

Analog Tetrode Adaptive Spike Detector

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Abstract

The detection of individual brain cells activity is essential to studying brain function. Most brain cells communicate by firing action potentials (spikes). Brain information is thought to be encoded in the timing between successive spikes. Neural data collected from tetrodes directly implanted in the neural tissue seems to provide highly accurate data. Detecting spikes and identifying the firing times of a specific neuron require analyzing the signals from the four tetrode conductors simultaneously and filtering useful information from any background noise. The computational simplicity of voltage thresholding makes it the most common method or the detecting action potentials buried in noise. Nevertheless, it is not straightforward to apply the technique to several channels simultaneously.

The proposed algorithm combines the four tetrode signals and compares the output against an adaptive voltage threshold detector. The signals are combined using an analog signal multiplication that emphasizes the times when all four signals are spiking. The adaptive threshold detector sets itself to the background noise level. The entire operation is done in analog and therefore makes the system low power and highly suitable for hardware implementation. This technique has been demonstrated in Matlab simulation using real tetrode data and is being adapted for an all-analog circuit implementation.

I. INTRODUCTION

Measuring, analyzing and interpreting the activity of individual brain cells are essential rudiments to studying brain function [1]. Most brain cells communicate by firing action potentials (spikes). Brain information is thought to be encoded in the timing between successive spikes.

For implanted circuitry, an analog hardware realization is advantageous over a digital realization because it has lower power consumption and it is smaller in size especially when the need of the analog-to-digital converter is eliminated.

Although there are many methods for recording neural activity, implanting tetrodes (4-wire electrodes) directly in the neural tissue seems to provide highly accurate data [2]. Detecting spikes and identifying the firing times of a specific neuron require analyzing the signals from the four tetrode conductors simultaneously and filtering useful information from any background noise.

Among all existing techniques for the detecting action potentials buried in noise, the computational simplicity of voltage thresholding makes it the most common method [3]. It also requires minimal hardware and often satisfies experimental demands. Nevertheless, it is not straightforward to apply the technique to several channels simultaneously.

II. METHODS

The proposed algorithm combines the four tetrode signals and compares the output against an adaptive voltage threshold detector. Real spike data are taken from simultaneous intracellular and extracellular tetrode recordings [4]. The signals are combined using an analog signal multiplication that emphasizes the times when all four signals are spiking (Fig. 1). The operation is done using a log-antilog multiplier. The four input signals are multiplied by first calculating their logarithm, adding the outputs and finally taking the antilogarithm [5].

The results from the analog multiplier are passed through an

adaptive threshold detector (Fig. 2). The algorithm measures the rms value of the background noise and adaptively sets the threshold to a multiple of rms. The detector however, only processes data from one channel and assumes the background noise to be Gaussian. The entire operation is done in analog and therefore makes the system low power and highly suitable for hardware implementation.

A. Signal Multiplication

The first stage of the algorithm is analog signal multiplication. It is used to emphasize the times when all four signals are spiking. The identity $\log XY = \log X + \log Y$ reduces multiplication to addition. The formula shows that two signal voltages are effectively multiplied if the logarithms of the signal voltages are added. Therefore the four input signals are multiplied by first calculating their logarithm, adding the outputs and finally taking the antilogarithm.

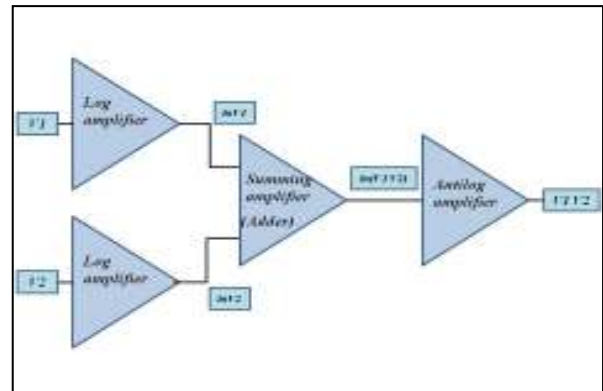


Fig. 1. Analog multiplication performed by log-antilog amplifiers

There are two basic circuits for logarithmic amplifiers (1) transdiode and (2) diode connected transistor. Most log amplifiers are based on the logarithmic relationship between

the collector current (flowing through the diode) I_C and the base-emitter voltage V_{BE} .

