Understanding the electrical behavior of the action potential in terms of elementary electrical sources

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Rodriguez-Falces J. Understanding the electrical behavior of the action potential in terms of elementary electrical sources. Adv Physiol Educ 39: 15–26, 2015; doi:10.1152/advan.00130.2014.—A concept of major importance in human electrophysiology studies is the process by which activation of an excitable cell results in a rapid rise and fall of the electrical membrane potential, the so-called action potential. Hodgkin and Huxley proposed a model to explain the ionic mechanisms underlying the formation of action potentials. However, this model is unsuitably complex for teaching purposes. In addition, the Hodgkin and Huxley approach describes the shape of the action potential only in terms of ionic currents, i.e., it is unable to explain the electrical significance of the action potential or describe the electrical field arising from this source using basic concepts of electromagnetic theory. The goal of the present report was to propose a new model to describe the electrical behaviour of the action potential in terms of elementary electrical sources (in particular, dipoles). The efficacy of this model was tested through a closed-book written exam. The new approach allowed students to appreciate that the amplitude and sign of the extracellular electrical potential arising from the action potential are determined by the spatial derivative of this intracellular source. The proposed model, which incorporates intuitive graphical representations, has improved students' understanding of the electrical potentials generated by bioelectrical sources and has heightened their interest in bioelectricity.

biomedical engineering; electrostatic theory; dipole; membrane potential; bioelectrical source; extracellular potential

ONE OF THE FIRST TOPICS addressed in bioelectricity courses is the description of the “elementary electrical sources,” such as monopoles and dipoles, and their associated electrical fields (2, 16). Subsequently, the theoretical fundamentals of membrane potentials at rest (which includes equilibrium potentials and resting potentials) and when the fiber is excited (the so-called action potential) are presented. The action potential represents the true “excitation source” in electrophysiology studies, as the propagation of this source along the muscle fiber yields an extracellular potential in the region outside the fiber that can be recorded by an electrode. The action potential consists of a rapid depolarization followed by a slower recovery to resting conditions. This apparently simple time course is the result of complicated changes in the conductance of Na⁺ and K⁺. Hodgkin and Huxley (8) derived a mathematical model to calculate Na⁺ and K⁺ conductances by fitting experimental measurements of ionic currents in the giant axon. Although the Hodgkin and Huxley equations provide a compact, comprehensive description of the AP, their daunting complexity makes them less suitable for teaching purposes. More importantly, the intricate formulation of Hodgkin and Huxley theory does not permit an easy interpretation of the electrical behavior of the AP.

Perhaps the major limitation of the Hodgkin and Huxley equations as a pedagogical tool is that they describe the shape of the action potential in terms of ionic currents only, i.e., they do not relate or express the profile of the action potential as a function of elementary electrical sources (monopoles and dipoles) (8). As a result, the electrical significance of the shape of the action potential is lacking in this model. For example, what is the “electrical” implication of having a rising (depolarization) phase followed by a falling (repolarization) phase (19)? Another limitation of the Hodgkin and Huxley model is that, as action potential is not expressed in terms of known electrical sources, it is difficult to predict how changes in the shape of this intracellular potential are translated into changes in the characteristics of the extracellular potential. This is a point of major importance in quantitative electromyography: to be able to infer alterations in the anatomic and physiological properties of the biological sources from “measurable” changes in waveform parameters of extracellular potentials (16, 23). In addition, an electrical model of the action potential based on elementary sources would facilitate the understanding of how the extracellular potential develops as the distance from the electrode to these sources increases.

A widespread incorrect assumption among students, as well as clinicians, is that the action potential exists only as a function of time. Representations of the action potential in the clinical neurophysiology field have surely contributed to this incorrect perception (5). However, because of its propagation along the fiber, an action potential also spreads out along the fiber as a function of space. In fact, at any moment after the fiber activation, an actual portion of membrane of ~10 mm is depolarized due to action potential propagation (4, 16). The spatial length of the action potential is of comparable order of magnitude as the distance from muscle fibers to the recording electrode in both intramuscular and surface electromyography recordings. This has a paramount importance as it implies that the action potential cannot be considered as a lumped (point) source, such as a monopole or a dipole; rather, it should be treated as a distributed source whose voltage varies gradually along the spatial extent of the muscle fiber.

Previous pedagogical studies on the principles underlying membrane potentials were more interested in explaining the effect of ionic currents and concentrations on the action potential than on describing the electrical significance of such potential. For example, Ribeiro-Filho et al. (17) demonstrated the relationship between the equilibrium potential for K⁺ and...
transmembrane electrical potential. In the same line, Wright (25) provided students a general view of the quantitative relationship that exists between transmembrane gradients for K⁺ and Na⁺. Other pedagogical works developed simple laboratory exercises to illustrate the generation of membrane potentials across plasma membranes (13) or simply to record transmembrane potentials (9, 26). However, to date, no study has proposed a model to describe the electrical field arising from the action potential in a simple, intuitive way.

