

TEACHING FIELD POTENTIALS: A MICROCOMPUTER SIMULATION OF THE NERVE ACTION POTENTIAL IN A BIDIMENSIONAL CONDUCTOR

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A computer simulation of the extracellular field potential recording of nerve activity is presented. An experimental setup composed of an oscilloscope, a nerve, a recording conductive surface, and a recording electrode is graphically simulated. The user may study the influence of the position of the recording electrode and of certain nerve properties (membrane potential, velocity of conduction and action potential duration), on the action potential shape. The different waves which constitute the action potential may be analyzed and their peak values plotted as a function of the independent variable (e.g. electrode distance from the nerve). Three-dimensional plots of a set of action potentials as a function of the independent variable may also be obtained. The simulation allows the user to study the basic factors which determine the configuration of an extracellularly recorded compound nerve action potential.

Keywords: Teaching; Simulation; Computer; Action potential; Field potential.

Introduction

Understanding the generation of field potentials is fundamental to comprehend the characteristics of diverse electrophysiological measurements performed in living organisms. Extracellularly recorded electrical activity of excitable cells may markedly vary, depending upon the geometry of the cells and the position of the recording electrode. Nevertheless, the analysis of the potentials that are set up in the surrounding medium allows to infer about the features of an excitable system. For example, the interpretation of the EEG and EKG, which are two of the most commonly performed physiological measurements, is based upon the theory and analysis of field potentials. Thus, for students in the biomedical sciences, it is essential to understand the elements which determine the configuration of an extracellular record.

Experiments commonly performed to study field potentials are based on the classical demonstration of Lorente de Nó [1] who in 1947 recorded the electrical activity of a bullfrog sciatic nerve laid upon a piece of filter paper soaked in saline solution. One of the nerve ends was submerged in an oil pool in contact with the stimulation electrodes. The indifferent electrode was placed in a corner of the conductive area. The active recording

electrode was moved and placed in different parts of the conductive paper. Hence, a map of the potential spread over the conducting media might be constructed [2]. Characteristically a triphasic record was observed: an initial wave front of positive polarity (P1), followed by a large amplitude negative potential (N) and a second positive potential (P2). When the recording electrode was moved away from the nerve, the amplitude of the record decreases, its shape remaining almost the same. However, if the active electrode was shifted near the point of origin, as well as to the end of the fibre, the relative amplitude and duration of the record waves vary as a function of the electrode position. (Fig. 1). Based on these experiments Lorente de N6 postulated the double dipole nature of excitation and recovery in nerve fibers.

The software here presented has been designed to reproduce Lorente de N6's experiments. The program may provide students with further insight regarding the mechanisms of impulse conduction and the characteristics of extracellularly recorded compound nerve action potentials. It allows the user to accurately map the geometry of a compound action potential in a two dimensional conductor. The program is designed for

