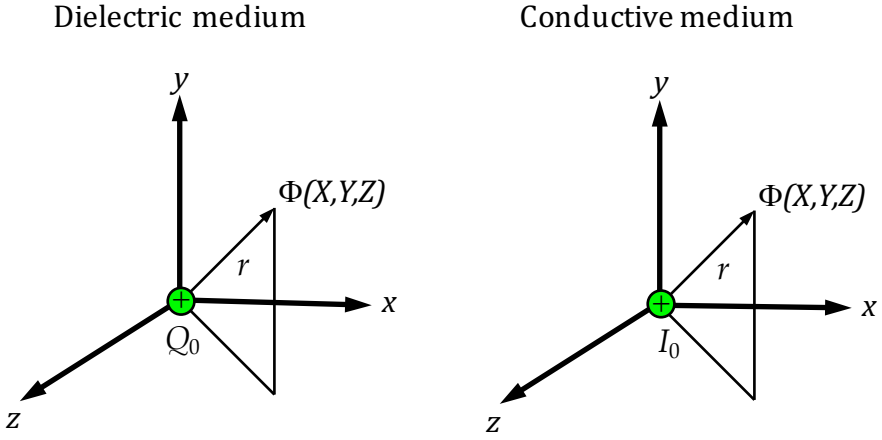
HANDOUT #2. ACTIVE FIBER AS BIOELECTRIC SOURCE

In this handout, we will discuss the potential field arising from a bioelectric source, in the form of an active, cylindrical fiber lying in a volume conductor.

A. Review of electrostatics. As a brief review of electrostatics and charge sources in a dielectric medium, a potential Φ will arise in space from a single point charge Q_0 at the origin (Fig. 1, left). Φ is a function of position (*X*,*Y*,*Z*), so we refer to it as a *potential field*.

Figure 1



Φ is given by

$$\Phi(X,Y,Z) = \frac{Q_0}{4\pi\varepsilon r} \tag{1}$$

where ε is the permittivity, and r is the distance from the measurement point (*X*,*Y*,*Z*) to the origin.

$$r = \sqrt{X^2 + Y^2 + Z^2} \tag{2}$$

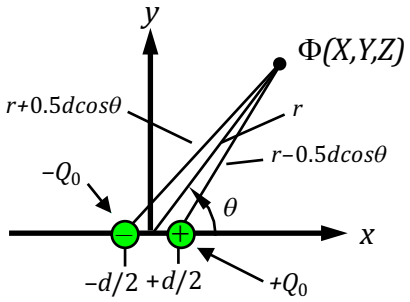
When we consider a conductive medium, Φ can arise from a point current I_0 at the origin (Fig. 1, right),

$$\Phi(X,Y,Z) = \frac{I_0}{4\pi\sigma r} \tag{3}$$

The reason (3) resembles (1) is that Φ in both media is constrained by physical laws to satisfy the same equation (Poisson's equation), where ε is used for the dielectric medium and σ for the conductive medium.

The point sources above are examples of *monopole* sources. For a charge *dipole* source, we have,

Figure 2



$$\Phi(X,Y,Z) = \frac{Q_0}{4\pi\varepsilon(r-0.5d\cos\theta)} - \frac{Q_0}{4\pi\varepsilon(r+0.5d\cos\theta)} \quad (4a)$$

$$\cong \frac{Q_0}{4\pi\varepsilon r}\left(1+\frac{1}{r}0.5d\cos\theta\right) - \frac{Q_0}{4\pi\varepsilon r}\left(1-\frac{1}{r}0.5d\cos\theta\right) \quad (4b)$$

$$= \frac{Q_0 d}{4\pi\varepsilon r^2}\cos\theta = \frac{p}{4\pi\varepsilon r^2}\cos\theta \quad (4c)$$

where $p = Q_o d$ is the charge dipole moment. Similarly, for a current dipole with source $+I_0$ at $x = d/2$ and $-I_0$ at $x = -d/2$,

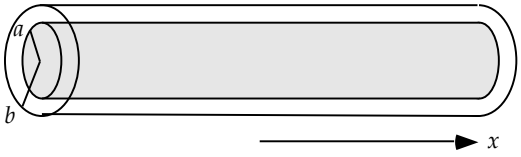
$$\Phi(X,Y,Z) = \frac{I_0 d}{4\pi\sigma r^2}\cos\theta = \frac{p}{4\pi\sigma r^2}\cos\theta \quad (5)$$

where $p = I_o d$ is the current dipole moment.