The objective of the present study was to propose a new pedagogically oriented model to describe the electrical behavior of the action potential in terms of elementary electrical sources (in particular, dipoles). According to the author’s teaching experience, the dipole-based presentation of the action potential is suitable for teaching purposes because it is grounded on basic concepts of electromagnetic theory that are familiar to biomedical engineering students. The proposed model is believed to be convenient for both students and clinicians as it underlines the distributed character of the AP. The model presented here is in keeping with the trend of modern education to combine the rigor of mathematical analysis with more intuitive approaches such as schematic representations.

The Spatial Profile of the Action Potential of Human Muscle Fibers: Distributed Sources

The striated muscle is composed of a large number of striated muscle cells, colloquially referred to as “muscle fibers.” These cylindrical cells are arranged parallel to one another. Each muscle fiber cell is surrounded by a plasma membrane called sarcolemma (10), which has the property of being excited by electrical impulses coming from the motoneuron. Muscle contraction is created via the repeated activation of several groups of muscle fiber, each of which is controlled by a single motoneuron through its motor axon (10). Figure 1B shows a portion of a muscle fiber attached, at the neuromuscular junction, to the terminal branch of its axon.

When the muscle fiber is at rest, the plasma membrane maintains a nearly constant potential difference between the intracellular and extracellular space (Fig. 1B). This voltage is normally referred to as the resting potential and has a value of about −80 mV (Fig. 1C). This negative polarization is shown in Fig. 1B by a number of layers of negative signs. The fiber cell is activated via a nerve impulse generated by the motoneuron. Once the impulse reaches the neuromuscular junction, the membrane abandons the “polarized” state and starts a “depolarization” toward positive voltage values. The depolarization phase is rather fast (typically 0.3 ms), and it is followed by a more gradual repolarization phase, which brings the membrane back to its resting (negative) potential. The combination of depolarization and repolarization transitions forms the so-called transmembrane voltage, which is defined as the electrical potential outside of the cell (extracellular) minus the potential inside the membrane (intracellular). Since the transmembrane voltage can be assumed to equal the intracellular action potential (IAP) (3, 16), from now on we will use the term IAP to refer to the action potential (i.e., our excitation source).

The transmembrane current flows through the muscle tissue “prompted” by local electrophysiological processes. In fact, this flow of current in the tissue (i.e., the volume conduction) is the mechanism that allows extracellular potentials to exist and to be recorded at a certain distance from the sources (muscle fibers). The principle of volume conduction can be viewed as the biophysical version of Ohm’s law: the transmembrane current that flows through an ideally infinite volume, whose electric impedance is the inverse of the tissue electrical conductivity, generates a potential (extracellular) at any point in the volume.

As described above, the generation of the IAP at the neuromuscular junction is not instantaneous; rather, it takes ~2 ms for depolarization and repolarization phases to be formed completely (Fig. 1A). Moreover, because of its propagation along the fiber, an IAP does not merely exist as a function of time, where $T_{in}$ is the duration of the IAP (normally around 2 ms). B: schematic representation of a portion of muscle fiber in which two excitation sources [IAP($x$)] are propagating with velocity $v$ from the neuromuscular junction (NMJ) to the tendons. The polarization of the fiber membrane is represented by a number of layers of negative signs. C: representation of the IAP as a function of space, with its depolarization and repolarization phases. L is the spatial length of the IAP (typically around 10 mm).
time: it also spreads out along the fiber as a function of space. The length of the IAP profile along the fiber \( (L) \) is defined by the product of the IAP duration \( (T_{in}) \) and the propagation velocity \( (v) \) (Fig. 1C). This means that, at any moment while an IAP is propagating along the fiber, an actual portion of membrane of \( \sim 10 \) mm is depolarized. This spatial distance is greater than the typical electrode-to-fiber distances in concentric needle electromyography and comparable with those of surface electromyography. The implication is that, to model correctly the electrical activity generated by the IAP, this source cannot be considered as a lumped (point) source, such as a monopole or a dipole; rather, the whole spatial profile of the IAP must be taken into account. This means that the IAP must be treated as a distributed source, i.e., a function formed by an ensemble (collection) of point sources, the characteristics of which are determined by the value of the IAP at the corresponding membrane point.

The main objective of the present study was to combine biophysical principles and electromagnetic field theory to demonstrate that the bioelectrical source of human muscle fibers can be described as a sequence of lumped sources distributed along its spatial profile. The following description of the IAP is presented in a progressive, step-by-step manner so that each new concept introduced builds on or incorporates the information learned in earlier sections. The starting point of our progressive approach is the theory of the double (dipole) layer, which will be extended to the membrane of excitable cells.