1) Transdiode log amplifier

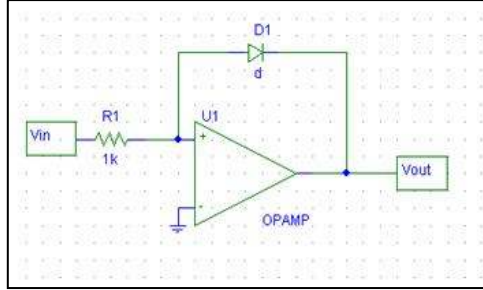


Fig. 2. Transdiode logarithmic amplifier

In a transdiode log amplifier, the input voltage V_{in} is converted by R_1 into current, which then flows through the diode's collector. The collector current is

$$I_C = I_S \left(e^{\frac{qV_D}{kT}} - 1 \right) = I_S \left(e^{\frac{V_D}{V_T}} - 1 \right)$$

Where V_D is the voltage across the diode, I_S is saturation current, $V_T = \frac{kT}{q}$ is thermal voltage, k is Boltzman's constant $1.3807 \times 10^{-23} \frac{\text{Joules}}{\text{Kelvin}}$, T is absolute temperature in Kelvin, and q is the electron charge $1.6 \times 10^{-19} \text{Coulombs}$.

For small forward bias voltages the exponential is very large because the thermal voltage is very small, therefore the subtracted '1' is negligible and the formula is often simplified to $I_C \approx I_S \cdot e^{\frac{V_D}{V_T}}$. At room temperature, $V_T = 25\text{mV}$, V_{out} is therefore

$$V_{out} = -V_D = -V_T \ln \left(\frac{I_C}{I_S} \right) = -\frac{V_T}{2.3} \lg \left(\frac{I_C}{I_S} \right) = -\frac{V_T}{2.3} \lg \left(\frac{V_{in}}{R_1 I_S} \right)$$

2) Anti-log (exponential) amplifier

An exponential or antilogarithmic amplifier performs the inverse function of that of log amps. Anti-log amplifier circuits include the same elements as log amplifier circuits but arranged in different feedback configuration (Fig. 9). Exchanging the position of the diode and resistor in log amp yields an anti-log amp.

The collector current is given by $I_C \approx I_S \cdot e^{\frac{V_D}{V_T}}$

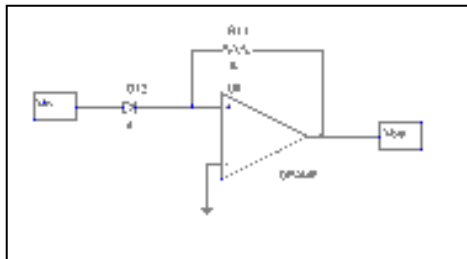


Fig. 3. Anti-log amplifier

B. Adaptive Threshold Spike Detection

The second stage of the algorithm is spike detection. The output from the analog multiplier is passed through an adaptive threshold detector.

The spike detection system was partially inspired by [6]. The author developed an algorithm which performs real-time spike detection and which can be implemented in a low power analog integrated circuit.

The author made two important assumptions (i) the neural data measured by an extracellular electrode was high-pass filtered to remove DC offset, and (ii) the background noise was Gaussian and therefore strictly described by its root mean square (equal to its standard deviation).

Since the background is assumed to be Gaussian with zero mean, the probability that the noise exceeds one standard deviation is 0.159. Conversely, a threshold adaptively tuned such that 15.9% of the signal exceeds it, will be equal to one standard deviation σ .

Figure 4 illustrates the adaptive spike detection algorithm. Comparator A with gain K is used in a feedback loop to servo the duty cycle of 0.159 and therefore sets the output voltage (V_1) to the rms value of the input voltage. This voltage is then amplified by N and used as a threshold level for the comparator B.

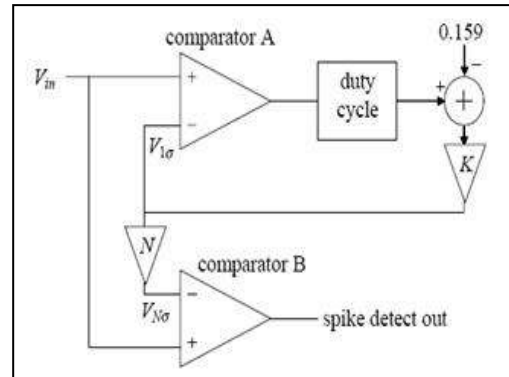


Fig. 4. Block diagram of the adaptive spike detection algorithm (3)

The adaptive threshold setting algorithm depends on a set of variables: K , N and duty cycle (the length of time the waveform is in logic high). These variables must be determined before any circuit implementation.

