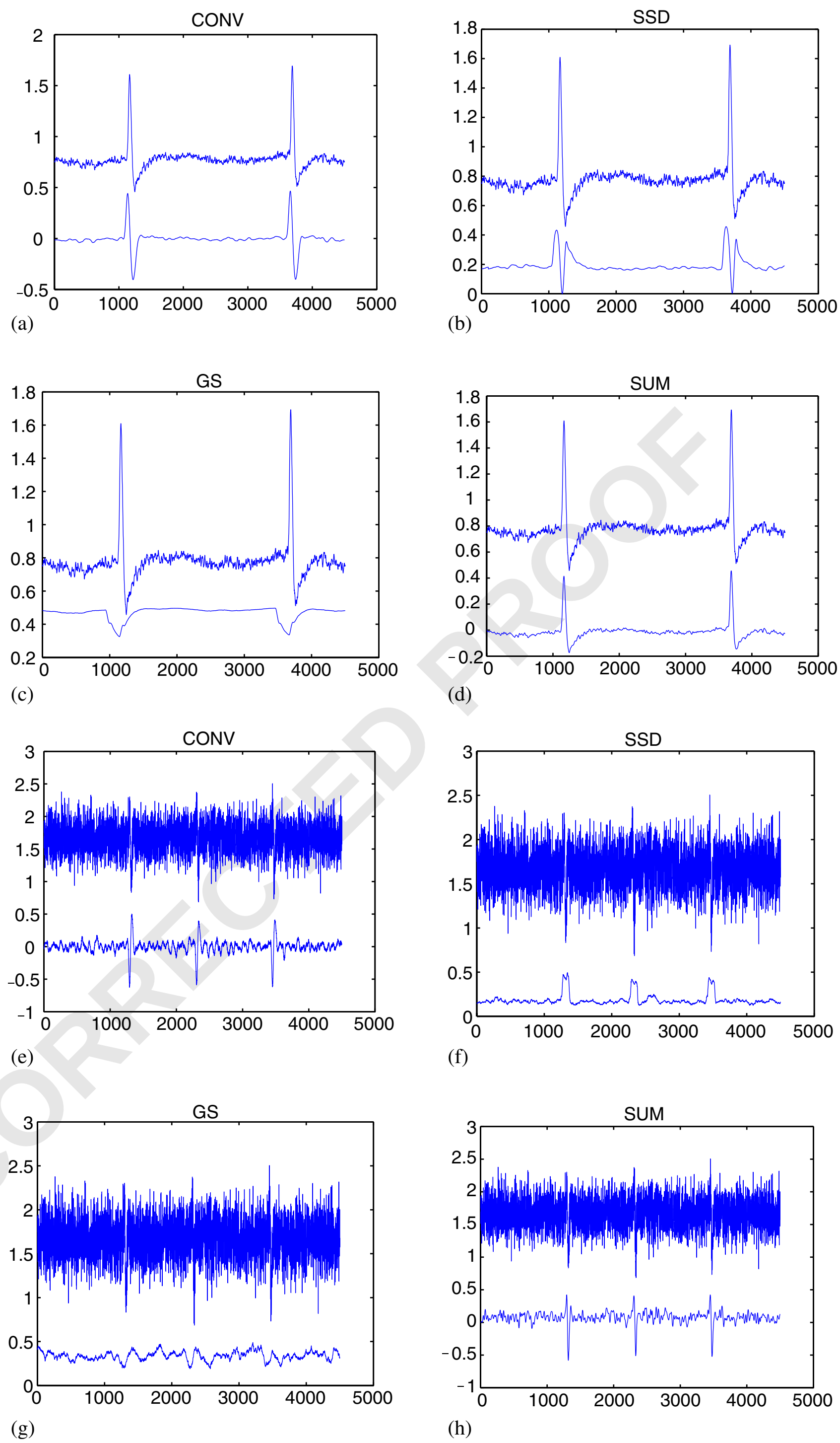

Fig. 1. In each graph (a)–(h), the upper trace is raw data, lower trace is processed data. Graphs (a)–(d) show high quality raw data (SNR = 9.82) transformed by CONV, SSD, GS and SUM. (e)–(h) show low-quality raw data (SNR = 1) similarly transformed. In each case the spikes are significantly enhanced except for GS in (g) where the spikes are less clear showing GS's susceptibility to noise.

$$\mathrm{CONV}(i) = s(i) * T = \sum_{k=1}^{n} s(i+k)T(n-k+1), \tag{1}$$

where $s(i)$ is the sampled signal, and $T(j)$ $(j = 1 \ldots n)$ is the template. Spikes are detected by thresholding the output function CONV.

