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Analysis of Bipolar External Excitation of Spherical Tissue by Spatially Opposed Current Source and Sink Points

Benjamin L. Schwartz and **Rosalind J. Sadleir**

School of Biological and Health Systems Engineering, Arizona State University, Tempe, AZ 85287, USA

Abstract

The recently increasing role in medical imaging that electrophysiology plays has spurred the need for its quantitative analysis at all scales—ions, cells, tissues, organs, etc.; so, here is presented a model of nerve tissue in a spherical volume excited by a point current source at one pole and a point current sink at the opposite pole. The sphere of tissue is described as an isotropic bidomain, consisting of the intra- and extra-cellular regions and the membrane that separates them, and is immersed in an infinite isotropic conductive bath. The system of coupled differential equations is solved by redefining the domains to be in terms of a monodomain and a membrane. The solution takes the form of an infinite sum of the product of certain transcendental functions. The study concludes with a numeric example in which the boundary conditions are shown to be satisfied, validating this analysis, paving the way for more sophisticated models of excitable tissue.

I. INTRODUCTION

The material properties of living tissue depend significantly on their states of health. Normal physiologic function also informs the living tissue's properties as seen in the correlation between neural activity and electrical impedance [1]. Recent work has shown that electrical impedance can be non-invasively measured with MRI techniques [2]. One such technique, magnetic resonance electrical impedance tomography (MREIT) [3], calls for injecting current into an object in synchrony with the pulse sequence of an MRI scan.

A. MR Electrical Impedance Tomography

Not unlike MR elastography, MREIT measures electrical activity by the phase that accrues in the complex MR signal. Whereas in MR elastography the phase accumulation is due to mechanical vibrations [4], with MREIT the phase accumulation is due to the magnetic field induced by electric current that is injected into a domain of interest. The phase image, then, is a map of the local magnetic fields from which current density can be computed, from which a map of electric conductivity can be rendered [3]. The ability to measure, non-invasively, the electrical properties of tissue has many possible applications. If that tissue is comprised of excitable cells like neurons, then its electrodynamic *behavior* may be studied, e.g. MREIT can possibly be used to detect neural activity directly [1]. Such advanced measurements necessarily demand careful modeling of tissue electrical properties.

B. Electrodynamic Modeling

Excitable tissues are comprised of cells, discrete units, mechanically connected, through which electric signals may propagate via action potentials [5]. While many have studied and modeled the behavior of individual cells in both sub- and supra-threshold conditions, it is also very important to understand excitability behavior at the tissue or *voxel*/level, i.e. the cells en masse, particularly in the context of medical imaging. The bidomain model [6], a generalization of the cable equation [7], addresses this need by avoiding the discrete constructs of tissue, assuming instead a continuum of two domains, intra- and extracellular, divided by a membrane and occupying the same volume [8]. Each domain represents an average, then, of all its individual components. If we momentarily consider only the two domains and the membrane dividing them, it becomes clear that any current leaving one domain must be a transmembrane current that enters the other domain. Thus the bidomain model is a set of differential equations, coupled by the transmembrane current. Ion current across the membrane is highly non-linear [5]; so, many researchers have resorted to finite difference or finite element models (FEM) to elucidate the behavior of active tissue [9] [10]. FEM can be an extremely powerful tool in solving initial-boundary value problems that can't be solved by analytic means, such as the propagation of an action potential through a finite volume of excitable tissue. In addition to the non-linearities inherent to active membranes, most anatomic geometry is not analytically tractable. Still, analytic solutions are invaluable when it comes to validating FEM. We have more faith in the solutions of FEM to an intricate problem if those methods have first been shown to agree with the analytic solution of a more straightforward problem. The objective of this study is to provide an analytic model of neural tissue which can be used to validate other modeling techniques. Altman and Plonsey have modeled a bundle of nerves as an isotropic infinite circular cylinder in an infinite conducting bath under steady state stimulation by an external point current source [11]. We solve the problem of a sphere of tissue immersed in an infinite conducting bath and stimulated by injection currents. The injection currents are modeled as a current point source and a point sink.

