A novel approach to teach the generation of bioelectrical potentials from a descriptive and quantitative perspective

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Rodriguez-Falces J. A novel approach to teach the generation of bioelectrical potentials from a descriptive and quantitative perspective. Adv Physiol Educ 37: 327–336, 2013; doi:10.1152/advan.00064.2013.—In electrophysiology studies, it is becoming increasingly common to explain experimental observations using both descriptive methods and quantitative approaches. However, some electrophysiological phenomena, such as the generation of extracellular potentials that results from the propagation of the excitation source along the muscle fiber, are difficult to describe and conceptualize. In addition, most traditional approaches aimed at describing extracellular potentials consist of complex mathematical machinery that gives no chance for physical interpretation. The aim of the present study is to present a new method to teach the formation of extracellular potentials around a muscle fiber from both a descriptive and quantitative perspective. The implementation of this method was tested through a written exam and a satisfaction survey. The new method enhanced the ability of students to visualize the generation of bioelectrical potentials. In addition, the new approach improved students’ understanding of how changes in the fiber-to-electrode distance and in the shape of the excitation source are translated into changes in the extracellular potential. The survey results show that combining general principles of electrical fields with accurate graphic imagery gives students an intuitive, yet quantitative, feel for electrophysiological signals and enhances their motivation to continue their studies in the biomedical engineering field.

THE STUDY OF ELECTROPHYSIOLOGY has experienced a rapid progress mainly due to the creative, meticulous, and accurate experimental studies conducted by many investigators. In past decades, research articles were conducted using mainly a descriptive approach, i.e., they reported their experimental findings primarily by precise explanations and with the aid of meaningful diagrams (15). Similarly, early textbooks in electrophysiology relied mainly on descriptions and illustrations to describe the phenomena, leaving little space for theoretical formulations and mathematical analysis. However, in recent years, the field has progressively incorporated the electromagnetic field theory, which allows one to describe electrophysiological phenomena from a quantitative perspective. Using this electromagnetic theory, authors have made an effort to develop theoretical formulations with which to explain their experimental observations (10, 15).

Generally, courses on bioelectricity (electrophysiology) begin with a presentation of the “elementary electrical sources,” monopoles and dipoles, and their associated electrical fields (2, 15). The second topic normally addressed is the excitable cell, which represents the “elementary electrophysiological source” that gives rise to both intracellular and extracellular action potentials (15). As an example, in the context of electromyography, activation of the excitable cell (muscle fiber) generates a voltage across its membrane (from now on referred to as intracellular potential), and the propagation of this voltage along the muscle fiber yields a potential in the region outside the fiber (hereafter referred to as extracellular potential). An in-depth understanding of the generation of extracellular potentials is of paramount importance as it provides the basis for a correct interpretation of electromyographic and electrocardiographic signals. However, most theoretical models proposed to characterize extracellular potentials have been developed for research purposes (1, 4, 12, 13, 14) and are less effective as a pedagogical tool. First, they use complex mathematical formulae that give no chance for transparent physical interpretations (1, 13). Second, with the exception of convolutional models (which allow one to recognize the excitation source and the system response) (4, 12), the rest of the approaches based on electromagnetic theory are much less intuitive (1, 14).

Perhaps the most significant drawback of traditional methods is that they do not facilitate the conceptualization of how the extracellular potential is progressively generated as the excitation source (the intracellular potential) propagates along the fiber. The inability to create a mental picture of the formation of the electrical field around a fiber is a critical problem that prevents students from acquiring the foundational knowledge with which to understand subsequent concepts in bioelectricity. A second disadvantage of classical methods is that they do not allow student to predict how changes in the shape of the intracellular potential are translated into changes in the morphology of the extracellular potential (1, 4). This is precisely one of the missions of quantitative electromyography (15, 18): to associate alterations in the waveform parameters of extracellular potentials with changes in the anatomic, physiological, and functional properties of the biological structures and sources. Moreover, these traditional approaches do not students permit to visualize how the extracellular potential develops with increasing distance from the source, and this is a crucial point since the distance from the electrode to the source cannot be controlled by the electrophysiologist (5, 17, 18).

There have been some attempts to show, in a pedagogical way, the formation of bioelectrical potentials, including standard laboratories (6, 8, 11, 16, 22), project-based laboratories (20), and theoretical methods (21). However, these approaches have been mainly focused on the intracellular potential. The formation of the extracellular electrical potential around a fiber is a complicated issue, mainly due to the fact that the excitation source is not a point (lumped) source but a distributed function whose voltage varies gradually along the spatial extent of the muscle fiber. Thus, a reasonable way to simplify the problem would be to approximate the spatial profile of the bioelectrical
source by a sequence of point sources and then to calculate the individual contribution of each point source to the total extracellular potential.