B. Active fiber model

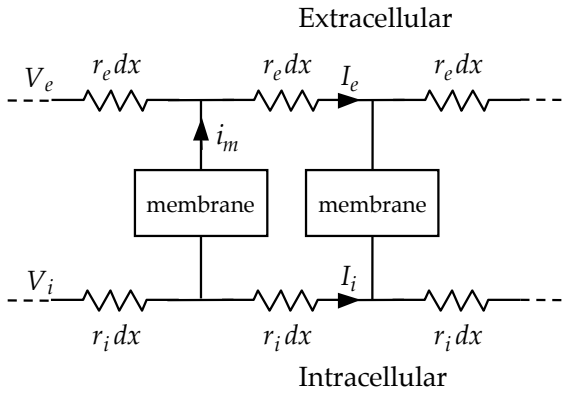
The linear core conductor model was developed by Hodgkin and Rushton [1] to describe 1-D propagation in cylindrical nerve fibers. It is applicable to the case where the fiber has a radius *a* and is surrounded by a restricted extracellular space, say with radius *b*.

Figure 3



The flow of extracellular and intracellular current is primarily along the fiber axis, and can be modeled as an electrical ladder network, the *core conductor model*.

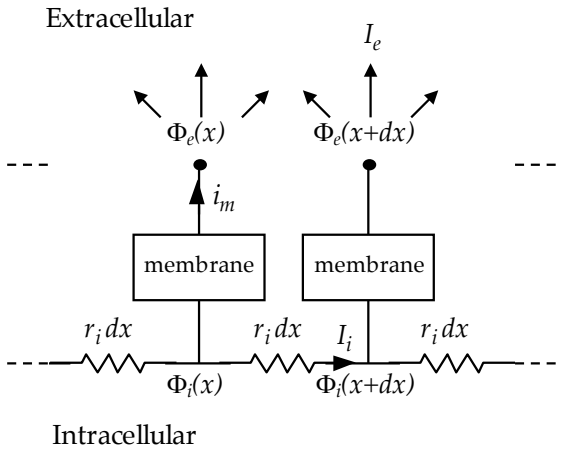
Figure 4



The extracellular and intracellular compartments are characterized by unit resistances per unit length r_e and r_i, and voltages V_e and V_i, respectively. Our focus is on active fibers that support propagating action potentials, but it will not be necessary to make any assumptions regarding the form of the membrane biophysical equations (e.g., passive RC circuit, Hodgkin-Huxley model, cardiac membrane model, etc.). We also assume that no current is being introduced into the system (such as from stimulus electrodes). V_e and V_i will vary both with position and with time.

However, we'd like to generalize the situation to where the fiber lies in a large volume conductor (i.e., b becomes very large), which would be more akin to a bioelectric source in, say a torso or head. Now the flow of extracellular current I_e will no longer be restricted to flow along the x-axis, and in fact can spread out in three-dimensions. The surface nodes of the fiber will now be represented as points lying in a 3D volume conductor from which extracellular current emanates. To symbolize the shift from electrical circuits to volume conductors, the voltages are now represented as electrical potentials, Φ_e and Φ_i.

Figure 5

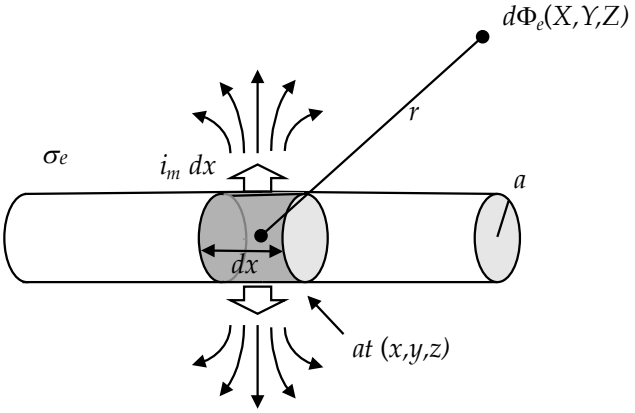


C. Equivalent source (monopole)

The flow of current (by convention, positive when flowing from inside to outside the fiber) across an incremental ring of fiber membrane can be considered to act approximately

as a point source of current in the extracellular space located at position (x,y,z).[1]