II. PROBLEM FORMULATION

A. Bidomain Tissue

Let there be given a sphere of isotropic nervous tissue in a uniform isotropic infinite conducting bath which contains a point current source and sink on opposite sides of the sphere, shown in Fig. 1. Due to the azimuthal symmetry, we neglect any dependence on ϕ throughout this analysis. The tissue is modeled as a bidomain, the interstitial and intracellular regions occupying the same volume, separated by a membrane which we hold to be passive. The steady-state bidomain equations for the tissue that couple the intra- and extracellular potentials, ϕ_i and ϕ_o , respectively, are given as

$$\nabla^2 \phi_i = I_m \rho_i, \quad (1a)$$

and

$$\nabla^2 \phi_o = -I_m \rho_o, \quad (1b)$$

where

$$I_m = (\phi_i - \phi_o) \frac{\beta}{R_m} \quad (2)$$

is the transmembrane current, ρ_i and ρ_o are the intra- and extracellular resistivities, R_m is the membrane resistance times unit area and β is the membrane's surface area to volume ratio.

B. Uncoupling

To solve for ϕ_i and ϕ_o we must first uncouple (1) by defining, after Tung [12], the transmembrane potential, V_m , and the monodomain potential, ψ ,

$$V_m = \phi_i - \phi_o, \quad (3a)$$

and

$$\psi = \frac{\rho_o}{\rho_o + \rho_i} \phi_i + \frac{\rho_i}{\rho_o + \rho_i} \phi_o, \quad (3b)$$

with ϕ_i and ϕ_o , then, given as

$$\phi_i = \frac{\rho_i}{\rho_o + \rho_i} V_m + \psi, \quad (4a)$$

and

$$\phi_o = -\frac{\rho_o}{\rho_o + \rho_i} V_m + \psi. \quad (4b)$$

If we put our expressions for the transmembrane current and potential into the difference of equations (1a) and (1b), we see that V_m is the solution to the scalar Helmholtz equation,

$$\nabla^2 V_m - \frac{V_m}{\lambda^2} = 0, \quad (5)$$

where the length constant is $\lambda = \sqrt{\rho_m / (\rho_i + \rho_o)}$, and $\rho_m = R_m / \beta$. If we apply the Laplacian operator to (3b), then we may insert (1) which will cancel everything on the right side, revealing that ψ is the solution to the Laplace equation,

$$\nabla^2 \psi = 0. \quad (6)$$

C. Conducting Bath

External to the sphere the potential, ϕ_e , is given by

$$\phi_e = \phi_{bath} + \phi_{source} + \phi_{sink}, \quad (7)$$

where ϕ_{source} and ϕ_{sink} are the fields due to the current points source and sink, respectively, and ϕ_{bath} is the secondary field which also satisfies the Laplace equation,

$$\nabla^2 \phi_{bath} = 0. \quad (8)$$

III. SOLUTIONS

A. Transmembrane Potential

In spherical coordinates with azimuthal independence, the Laplacian operator on a function, $\nabla^2 f$, is given as [13]

$$\nabla^2 f = \frac{\partial^2 f}{\partial r^2} + \frac{2}{r} \frac{\partial f}{\partial r} + \frac{1}{r^2} \frac{\partial^2 f}{\partial \theta^2} + \frac{\cot(\theta)}{r^2} \frac{\partial f}{\partial \theta}. \quad (9)$$

Thus, assuming the product solution of $V_m(r, \theta) = R(r)\Theta(\theta)$, from the separation of variables, (5) yields

$$\frac{\partial^2 R(r)}{\partial r^2} + \frac{2}{r} \frac{\partial R(r)}{\partial r} - \left(\frac{1}{\lambda^2} + \frac{\alpha}{r^2} \right) R(r) = 0, \quad (10a)$$

and

$$\frac{\partial^2 \Theta(\theta)}{\partial \theta^2} \cot(\theta) - \frac{\partial \Theta(\theta)}{\partial \theta} + \alpha \Theta(\theta) = 0, \quad (10b)$$

where $\alpha = n(n+1)$, and whose solutions' product give us V_m i.e.

$$V_m(r, \theta) = \sum_{n=0}^{\infty} \left(a_n i_n\left(\frac{r}{\lambda}\right) + b_n k_n\left(\frac{r}{\lambda}\right) \right) P_n(\cos(\theta)), \quad (11)$$

where i_n and k_n are the modified spherical Bessel function of the first and second kind [14], respectively, of order n , P_n is the Legendre polynomial of order n [16], a_n is the coefficient we determine from the boundary conditions, and b_n must be 0 since we need the potential to remain analytic at the origin.