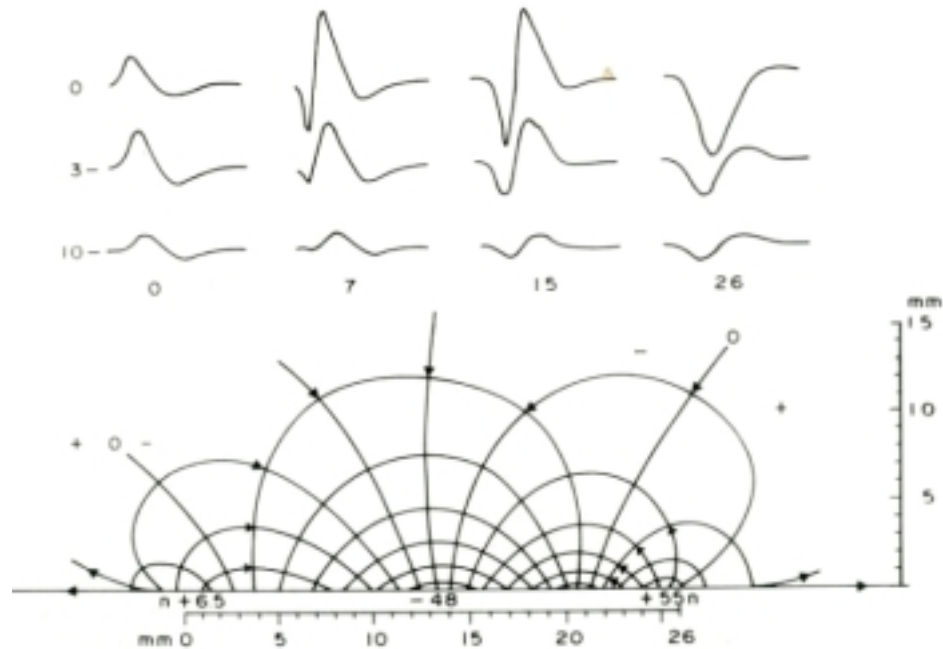


Fig. 1. Experimental records obtained by Lorente de N6 from a frog sciatic nerve. Upper panel, a set of twelve records taken at variable distances to the nerve are shown. By displacing the electrode away from the nerve (0, 3 and 10 mm), the record amplitude decreases with no change in its shape, revealing the decay of field potential with the distance. Displacing the electrode longitudinally alongside the nerve (0, 7, 15 and 26 mm), modifies the relative amplitude and duration of the action potential components, revealing the double dipole nature of the action potential. Lower panel, the isopotential lines shows that the field set up in the conductive medium is characterized by a front of positive polarity, a high amplitude negative area, and a recovery phase of positive polarity (modified from Lorente de N6 [1]).

students at undergraduate and graduate levels. Preliminary results have been communicated in abstract form [3, 4].

Software Description

Program Basis

From an extracellular recording standpoint, current which flows out of a cell will appear as a current source, whereas current which flows into the cell will appear as a current sink [5, 6]. During the passage of an action potential, currents flow into the cell forming a sink in the active region, current flowing along the inside of the axon to the adjacent resting parts of the cell, and outwards through the membrane, closing the circuit. The boundaries between the active and inactive domains constitute an area of opposite sign charges, and can be equated with two dipoles [6-9]. One, with its positive pole in the direction of propagation, and a second one with inverted polarity. Thence, if an action potential passes near a monopolar electrode, the potential recorded depends on the linear addition of the potentials contributed by each dipole.

From the foregoing, it can be understood that the nerve action potential may be simulated by a double dipole model [8, 9]. This approach was used in this simulation. Action potentials which travel along a nerve segment, have been simulated as two opposite dipoles. The smoothly rising and falling phases of the action potential were simulated as a square wave, approach which is quantitatively inaccurate, but greatly simplifies the computation required for the simulation [6, 10, 11]. The record is obtained by calculating the projection of each vector (depolarization and repolarization vectors) upon a line conceived between their trailing and the electrode. In a conducting medium, the potential that would be generated at any point by such current dipoles would be given by:

$$V = \frac{V_{\text{mem}} - E_{\text{Na}}}{4.0 \pi \sigma (1 / \theta r^+ - 1 / \theta r^-)}$$

in which V_{mem} is the resting membrane potential value, E_{Na} is the equilibrium potential for sodium, σ is the medium conductivity and θr^+ , θr^- are the projections of the vectors set up by the source and sink respectively [6]. In this simulation, σ and E_{Na} are assumed to be constant. The two vectors are separated by the active region, which is the area of inverted polarity, and is defined on the basis of the duration and velocity parameters selected for the nerve action potential. A correction factor accounts for border conditions at both ends of the nerve [12].

Program operation

The program has been developed in Turbo PascalTM; it is designed to operate in an IBM-PC or compatible machine, equipped with a color graphics RGB adapter, 256 K of RAM, and one disk drive. Use of the optional 8087 mathematical coprocessor is recommended since it speeds up the program operation. The program has been fully debugged and no computer expertise seems necessary to use it. Input-output protection