The test data for this project consist of real cortical recordings. Therefore, the assumption made by the author about the background noise being Gaussian would not be appropriate for the proposed design.

Nevertheless, the system is expected to work for non-Gaussian background if the parameters shown in figure 4 are suitably chosen. With an amplification constant $N=1$, the output of the feedback loop V_1 will lead to errors in estimating the rms level of the noise because it is too low to distinguish between spikes (correct detections) and background noise (false alarms). Selecting a large amplification constant N will set a threshold high enough to discriminate non-Gaussian noise. In addition, spikes occur

rarely (1% of the time) and should not affect the rms noise estimate.

III. PRELIMINARY RESULTS

A. Signal Multiplication

Multiplication was simulated in Matlab using the identity $\log XY = \log X + \log Y$, which reduces multiplication to addition. The algorithm was tested on tetrode neural recordings from (2). As shown in the waveform, the algorithm succeeded in capturing the times when all four signals spike.

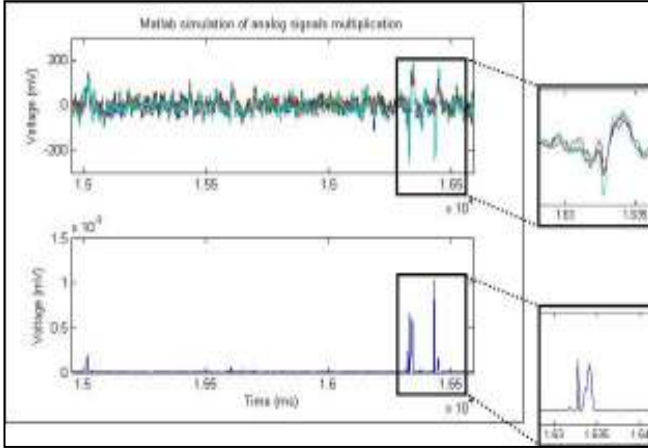


Fig. 5. Matlab simulation of analog signals multiplication

To verify the multiplier's performance, the Matlab simulation was examined under four different conditions:

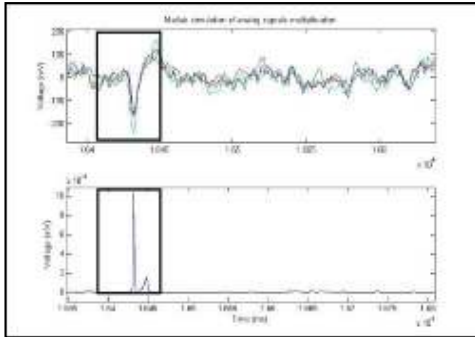


Fig. 6. When all four tetrode channels are spiking

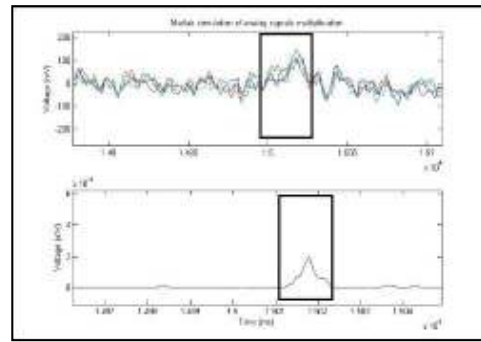


Fig. 7. When three tetrode channels are spiking

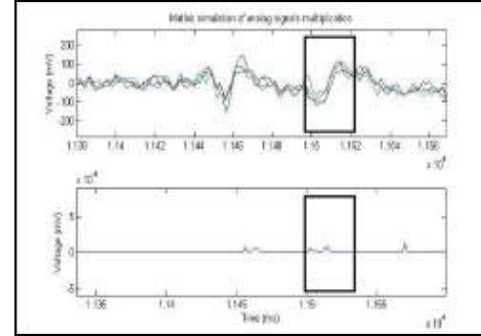


Fig. 8. When two tetrode channels are spiking

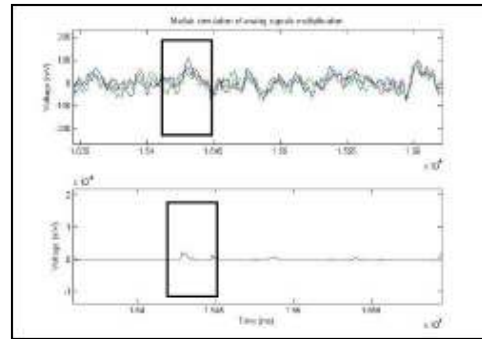


Fig. 9. When only one tetrode channel are spiking

The multiplier succeeds in combining simultaneous observations of the same event as recorded by the four channel tetrode. As shown by the graphs, the output's amplitude increases as the number of spiking channels increase. When only one channel is spiking, the output is very small and may be missed by the threshold spike detector. However the goal is to detect the times when all four tetrode conductors are spiking.