B. Monodomain Potential

For the product solution of $\psi(r, \theta) = \mathcal{R}(r)\mathcal{Q}(\theta)$, we separate (6) into

$$\frac{\partial^2 \mathcal{R}(r)}{\partial r^2} + \frac{2}{r} \frac{\partial \mathcal{R}(r)}{\partial r} - \frac{\alpha}{r^2} \mathcal{R}(r) = 0, \quad (12a)$$

and

$$\frac{\partial^2 \Theta(\theta)}{\partial \theta^2} \cot(\theta) - \frac{\partial \Theta(\theta)}{\partial \theta} + \alpha \Theta(\theta) = 0, \quad (12b)$$

whence

$$\psi(r, \theta) = \sum_{n=0}^{\infty} (c_n r^n + d_n r^{-n-1}) P_n(\cos(\theta)). \quad (13)$$

For analyticity, since the monodomain includes the origin, we hold that $d_n = 0$ leaving the coefficient, c_n , to be determined from the boundary conditions.

C. External Potential

From (7) we see that the external potential is the sum of the potential due to the source and sink points and the secondary field. Since ϕ_{bath} satisfies the axially symmetric Laplace

equation and is in a region that does not include the origin, we can immediately write its solution as

$$\phi_{bath}(r, \theta) = \sum_{n=0}^{\infty} e_n r^{-n-1} P_n(\cos(\theta)), \quad (14)$$

determining e_n from the boundary conditions. The potentials due to the current source and sink points with magnitude I_0 are given as [15]

$$\phi_{source} = \frac{I_0 \rho_e}{4\pi R_{source}}, \quad (15a)$$

and

$$\phi_{sink} = \frac{-I_0 \rho_e}{4\pi R_{sink}}, \quad (15b)$$

where ρ_e is the resistivity of the conducting bath, and R_{source} and R_{sink} are the distances from their respective points to any point (r, θ) in the problem domain. From Fig. 1 it is clear that

$$R_{source}(r, \theta) = \sqrt{b^2 + r^2 - 2br \cos(\theta)}, \quad (16a)$$

and

$$R_{sink}(r, \theta) = \sqrt{b^2 + r^2 + 2br \cos(\theta)}, \quad (16b)$$

which, considering the generating function of the Legendre polynomial [16], allows us to rewrite the expressions for the points' potentials in (15) as

$$\phi_{source}(r, \theta) = \frac{I_0 \rho_e}{4\pi} \sum_{n=0}^{\infty} \frac{g_{<}^n}{g_{>}^{n+1}} P_n(\cos(\theta)), \quad (17a)$$

and

$$\phi_{sink}(r, \theta) = \frac{-I_0 \rho_e}{4\pi} \sum_{n=0}^{\infty} \frac{(-g_<)^n}{g_>^{n+1}} P_n(\cos(\theta)), \quad (17b)$$

where $g_< = \min(r, b)$ and $g_> = \max(r, b)$.

IV. BOUNDARY CONDITIONS

The three boundary conditions at the tissue-bath interface [17], through which we will determine the unknown coefficients, b_n , c_n , and e_n , are continuity of external and extracellular potentials,

$$\phi_e(a, \theta) = \phi_o(a, \theta), \quad (18)$$

continuity of normal current between bath and interstitium,

$$\rho_e^{-1} \frac{\partial \phi_e(r, \theta)}{\partial r} \Big|_{r=a} = \rho_o^{-1} \frac{\partial \phi_o(r, \theta)}{\partial r} \Big|_{r=a}, \quad (19)$$

and no intracellular normal current,

$$\rho_i^{-1} \frac{\partial \phi_i(r, \theta)}{\partial r} \Big|_{r=a} = 0. \quad (20)$$