**Modeling the Electrical Behavior of the Action Potential**

**Step 1: the concept of the double dipole layer.** The pioneer research of Helmholtz (7) established the principle of the electromotive surface, which provided the basis for the understanding of the potentials produced by excitable fibers. To develop his theory, the author brought in the concept of an electric double (dipole) layer and suggested that it can be applied to solve certain boundary problems in potential theory. Specifically, Helmholtz proposed that the potential produced by a uniform double layer at a point \( (P) \) in the surrounding medium \( [V(P)] \) can be calculated as the product of the solid angle \( (\Omega) \) subtended by the layer at \( P \) and the dipole moment of the layer \( (\Phi_{DL}) \), as shown in Fig. 2A. The dipole moment \( \Phi_{DL} \) is the product of the amount of charges per unit area and the layer thickness. In Fig. 2A, it is important to note that the fields of the negative and positive charges cancel, but the negative charges win out because they are slightly closer to \( P \), resulting in a negative potential at \( P \).

Let us now assume a closed surface with a double layer that is uniformly polarized (like the membrane of a muscle fiber membrane at rest). In this case, both the outer and inner layers of the closed surface (labeled as “out” and “in” in Fig. 2B) are “seen” under the same solid angle \( (\Omega) \) from the point of observation \( (P) \) as these layers are identical. However, the outer and inner layers “face” \( P \) with different signs. As a result, the potentials produced by these layers at this point have the same magnitude but opposite sign \( [V_{OUT}(+) \text{ and } V_{IN}(-)] \) as shown in Fig. 2B.

**Step 2: extending the concept of the double dipole layer to the membrane of excitable cells.** The concept of the double-layer source, however, had to wait almost a century before Wilson et al. (24) demonstrated that it can be applied to describe the electrical field around excitable cells. Wilson and colleagues proposed that, in terms of electrical properties, the membrane of an excitable cell essentially behaves as a double (dipole) layer. This idea is based on two important assumptions. First, since a potential difference exists across the thin membrane of an excitable cell, the inner and outer surfaces of the cell membrane can be associated to the oppositely signed layers defined by Helmholtz. Second, as the membrane can be considered a capacitor, the amount of charge per unit area at a certain point of the membrane is directly proportional to the value of the action potential at this point.

In the following sections, we will assume that our excitable cells have cylindrical shape, so that they resemble more closely the polygonal geometry of skeletal muscle fiber cells. This simplification will facilitate the description of the electrical field arising from an action potential and, in addition, is more consistent with the objective of the present work.

**Step 3: modeling the fiber membrane as polarized disks.** Let us consider a cylindrical uniformly polarized fiber that forms a closed surface. We now open such fiber at its right end by making a vertical cut through its cross-section, thereby removing the polarized disk-B, as shown in Fig. 3A. Under these conditions, the potential at \( P \) due to the opened fiber alone \( (V_{OP}) \) is not zero. However, by putting disk-B back into its original position, a completely closed polarized surface is
Fig. 3. A: schematic representation of a uniformly polarized fiber membrane opened at one of its ends and the extracellular potential generated by this fiber at P ($V_{OF}$). B: the extracellular potential produced at P by the opened fiber and the polarized disk that makes the membrane closed (disk-B) taken together should be zero, as they form a closed polarized surface. C: polarized disk-A, obtained by reversing the polarity of the charges of disk-B, produces a potential identical to that produced by the opened membrane.

Let us regard this potential as the sum of two separate contributions: $V_{OF}$ and the potential of disk-B at P ($V_{DISK-B}$). Since the potential at P must be zero, we have that $V_{OF} + V_{DISK-B} = 0$, which, in turn, means that $V_{OF}$ and $V_{DISK-B}$ are equal in magnitude but opposite in sign. Therefore, a double-layer disk with the polarity of the charges reversed ($V_{DISK-A}$; Fig. 3C) can replace the rest of the opened polarized fiber surface.

Let us now consider a portion of cylindrical uniformly polarized fiber that is opened at its two ends (Fig. 4B). Based on the above reasoning, this “opened” fiber could be replaced by two double-layer disks (located at the ends) with polarities opposite to those of the disks, which would make the fiber a closed surface (see above for details).

Let the fiber in A be opened at its two ends, it can be replaced by two polarized disks whose polarity is opposite to that of the disks that makes the membrane closed.

**Step 4:** modeling the transmembrane voltage as two stacks of double-layer disks distributed along the fiber. At this point, it is convenient to remember that our excitation source (i.e., the IAP) is not a lumped (point) source that occupies an infinitesimal portion of the fiber; rather, it spreads out along the fiber as a function of space, with a length of ~10 mm (Fig. 5A) (15, 16). However, it would be possible to represent the profile of such “distributed” source through a number of steps (or cylinders) of equal length (dx) that are opened at their ends. Since dx is infinitesimal, each step can be assumed to be uniformly depolarized according to the magnitude of the excitation IAP at the corresponding membrane portion (Fig. 5B).