The objective of this study is to present a novel pedagogical-oriented method to conceptualize the formation of extracellular potentials around a muscle fiber from both a descriptive and quantitative perspective. The proposed method is believed to be particularly convenient for biomedical engineering and medical students as it is based on basic concepts of electrostatic theory with which they are already familiar. Special emphasis is directed toward facilitating an intuitive perception of how the different portions of the excitation source give rise to the different parts of the extracellular potential. Thus, the approach presented here is in line with the trend of modern science of combining the rigor and accuracy of mathematical formulations with more intuitive descriptions and graphic representations.

METHODS

Overview of the Bioelectricity Course

Context of the study. The Public University of Navarra (Pamplona, Spain) has offered a Master’s Degree program in Biomedical Engineering since 2007. Ever since then, the Bioelectricity course has been included as a compulsory subject in the Master’s Degree program. Thus, the present study describes the methodology used and evaluation results obtained during the last 6 academic years. An average of 19 ± 4 students has been enrolled in the Bioelectricity course each year. The only prerequisite for entering the course is that students must have completed a degree program in Engineering or Medical Sciences.

Educational backgrounds. Over the years, students attending the Bioelectricity course could be roughly divided into two groups according to their educational background. The first profile includes students knowledgeable in signal processing, signal analysis, and computer programming. The majority of these students have graduated from the Telecommunication Engineering degree and represented ~50% of total students in the course. The second profile comprised students with advanced skills of mechanical engineering and industrial design. This group contained ~30% of total students in the course. The rest of the students (~20%) exhibited good knowledge in different areas, such as computer science, physics, or biology. As can be seen, most of our students had little or no previous knowledge on physiology and biology. To overcome this lack of background, the first lectures were devoted to basic knowledge of physiology, anatomy, and biological systems.

Learning objectives of the topic. The main learning goals of this topic were classified in four groups:

A. Polarization of the membrane in passive (resting) and active (excited) conditions
   A1. Understand the concepts of membrane polarization and transmembrane voltage
   A2. Appreciate that the transmembrane voltage is not lumped but distributed along the spatial length of the fiber
   A3. Know the elementary electrostatic sources (monopoles and dipoles)
   A4. Recognize that the intracellular potential can be modelled as a sequence of lumped dipoles

B. Generation of intracellular potentials
   B1. Recognize the basic features of nerve and muscle intracellular action potentials (IAPs)
   B2. Understand that intracellular potentials are the result of exchange of ions across the fiber membrane
   B3. Comprehend the Hodgkin and Huxley model for the cell membrane during an action potential

C. Generation of extracellular potentials
   C1. Know the extracellular potentials generated by electrostatic monopoles and dipoles
   C2. Understand the extracellular potentials generated by a dipole propagating along a muscle fiber
   C3. Understand the extracellular potentials generated by the bioelectrical source (IAP) propagating along a muscle fiber
   C4. Understand the formation of the extracellular potential in terms of the potentials generated by the dipoles modeling the IAP
   C5. Appreciate that the formation of the extracellular potential is the result of interactions between positive and negative fields and so that the phenomenon of cancellation is present

D. Effects of fiber-to-electrode distance and IAP on extracellular potentials
   D1. Appreciate that the formation of the extracellular potential is strongly dependent on the fiber-to-electrode distance
   D2. Understand that the formation of the extracellular potential is highly dependent on the spatial length of the IAP

Presentation of the Bioelectrical Source as a Sequence of Lumped Dipoles

Striated skeletal muscle is made up of individual components known as “muscle cells,” sometimes colloquially referred to as “muscle fibers.” These elongated, cylindrical cells are arranged parallel to one another, and each one is surrounded by a plasma membrane called the sarcolema (9). The motor unit is the system formed by a single motoneuron and all the muscle fibers that it innervates and represents the anatomic and functional unit of a skeletal muscle (Fig. 1A). Muscle contraction is generated by the repeated activation of several motor units.

The plasma membrane of the muscle fiber actively maintains a nearly constant potential difference between the intracellular and extracellular space. This voltage is normally referred to as the resting potential and has a value of about ~80 mV (Fig. 1B). Thus, under resting conditions, the muscle fiber can be said to be “negatively polarized” (19). The muscle cell is activated by electrical impulses coming from the motoneuron. This forces the cell membrane to abandon its “polarized” state and to start a rapid “depolarization” toward positive voltage values, which is followed by a more gradual repolarization back to the resting (negative) potential. The combination of depolarization and repolarization transitions forms the so-called transmembrane voltage, typically referred to as an action potential. The transmembrane voltage is defined as the electrical potential outside of the cell (extracellular) minus the potential inside the membrane (intracellular). The extracellular potential is practically zero, and thus the transmembrane voltage approximately equals the IAP (3, 15).