Solving (18), (19), and (20) yields

$$b_n = I_0 \lambda n(2n+1) ((-a)^n - a^n) q^{-1} \times b^{-n-1} \frac{\rho_e \rho_o}{4\pi} (\rho_i + \rho_o), \quad (21)$$

$$c_n = I_0 (2n+1) a^{-1} (a^n - (-a)^n) \frac{\rho_e \rho_i \rho_o}{4\pi} q^{-1} \times b^{-n-1} \left(\lambda n i_n \left(\frac{a}{\lambda} \right) - a i_{n+1} \left(\frac{a}{\lambda} \right) \right), \quad (22)$$

and

$$e_n = I_0 n a^{n+1} (a^n - (-a)^n) \frac{\rho_e}{4\pi} q^{-1} b^{-n-1} \times \left(a(\rho_e(\rho_i + \rho_o) - \rho_i \rho_o) i_{n+1} \left(\frac{a}{\lambda} \right) - \lambda n (\rho_e - \rho_o) (\rho_i + \rho_o) i_n \left(\frac{a}{\lambda} \right) \right), \quad (23)$$

where

$$q = \lambda n (\rho_i + \rho_o) (n \rho_e + (n+1) \rho_o) i_n \left(\frac{a}{\lambda} \right) - a i_{n+1} \left(\frac{a}{\lambda} \right) (n \rho_e (\rho_i + \rho_o) + (n+1) \rho_i \rho_o), \quad (24)$$

completely determining all potential fields.

V. EXAMPLE AND CONCLUDING REMARKS

To demonstrate our model, let us give an example. We use inputs in the range of known biologically realistic values [6] and list them in Table I. All computations were done on Mathematica 10 (Wolfram Research, Champaign, Illinois). We increased the upper limit of summation until the solution stabilized to five places to the right of the decimal point, at $n = 11$. Fig. 2 shows the interstitial potential of the sphere in the middle of the external field. The dashed line indicates the circumference of the sphere. We see that the potentials, ϕ_o and ϕ_e , are continuous across the dashed line. Fig. 3 shows the expected results. By inspection it is clear that the transmembrane potential, indicated by the dotted line, is the difference between the intracellular and extracellular potentials, indicated by the dot-dashed and solid lines, respectively. The horizontal axis in Fig. 3 is coincidental with the vertical white line in the center of Fig. 2, and the vertical lines at $y = -2$ and 2 indicate the interface between the tissue and conducting bath. Finally we note that the potential generally increases from left to right, i.e. from the point sink to the point source. Neither of those points is shown in Fig. 2 and Fig. 3 because it would obscure the behavior within and immediately surrounding the sphere.

We have shown that all the boundary conditions are satisfied. We can use this work to validate our numeric modeling of the aplysia abdominal ganglion in a MERIT context [18], but this analysis can also be seen as but a first step toward more realistic models. Future analytic modeling will examine the impact of anisotropy on current behavior in spheroidal tissue geometries. Additionally we plan to incorporate the bilayer sonophore model of Plaksin et al. [19] to our MREIT injection current problem and as well as use the decomposition method of Adomian et al. [20] to find an *analytic* approximation, rather than a strictly numeric one.

