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Numerical Methods for Bioelectric Field Problems

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1 Introduction

Computer modeling and simulation continue to grow more important to the field of Bioengineering. The reasons for this growing importance are manyfold. First, mathematical modeling has been shown to be a substantial tool for the investigation of complex biophysical phenomena. Second, since the level of complexity one can model parallels existing hardware configurations, advances in computer architecture have made it feasible to apply the computational paradigm to complex biophysical systems. Hence, while biological complexity continues to outstrip the capabilities of even the largest computational systems, the computational methodology has taken hold in bioengineering and has been used successfully to suggest physiologically and clinically important scenarios and results.

This section provides an overview of numerical techniques which can be applied to a class of bioelectric field problems. Bioelectric field problems are found in a wide variety of biomedical applications which range from single cells [1], to organs [2], up to models which incorporate partial to full human structures [3, 4, 5]. We describe some general modeling techniques which will be applicable, in part, to all the aforementioned applications. We focus our study on a class of bioelectric volume conductor problems which arise in electrocardiography and electroencephalography.

We begin by stating the mathematical formulation for a bioelectric volume conductor, continue by describing the model construction process, and follow with sections on numerical solutions and computational considerations. We conclude with a section on error analysis coupled with a brief introduction to adaptive methods.

2 Problem Formulation

As noted in the chapter on Volume Conductor Theory, most bioelectric field problems can be formulated in terms of either the Poisson or the Laplace equation for electrical conduction. Since Laplace's equation is the homogeneous counterpart of the Poisson equation, we will develop the treatment for a general three-dimensional Poisson problem and discuss simplifications and special cases when necessary.

A *typical* bioelectric volume conductor can be posed as the following boundary value problem:

$$\nabla \cdot \sigma \nabla \Phi = -I_V \qquad \text{in } \Omega, \tag{1}$$

where Φ is the electrostatic potential, σ is the electrical conductivity tensor, and I_V is the current per unit volume defined within the solution domain, Ω. The associated boundary conditions depend on what type of problem one wishes to solve. There are generally considered to be two different types of direct and inverse volume conductor problems.

One type of problem deals with the interplay between the description of the bioelectric volume source currents and the resulting volume currents and volume and surface voltages. Here, the problem statement would be to solve (1) for Φ with a known description of I_V and the Neumann boundary condition:

$$\sigma \nabla \Phi \cdot \mathbf{n} = 0 \qquad \text{on } \Gamma_T, \tag{2}$$

which says that the normal component of the electric field is zero on the surface interfacing with air (here denoted by Γ_T). This problem can be used to solve two well known problems in medicine, the direct EEG (electroencephioliography) and ECG (electrocardiography) volume conductor problems. In the direct EEG problem, one usually discretizes the brain and surrounding tissue and skull. One then assumes a description of the bioelectric current source within the brain (this usually takes the form of dipoles or multipoles) and calculates the field within the brain and on the surface of the scalp. Similarly, in one version of the direct ECG problem, one utilizes descriptions of the current sources in the heart (either dipoles or membrane current source models such as the FitzHugh Nagumo and Beeler Reuter, among others) and calculates the currents and voltages within the volume conductor of the chest and voltages on the surface of the torso. The inverse problems associated with these direct problems involve estimating the current sources I_V within the volume conductor from measurements of voltages on the surface of either the head or body. Thus, one would solve (1) with the boundary conditions:

$$\Phi = \Phi_0 \qquad \text{on } \Sigma \subseteq \Gamma_T \tag{3}$$

$$\sigma \nabla \Phi \cdot \mathbf{n} = 0 \qquad \text{on } \Gamma_T. \tag{4}$$

The first is the Dirichlet condition, which says that one has a set of discrete measurements of the voltage of a subset of the outer surface. The second is the natural Neumann condition. While it doesn't look much different than the formulation of the direct problem, the inverse formulations are ill-posed. The bioelectric inverse problem in terms of primary current sources does not have a unique solution, and the solution doesn't depend continuously on the data. Thus, to obtain *useful* solutions, one must try to restrict the solution domain (i.e. number of physiologically plausible solutions) [11] for the former case, and apply so-called *regularization* techniques to attempt to restore the continuity of the solution on the data in the latter case.