The main objective of the present study is to provide an intuitive approach to understand the generation of the extracellular potential as a result of the propagation of the IAP along the skeletal muscle fiber (Fig. 1A). To do this, the first step is to assume that our bioelectrical source (i.e., the IAP) can be described as a sequence of infinite lumped dipoles distributed along its spatial profile, as shown in Fig. 1C. The basis for this approximation can be found in Dimitrov and Dimitrov (5). Based on the author’s teaching experience, the dipole-based presentation of the IAP is very convenient for pedagogical purposes as it allows students to conceptualize a “complex” bioelectrical source, such as the IAP function, as a collection of simpler and well-known elementary sources, such as the dipole. The mathematical formulation and graphic representation of the extracellular potential produced by a “static” dipole and a “propagating” dipole are present next.

Extracellular Potential Generated by “Static” and “Moving” Dipoles

Electrostatic dipole potential. A dipole consists of two point electric charges of opposite polarity separated by a small distance. In the context of bioelectricity, a dipole is a combination of a current
source and a current sink located in close proximity to one another. The electrical potential generated by a dipole at a field point \( P \) can be computed as the sum of the fields generated by the “sink” and the “source,” where the distance from the sink to point \( P \) is \( r \), whereas that from the source to point \( P \) is \( r_1 \). The geometry is shown in Fig. 2. The total dipole field \( \Phi_d \) can be calculated as follows:

\[
\Phi_d = -\frac{I_0}{4\pi\sigma} \times \frac{1}{r} + \frac{I_0}{4\pi\sigma} \times \frac{1}{r_1}
\]  

(1)

where \( I_0 \) is the strength of two equal oppositely charged point sources and \( \sigma \) is the conductivity of the muscle tissue. If the distances \( r \) and \( r_1 \) are large compared with the separation between the sink and source (\( d \)), then \( r_1 \) can be expressed in terms of \( r \) as follows:

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

(2)

Accordingly, \( \Phi_d \) can be found from Eq. 1 as follows:

\[
\Phi_d = -\frac{I_0}{4\pi\sigma} \times \frac{\partial (1/r)}{\partial d} \times d
\]  

Fig. 2. Dipole configuration as two equal oppositely charged point sources of strength \( I_0 \) whose separation (\( d \)) is small. The potential produced by the dipole is calculated at point \( P \). \( r \), distance from the sink to point \( P \); \( r_1 \), distance from the source to point \( P \); \( \vec{a}_s \), source-to-field unit vector; \( \theta \), angle; \( \vec{p} \), an example single dipole traveling along a muscle fiber from the neuromuscular junction (NMJ) toward the tendon.

In Eq. 3, the partial derivative \( \partial (1/r)/\partial d \) should be interpreted as the rate of change in the field that results from displacing \( I_0 \) in the direction of displacement \( d \) (i.e., in the \( x \)-axis). Thus, the partial derivative can be rewritten as follows:

\[
\frac{\partial (1/r)}{\partial d} = \nabla (-) \times \vec{a}_s
\]  

(4)

where \( \vec{a}_s \) is a unit vector in the direction of displacement \( d \). Substituting Eq. 4 in Eq. 3 yields the following:

\[
\Phi_d = -\frac{I_0}{4\pi\sigma} \times \left[ \nabla (-) \times \vec{a}_s \right] \times d
\]  

(5)

For a mathematically defined dipole, the approximations \( d \to 0 \) and \( I_0 \to \infty \) must be fulfilled such that \( I_0 \times d = p \) (where \( p \) is a dipole) remains constant and finite. Equation 5 can then be written as follows:

\[
\Phi_d = \frac{1}{4\pi\sigma} \times \nabla (-) \times \vec{a}_s \times p
\]  

(6)

Now, the gradient operation allows the following expression:

\[
\nabla (-) = \frac{\vec{a}_s}{r^2}
\]  

(7)

where \( \vec{a}_s \) is the source-to-field unit vector. Consequently, from Eq. 6, \( \Phi_d \) can be expressed as follows:

\[
\Phi_d = \frac{\vec{a}_s \times \vec{a}_s \times p}{4\pi\sigma \times r^2}
\]  

(8)

The product of the unit vectors can be computed as follows:

\[
\vec{a}_s \times \vec{a}_s = \cos \theta
\]  

(9)

where \( \theta \) is the polar angle between the vectors. Substituting Eq. 9 in Eq. 8 yields one of the most used expression for the field produced by a dipole (\( p \)) lying along the \( x \)-axis:
Potential generated by a single dipole propagating along the muscle fiber. Let us consider a hypothetical scenario in which one single dipole (p) is traveling along a muscle fiber from the neuromuscular junction toward the tendon, as shown in Fig. 3A. Such a scenario does not represent a real situation in physiology as human bioelectrical sources are always formed by a collection of dipoles of different magnitudes (5). However, for teaching purposes, it is useful to isolate the activity of a unit dipole as it allows us to calculate the different magnitudes (5).

