

Smoothing and thresholding in neuronal spike detection

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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.

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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 capacitive, resulting in weak noisy signals whose shape may differ from intracellularly recorded spikes. Extracellularly re-

corded 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

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(ii) those that search for an event that crosses an amplitude threshold [1] or whose first derivative [6], energy [3] or 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

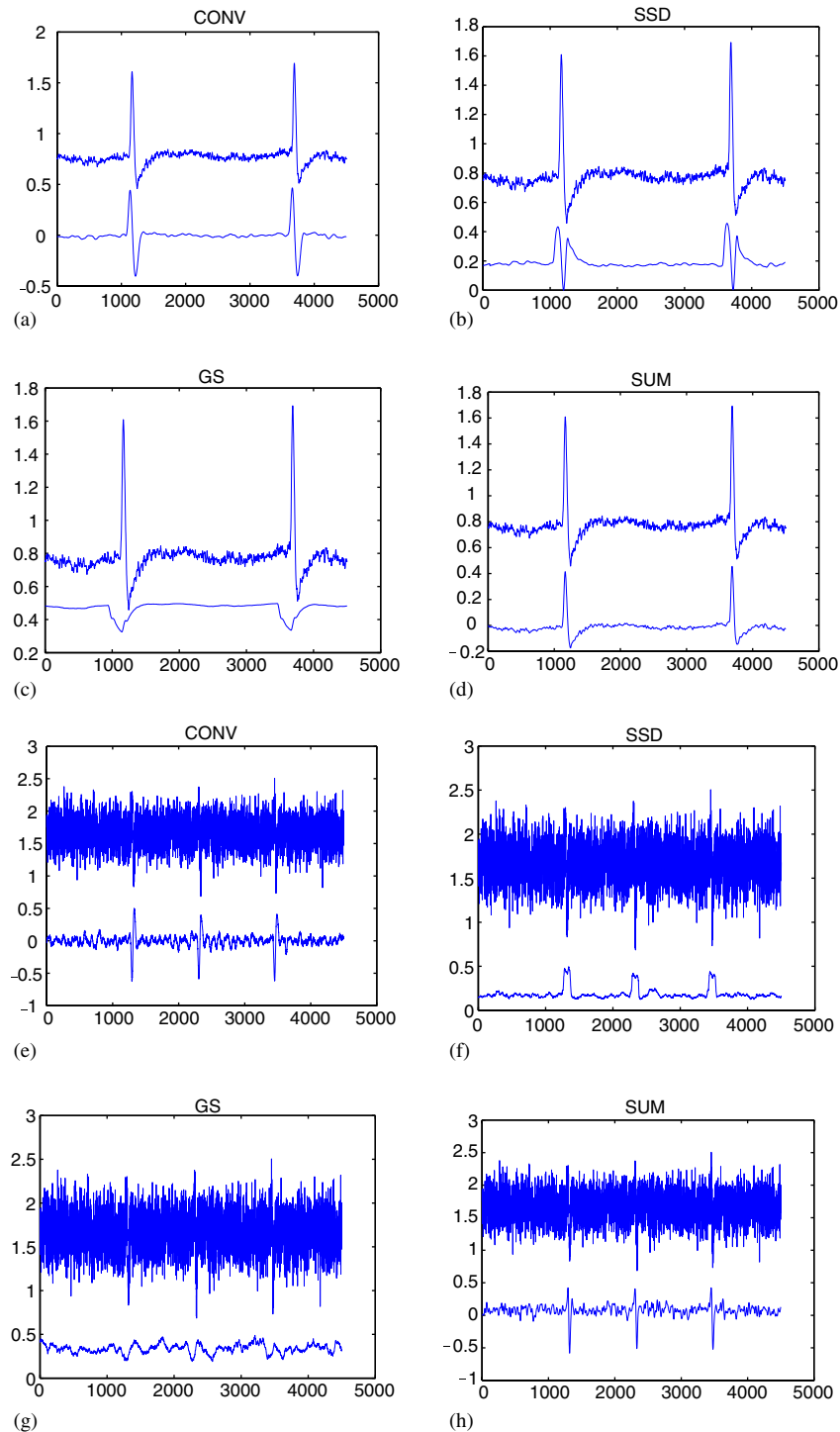


Fig. 1. In each graph (a)–(h), the upper trace is raw data, lower trace is processed data. Graphs (a)–(d) show high quality raw data ($\text{SNR} = 9.82$) transformed by CONV, SSD, GS and SUM. (e)–(h) show low-quality raw data ($\text{SNR} = 1$) similarly transformed. In each case the spikes are significantly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

correlated to the template (see Fig. 1(a,e)).

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

where $s(i)$ is the sampled signal, and $T(j)$ ($j = 1 \dots n$) 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.