As described above, each of these “open” steps could then be substituted by two double-layer disks with different polarity located at its two ends (Fig. 6A). By doing this, two layers with opposite polarity [represented by disks of different colors obtained, which implies that the potential at P due to the opened fiber and disk-B taken together should be zero (Fig. 3B). Let us regard this potential as the sum of two separate contributions: $V_{OF}$ and the potential of disk-B at P ($V_{DISK-B}$). Since the potential at P must be zero, we have that $V_{OF} + V_{DISK-B} = 0$, which, in turn, means that $V_{OF}$ and $V_{DISK-B}$ are equal in magnitude but opposite in sign. Therefore, a double-layer disk with the polarity of the charges reversed ($V_{DISK-A}$; Fig. 3C) can replace the rest of the opened polarized fiber surface.

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An electrical dipole is defined as a pair of equal electric charges of opposite polarity separated by finite distance from each other (Fig. 7A). The electrical potential generated by a dipole at $P$ [$V_d(P)$] can be computed as the sum of the fields generated by the negative and positive charges, as follows:

$$V_d(P) = \frac{I_0}{4\pi\sigma} \times \frac{1}{r} + \frac{I_0}{4\pi\sigma} \times \frac{1}{r_1}$$

where $I_0$ is the strength of the charge and $\sigma$ is the electrical conductivity. If the distances $r$ and $r_1$ are large compared with the separation between the sink and the source ($d$), then $r_1$ can be expressed in terms of $r$ as follows:

$$\frac{1}{r_1} = \frac{1}{r} + \frac{\partial (1/r)}{\partial d} \times d$$

Substituting Eq. 2 into Eq. 1 yields the following:

$$V_d(P) = \frac{I_0}{4\pi\sigma} \times \frac{\partial (1/r)}{\partial d} \times d = \frac{I_0}{4\pi\sigma} \times \left[ \nabla \left( \frac{1}{r} \right) \times \vec{a}_x \right] \times d$$

In Eq. 3, the partial derivative $\partial (1/r) / \partial d$ represents the rate of change in the field that results from displacing $I_0$ in the direction of the displacement $d$ (i.e., in the $x$-axis); therefore, it can be replaced by the gradient of $1/r$ in the $x$-axis. $\vec{a}_x$ is an unit vector in the direction of the displacement $d$.

For a mathematically defined dipole, the approximations $d \to 0$ and $I_0 \to \infty$ must be fulfilled such that $I_0 \times d = p$ remains constant and finite (where $p$ is the strength of the dipole). Equation 3 can then be written as follows:

$$V_d(P) = \frac{I}{4\pi\sigma} \times \nabla \left( \frac{1}{r} \right) \times \vec{a}_x \times p$$

Now the gradient operation can be expressed as follows:

$$V_d(P) = \frac{I}{4\pi\sigma} \times \left( \vec{a}_x \times p \right)$$
Consequently, combining Eqs. 4 and 5 leads to the following:

\[ V_d(P) = \frac{\mathbf{a}_s \times \mathbf{a}_s \times p}{4\pi\sigma \times r^2} \] (6)

The product of the unit vectors can be computed as \( \mathbf{a}_s \times \mathbf{a}_s = \cos \theta \), where \( \theta \) is the polar angle between the vectors. Substituting this expression into Eq. 6 yields one of the most used expressions for the field produced by a dipole \( p \) lying along the \( x \)-axis:

\[ V_d(P) = \frac{p}{4\pi\sigma} \times \frac{\cos\theta}{r^2} \] (7)

As described by Helmholtz (see Step 1: the concept of the double dipole layer), the potential generated by a polarized disk immersed in an infinite homogeneous medium at any point outside the disk (Fig. 7A) can be calculated as follows:

\[ V(P) = \Phi_{DL} \times \Omega \] (8)

where \( \Phi_{DL} \) is the dipole moment of the layer and \( \Omega \) is the solid angle subtended by the disk at \( P \) (Fig. 7B). In Fig. 7B, the magnitude of the solid angle subtended by the disk-CD can be calculated as follows using an infinite series:

\[
\Omega = 5 \frac{\cos\theta}{r^2} - \pi \left[ \frac{1 \times 3 a^4}{4} P_3(\cos\theta) - \frac{1 \times 3 \times 5 a^6}{4 \times 6} P_6(\cos\theta) \ldots \text{etc.} \right]
\] (9)

where \( S \) is the disk area, \( a \) is the disk radius, \( r \) is the distance from the disk center to \( P \), and \( \theta \) is the angle between the \( x \)-axis and the direction of the source-to-field unit vector. \( P_m(\cos\theta) \) represents the \( m \)th coefficient of Legendre. The series shown in Eq. 1 is convergent if the ratio of \( a \) to \( r \) is < 1.

If the radius of the disk (that of the muscle fiber) is small, then the solid angle subtended by it at any relatively distant \( P \) is nearly equal to \( (S \times \cos\theta)/r^2 \). For a disk polarized with a dipole moment \( \Phi_{DL} \), the potential at \( P \) can then be approximately defined by the following equation:

\[ V(P) = \Phi_{DL} \times \frac{S \cos\theta}{r^2} \] (10)

The similarity between Eqs. 7 and 10 implies that the potentials generated by a polarized disk and a dipole are equivalent. For this to be true, the single source and single sink of the dipole must lie very close together upon the axis of the disk and equidistant from its center, as shown in Fig. 7C. Note that the strength of this dipole is proportional to the product of the area of the disk (\( S \)) and the intensity to which it is polarized (\( \Phi_{DL} \)).