By defining $\phi_d$ as the hypothetical potential that this dipole would generate at a certain point to isolate the activity of a unit dipole as it allows us to calculate the different magnitudes (5). However, for teaching purposes, it is useful to use the dipole equations presented above, and more specifically Eq. 10, to illustrate how the detection conditions affect the characteristics of potential generated by a dipole. More specifically, we show the influence of fiber-to-electrode distance (the so-called radial distance) on both the amplitude and duration of the dipole potential. As shown in Fig. 4A, when the electrode is placed in close proximity to the fiber ($r < 0.2$ mm), the resulting potential is of large amplitude and short duration, whereas for electrode locations further away from the fiber (as shown in Fig. 4B), the generated dipole potential is significantly smaller and wider. The observed changes in amplitude should not be surprising as Eq. 10 predicts a decrement in the magnitude of the dipole potential with increasing $r$. The explanation as to why the duration of the potential is so greatly influenced by $r$ is shown in Fig. 4. When the electrode is close to the fiber (Fig. 4A), the distance from the moving dipole to the recording point ($d$) and $r$ are of the same order of magnitude for a very narrow portion of the fiber. In contrast, when the electrode is far from the fiber, $d$ and $r$ take comparable values for a much longer piece of the fiber (Fig. 4B).

**Lines of positive and negative maxima of a dipole source.** As described above, the IAP source can be modeled as a sequence of infinite dipoles, and the potential generated by each of these dipoles when they propagate along the fiber is highly dependent on $r$. As a consequence, understanding of the interactions between the potentials arising from all the dipoles that form the IAP and visualization of how these interactions change with $r$ can be extremely complicated. To facilitate the conceptualization of the above interactions, it will be useful to have a simple representation of the potential produced by a dipole at different $r$ values, as described above.

Let us consider a scenario where three electrodes placed at different $r$ values ($r_1 < r_2 < r_3$) are recording the electrostatic activity generated by a single dipole propagating along a fiber, as shown in Fig. 5A. The general definition of $r$ is as follows: $r = \sqrt{(y^2 + z^2)}$. As shown in Fig. 5, we assume that $z = 0$ (i.e., the electrode is placed in the plane $z = 0$), and therefore one can safely says that $y = r$. The potentials recorded by each of the three electrodes are plotted as a function of space in Fig. 5B. In Fig. 5B, the points of maximum and minimum voltage are indicated for each potential. As shown in Fig. 5B, as $r$ increases, the $x$-coordinate of the maximal point of the potential is displaced further away from the zero line ($l_{x1} < l_{x2} < l_{x3}$).

For a potential recorded at a known radial distance $r$, it will be highly desirable to derive the mathematical expression that provides the position in the $x$-axis of the maximum of such potential relative to the zero line ($x$). To do this, let us consider the dipole $p$ shown in Fig. 2. For the sake of clarity, the electrostatic field generated by a dipole is presented again:

$$\phi_d = -\frac{I_0}{4\pi\sigma} \times \frac{1}{r} + \frac{I_0}{4\pi\sigma} \times \frac{1}{r_1} \quad (11)$$

By defining $e$ as $e = I_0/4\pi\sigma$, Eq. 11 can then be expressed as follows:

$$\phi_d = \frac{e}{r_1} - \frac{e}{r} = \frac{r - r_1}{r_1 \times r} = \frac{e}{r_1 \times r} \quad (12)$$

The difference $r - r_1$ can be expressed as a function of $d$ and $\theta$. Equation 12 can then be rewritten as follows:

Fig. 3. A: schematic representation of a single dipole propagating along a muscle fiber with velocity $v$ from the NMJ toward the tendon. B: extracellular potential recorded at the electrode as a result of the dipole propagation.
Thus, for a given radial distance ($r_i$), the position ($r_1$ and $r_2$) or the source of the dipole). The assumption $r_1 \approx r$ is then valid, which yields the following:

$$\Phi_d = e \frac{d \cos v}{r_1} \times r$$

where $v$ is velocity. For distances typical of needle electrode recordings, $r$ and $r_1$ are several orders of magnitude larger than $d$ (the distance between the sink and the source of the dipole). The assumption $r_1 \approx r$ is then valid, which yields the following:

$$\Phi_d = e \frac{d}{r^2} \times \frac{x}{r} = e \times \frac{d x}{r} = e \times \frac{x}{r} \left(\frac{x^2 + y^2}{x^2}ight)$$

To obtain position of the maxima, it is necessary to calculate $\frac{d \Phi_d}{dx} = 0$, from which we obtain the following:

$$x = \pm \frac{y}{\sqrt{2}} = \pm 0.7 \times y$$

Thus, for a given radial distance ($r = y$), the position (in the x-axis) of the maximal points can be obtained using Eq. 15. More importantly, Eq. 15 provides the expression of the lines that contain the position of the extreme points of the field from the zero line (Fig. 5C).