References

1. Sadleir RJ, Grant SC, Woo EJ. Can high-field MREIT be used to directly detect neural activity? Theoretical considerations. *NeuroImage*. Aug; 2010 52(1):205–216. [PubMed: 20382240]
2. Zhang X, Liu J, He B. Magnetic-resonance-based electrical properties tomography: a review. *IEEE Rev Biomed Eng*. Jan.2014 7:87–96. [PubMed: 24803104]
3. Woo, EJ., Seo, JK., Lee, SY. Magnetic resonance electrical impedance tomography (MREIT). In: Holder, DS., editor. *Electrical Impedance Tomography: Methods, History, and Applications*. Vol. ch. 9. Institute of Physics Publishing Ltd; 2005. p. 239-294.
4. Muthupillai R, Ehman RL. Magnetic resonance elastography. *Nat Med*. May; 1996 2(5):601–603. [PubMed: 8616724]
5. FitzHugh, R. Mathematical models of excitation and propagation in nerve. In: Schwan, HP., editor. *Biological Engineering*. Vol. ch. 1. McGraw-Hill, Inc; 1969. p. 1-85.
6. Malmivuo, J., Plonsey, R. *Bioelectromagnetism: Principles and Applications of Bioelectric and Biomagnetic Fields*. Vol. ch. 9. Oxford University Press, Inc; New York, NY: 1995. p. 159-168.
7. Rall, W., Agmon-Snir, H. Cable theory for dendritic neurons. In: Koch, C., Segev, I., editors. *Methods in Neuronal Modeling: From Ions to Networks*. 2. Vol. ch. 2. MIT Press; Cambridge, MA: 1998. p. 27-92.
8. Plonsey R. The use of a bidomain model for the study of excitable media. *Lect Math Life Sci*. Nov. 1989 21:123–149.
9. Martinek J, Stickler Y, Reichel M, Mayr W, Rattay F. A Novel Approach to Simulate Hodgkin? Huxley-like Excitation With COMSOL Multiphysics. *Artif Organs*. Aug; 2008 32(8):614–619. [PubMed: 18782131]
10. Yin, S., Dokos, S., Lovell, NH. Bidomain modeling of neural tissue. In: He, B., editor. *Neural Engineering*. Vol. ch. 8. Springer; New York, NY: 2013. p. 389-404.
11. Altman KW, Plonsey R. Development of a model for point source electrical fibre bundle stimulation. *Med Biol Eng Comput*. Sep.1988 26:466–475. [PubMed: 3256735]
12. Tung, L. PhD dissertation. Vol. ch. 4. Mass. Inst. Tech; Cambridge, MA: Jun. 1978 A Bi-Domain Model for Describing Ischemic Myocardial D-C Potentials; p. 59-102.
13. Moon, P., Spencer, DE. *Field Theory Handbook*. Springer-Verlag; Berlin, Germany: 1981. p. 1-48.sec. 2
14. Ben-Menahem, A., Singh, SJ. *Seismic Waves and Sources*. Springer-Verlag; New York, NY: 1981. p. 967-983.app. D
15. Malmivuo, J., Plonsey, R. *Bioelectromagnetism: Principles and Applications of Bioelectric and Biomagnetic Fields*. Vol. ch. 8. Oxford University Press, Inc; New York, NY: 1995. p. 148-158.
16. Bell, WW. *Special Functions for Scientists and Engineers*. Vol. ch. 3. Dover Publications, Inc; Mineola, NY: 2004. p. 42-91.
17. Roth BJ. A comparison of two boundary conditions used with the bidomain model of cardiac tissue. *Ann Biomed Eng*. Feb; 1991 19(2):669–677. [PubMed: 1781568]
18. Sadleir RJ. A bidomain model for neural tissue. *Int J Bioelectromagn*. Jan; 2010 12(1):2–6.
19. Plaksin M, Shoham S, Kimmel E. Intramembrane cavitation as a predictive bio-piezoelectric mechanism for ultrasonic brain stimulation. *Phys Rev X*. Jan.2014 4(1):011004.
20. Adomian, G., Witten, M., Adomian, GE. A new approach to the solution of neurological models: application to the hodgkin-huxley and the fitzhugh-nagumo equations. In: Beckmann, MJ.Gopalan, MN., Subramanian, R., editors. *Stochastic Processes and their Applications*. Springer; Berlin, Germany: 1991. p. 99-113.

Fig. 1.

The volume of tissue is referred to spherical coordinates (r, ϕ, θ) , with its center coinciding with $r=0$. The source and sink points are on a line, their distance bisected by the origin that axial symmetry is achieved. The distances, R , are from the source and sink points to a point in the isotropic conducting bath.

Fig. 2.

The sphere of tissue in a conducting bath. The shade of gray corresponds to the potential at any point in the region of interest, i.e. the lighter the shade, the higher the potential and vice versa. The dashed line indicates the circumference of the sphere. The white line is the horizontal axis in the plot in Fig. 3.

Fig. 3.

The intracellular (dot-dashed), extracellular (solid), transmembrane (dotted), and bath (dashed) potentials are shown as a function of y , along the white line where $x = 0$ in Fig. 2. The vertical lines at $y = -2$ and 2 correspond to the radius of the sphere, $r = a$.

TABLE I

Modeling inputs

Parameter	Value
Interstitial resistivity, ρ_o	$0.19 \Omega m$
Intracellular resistivity, ρ_i	$0.29 \Omega m$
Transmembrane resistivity, ρ_m	$0.15 \Omega m$
Bath resistivity, ρ_e	$0.29 \Omega m$
Interstitial point source, I_o	$1.385 mA$
Tissue radius, a	$2 mm$
Point source distance, b	$4 mm$