Figure 6



Assuming that the fiber is aligned along the x-axis, the incremental extracellular potential $d\Phi_e(X,Y,Z)$ that results from a ring of membrane with length dx is very nearly that arising from a point source in an infinite volume conductor, located at position (x,y,z). From (3):

$$d\Phi_e = \frac{i_m dx}{4\pi\sigma_e r} \tag{6}$$

where σ_e is the conductivity of the extracellular space, i_m is the line density of membrane current (units of amp/cm) emerging into the extracellular space, and r is,

$$r = \sqrt{(x-X)^2 + (y-Y)^2 + (z-Z)^2} \tag{7}$$

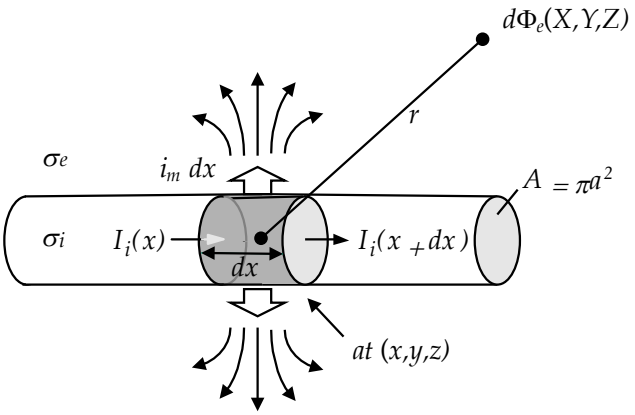
Taking a line integral along x over the length L of the fiber superimposes the extracellular potentials arising from each incremental segment of the fiber, and the total extracellular potential at (X,Y,Z) is therefore,

$$\Phi_e(X,Y,Z) = \frac{1}{4\pi\sigma_e}\int_L \frac{i_m}{r}\,dx \tag{8}$$

The source i_m in (8) can be expressed instead in terms of the transmembrane potential V_m through consideration of the flow of current through the fiber. From charge conservation and Fig. 7,

[1] For this approximation to be valid, what do you think should be the relative size of r compared with a?

Figure 7



$$i_m = -\frac{\partial I_i}{\partial x}. \tag{9}$$

If the intracellular potential Φ_i is relatively uniform across the cross-section of the fiber, then from the constitutive law of conduction (electric field generalization of Ohm's law),

$$\frac{I_i}{\pi a^2} = -\sigma_i \frac{\partial \Phi_i}{\partial x}. \tag{10}$$

Note that although Φ_i varies only along the x-direction, we still use partial derivatives in (9) and (10) because I_i and Φ_i can also vary with time. Combining (8) through (10),

$$i_m = \pi a^2 \sigma_i \frac{\partial^2 \Phi_i}{\partial x^2}. \tag{11}$$

Strictly speaking, (11) is only *approximate*, since the fiber itself was assumed to be "transparent" to the flow of extracellular current, so that (6) could be assumed. The perturbation of Φ_e by the fiber itself can be determined by the application of Green's theorem, which allows the potentials across the entire surface of the fiber to be accounted for. While the derivation is somewhat involved and beyond the scope of this discussion, the *exact* expression for i_m can be shown to be,

$$i_m = \pi a^2 (\sigma_i \frac{\partial^2 \Phi_i}{\partial x^2} - \sigma_e \frac{\partial^2 \Phi_e^S}{\partial x^2}) \tag{12}$$

where Φ_e^S in (12) is evaluated on the fiber surface. Note the difference between (12) and (11) is the presence of an additional term that is a function of Φ_e^S.

Under some not uncommon conditions, i_m will be proportional to $\partial^2 V_m / \partial x^2$. This can be seen by rewriting (12) as,

$$i_m = \pi a^2 [\sigma_i \frac{\partial^2 \Phi_i}{\partial x^2} - \sigma_i \frac{\partial^2 \Phi_e^S}{\partial x^2} + (\sigma_i - \sigma_e) \frac{\partial^2 \Phi_e^S}{\partial x^2}] \tag{13a}$$

$$= \pi a^2 [\sigma_i \frac{\partial^2 V_m}{\partial x^2} + (\sigma_i - \sigma_e) \frac{\partial^2 \Phi_e^S}{\partial x^2}] \tag{13b}$$