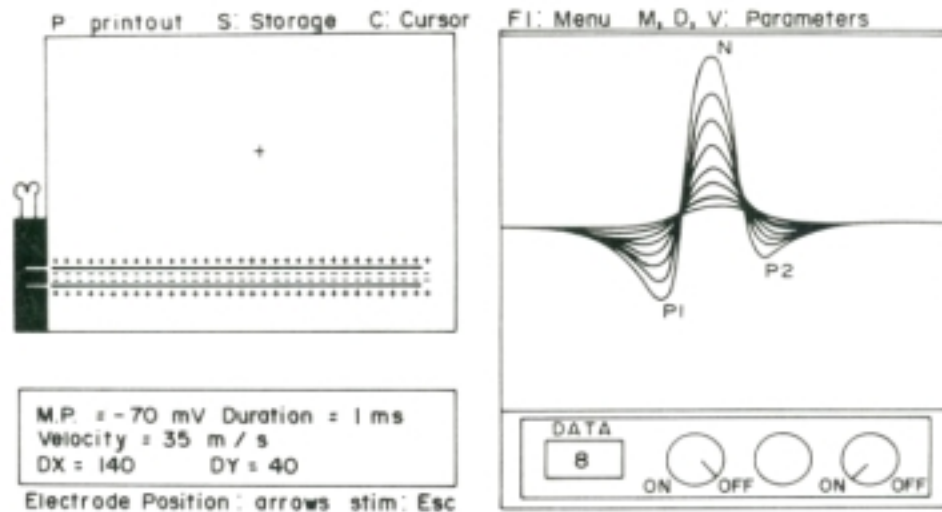


Fig. 2. Printout of the main program display. The simulated oscilloscope is shown to the right. To the left, a nerve with its characteristic polarization is presented. The exploring electrode is represented by a cross. The electrode may be displaced by using the arrow keys. The keys M, V, and D are used for parameter modifications (M: membrane potential; V: velocity of conduction; D: action potential duration). The oscilloscope knobs shows storage mode and background screen aspect, which are set on-off with the S and W keys. The records shown on the oscilloscope screen were generated while displacing the electrode away from the nerve (increasing dy). P1, N and P2 designate the main components of the nerve field potential.

schemes are included to the extent needed to avoid errors. Disk data storage and retrieval, and routines for printing the graphs obtained have also been implemented.

From the main Menu the user may choose several options: (a) work on the simulated experimental setup, (b) read data from diskette, (c) printout a table of results, (d) graphically analyze the results, (e) store the data in diskette for further analysis, (f) activate or deactivate sound prompts.

The simulated experimental setup consists of an oscilloscope, shown at the right side of the screen, and the nerve preparation shown to the left. The nerve is schematically represented with negative charges inside it, and positive charges outside (Fig. 2). The user is allowed to vary the nerve parameters (eg. conduction velocity, membrane potential, action potential duration) and to position the active electrode in any place of the simulated saline soaked surface. The oscilloscope display may also be modified, selecting persistence of the images and screen background (black or white). The action potential is triggered by pressing the Esc key. The electrical polarity across the nerve membrane becomes momentarily reversed, graphically simulating the passage of an action potential, while the record appears on the oscilloscope screen. Once a record has been obtained, a cursor may be activated allowing exact numerical measurements. Values of the electrode position, oscilloscope display characteristics and nerve parameters are easily selectable

and continuously shown on the screen, in a data box located below the simulated nerve preparation.

The user designs an experiment by selecting an independent variable, and studying its influence upon the shape and amplitude of the action potential components. Selectable independent variables are: the distance from the electrode to the nerve (dy), the position of the electrode along the longitudinal axis of the nerve (dx), the value of the membrane potential (M), the conduction velocity (V) and the duration of the action potential (D). The program allows the user to plot the peak amplitudes and latencies of the action potential components, as a function of the independent variable. Care must be taken in designing a logical experiment by studying the influence of only one variable at a time. Otherwise, graphs might be difficult to interpret and sometimes appear nonsensical, as happens in reality with a badly designed experiment. User is also allowed to plot the potentials obtained in a three-dimensional graph, in which the independent variable is plotted in the z axis as a function of the voltage in the ordinate and time in the abscissa. This kind of plots allows the user to visually inspect a whole set of records, maintaining contact with the crude data.

Results

Figure 2 depicts the simulated experimental setup and the records obtained by moving the recording electrode away from the nerve (dy) maintaining constant its position in relation to the long axis of the nerve (dx). In the simulation, the negative waves are always represented upwards. The record amplitude decreases while its shape remains