In Eq. 15, the positive sign corresponds to the line that comprises the potential maxima ($A^+$), whereas the negative sign refers to the line containing the negative maxima ($A^-$). The lines of positive and negative maxima afford for a clear, straightforward representation of the potential produced by a dipole at different radial distances.

### Extracellular Potential Generated by the IAP at Different Radial Distances Using Lines of Positive and Negative Maxima

**Influence of r on the formation of the extracellular potential.** As established by Dimitrova and Dimitrov (5), the IAP source can be described as a collection of infinite lumped dipoles distributed along its spatial profile, as shown in Fig. 6A. The magnitude of each dipole is determined by the spatial derivative of the potential profile along the fiber. This can be appreciated from the schematic representation shown in Fig. 6A, where the size of the positive and negative charges gives an indication of the strength of each dipole. The orientation of the dipoles [i.e., leftward ($++$) or rightward ($--$)] is determined by the sign of the IAP derivative. Note that all dipoles lying on the IAP depolarization phase ($A_1$) are oriented rightward, whereas those lying on the repolarization phase ($B$) are oriented leftward.

To facilitate the visualization of the extracellular potential generated by the dipoles lying on the IAP spatial profile, in Fig. 6B, each dipole is substituted by a solid line and a dashed line containing the positions of the positive and negative maxima, respectively, of the field produced by the dipole at different $r$ values. In Fig. 6B, the dipoles located at the points of steepest rise ($A_0$) and decay ($B_0$) along...
the IAP profile can be easily identified by their corresponding lines, which are thicker than the others. The spatial distance between \( A_0 \) and \( B_0 \), also referred to as IAP spike width, is the portion of the skeletal muscle fiber delimited between the points of steepest rise and decay along the IAP profile. The IAP spike width is a critical parameter for the formation of the total extracellular potential (see Influence of the IAP spike width on the extracellular potential for details).

In Fig. 6B, \( r \) values are shown on the y-axis, i.e., perpendicular to the fiber’s longitudinal axis. Interactions between the fields of the oppositely directed dipoles depend on \( r \). These interactions refer to the scenarios where the negative or positive maxima of one dipole, \( A_i \), is produced in the region where other oppositely directed dipole, \( B_j \), produces its negative or positive maxima. For small values of \( r \), interactions between the negative maxima of dipoles \( A_i \) and \( B_j \) are small. As an example, for \( r_1 \), only the negative maxima lines of \( A_1 \) and \( A_2 \) coincide with those of \( B_1 \) and \( B_2 \), respectively. As \( r \) increases, more and more dipoles with stronger moments start interacting. When \( r = r_2 \), for example, the negative maxima lines of \( A_0 \), \( A_1 \), \( A_2 \), and \( A_3 \) coincide with those of \( B_0 \), \( B_1 \), \( B_2 \), and \( B_3 \), respectively.

At a given \( r \) value and longitudinal position along the fiber, the sign of the extracellular potential is determined by interactions between oppositely directed dipoles for that specific \( r \) value and position. As an example, the positive and negative signs shown at the top of Fig. 6B represent the polarity of the extracellular potential at \( r = r_2 \). As shown in Fig. 6B, all dipoles lying on the IAP rising phase contribute to the first positive phase of the extracellular potential. Similarly, all dipoles on the IAP repolarization phase contribute to the second positive phase of the potential. In addition, the sources contained in the space delimited by dipoles \( A_0 \) and \( B_0 \) (i.e., \( A_1, A_2, B_1, B_2 \), etc.) generate a negative field that overlaps more and more as \( r \) increases.

Another important observation to make is that the lines of positive and negative maxima are inclined. This observation helps students to reflect on the fact that the potential of each dipole widens as the distance from the observation point to the source increases (see Fig. 4). This inherent spreading of the electrical field explains why the duration of extracellular potentials increases with increasing fiber-to-electrode distance, as shown in Fig. 6C.

Influence of the IAP spike width on the extracellular potential. In Influence of \( r \) on the formation of the extracellular potential, it was shown that the formation of the extracellular potential results from interactions between the fields of oppositely directed dipoles lying on the IAP rising and falling phases and that such interactions are strongly dependent on the fiber-to-electrode distance. The next step is to illustrate to students that the degree of interaction between the fields produced by the two IAP phases also depends on the spatial separation between the phases, i.e., the so-called IAP spike width.

We consider a simplified model of the IAP source in which the depolarization and repolarization phases are represented by two oppositely directed dipoles located at the points of steepest rise and decay along the IAP spatial profile, respectively (Fig. 7, A and B). In Fig. 7, C and D, each dipole is substituted by a solid line and a dashed line representing the positions of the positive and negative maxima, respectively. Below the maxima line plots, we show the potentials produced by these dipoles in the space domain at different \( r \) values: \( r_1 \), \( r_2 \), etc.
Note that the potentials corresponding to dipoles $D_0$ and $A_0$ are smaller than those corresponding to dipoles $F_0$ and $B_0$, as the repolarization phase of the IAP is more gradual (less slope) than the depolarization phase.