The proportionality between i_m and $\partial^2 V_m/\partial x^2$ occurs, for example when the second derivative of extracellular potential at the fiber surface is much smaller than that of the transmembrane voltage (as is approximately the case when a single fiber is immersed in a large volume bath), or when the conductivities of the intracellular and extracellular spaces are similar. In these cases,

$$i_m \cong \pi a^2 \sigma_i \frac{\partial^2 V_m}{\partial x^2} \qquad \left(\text{if } \frac{\partial^2 \Phi_e^S}{\partial x^2} \ll \frac{\partial^2 V_m}{\partial x^2} \text{ or } \sigma_i \approx \sigma_e\right) \quad (14)$$

so that (8) becomes,

$$\Phi_e(X,Y,Z) = \frac{1}{4\pi\sigma_e}\int_L \frac{1}{r}\pi a^2 \sigma_i \frac{\partial^2 V_m}{\partial x^2} dx \qquad (15a)$$

$$\Phi_e(X,Y,Z) = \frac{a^2\sigma_i}{4\sigma_e}\int_L \frac{1}{r}\frac{\partial^2 V_m}{\partial x^2} dx \qquad (15b)$$

Bottom line: (15b) tells us that net current is driven across the fiber's membrane and acts as a monopole current source in the volume conductor. The axial density of the current source is proportional to the second derivative of V_m, and is given by (14).

D. Equivalent source (dipole). Because free charge cannot accumulate or deplete in steady-state in a volume conductor, the net flow of i_m current across the entire length of the fiber must integrate to zero. For example, "action" current flows in a closed loop between activated, depolarized cells and resting, polarized cells.

Figure 8 [2]

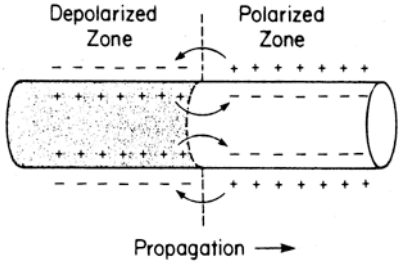
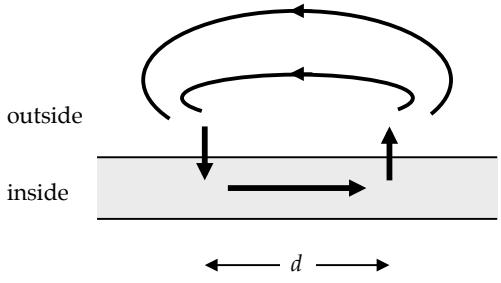


Fig. 2-9. The role of local currents in the propagation of a wave of excitation down a cardiac fiber.

From the viewpoint of the extracellular space, current crosses the fiber membrane and "appears" just in front of the depolarizing wavefront, traverses a short distance and then "disappears" just behind the wavefront.

Figure 9



Thus, there is a source and sink of *extracellular* current (which accompany closed current loops that traverse the cell membrane) that are separated by a distance d roughly equal to the propagation velocity times the duration of the action potential upstroke (of the order of 0.5 m/sec times 1.0 msec = 0.5 mm for cardiac fibers). This is precisely the characteristic of a current dipole.

With this concept in mind, we would like to recast (15b) into a form where the current sources are dipoles instead of monopoles. To do this, we integrate (15b) by parts:

$$\int a\frac{db}{dx}dx = ab - \int b\frac{da}{dx}dx \tag{16a}$$

where,

$$a = \frac{1}{r} \text{ and } b = \frac{\partial V_m}{\partial x} \tag{16b}$$

$$\Phi_e(X,Y,Z) = \frac{a^2\sigma_i}{4\sigma_e}\int_L \left[\frac{1}{r}\frac{\partial}{\partial x}\left(\frac{\partial V_m}{\partial x}\right)\right]dx = \frac{a^2\sigma_i}{4\sigma_e}\left(\frac{1}{r}\frac{\partial V_m}{\partial x}\right)_{-\infty}^{\infty} - \frac{a^2\sigma_i}{4\sigma_e}\int_L \frac{\partial(1/r)}{\partial x}\frac{\partial V_m}{\partial x}dx \tag{17}$$