In the particular case of a skeletal muscle fiber cell, the equivalence between the potentials generated by a polarized disk and a dipole can be considered valid because the following two conditions are fulfilled. First, the diameter of human muscle fibers (typically ranging from 20 to 90 \( \mu \)m) is much smaller than the distance from the fiber axis to the recording point of the electrode except, perhaps, in the case of single-fiber electromyography recordings (22). Second, in the model proposed above, the fiber membrane is divided into steps (or cylinders) of infinitesimal length (\( dx \)), which means that the proximity between the source and single sink of the dipole is granted. In this connection, Plonsey (15) estimated that the error caused by such a source simplification is < 5% provided that the radial distance is five fiber radii or greater from the fiber axis.

Step 6: **modeling the action potential as a sequence of point dipoles distributed along its spatial profile.** Once the correspondence between the electrical behavior of polarized disks and dipoles has been proven, the presentation of the IAP as two stacks of double-layer disks distributed along the fiber (Fig. 8A, **top**) can be considered, to all practical purposes, equivalent to a model consisting of a collection of dipoles of different polarity lying along the fiber axis (Fig. 8A, **bottom**). Whereas this last presentation is intuitive and allows the student to recognize the distributed character of the excitation source (IAP), it does not permit an association of the direction and strength of the dipoles with the changes in voltage of the IAP.
along the spatial extent of the fiber. Thus, a more convenient way to “picture” this new IAP model is to place the different dipoles along the spatial profile of the IAP, as shown in Fig. 8D. With this presentation, it can be readily appreciated that the direction of the dipoles is determined by the sign of the IAP spatial derivative. As a result, the dipoles lying on the depolarization (rising) phase all have the same polarity, which is opposite to that of the dipoles distributed along the depolarization (falling) phase. Moreover, this graphical description helps the student realize that the strength of a given dipole is determined by the slope (derivative) of the IAP spatial derivative at the corresponding point of the membrane. This can be visually appreciated in Fig. 8D, where the differences in strengths of the distributed dipoles are represented by the different sizes of the dipoles (note that the dipoles located at the points of steepest rise and decay along the IAP profile have the largest sizes).

**Application of the Dipole-Based IAP Presentation**

Once the electrical model of the IAP spatial profile has been introduced, the next educational goal is to show students how this IAP presentation can facilitate the understanding of the formation of extracellular potentials.

The first application of the dipole-based IAP model is to illustrate how the different portions (phases) of the extracellular potential are generated as the IAP propagates along the fiber. To do this, let us consider the scenario shown in Fig. 9, which shows...
an electrode recording (recording point $P$) of the electrical activity generated by an IAP traveling toward the right tendon. The polarity of the extracellular potential produced at $P$ by the IAP is determined by the sign of the field generated by the dipoles of this IAP as they are “seen” from this point. In Fig. 9A, for example, $P$ is only directly exposed to the positive field of the dipoles that lie on the IAP rising phase, and, as a result, the extracellular potential produced at $P$ is positive. When the peak of the IAP is lined up with the electrode, as in Fig. 9B, $P$ is exposed to only the negative charges of dipoles, which results in the formation of the negative peak of the extracellular potential. When the IAP has been completely surpassed the electrode vertical and is close to the tendon, as in Fig. 9C, $P$ is only directly exposed to the positive field of the dipoles lying on the IAP falling phase, and, consequently, the extracellular potential produced at $P$ is positive again.

Another application of the dipole-based presentation of the IAP is to help students to predict how changes in the spatial profile of the IAP influence the characteristics of the extracellular potential. Let us consider two muscle fibers, one from a healthy subject and the other from a patient with severe impairment of the membrane. Because of the disease process, let us assume that the propagation velocity in the “impaired” fiber doubles that of the normal fiber. In this case, the spatial extension of the IAP ($2L$) in the former fiber will be twice as long as that of the normal fiber ($L$). With the amplitude of the IAP unchanged and the spatial profile significantly widened, the strengths of the dipoles lying on the profile of the “diseased IAP” are considerably reduced. As a result, the extracellular potentials generated in the diseased fiber (Fig. 10B) have smaller amplitude and longer spatial extension than those arising from the normal fiber (Fig. 10A).