Let us imagine two IAPs with different spike widths, one long and one short, such as those shown in Fig. 7, A and B, respectively. The degree of interaction between the fields of the oppositely directed dipoles at a given $r$ value can be totally different for the narrow and wide IAPs. As an example, for the narrow IAP, the negative maxima of $A_0$ and $B_0$ coincide when the $r$ value is $r_2$ (point $I_2$ in Fig. 7D), which means that the negative peaks of the potentials produced by $A_0$ and $B_0$ overlap completely at this $r$ value (Fig. 7H). In contrast, for the long IAP, the negative maxima of $D_0$ and $F_0$ are still far apart at $r_2$ (Fig. 7C), and, therefore, the negative phases of the potentials of $D_0$ and $F_0$ are not fully aligned (Fig. 7G).

For long $r$ values, such as $r_3$ and above, the negative maxima of dipole $A_0$ is produced in the region where dipole $B_0$ produced a positive field (Fig. 7D). Interacting, the overlapping potentials start cancelling each other (Fig. 7F). For the long IAP, however, the negative maxima of $D_0$ and $F_0$ just coincide for $r_3$ (Fig. 7C), and so for this long $r$ value a low degree of cancellation occurs between the corresponding dipole potentials (Fig. 7E). For small $r$ values, such as $r_1$, the interaction between the negative maxima of oppositely directed dipoles is small for both narrow and wide IAPs (Fig. 7, C and D). At this distance, the potentials produced by $A_0$ and $B_0$ overlap only slightly (Fig. 7J), whereas the potentials produced by $D_0$ and $F_0$ do not even touch each other (Fig. 7I).

### Teaching Plan

Teaching the generation of IAPs and extracellular electrical potentials comprised approximately half of the hours assigned to the bioelectricity course. The theoretical knowledge described above is only a fraction of the content taught in relation to intracellular and
extracellular potentials. Such theoretical concepts were presented to the students as an advanced approach (or explanation) to gain a deeper understanding on the formation of electrical potentials in the human body. Thus, the content presented here were extended by other theoretical material (10, 15, 17) as well as by practical sessions involving simulation programs written in Matlab (17). In total, four lectures (of ~90 min each) were devoted to showing students the theoretical material presented here. These informational lectures covered the topics embedded in the learning objectives as follows. The first lecture addressed the polarization of the muscle fiber membrane and the concept of depolarization-repolarization. During this lecture, the intracellular potential was presented as the result of the exchange of ions (Na⁺, K⁺, and Cl⁻) across the fiber membrane. Hodgkin and Huxley equations were then explained to provide students with the precise mechanism by which the ions flow across the membrane during an action potential. The second lecture described all aspects related to the potentials generated by an electrostatic dipole and by a dipole propagating along a muscle fiber. The third lecture was aimed at showing that the extracellular potential generated by the IAP is the result of interactions between the fields of dipoles lying on the IAP spatial profile and that such interactions are strongly dependent on the fiber-to-electrode distance. Finally, the fourth lecture showed the influence of the IAP spike width on the extracellular potential.

Assessment of the Topic and Feedback From Students

The degree of understanding of the contents of the Bioelectricity course was assessed by a closed-book 2-h written exam consisting of 12 questions. Among the 12 questions, 4 questions were focused on the learning objectives outlined here. The questions were mostly theoretical and included providing a descriptive explanation of a given phenomenon, finding the mathematical solution of a problem, interpreting the shape of a certain extracellular potential, or predicting the extracellular potential generated under certain conditions. To obtain students’ opinions with regard to the contents and methodology adopted in the present study, students were required to fill in a short survey consisting of the points shown in Table 1.

### RESULTS

In general, students acquired a good understanding of the generation of both intracellular and extracellular potentials. A summary of the scores obtained on the different learning objectives is shown in Table 2. As shown in Table 2, students obtained high marks in questions pertaining to the polarization of the membrane under resting and excited conditions. They recognized that these concepts were difficult to comprehend and that the schematic figures provided were necessary to create a mental picture of the electrical phenomena. Students also achieved a deep comprehension of the generation of the intracellular potential. Table 2 also shows that the students understood that the extracellular potential is the result of the propagation of the source (dipole or intracellular potential) along the fiber (Figs. 3–6). Students reported that modeling the IAP spatial profile as a sequence of dipoles aided in the conceptualization of the generation of extracellular potential and that the lines of positive and negative maxima play an important role in this respect. In addition, students obtained high marks in the third learning objective, which suggests that