Sum-of-squared differences (SSD) template matching: SSD originates in image matching applications such as tracking and stereo matching [8]. SSD measures the Euclidean difference between each point in the template and each corresponding point in the signal section.

$$\mathrm{SSD}(i) = \sum_{j=1}^{n} (s(i+j) - T(j))^2. \tag{2}$$

Clearly the signal and template must have the same polarity. Further, the signal amplitude will matter: if there is a mismatch, then the peaks and troughs will be less pronounced. The output of SSD (see Fig. 1(b,f)) is thresholded to detect the spikes. SSD is sensitive to outliers and template variations.

Gaussian sampling (GS) template matching: GS was inspired by maximum likelihood (ML) template matching in image processing [9]. GS transforms the template T into a two-parameter distribution, $(\hat{\mu}, \hat{\sigma})$ using ML estimation [11]. Sections s of the signal are transformed into standard normal variates (GS) which are then read out from the standard normal table where: $\mathrm{GS}(i) = \sum_{j=1}^{n} \phi((s(j) - \hat{\mu})/\hat{\sigma})$, where ϕ is the standard normal distribution. GS is thresholded. Spikes are characterised by a dip in the output as seen in Fig. 1(c,g).

Summation (SUM): This technique does not require a template. To help resolve weak spikes, we average neighbouring points in order to get smoothed data (see Eq. (3) from Ref. [5]).

$$s_i(w) = \frac{\sum_{j=i-m}^{i+m} s_j}{2m+1}, \quad s_i(z, w) = \sum_{j=i-m}^{i+m} \cdots \sum_{h=l-m}^{l+m} s_h. \tag{3}$$

The parameter $w = 2m + 1$ (m integer) requires to be chosen. z is the number of summations to be done. This method smoothens the data as can be seen in Fig. 1(d,h). Spike events are detected by thresholding the output function.

Normalised cumulative energy difference (NCED): This method was inspired by the fact that the energy in a spike (positive or negative going) should be greater than that in noise of the same length. To compute NCED we compute the total energy E_{tot} of the signal. After this, the normalised cumulative energy (NCE) $E(t)$ in the signal segments is computed.

$$E_{\mathrm{tot}} = \int_0^L s(t)^2 \, \mathrm{d}t, \quad E(t) = \frac{\int_0^t s(\tau)^2 \, \mathrm{d}\tau}{E_{\mathrm{tot}}}, \tag{4}$$

