1983

Computer Pattern Recognition of Action Potentials

Ronald S. Remmel
University of Arkansas for Medical Sciences

COMPUTER PATTERN RECOGNITION
OF ACTION POTENTIALS

RONALD S. REMMEL[*]
Department of Physiology and Biophysics
University of Arkansas for Medical Sciences
4301 W. Markham Street
Little Rock, Arkansas 72205

ABSTRACT

A general method of pattern recognition was applied to the problem of recognizing extracellularly-recorded neuronal action potentials in the presence of noise and other pulses. A PDP11/23 performed the calculations. There were four stages: 1.) A bandpass filter attenuated noises; 2.) the data input program digitized the signal every 55 μsec. If the signal exceeded a threshold, 12 samples of the signal and the time were written onto the disk; 3.) the pulse discriminating program recognized an action potential by fitting the 12 points with this function:

$$v(t) = (a + bt + ct^2) \exp(-t/\tau).$$

For each pulse the computer determined values of the parameters giving the best fit through use of the least squares technique. For acceptance, the total pulse height and the position of the zeroes of $v(t)$ must fall within limits; 4.) occasionally a pulse may be missed or an extra one recorded. The computer displayed the complete pulse train and the operator moved a cursor to insert or delete pulses.

INTRODUCTION

Signals in the nervous system are transmitted along axons as pulses of electricity called action potentials. If a microelectrode is inserted inside a neuronal cell body or axon, a resting potential of about -60 mV is measured with respect to the extracellular fluid. The resting potential is a thermodynamic consequence of the fact that the intracellular potassium concentration is much HIGHER than outside. In contrast, the intracellular sodium concentration is much LOWER than outside. These concentrations are maintained by the cell's sodium-potassium pump.

An action potential is a positive-going pulse of about 100 mV amplitude and about 0.5 msec duration superimposed upon the resting level (Ganong, 1981). The rising phase of an action potential occurs when membrane channels selectively permeable to sodium ions open and sodium ions rush into the cell. This inrush of positive charges causes the membrane potential to go positive. The failing phase is caused by the sodium channels closing and potassium channels opening. The outflow of potassium ions leaves a net negative charge inside, causing the membrane potential to return to its negative resting potential. This voltage wave propagates rapidly down the axon at speeds up to 120 m/sec with no attenuation in amplitude. Action potentials are usually initiated by excitatory synapses. Standard textbooks give further details (Ganong, 1981).

An intracellular recording of action potentials is difficult to obtain in the alert, behaving animal because the microelectrode is easily jarred out of the cell. It is easier to record action potentials extracellularly by inserting a microelectrode into the brain to within 50 μm of a neuronal cell body. The pulses are ~ 1 mV in amplitude and generally negative-positive biphasic waves. The negative phase is caused by sodium ions moving away from the microelectrode into the cell. The positive phase is caused by potassium ions moving out of the cell towards the microelectrode.

Typically the height of recorded action potentials is only 3-20 times the noise level of 30 μV. This noise is caused by the thermal motion of charges in the electrode and amplifier. The usual method to distinguish between neuronal pulses and noise is to use an electronic circuit called a discriminator, which gives an output pulse only when the signal exceeds a preset voltage. However, sometimes a large noise transient is mistaken for an action potential.

We present a new method for distinguishing between action potentials of interest and noise and background units. The method has four stages: 1.) an analog bandpass filter attenuates the noise; 2.) the computer writes onto disk 12 digitized samples of each pulse; 3.) offline the computer fits this function to the 12 points:

$$v(t) = (a + bt + ct^2) \exp(-t/\tau).$$

This function was chosen because it has a biphasic shape which is very similar to that of an extracellularly recorded action potential. The pulse is rejected if its height or if the shape of $v(t)$ deviates beyond limits; 4.) another computer program allows editing the data file for apparently missing or extra pulses. More details have been presented in another publication (Remmel, 1983).

MATERIALS AND METHODS

Action potentials were recorded extracellularly with glass micropipettes in the pons of alert cats making eye movements (Remmel and Skinner, 1981). We recorded the neuronal signal in direct mode on a TEAC A-2340SX high-fidelity tape recorder for computer analysis at a later time. The computer belongs to the NSF EPSCOR Program (Neuroscience Component) and is a D.E.C. PDP11/23 (MINC-11) with the following equipment:

128 KByte of MOS-FET memory (only 64 KByte used)
dual RL01 disks (5 MByte each)
ADV11-A analog-to-digital converter (A/D)
KEF11-AA floating point processor
VT105 graphics terminal
Nicolet Zeta plotter

The bandpass filter

Electrode and amplifier noise, a major source of spurious pulses, is attenuated by the analog bandpass filter (Fig. 1a). Component values were selected to optimize the pulse height relative to white noise (equal noise energy at all frequencies). The filter passes 300-3000 hZ (Fig. 1b); the pulse (Fig. 1c), although attenuated to 40%, is qualitatively unchanged.