**Overview of the Bioelectricity Course**

**Framework of the study.** A Masters Degree Program in Biomedical Engineering has been offered by the Public University of Navarra (Pamplona, Spain) since the academic year of 2007/2008. The contents presented in the present study are included in the Bioelectricity course, which has formed part of the Masters Degree Program since its beginning. Therefore, the results of teaching the dipole-based description of the IAP presented here have been collected during the last 7 yr. An average of 17 ± 4 students have participated in the Bioelectricity course each year. The only prerequisite to enter the Masters Degree Program is that students must have completed a Degree Program in Engineering or Medical Sciences. The main learning goals of the Bioelectricity course are listed below:

1. Understand the membrane potentials when the fiber is at rest.
2. Understand the membrane potentials when the fiber is excited.
3. Understand the generation of extracellular potentials.
4. Know the theoretical and practical aspects of electromyography, electrocardiology, and electroencephalography.

**Educational backgrounds of students**

Students enrolled in Bioelectricity course during the last 7 yr fell into two broad groups on the basis of their background.
profile. The first profile (comprising ~50–60% of students of the course) was characterized by a strong knowledge of signal processing analysis and signals and systems theory. The majority of these students graduated with a Telecommunication Engineering degree. The second profile (which represent ~20–30% of students) was characterized by an advanced knowledge of mechanics and industrial design. The rest of the students exhibited good knowledge in different areas, such as computer science, physics, or biology. Irrespective of their previous background, students must have a solid knowledge of mathematics and physics as well as a good understanding of electromagnetic theory before attempting to learn the material presented here.

Learning objectives of the topic. The learning goals of this topic were classified into the following four groups:

1. Elementary electrical sources and fields
   1.1. Recognize the elementary electrostatic sources (monopoles and dipoles).
   1.2. Know the mathematical expressions of the potentials produced by monopoles and dipoles.

2. Potentials produced by double-layer surfaces (disks)
   2.1. Understand the concept of the solid angle in both opened and closed double-layer surfaces.
   2.2. Recognize that the potential produced by a closed polarized surface at a point outside the surface is zero.
   2.3. Appreciate that a piece of fiber membrane can be substituted by two double-layer disks with different polarity located at its two ends.
   2.4. Know that the potential produced by a polarized disk is equivalent to that produced by a point dipole whose moment is proportional to that of the disk area.

3. Membrane potentials when the fiber is excited (dipole-based presentation of the IAP)
   3.1. Understand that voltage- and space-clamp montages allow an ability to cancel membrane capacitive current and know how these configurations can be used to separately measure Na⁺ and K⁺ currents.
   3.2. Understand that the overall objective of the Hodgkin and Huxley equations was to model the changes in the conductance of Na⁺ and K⁺ during the action potential.
   3.3. Know the depolarization and repolarization phases of an action potential and their duration.
   3.4. Appreciate that the depolarization and repolarization phases of the action potential correspond to the amplitude of the generated extracellular potential.
   3.5. Recognize that the potential can be modeled as a sequence of lumped dipoles.
   3.6. Understand that the slope of the spatial profile of the action potential corresponds to the amplitude of the generated extracellular potential.
   3.7. Understand that the sign of the electrical field generated by the depolarization phase of the IAP is opposite to that of the repolarization phase.

4. Application of the dipole-based IAP presentation
   4.1. Appreciate that the extracellular potential is generated as a result of the propagation of the intracellular potential along the fiber.
   4.2. Understand that the amplitude characteristics of an extracellular potential depend on the spatial profile of its corresponding intracellular potential.

Teaching Plan

Nearly half of the Bioelectricity course was devoted to teach the generation of intracellular and extracellular electrical potentials. The dipole-based IAP model presented here represents only a part of the topics related to membrane potentials at rest and under excited conditions. Thus, the contents presented in the present study were extended by other theoretical material (12, 16, 18, 20) as well as by a number of simulation programs written in Matlab (18). Specifically, each student was given a
list of tasks to be accomplished, which include the execution of computer programs to demonstrate a certain concept, modifying the parameters of various algorithms, and writing their own simulation programs. A total of four informational lectures (of ~90 min each) were given to show students the theoretical material presented here. These lectures covered the learning objectives outlined above.

Assessment of the Topic and Feedback From Students

Knowledge acquired during the theoretical sessions was evaluated by means of a closed-book 2-h written exam consisting of 12 questions. Of the 12 questions, 4 questions evaluated the learning objectives set in the present study. Most of the questions were concerned purely with theory, which included finding the mathematical solution of a problem, predicting the effects of changes in the shape of the IAP on the characteristics of extracellular potentials, and providing descriptive explanations of the membrane potentials at rest and under excited conditions. In addition, to measure the level of student satisfaction with the contents and methodology adopted in the present study, students were asked to fill in a short questionnaire. For each of the points in the questionnaire, students chose a score between 0 and 10.