B. Spike detector

The adaptive threshold spike detector algorithm was developed using Matlab.

Initially, the code consisted of a small routine where the key parameters: (1) The gain K , (2) The duty cycle which is nothing but a filter and (3) the constant N which is a multiple of the standard deviation. The code was first tested on random Gaussian noise to obtain a range for these parameters.

The comparator's gain K was the first parameter to be tested. The values tried ranged from 10 to 200. The filter's values ranged from 0.1 to 1.

The amplifying constant N was manually selected according to the output on the graph.

The code computes all possible combinations of the three parameters of interest for 100 Mbytes of data.

The output shown below consists of a drop down menu where the user selects the values for the gain and filter depth, and a waveform categorizing the detected spikes as being correct (caused by the target neuron) or false alarms (caused the background noise). An ideal detector follows the left and top limits of the graph.

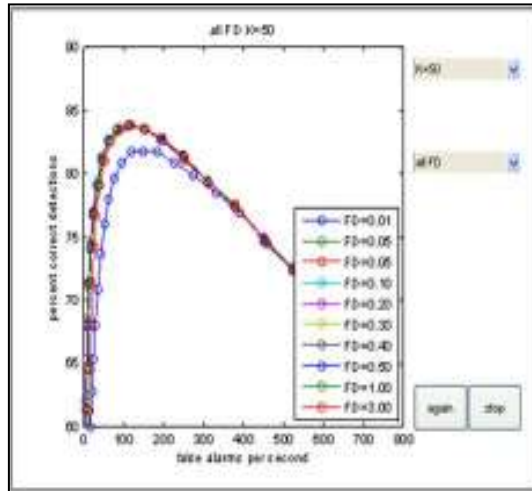


Fig. 10. Percentage of correct spikes vs. false alarms per second

IV. FUTURE WORK

First, the multiplier's output will be applied to the adaptive spike detector through a Matlab simulation to determine the best combination of parameters (gain and duty cycle). These values will be used in the circuit design step. The spike detector must maximize the number of correct detections while reducing the number of false alarms. The results will be compared to the neural data with precisely known correct spikes percentage.

The second step is circuit design. Values of the analog multiplier circuit components will be calculated. The circuit will consist of operational amplifiers

The parameters values of the spike detector will be used to design the adaptive spike detector. The duty cycle of comparator A (Fig. 4) will be calculated using an operational transconductance amplifier (OTA) to realize a low pass filter.

After determining all components of the spike detector, the overall system will be validated by simulating in Tanner EDA, providing an all-analog circuit implementation. The test data will consist first of white noise to verify the circuit is not detecting any spikes, then real neural data for which spike times are known precisely.

The overall goal is an integrated circuit that is part of a wireless BMI. Consequently, the spike detection circuit must process the signals from an implanted tetrode, performs spike detection, then transmits the action potentials to a receiver that sorts the spikes and controls a prosthesis. Therefore, minimizing chip area and power consumption is key in the overall system design.

V. CONCLUSIONS

A method for neural spike detection has been presented. In comparison to other existing techniques, the novelty of the research proposed here is in combining the simultaneous signals from four tetrode conductors and applying the output to an all-analog adaptive-threshold spike detector.

An analog multiplier was designed to combine the four tetrode signals. An algorithm for the adaptive threshold detector was developed. Matlab validations with real neural data were used to test the analog multiplier and the adaptive spike detector.

In selecting spike detection algorithms for this study, emphasis was placed on a design that is well suited for implementation in a low power wireless BMI system.

Although it may seem that 100% correct spike detection is required to successfully drive a prosthesis, the physiological properties of cortical ensembles are adaptive and can change as a function of experience and training. So the existence of cortical plasticity must be taken into account in the design of an efficient BMI.

VI. REFERENCES

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