The data input program

This MACRO-11 program digitizes data in real time and stores it on the disk for later analysis. The operator types in the trigger level,

[*]Present address: Biomedical Engineering Department, Boston University, 110 Cummington St., Boston, Mass. 02215.
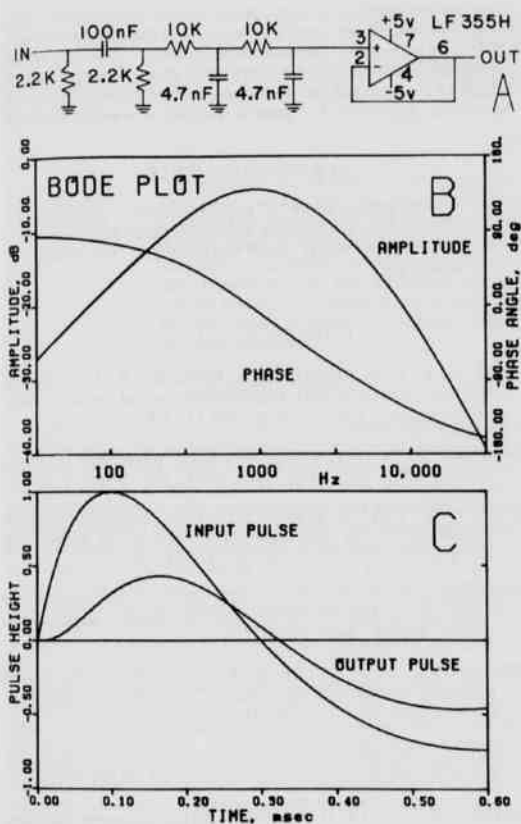
Ronald S. Remmel

Figure 1. A bandpass filter for action potentials (A). The unity-gain amplifier (National type LF355H) functions to drive subsequent circuits. The filter has sharp cut-off at high frequencies (Bode plot, B) in order to attenuate electrode and amplifier noise. The filter blocks D.C. and attenuates low frequencies such as 60 Hz. For a biphasic pulse put into the filter (C), a computer program numerically solved the differential equations to give the output pulse shape. It is attenuated to 40% but otherwise little changed.

Figure 2. Curves fit to the 12 voltage measurements (55 μsec apart) for pulses from an abducens interneuron (unit 98.98). The function fit to the points is described in the text. A-B: Acceptable pulses. C-H: Rejected pulses. The following are the reasons for rejection: The second zero of the fitted function is too far to the right in C and D and too far to the left in E and F. In G the pulse height is too small. No zeroes occurred in H.

which is set low but not so low that the computer is inundated with small noise pulses. The A/D converter samples the signal every 55 μsec. If the sample exceeds the trigger level, more samples are taken until 12 are accumulated, including the one preceding the trigger. We call these samples y_i (i = 1 to 12). The 12 samples and the time of the pulse are written onto disk. One disk can hold about 30 min. of data.

The pulse discriminating program

This FORTRAN program reads a disk file, rejects bad pulses, and writes only the time of accepted pulses back onto the disk. The following function is fit to the 12 voltage samples for each pulse by the least squares technique:

$$v(t) = (a + bt + ct^2) \exp(-t/\tau).$$

The polynomial is an inverted parabola (one maximum and two zeroes);
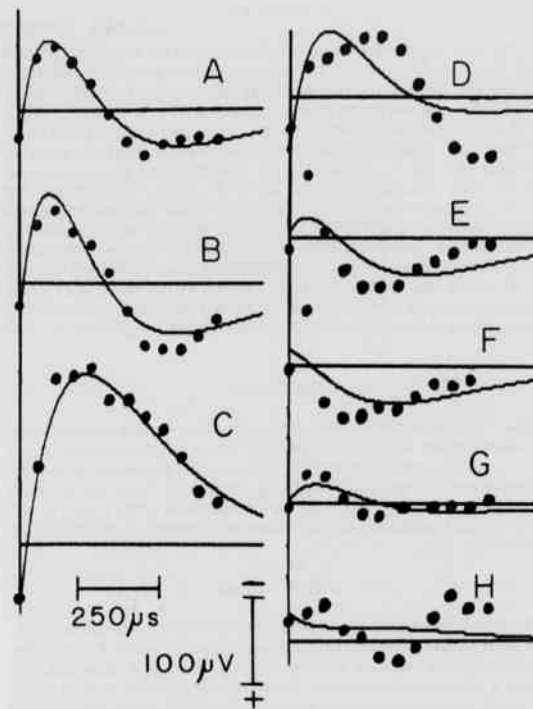
the exponential causes a decay at long times and produces a minimum (Fig. 2a). This function thus has an ideal shape for describing action potentials. The operator chooses one τ giving good fits for good pulses. the computer then calculates a, b and c by the least squares technique, that is, by minimizing S:

$$S = \sum_{i=1}^{12} (y_i - v(t_i))^2,$$

where $t_1 = 0$ μsec, $t_2 = 55$ μsec, etc.