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

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: $\text{GS}(i) = \sum_{j=1}^n \phi((s(j) - \hat{\mu})/\hat{\sigma})$, 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]).

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

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.

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

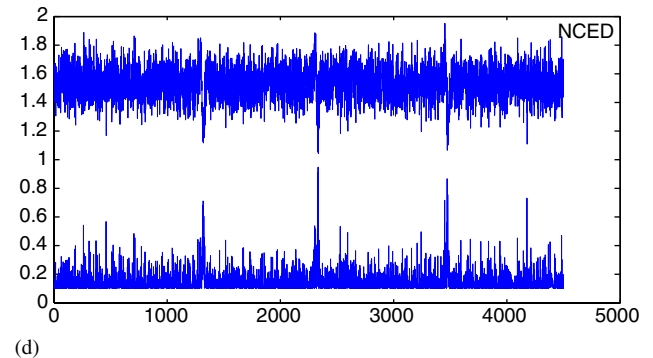
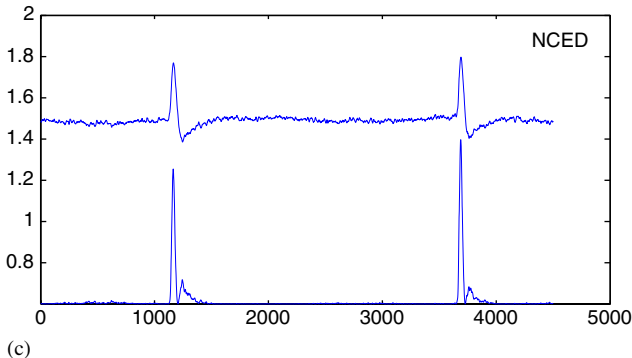
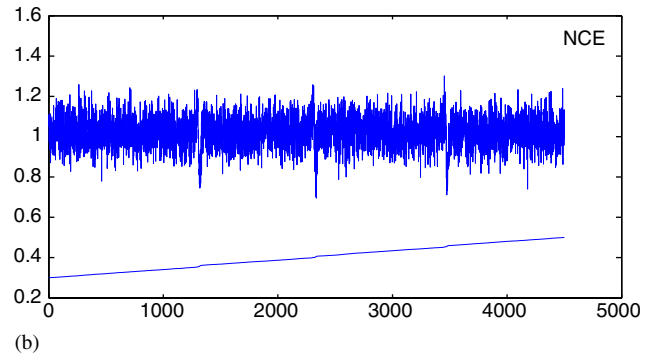
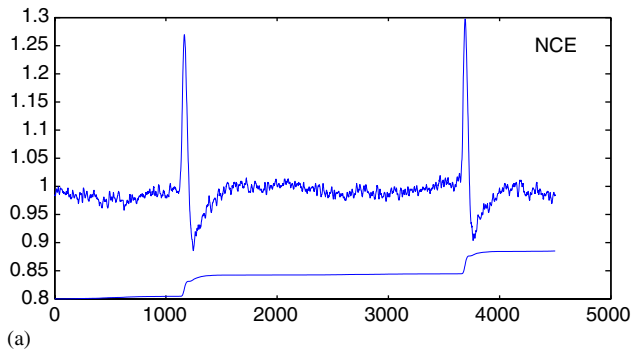


Fig. 2. Graphs (a) and (b) show a plot of $E(t)$ (NCE) applied to high- and low-quality raw data. It is clear that $E(t)$ increases sharply at spikes in (a) but less so in (b) due to noise. Graphs (c) and (d) show a plot of $E'(t)$ applied to raw data. $E'(t)$ clearly peaks at spikes for both high SNR (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).

where L is the signal length. $E'(t)$ has a value significantly 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 ($\text{SNR} = \frac{(S+N)}{N}$ where $(S+N)$ is the power of a signal component with a spike and noise, 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 $E' \leq 1$ there are no spikes in the signal,

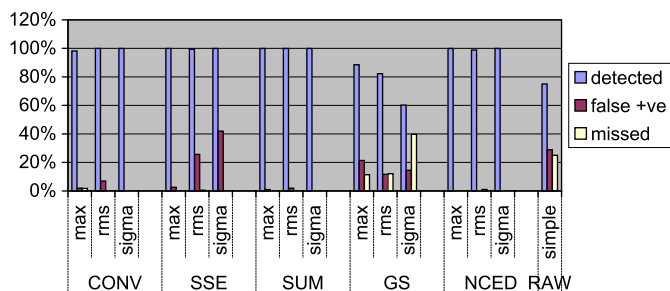


Fig. 3. Summarised results. The thresholding criteria used are maxima/minima (max), root mean square (rms), standard deviation (sigma) of the output from each of the techniques discussed. These techniques are compared with the simple thresholding of the raw data (RAW).

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.

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.

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