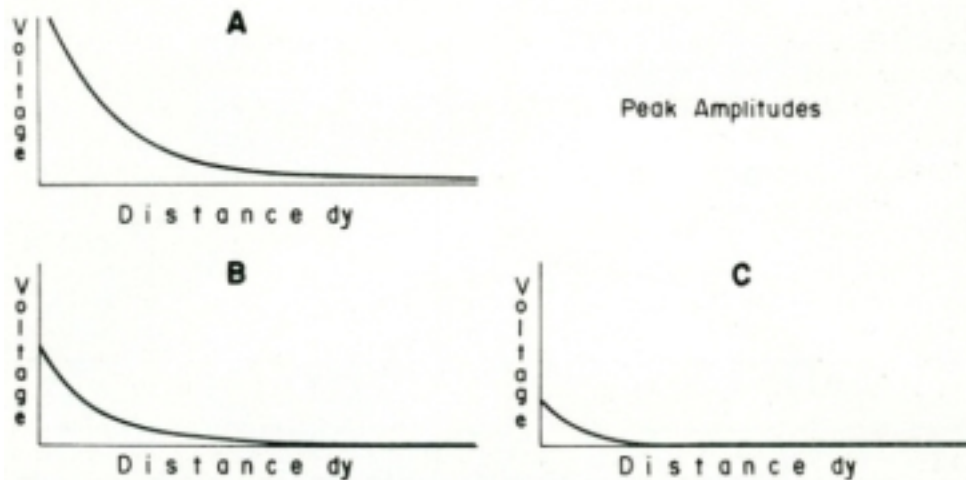


Fig. 3. Plots of the peak amplitude of field potential components as a function of the distance from the electrode to the nerve (dy). In A, the peak value of N, In B and C peak values of P1 and P2 respectively. The graphs reveal that the field potential amplitude diminishes exponentially as the distance from the nerve to the electrode is increased.

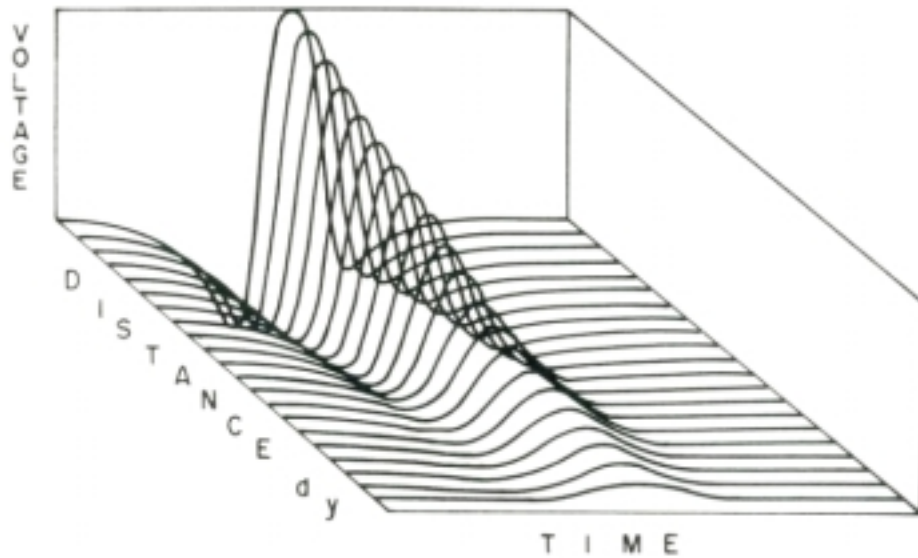


Fig. 4. Three dimensional plots of records generated while displacing the electrode away from the nerve. All the other parameters were kept constant. The amplitude of the field potential decreases while the latency and the shape of the compound action potential remain almost the same.