The first term on the right-hand side of (17) goes to zero at the limits of integration for an infinitely long fiber (V_m is constant, and r goes to infinity), so (17) becomes,

$$\Phi_e(X,Y,Z) = -\frac{a^2\sigma_i}{4\sigma_e}\int_L \frac{\partial(1/r)}{\partial x}\frac{\partial V_m}{\partial x}dx = -\frac{a^2\sigma_i}{4\sigma_e}\int_L \frac{x}{r^3}\frac{\partial V_m}{\partial x}dx \tag{18}$$

Since (see Fig. 2),

$$x = r\cos\theta \tag{19}$$

then,

$$\Phi_e(X,Y,Z) = -\frac{a^2\sigma_i}{4\sigma_e}\int_L \frac{1}{r^2}\left(\frac{\partial V_m}{\partial x}\right)\cos\theta\, dx \tag{20}$$

Comparing (20) to (5), we can define

$$\tau_l = -\pi a^2\sigma_i\frac{\partial V_m}{\partial x} \tag{21}$$

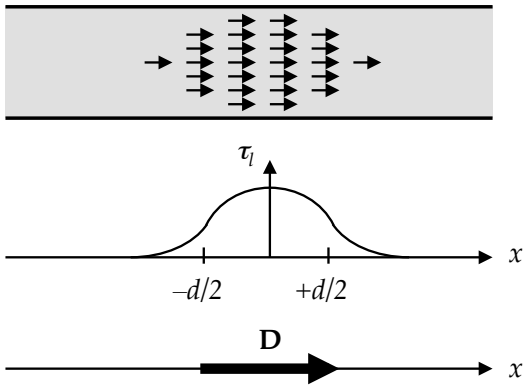
where τ_l is a line density of axial dipole sources (with units of amp-cm per cm), so that (20) becomes,

$$\Phi_e(X,Y,Z) = \frac{1}{4\pi\sigma_e}\int_L \frac{1}{r^2}\tau_l\cos\theta\, dx \tag{22}$$

Bottom line: (22) tells us that net current is driven in loops across the fiber's membrane and act like a dipole current source in the volume conductor. The axial density of the dipole source is proportional to the first derivative of V_m, and is given by (21).

E. Total dipole source strength. The axial density of dipole sources τ_l at the activation wavefront varies as the negative spatial gradient of transmembrane potential $\partial V_m/\partial x$ and would look something like Fig. 10 for a wavefront propagating from left to right.

Figure 10



The integral of the axial density allows us to represent the activation wavefront by a *lumped dipole* **D** with magnitude *D* and direction along *x* provided that Φ is measured far from the source; i.e., *r* >> *d*:

$$\Phi_e(X,Y,Z) = \frac{1}{4\pi\sigma_e}\int_L \frac{1}{r^2}\tau_l \cos\theta \, dx \approx \frac{\cos\theta}{4\pi\sigma_e r^2}\int_L \tau_l \, dx = \frac{D\cos\theta}{4\pi\sigma_e r^2} \qquad (23)$$

The total dipole source in any given interval $[x_1, x_2]$ along the fiber can be obtained by integrating the dipole source density, and total dipole strength *D* obtained by,

$$D = \int_{x_1}^{x_2} \tau_l \, dx = -\pi a^2 \sigma_i \int_{x_1}^{x_2} \frac{\partial V_m}{\partial x} dx = -\pi a^2 \sigma_i [V_m(x_2) - V_m(x_1)] \qquad (24)$$

If the interval $[x_1, x_2]$ spans the upstroke of the action potential, then we get the very simple relationship,

$$D = -\pi a^2 \sigma_i \left[V_{rest} - V_{peak}\right] = \pi a^2 \sigma_i \left[V_{peak} - V_{rest}\right] \qquad (25a)$$

where V_{rest} and V_{peak} refer to the resting and peak voltages of the action potential. Therefore, *the total dipole strength associated with electrical activation is proportional to the amplitude of the action potential*.

Φ_e is depicted in Fig. 11 as an *isopotential contour map*.