For acceptance, the locations of the zeroes of v(t) must fall within the limits specified by the operator. The height of the pulse also must fall within limits. Summary statistics printed at the end show the number of accepted and rejected pulses and histograms of the pulse heights and of the two zeroes. This program takes 80 msec/pulse.

The pulse insertion-deletion program

Sometimes a pulse is missed or an extra one recorded. This program displays a graph of the instantaneous interspike frequency (ISF, which equals 1/Δt, where Δt is the time between two pulses). If the neuron fires at a steady rate, the missing or extra pulses are easily seen on this graph. The operator moves a cursor to point to the location of the defect and the computer inserts or deletes pulses.

Computer Pattern Recognition of Action Potentials

RESULTS

The operator can view on the graphics terminal the 12 voltage samples and the fitted function v(t) for accepted and/or rejected pulses (Fig. 2). For this neuron, the threshold was set to -32 μV. The τ was set to 150 μsec, a value giving good fits. The reasons for rejecting pulses C-H are given in the caption. For accepted pulses (A,B) the fitted curve showed little variation in shape from pulse to pulse. The most sensitive measure of shape was found to be the time difference between the two zeroes on the abscissa, which was 243 $\pm$ 17 μsec (av. and std. dev. for 27,147 good pulses for the neuron of Fig. 2). The 17 μsec standard deviation is much less than the 55 μsec between samples, implying that the computer had "interpolated" between points. For this neuron the total pulse height (difference between the maximum and minimum) was 165 $\pm$ 44 μV on the average for good pulses and fluctuated during the recording because the microelectrode moved relative to the cell. Thus although the pulse height fluctuated, the zeroes varied little.

DISCUSSION

Pattern recognition involves determining how similar the pattern of measured points is to a model pattern. Let us call those points (x_i, y_i) for n points. A general procedure is to describe the model pattern by a mathematical function $v(x,a,b,...)$, which may have one or more adjustable parameters $a,b,...$. This function is fit to the points by the least squares method, i.e., the following function is minimized by adjusting $a,b,...$:

$$S = \sum_{i=1}^{n} (y_i - v(x_i,a,b,...))^2.$$

(The least squares method is nearly identical to the chi-square method, the latter simply having statistical weights multiplying each term.) The minimization in our case involves solving 3X3 matrix equations, for which a subroutine is available. If the fit is bad (sum of squares large) or if the parameters deviate beyond prescribed limits, the event is rejected — it's not like the pattern. I have previously used this method for testing whether millions of particle reactions detected in a high-energy physics experiment were consistent with a reaction in which a positive kaon decayed into three charged pions (Ford et al., 1972).

My method fits 12 points with a 4-parameter function. More details of the pulse shape can be fit by the template method of Prochazka and Kornhuber (1973), which is a least squares method. The contour-fitted amplitude window used by Kent (1971) tests complex waveforms without much computer times, but does no smoothing as is done by this least squares method. Other methods extract features of the pulse from the digitized points. For instance, the methods of Mishelevich (1970) and of Vibert and Costa (1979) calculate the maximum and minimum amplitudes, the time between the maximum and the subsequent zero crossing, and the time between the maximum and the minimum. These methods provide no smoothing nor interpolation of points.

My method employs a least-squares fit of a 4-parameter function having a biphasic shape which is very similar to that of an action potential. Pattern recognition is accomplished as follows: An action potential is represented as a point in a 4-dimensional space; those points falling outside of a certain volume in that space are rejected as being unlike the pattern. This method of pattern recognition is widely applicable.

LITERATURE CITED

FORD, W. T., P. A. PIROUE, R. S. REMMEL, A. J. S. SMITH, and P. A. SOUDER. 1972. Experimental study of the tau $\pm$ decay matrix element, Physics Letters 38B:335-338.

GANONG, W. F. 1981. Review of medical physiology, 10th ed., Lange Medical Publ., Los Altos, Calif., pp. 29-39.

KENT, E. W. 1971. An educable wave form recognition program suitable for on-line discrimination of extracellular single units, Electroenceph. clin. Neurophysiol. 31:618-620.

MISHELEVICH, D. J. 1970. On-line real-time digital computer separation of extracellular neuroelectric signals, IEEE Trans. biomed. Engng., BME 17:147-150.

PROCHAZKA, V. J., and H. H. KORNHUBER. 1973. On-line multi-unit sorting with resolution of superimposed potentials, Electroenceph. clin. Neurophysiol. 34:91-93.

REMMEL, R. S. 1983. A computerized discriminator for action potentials, Electroenceph. clin. Neurophysiol 56:528-530.

REMMEL, R. S., and R. D. SKINNER. 1981. Cat neurons related to horizontal eye position located ventral to the 6th nucleus, Neurosci. Abst. 7:623, abst. 204.2.

VIBERT, J. F., and J. COSTA. 1979. Spike separation in multiunit records: A multivariate analysis of spike descriptive parameters, Electroenceph. clin. Neurophysiol. 47:172-182.