### Table 1. Evaluation of students’ satisfaction with the teaching methods

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<tr>
<td>1. Concepts were clearly explained in the learning material provided</td>
<td>7.9 ± 1.8</td>
<td>7.2 ± 1.3</td>
<td>7.0 ± 1.3</td>
<td>8.1 ± 1.1</td>
<td>7.1 ± 1.5</td>
<td>8.6 ± 0.7</td>
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<td>2. The proposed method was clearly related to electromagnetic field theory</td>
<td>7.5 ± 1.3</td>
<td>6.9 ± 1.3</td>
<td>7.8 ± 1.5</td>
<td>7.6 ± 1.7</td>
<td>7.8 ± 1.6</td>
<td>9.2 ± 1.2</td>
</tr>
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<td>3. The topic affected your motivation to continue your education in the biomedical engineering field</td>
<td>7.9 ± 1.3</td>
<td>8.8 ± 1.2</td>
<td>8.5 ± 1.8</td>
<td>8.3 ± 1.5</td>
<td>8.7 ± 1.0</td>
<td>9.3 ± 0.9</td>
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<td>4. The methodology was intuitive and easy to grasp</td>
<td>8.1 ± 0.7</td>
<td>7.5 ± 1.5</td>
<td>8.3 ± 0.9</td>
<td>8.7 ± 0.9</td>
<td>8.2 ± 0.9</td>
<td>8.9 ± 0.9</td>
</tr>
<tr>
<td>5. Overall, I am satisfied with the sessions</td>
<td>8.2 ± 1.3</td>
<td>7.8 ± 1.7</td>
<td>8.8 ± 1.5</td>
<td>8.5 ± 1.4</td>
<td>8.3 ± 1.7</td>
<td>8.7 ± 1.5</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, number of students. Students’ degree of satisfaction was determined on a scale from 1 to 10, where 1 = completely unsatisfied and 10 = completely satisfied.

### Table 2. Level of attainment of the learning objectives of the topic

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>A. Polarization of the membrane under passive and active conditions</td>
<td>7.2 ± 1.2</td>
<td>6.8 ± 1.7</td>
<td>7.8 ± 0.9</td>
<td>7.8 ± 1.3</td>
<td>7.9 ± 1.5</td>
<td>8.6 ± 1.3</td>
</tr>
<tr>
<td>B. Generation of intracellular potentials</td>
<td>6.9 ± 1.0</td>
<td>6.9 ± 0.97</td>
<td>7.2 ± 1.4</td>
<td>7.9 ± 1.1</td>
<td>7.5 ± 1.8</td>
<td>8.3 ± 1.0</td>
</tr>
<tr>
<td>C. Generation of extracellular potentials</td>
<td>7.4 ± 1.4</td>
<td>7.8 ± 1.3</td>
<td>8.9 ± 1.1</td>
<td>8.0 ± 1.2</td>
<td>8.5 ± 1.2</td>
<td>8.7 ± 1.2</td>
</tr>
<tr>
<td>D. Effects of fiber-to-electrode distance and intracellular action potential on extracellular potentials</td>
<td>6.3 ± 1.9</td>
<td>6.9 ± 1.4</td>
<td>7.5 ± 2.1</td>
<td>7.3 ± 1.8</td>
<td>7.3 ± 1.6</td>
<td>8.3 ± 1.2</td>
</tr>
</tbody>
</table>

Values are examination grades in means ± SD; n, number of students. Learning objectives were assessed on a scale from 1 to 10.
they were aware of the influence of $r$ on the formation of the electrical potential.

The results of students’ satisfaction with regard to the teaching approach presented here are shown in Table 1. Students followed the lecturer’s explanations with interest and great attention (point 4). They were able to assimilate most of the concepts thanks to their solid background in mathematics and physics and also because they felt attracted by the topic (points 3 and 4). Overall, students were satisfied with the development of the course, and their comments were very positive (points 1, 2, and 5). Students agreed that the material and approaches presented here made the Bioelectricity course appealing (points 3 and 4), which increased their motivation to continue their studies in the Master’s Degree program of Biomedical Engineering. It should be mentioned that all data presented here regarding student satisfaction and test scores were taken while the teaching plan outlined in Learning Objectives of the Topic was in use, i.e., there are no data from students taught before this teaching plan was used.

**DISCUSSION**

**Innovative Contribution**

The generation of extracellular potentials has been traditionally addressed from a research perspective. Consequently, most methods aimed at calculating extracellular potentials have been more interested in offering an accurate modeling of the phenomena (1, 13, 14) and/or in improving the computational efficiency (4, 12) than in providing an intuitive, approachable description of how the potential is actually generated. As an example, in 1974, Plonsey (13) proposed an approach based on formal solutions of Laplace’s equation with a complex formulation that gave no chance for transparent physical interpretations. An important step toward the simplification of Plonsey’s model was made by Andreassen and Rosenfalck (1) in 1981. Perhaps the most intuitive presentation to date of extracellular potentials was the convolutional model introduced by Nandekar and Stalberg (12) and Dimitrov and Dimitrova (4). Convolutional models, however, still lacked the necessary physical transparency, and, therefore, they are not suitable methods for teaching.