where L is the signal length. $E'(t)$ has a value significantly

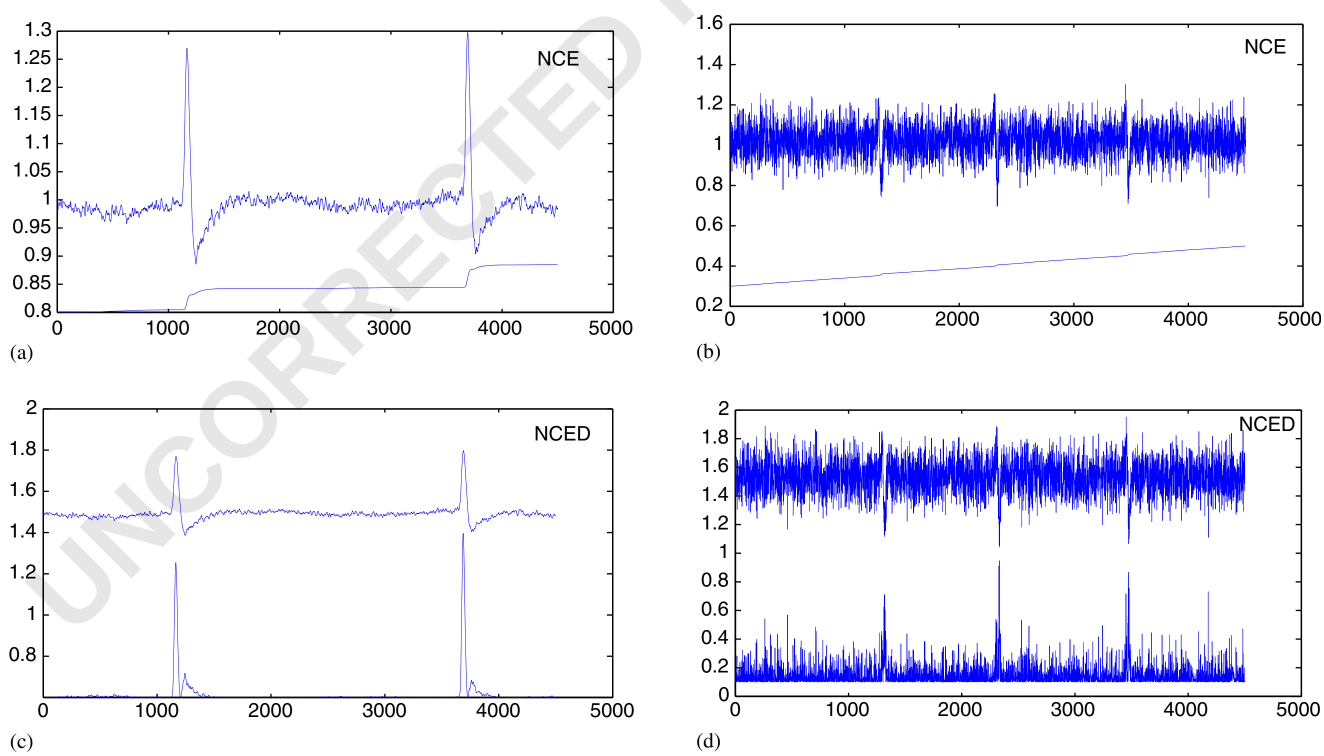

Fig. 2. Graphs (a) and (b) show a plot of $E(t)$ (NCE) applied to high- and low-quality raw data. It is clear that $E(t)$ increases sharply at spikes in (a) but less so in (b) due to noise. Graphs (c) and (d) show a plot of $E'(t)$ applied to raw data. $E'(t)$ clearly peaks at spikes for both high SNR (c) and low SNR (d). Note: Y-axis was normalised, actual peak values of $E'(t)$ are 40.8 in (c) and 17.1 in (d).

greater than 1 for spike events and is less than 1 elsewhere (see Fig. 2). This simplifies automatic threshold setting, a problem with the other methods discussed above.

3. Results, discussion and conclusions

Each detection technique was tested on five 1 s long real physiological data sets recorded at 10 Ksamples/s from hippocampal slices using an MCS rack. The SNR of the data ranges from 1 to 4.70 ($\mathrm{SNR} = \overline{(S+N)}/\overline{N}$ where $\overline{(S+N)}$ is the power of a signal component with a spike and noise, $\overline{N}$ is the power of the noise alone). Thresholds were calculated using a quarter of the sample points. These were broken up into R vectors of length Q, starting from random points (k) in the data. Three different thresholds were computed, RMS, MAX and SIGMA. RMS is the average root mean square of the vectors. MAX uses the average maxima (M) and minima (m) of these vectors. SIGMA uses the mean of these vectors plus a number of standard deviations of this mean.

Fig. 3 summarises results from the five techniques (CONV, SSD, GS, SUM and NCED) and the three thresholding criteria (max, rms, sigma). All perform better than simple amplitude thresholding (simple) of the raw data (RAW). NCED and SUM perform best, better than template based methods. Their main advantage over the template based methods is that they are independent of spike shape. NCED and SUM have inherent smoothing. SSD has a good detection rate but is marred by a high false positive percentage. Of the template based methods, GS performed worst perhaps because it only uses the template to estimate the two distribution parameters whereas the other methods (CONV, SSD) use the whole template. (It may be that better (or multiple) templates would improve results.) For CONV, SSD, GS and SUM the threshold has to be reset for new data. With NCED threshold setting is automatable because the gradient, $E'(t)$ is high where there is a spike almost independent of spike shape and polarity. For NCED, if $E' \leqslant 1$ there are no spikes in the signal, although $E' > 1$ does not necessarily imply a spike. SSD is sensitive to spike polarity because the detection is based on a template spike. It can thus miss spikes whose polarity and amplitude differ from the template. Spike polarity does not affect GS as long as the shape of the spikes stay the same.

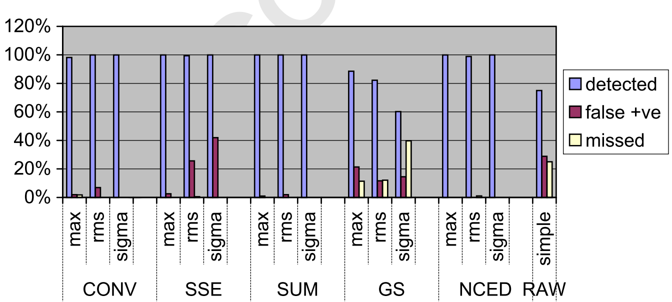

Fig. 3. Summarised results. The thresholding criteria used are maxima/minima (max), root mean square (rms), standard deviation (sigma) of the output from each of the techniques discussed. These techniques are compared with the simple thresholding of the raw data (RAW).