Results

Students in the Bioelectricity course responded positively to the lectures related to the dipole-based IAP model. A summary of the scores obtained on the different learning objectives is shown in Table 1. As shown in Table 1, students obtained high marks in questions pertaining to elementary electrical sources and their associated fields. Initially, some students showed difficulties in understanding the concept of the double layer. In fact, students recognized that the theory of the solid angle and double layer was new to them. However, when this concept was applied to the membrane of an excitable cell, they assimilated it more easily, as demonstrated by the results shown in Table 1. Table 1 also shows that students were able to understand that the IAP spatial profile can be modeled as a sequence of lumped dipoles (third learning objective). Some students commented on the fact that the schematic figures that accompanied the explanations were especially helpful to conceptualize the distributed character of the IAP source. In addition, students were able to appreciate how changing the spatial profile of the IAP resulted in changes in the strength of its constituent dipoles, which, in turn, influenced the amplitude of extracellular potentials. Also, students were able to recognize how the different phases of the extracellular potential are generated as the IAP propagates along the fiber.

Data of students’ satisfaction with the teaching methods described in the present study are shown in Table 2. Table 2 shows that most students were highly satisfied with the theoretical lectures. This finding was partly attributed to the fact that these lectures were students’ first contact with a biological system and because they were attracted by the topic (points 3 and 4). Students also appreciated the fact that the proposed model for the IAP was presented in a progressive, step-by-step manner so that each new concept introduced incorporated information learned in earlier sections (points 1, 2, 4, and 5). In addition, students agreed that the material and methods presented here made the learning process easy and convenient (points 1, 4, and 5).

Discussion

Innovative contribution. After the pioneering studies of Helmholtz (7), a great effort has been put into determining an accurate representation of the excitation source of human muscle fibers. Most of this effort has come from the research community, and, as a result, the majority of IAP models that can be found in the literature are unsuitably complex for teaching purposes. The first key contribution was made by Wilson et al. (24), who put forward the idea that the action potential can be approximated as stacks of double-layer disks. This theory was further developed by Lorente de Nó (11), who demonstrated that each double-layer disk could be substituted by one single-layer source. It must be stressed that the source descriptions proposed by Wilson et al. and Lorente de Nó were relatively easy to understand and that they could have been easily adapted for teaching purposes had the authors pursued this goal.

Table 1. Level of attainment of the learning objectives of the topic

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<tbody>
<tr>
<td>Number of students</td>
<td>13</td>
<td>18</td>
<td>26</td>
<td>24</td>
<td>18</td>
<td>15</td>
<td>12</td>
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<tr>
<td>Learning objectives</td>
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<tr>
<td>1. Elementary electrical sources and fields</td>
<td>7.4 ± 1.3</td>
<td>7.9 ± 1.3</td>
<td>7.5 ± 1.4</td>
<td>8.4 ± 1.0</td>
<td>8.6 ± 1.4</td>
<td>8.4 ± 1.0</td>
<td>8.2 ± 0.9</td>
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<tr>
<td>2. Potentials produced by double-layer surfaces (disks)</td>
<td>6.2 ± 1.0</td>
<td>6.8 ± 1.1</td>
<td>7.2 ± 1.5</td>
<td>7.6 ± 1.3</td>
<td>7.3 ± 0.9</td>
<td>7.5 ± 1.2</td>
<td>7.3 ± 1.0</td>
</tr>
<tr>
<td>3. Membrane potentials when the fibre is excited (dipole-based presentation of the IAP)</td>
<td>7.3 ± 1.2</td>
<td>7.9 ± 1.2</td>
<td>8.2 ± 1.4</td>
<td>8.1 ± 1.7</td>
<td>8.6 ± 1.5</td>
<td>7.9 ± 1.2</td>
<td>8.2 ± 1.3</td>
</tr>
<tr>
<td>4. Application of the dipole-based IAP presentation</td>
<td>7.0 ± 1.2</td>
<td>7.3 ± 1.1</td>
<td>7.8 ± 1.3</td>
<td>8.3 ± 1.4</td>
<td>8.4 ± 1.3</td>
<td>8.0 ± 0.9</td>
<td>8.2 ± 1.1</td>
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</table>

Values are means ± SD; examination grades were scored from 1 to 10. Most students were highly satisfied with the theoretical lectures. This finding was partly attributed to the fact that these lectures were students’ first contact with a biological system and because they were attracted by the topic (points 3 and 4). Students also appreciated the fact that the proposed model for the intracellular action potential (IAP) was presented in a progressive, step-by-step manner so that each new concept introduced incorporated information learned in earlier sections (points 1, 2, 4, and 5). In addition, students agreed that the material and methods presented here made the learning process easy and convenient (points 1, 4, and 5). Data of students’ satisfaction with the teaching methods described in the present study are shown in Table 2.
Unfortunately for teaching, the idea of presenting the excitation source as a collection of elementary (point) sources was abandoned after the major works of Wilson et al. and Lorente de Nó. Subsequent authors were more interested in providing a model of the action potential that improves accuracy and/or enhances computational efficiency. This was achieved using analytic functions that closely resembled the profile of transmembrane voltages recorded experimentally. Clark and Plonsey (4) were the first to realize that the distribution of a transmembrane potential can be approximated mathematically. The authors found that the analytic function that provided the best fit consisted of a sum of three exponential distributions. Another widely known mathematical expression of the IAP was introduced by Rosenfalck (21) in 1969 and consisted of a combination of polynomial and exponential functions. This analytic function was highly appreciated by subsequent authors, who continued to use it with minimal modifications (1, 14). Perhaps the most pedagogically oriented analytic model of the IAP was proposed by Dimitrov and Dimitrova (6), which allowed the possibility of making independent changes in depolarization and repolarization phases of the IAP.