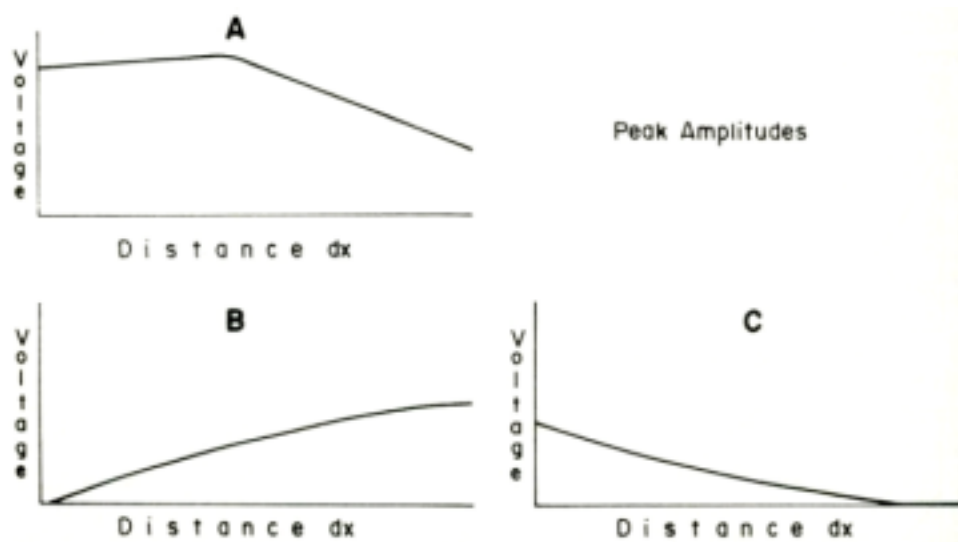


Fig. 5. Graphs of the peak amplitude of the action potential waves plotted as a function of the position of the electrode alongside the nerve (dx). In A, the curve reveals that the amplitude of the negative component increases as the electrode approaches the center of the nerve, then it diminishes as the electrode is moved toward the cut end of the nerve. In B, P1 increases as the electrode is moved away from the nerve entrance to the conductive paper. In C, the amplitude of P2 decreases as the electrode approaches the cut end of the nerve. These graphs reveal that the contribution of each dipole to the field potential, depends on it being leaving or approaching the recording electrode.

almost the same. Plots of the peak amplitude of each wave (positive-negative-positive) as a function of the distance between the electrode and the nerve show that the field potential amplitude diminishes exponentially as distance from the nerve (dy) increases (Fig. 3). Figure 4 shows a three-dimensional plot of a series of records obtained with the same experimental paradigm (increment dy , while dx is kept constant). It could be clearly appreciated that the only effect of moving the electrode away from the nerve is to reduce the amplitude of the potentials recorded, with no modification of the relative duration and amplitudes of the waves which compose the action potential.

If the electrode is displaced in dx while dy is maintained constant, the amplitude and the duration of the different waves of the record vary as a function of the electrode position. Figure 5 shows the plots of the peak amplitudes which result when the electrode is moved alongside the nerve. The peak amplitude of the negative wave remains almost constant, except for the records made in the neighborhood of the cut end of the nerve (Fig. 5A). In this region, the negative potential diminishes its amplitude and spreads for a longer time. The amplitude of the positive waves also varies depending on the electrode position, the depolarization wavefront being more prominent when the recording is performed near the entry of the nerve to the conductive sheet (Fig. 5C). As the electrode is brought to the center of the nerve, the typical positive-negative-positive wave develops. Finally, as the electrode is moved toward the cut end of the nerve, the repolarization elicited wave becomes more prominent (Fig. 5B). Figure 6 shows a three-dimensional plot

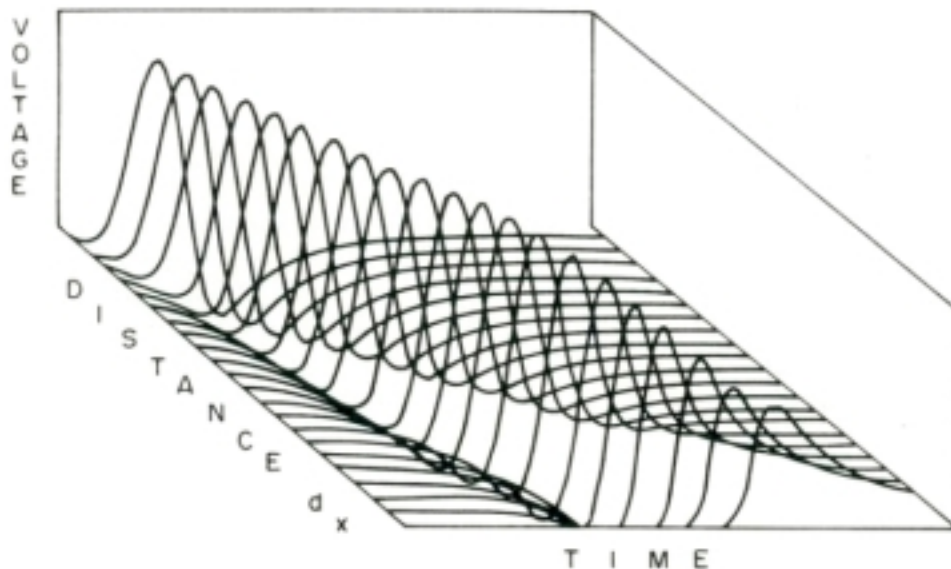


Fig. 6. Three-dimensional plot created with a set of records obtained while shifting the electrode in dx . The latency and shape of action potential change as a function of the electrode position. At the end of the nerve segment, a mainly positive potential will be recorded, since the segment is being approached by the action potential but, being unexcitable at its end, no inward current will be generated.