Complete understanding (and visualization) of how the extracellular potential is formed as a result of the propagation of the excitation source along the fiber is difficult for various reasons. First, the bioelectrical source (i.e., the intracellular potential) is not a “point source” but rather a “distributed function,” i.e., a voltage that varies gradually along the spatial length of the fiber for ~5–10 mm (5). Second, the bioelectrical source is not a monotonous function but a function formed by two portions of opposite slope: the so-called rising and falling phases. Finally, the assumption that the intracellular potential is the excitation source is only a simplification: the “true” excitation source is the first or second spatial derivative of the intracellular potential (4, 12). In view of the above exposition, it is clear that the main obstacle for the understanding of extracellular potential generation is that the conventional presentation of the IAP (as a continuous, distributed function) is unsuitable for teaching purposes. It has been the belief of the author that a more pedagogical approach consists on substituting the IAP source for a collection of well-known elementary sources, such as the dipoles.

The dipole-based presentation of the bioelectrical source offers students the possibility of learning the formation of the extracellular potential using basic concepts of electrostatic theory with which they are already familiar. This is a crucial aspect of our model as it helps increasing to students’ confidence and allows them to apply their previous knowledge. In addition, since the proposed description of the excitation source is grounded on electrostatic theory, it has general character, i.e., it is applicable for any shape of the bioelectrical source.

The dipole-based presentation of the bioelectrical source is not only suitable for the biomedical engineering profile but is also appropriate and helpful for other profiles, such as medical students and biomedical research students. Specifically, medical students, with a deep knowledge of the physiological mechanisms governing the generation of intracellular potentials, will be able to relate the physiological behavior of the cell membrane (exchange of ions, Hodgkin and Huxley equations, etc.) with its biophysical-electromagnetic behavior (sequence of dipoles lying along the IAP profile and the potential generated by each dipole). As an example, if a decline of the inward current of Na$^+$ occurs in the early stages of the membrane depolarization (slower depolarization phase), a medical student should instantaneously link this decline with a decrease in the strength of the dipoles lying on this IAP phase and, therefore, with a reduction of the extracellular potential.

**Benefits for Learning**

Modeling the IAP spatial profile as a sequence of infinite dipoles enormously facilitates the conceptualization of the formation of the extracellular field as it allows students to recognize the individual contribution of each small portion of the IAP profile (i.e., each dipole) to the total potential. To fully exploit the possibilities of the above dipole-based IAP model, each dipole must be accompanied by lines containing the positive and negative maxima of the dipole field at different $r$ values. The combination of a source model consisting of a collection of dipoles together with their associated maximal lines brings the following advantages for the students:

1. It allows students to appreciate that the formation of the extracellular potential results from interactions between the fields of all dipoles lying on the IAP spatial profile.
2. It permits students to realize that such interactions are strongly dependent on the fiber-to-electrode distance.
3. It allows students to understand that interactions between oppositely directed dipoles can be additive or subtractive, depending on the $r$ value.
4. It allows students to feel the impact of the IAP spike width on interactions between the dipoles.
5. It permits students to identify which parts of the IAP profile are more critical for the generation of each of the extracellular potential phases.
6. The observation that maxima lines are inclined help students to reflect on the fact that the potential of each dipole widens with increasing fiber-to-electrode distance.
7. The presentation of the source as a sequence of dipoles in itself helps students to reflect on the distributed character of the source.

The model of the bioelectrical source presented here (dipoles distributed along the IAP profile together with lines of negative and positive maxima) provided the necessary tools for students
to calculate extracellular potentials under a wider range of conditions. As stated above, the model is of general applicability, which implies that students can use it to predict the potential arising from any bioelectrochemical source for any distance between the source and the recording point. The theoretical material presented here can also be used to interpret and validate the potentials obtained from heart or brain cells, thereby contributing to improve the backgrounds of biomedical engineers, physicians, and researchers.

Conclusions

In this study, a new method to describe the generation of extracellular potentials around a muscle fiber using both descriptive and quantitative tools is presented. The new method is an attempt to overcome the limitations of classical approaches to bioelectrical potentials that involve complicated mathematical machinery that gives no chance for physical interpretation. The proposed method combines electromagnetic field theory with intuitive graphic representations to facilitate students to conceptualize the formation of extracellular potentials. The method has proved to be successful in helping students to visualize how the different parts of the excitation source give rise to the different parts of the extracellular potential. Moreover, the approach is particularly convenient to illustrate the influence of fiber-to-electrode distance and shape of the excitation source on the formation of the extracellular field. Feedback from students indicates that combining general principles of electrical fields with accurate graphic imagery increases their confidence (as it allows them to apply their previous knowledge) and gives them an intuitive feel for electrophysiological phenomena.

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.

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