While the above analytic approximations are able to synthesize action potentials with high precision and low computational cost (two desirable features in research), they do not allow students to predict the characteristics of the electrical potential generated by this excitation source (an essential aspect in education). These analytic approximations, for example, do not permit an anticipation of how the spatial profile of the IAP profile would influence the amplitude of the electrical potential generated by this potential, as shown in Fig. 10. This represents an important limitation, as it prevents students from understanding that the slope of the IAP spatial profile corresponds to the amplitude of the generated extracellular potential (a learning objective of the present topic). In addition, in general, available analytic functions do not afford independent control of depolarization and repolarization phases of the IAP, which makes it impossible to dissociate the contribution of each of these phases to the extracellular potential generated (see Fig. 9). This is another important weakness of these formal approaches, as they do not permit students to realize that the fields generated by rising and falling portions of the IAP are of opposite polarity.

**Benefits for learning.** The spatial model of the IAP presented here is highly beneficial for students as it makes them reflect on the distributed character of this source. In this regard, it is important to provide students a clear justification for why the excitation source should be treated as a distributed function: the spatial length of the IAP is \( \approx 10 \) mm, and this length is greater to or comparable with the detection distance (i.e., distance from muscle fibers to the recording electrode) in both intramuscular and surface electromyography recordings. As a result, the IAP spatial profile is not “seen” as a point source from the electrodes; rather, it is seen as a collection of point sources, the characteristics of which are determined by the value of the IAP at the corresponding membrane point. Another way to understand the distributed character of the IAP is that the gradual variation of the IAP voltage along the spatial extent of the fiber greatly influences the characteristics of the generated extracellular potential.

Another important feature of the dipole-based presentation of the IAP is that this description helps students understand that the excitation source does not exist only as a function of time; at any moment while an IAP is propagating along the fiber, an actual portion of membrane of \( \approx 10 \) mm is depolarized. In fact, the amplitude characteristics of the electrical field generated by the IAP are more coupled to the spatial than to the temporal profile of this function, as explained above (Modeling the Electrical Behavior of the Action Potential, Step 6: modeling the action potential as a sequence of point dipoles distributed along its spatial profile).

Since the dipole-based model of the IAP is based on elementary electrical sources, the electrical potential arising from distributed sources can be explained using basic concepts of electromagnetic theory with which students are already familiar. This makes us believe that our IAP presentation has a clear pedagogical orientation as it allows students to apply their previous knowledge. Moreover, the fact that our description of the excitation source is based on principles of classical electromagnetic theory makes it generalizable to bioelectrical sources of other excitable cells in the human body (such as nerve and cardiac cells).

Representation of the IAP as a sequence of lumped dipoles distributed along its spatial profile provides an approach to the excitation source that is more accessible and amenable to
adaptation for teaching purposes. Just as the voltage of the IAP varies gradually along the spatial extent of the fiber membrane, a number of dipoles of different strengths and orientation are lying along the spatial profile of this excitation source. The IAP description presented here provides students the necessary tools to predict the strength and sign of these dipoles. The construction of the IAP model is made in a progressive, step-by-step manner, and this is advantageous for the students to address the learning objectives stated above (in Learning objectives of the topic).

Conclusions. In the present study, a new pedagogically oriented model to describe the electrical behavior of the intracellular action potential of human muscle fibers is presented. The model is based on basic concepts of electromagnetic field theory, and it also incorporates detailed graphic imagery to help students conceptualize the electrical potential arising from the bioelectrical source. The proposed model presents the action potential as a collection of dipoles distributed along its spatial profile. The approach responds to the needs of biomedical engineering to understand that the bioelectrical source of muscle fibers has a distributed character and that it does not merely exist as a function of time; it also spreads out along the fiber as function of space. In addition, the proposed model has proved useful in showing students that 1) the amplitude of the electrical potential generated by the bioelectrical source is proportional to the derivative of the spatial profile of this source and 2) the electrical potentials produced by rising and falling phases of the bioelectrical source have opposite polarity. Data from student evaluations indicate that presenting the bioelectrical source in terms of elementary electromagnetic sources allowed students to obtain a deeper understanding of the formation of electrical potentials and clearly increased their motivation to obtain their Master of Biomedical Engineering degree.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: J.R.-F. conception and design of research; J.R.-F. performed experiments; J.R.-F. analyzed data; J.R.-F. interpreted results of experiments; J.R.-F. prepared figures; J.R.-F. drafted manuscript; J.R.-F. edited and revised manuscript; J.R.-F. approved final version of manuscript.

REFERENCES