Five spike detection techniques and three thresholding criteria have been developed and compared on real physiological data. NCED and SUM provide the best overall result. SNR, noise characteristics, and spike detection performance are interdependent. High-frequency noise implies initial smoothing. Low SNR entails better spike detection techniques: NCED has proven best here since signal integration provides smoothing and is automatable. In addition, this method can be followed by multi-template-based spike sorting, and is amenable to implementation in digital electronics for near real-time processing since it does not require template generation.

Acknowledgements

The authors gratefully acknowledge the financial support of the EPSRC grant number R65602/02 and the help and advice of Dr. D. McLean.

References

[1] H. Bergman, M.R. DeLong, A personal computer-based spike detector and sorter: implementation and evaluation, J. Neurosci. Methods 41 (1992) 187–197.
[2] E.M. Brown, R.E. Kass, P.P. Mitra, Multiple neural spike train data analysis: state of the art and future challenges, Nat. Neurosci. 7 (5) (2004) 456–461.
[3] K.H. Kim, S.J. Kim, Neural spike sorting under nearly 0-db signal-to-noise ratio using nonlinear energy operator and artificial neural-network classifier, IEEE Trans. Biomed. Eng. 47 (10) (2000) 1406–1411.
[4] M.S. Lewicki, A review of methods for spike sorting: the detection and classification of neural potentials, Network Comput. Neural Syst. 9 (1998) R53–R78.
[5] M.A. Mariscotti, A method for automatic identification of peaks in the presence of background and its application to spectrum analysis, Nucl. Instrum. Methods 50 (1967) 309–320.
[6] S. Mukhopadhyay, G.C. Ray, A new interpretation of the nonlinear energy operator and its efficacy in spike detection, IEEE Trans. Biomed. Eng. 45 (2) (1998) 180–187.
[7] Z. Nenadic, J.W. Burdick, Spike detection using continuous wavelet transform, IEEE Trans. Biomed. Eng. 52 (1) (2005) 74–87.
[8] C.F. Olson, Maximum-likelihood template matching, in: IEEE Computer Society Conference on Computer Vision and Pattern Recognition, Hilton Head, South Carolina, 2000, pp. 52–57.
[9] C. F Olson, Maximum-likelihood image matching, IEEE Trans. Pattern Anal. Mach. Intell. 24 (6) (2002) 853–857.
[10] K.G. Oweiss, D.J. Anderson, A multiresolution generalized maximum likelihood approach for the detection of unknown transient multichannel signals in colored noise with unknown covariance, in: Proceedings of ICASSP, vol. 3, August 2002, pp. 2993–2996.
[11] W.H. Press, S.A. Teukolsky, W.T. Vetterling, B.P. Flannery, Numerical Recipes in C++, second ed., Cambridge University Press, Cambridge, 2002.
[12] M. Salganicoff, M. Sarna, L. Sax, G.L. Gerstain, Unsupervised waveform classification for multi-neural recording: a real-time software-based system I, J. Neurosci. Methods 25 (1988) 181–188.

Leslie S. Smith received the B.Sc. Degree in 1973, and the Ph.D. in 1981, both from Glasgow University. From 1980–1983 he was a lecturer at Glasgow University. Since 1984 he has worked at Stirling University, where he is now Professor of Computing Science. His research interests are in engineering approximations to early auditory processing, neural/electronic interfacing and neuromorphic systems. Professor Smith is chair of the UKRI Chapter of the IEEE Computational Intelligence Society.

Nhamo Mtetwa received the B.Sc. Degree in 1993 from University of Zimbabwe, M.Sc. degree in Computer Science 1996 from National University of Science and Technology (NUST), Zimbabwe, M.Sc. degree in High Performance Computers and Computation in 1999 from University of Warwick, England and the Ph.D. in 2003, from University of Stirling, Scotland. From 1994–1996 he was a teaching assistant at NUST, Zimbabwe, 1997 lecturer at NUST, 1998 R&D Software Engineer at SIRDC, Zimbabwe. Since October 2002 to date he is working as a Research fellow at Stirling University. His research interests are in data analysis techniques, and simulation and modelling of neuronal systems and recently of business processes as well.