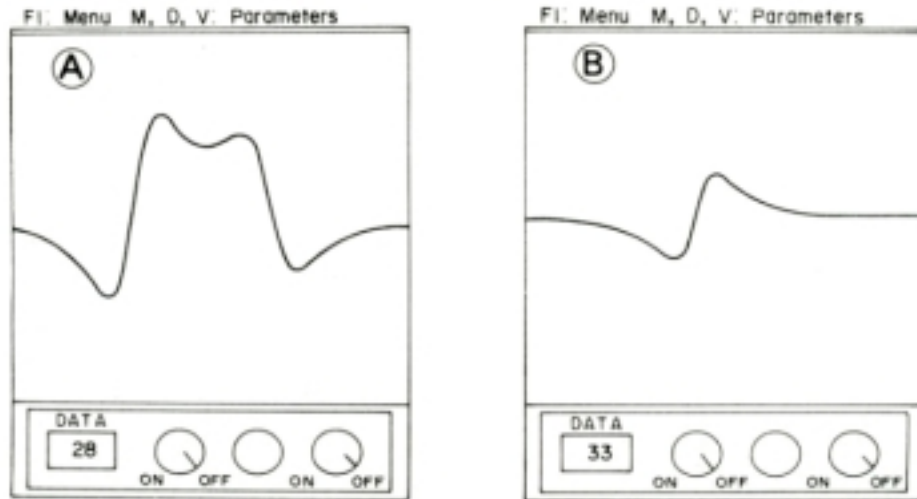


Fig. 7. Effect of dipole distance upon the record shape. Since the action potential is calculated in basis of the addition of the depolarization and repolarization vectors, changing the dipole distance strongly influences the shape of the record. In A, the action potential duration was increased from 1 to 5 ms. A hollow of the negative wave develops revealing the contribution of each dipole to the action potential. In B, the action potential duration was zero, thus the record is similar to that of a single dipole.

of a series of records obtained with the same experimental paradigm, that is maintaining dy constant as dx changes. The records show that latency and shape of action potential vary as a function of dx . At the point of origin, as well as at the end of the nerve segment, potential shape will tend to be dominated by positive waves. This is due to the fact that these points are continuously being leaving or approached by the action potential, thus the contribution of the current sources to the field potential becomes more intense.

If the separation between depolarization and repolarization dipoles of an action potential is increased, either by increasing the velocity of conduction or the action potential duration, the negative wave of the action potential becomes diphasic, revealing the contribution of each dipole to the generation of the field potential (Fig. 7A). In contrast, if the separation between depolarization and repolarization vectors is made to be zero, the record obtained reproduces the field potential of a single dipole. Typically a diphasic potential develops (Fig. 7B).

Conclusion

The simulation allows the user to completely reproduce Lorente de Nó's experiment, which is a classical demonstration in general physiology courses. The program has been used in several graduate general physiology courses taught at our University. By using the simulation before the experimental preparation, the students acquainted themselves with the required setup, with the results that should be expected, and how to analyze them in order to obtain the maximum information from the experiment, thus increasing their

experimental success. Based on the analysis of the results they were able to understand the importance of not varying two parameters at a time.

The simulation has been designed in an interactive form; nerve action potential animation and continuous display of nerve recordings and graphics, along with the freedom to select the characteristics of the oscilloscope display, maintains the user's interest. An introductory text tutorial and a users guide, both written in Spanish and English, allows usage of the program without the mediation of a teacher.

In this simulation no consideration has been given to other variables which might be relevant in determining the characteristics of a compound nerve action potential recording, such as: inhomogeneities of the conducting media, morphology changes of the segment being recorded (i.e. branching of the nerve), variations in the ionic composition of the conducting medium, etc.

We think that the use of computer simulations in general physiology courses should be highly recommended. It permits the students to advance in their comprehension of the illustrated phenomena [13], and also, to realize the basics of some elementary computational models, and the way in which algorithms and computer constructs are performed. Hence, students should be encouraged to use the simulation not only for the specific purposes for which it has been designed, but to understand the way in which the process has been simulated, and the minimal elements which were considered as essential to model a complex physiological phenomenon [14, 15].

Availability

A diskette containing the program is freely available from the authors, either in Spanish or English, by sending a blank diskette and 5.00 US dollars (or its equivalent in diskettes) for postage handling.

Also available at: <http://www.fisio.buap.mx>

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