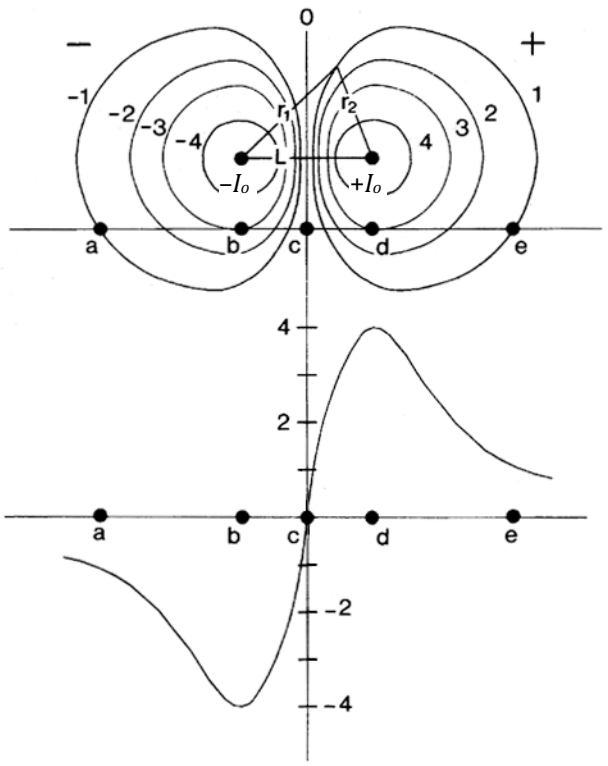


Figure 11 (adapted from [3])

The lower panel of Fig. 11 shows the variation in potential along a linear path passing through the points a through e, located a distance, say r_3, from the dipole axis. Thus, if the dipole is moving with the activation wave (say, from left to right in Fig. 11), the field at a point a distance r_3 from the dipole trajectory would measure this same sequence of potentials over time (actually, it would be reversed left to right – why?).

F. Example 1. To illustrate the concepts above, we consider a triangularized approximation to the action potential.

Figure 12 [4]

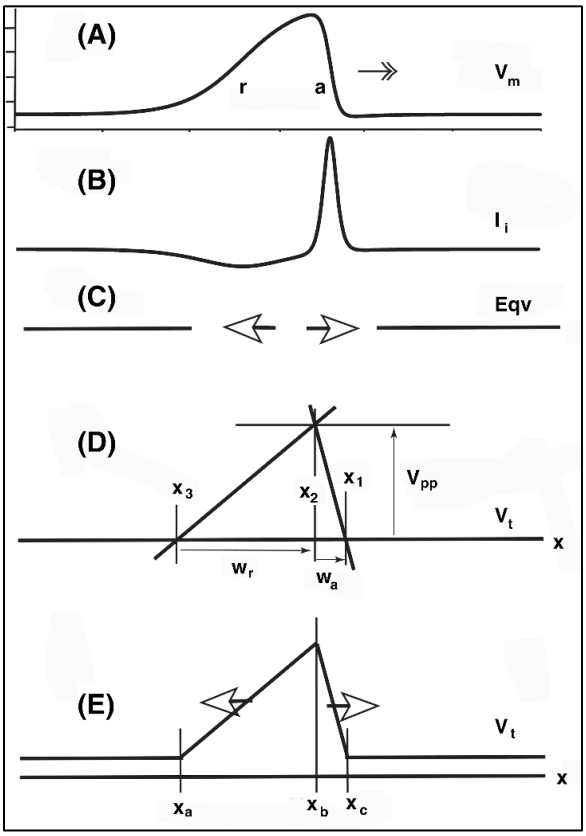


Figure 8.9. Dipole Sources. The action potential $V_m(x)$ and its first spatial derivative are given along with the approximating triangularized action potential $V_t(x)$ and axial current I_i, as found from the spatial derivative of V_m. Depolarization and repolarization spatial widths w_d and w_r are for the approximating triangular action potential.

More on this will be covered as a homework assignment.

References

1. Hodgkin AL and Rushton WAH. The electrical constants of a crustacean nerve fibre. *Proc Roy Soc London Ser B* 133:444-479, 1946.
2. Berne, R.M. and Levy, M.N. (1992), Cardiovascular Physiology, C.V. Mosby Co., St. Louis
3. de Bakker, J.M.T., Hauer, R.N.W. and Simmers, T.A. (1995). Activation mapping: unipolar versus bipolar recording. In: Cardiac Electrophysiology: From Cell to Bedside (Zipes, D.P. and Jalife, J., eds), 2nd edition, W.B. Saunders Co, Philadelphia, Chap. 94, pp. 1068-1078.
4. Plonsey R and Barr RC. Bioelectricity: A Quantitative Approach, 3rd ed, Chap. 8 (Extracellular fields). Springer, New York, 2007.