Another bioelectric direct/inverse formulation poses both the problems in terms of scalar values at the surfaces. For the EEG problem, one would take the surface of the brain (cortex) as one bounded surface and the surface of the scalp as the other surface. The direct problem would involve making measurements of voltage of the surface of the cortex at discrete locations and then calculating the voltages on the surface of the scalp. Similarly, for the ECG problem, voltages could be measured on the surface of the heart and used to calculate the voltages at the surface of the torso, as well as within the volume conductor of the thorax. To formulate the inverse problems one uses measurements on the surface of the scalp (torso) to calculate the voltages on the surface of the cortex (heart). Here we solve Laplace's equation instead of Poisson's equation, because we are interested in the distributions of voltages on a surface instead of current sources within a volume. This leads to the following boundary value problem:

$$\nabla \cdot \sigma \nabla \Phi = 0 \qquad \text{in } \Omega \tag{5}$$

$$\Phi = \Phi_0 \qquad \text{on } \Sigma \subseteq \Gamma_T \tag{6}$$

$$\sigma \nabla \Phi \cdot \mathbf{n} = 0 \qquad \text{on } \Gamma_T. \tag{7}$$

For this formulation, the solution to the inverse problem is unique [17]; however, there still exists the problem of continuity of the solution on the data. The linear algebra counterpart to the elliptic boundary value problem is often useful in discussing this problem of noncontinuity. The numerical solution to all elliptic boundary value problems (such as the Poisson and Laplace problems) can be formulated in terms of a set of linear equations, $\mathbf{A\Phi} = \mathbf{b}$. For the solution of Laplace's equation, the system can be reformulated as:

$$A\Phi_{in} = \Phi_{out}, \tag{8}$$

where Φ_{in} is the vector of data on the inner surface bounding the solution domain (the electrostatic potentials on the scalp or heart, for example), Φ_{out} is the vector of data which bounds the outer surface (the subset of voltage values on the surface of the cortex or torso, for example), and A is the *transfer matrix* between Φ_{out} and Φ_{in}, which usually contains the geometry and physical properties (conductivities, dielectric constants, etc.) of the volume conductor. The direct problem is then simply (well) posed as solving (8) for Φ_{out} given Φ_{in}. Likewise, the inverse problem is to determine Φ_{in} given Φ_{out}.

A characteristic of A for ill-posed problems is that it has a very large condition number. In other words, the ill-conditioned matrix A is very near to being singular. Briefly, the condition number is defined as $\kappa(A) = \|A\| \cdot \|A^{-1}\|$ or the ratio of maximum to minimum singular values measured in the L_2 norm. The ideal problem conditioning occurs for orthogonal matrices which have $\kappa(A) \approx 1$, while an ill-conditioned matrix will have $\kappa(A) \gg 1$. When one inverts a matrix which has a very large condition number, the inversion process is unstable and is highly susceptible to errors. The condition of a matrix is relative. It is related to the precision level of computations and is a function of the size of the problem. For example, if the condition number exceeds a linear growth rate with respect to the size of the problem, the problem will become increasingly ill-conditioned. See [36] for more about the condition number of matrices.

A number of techniques have arisen to deal with ill-posed inverse problems. These techniques include truncated singular value decompostion (TSVD), generalized singular value decompostion (GSVD), maximum entropy, and a number of generalized least squares schemes, including Twomey and Tikhonov regularization methods. Since this section is concerned more with the numerical techniques for approximating bioelectric field problems, the reader is referred to [12, 13, 14, 15] to further investigate the regularization of ill-posed problems. A particularly useful reference for discrete ill-posed problems is the Matlab package developed by Per Christian Hansen which is available via netlib [16].

3 Model Construction and Mesh Generation

Once we have stated or derived the mathematical equations which define the physics of the system, we must figure out how to solve these equations for the particular domain we are interested in. Most numerical methods for solving boundary value problems require that the continuous domain be broken up into discrete elements, the so-called *mesh* or *grid*, which one can use to approximate the governing equation(s) using the particular numerical technique (finite element, boundary element, finite difference, or multigrid) best suited to the problem.

Because of the complex geometries often associated with bioelectric field problems, construction of the polygonal mesh can become one of the most time consuming aspects of the modeling process. After deciding upon the particular approximation method to use (and the most appropriate type of element), we need to construct a mesh of the solution domain which matches the number of degrees of freedom of our fundamental element. For the sake of simplicity, we will assume that we will use linear elements, either tetrahedrons, which are usually used for modeling irregular three-dimensional domains, or hexahedrons used for modeling regular, uniform domains.

There are several different strategies for discretizing the geometry into fundamental elements. For bioelectric field problems, two approaches to mesh generation have become standard: the *divide and conquer* (or subsequent subdivision) strategy; and the so-called *Delaunay triangulation* strategy.

In using the divide and conquer strategy one starts with a set of points which define the bounding surface(s) in three dimensions (contours in two dimensions). The volume (surface) is repeatedly divided into smaller regions until a satisfactory discretization level has been achieved. Usually, the domain is broken up into eight-node cubic elements, which can then be subdivided into five (minimally) or six tetrahedral elements if so desired. This methodology has the advantage of being fairly easy to program; furthermore, commercial mesh generators exist for the divide and conquer method. For use in solving bioelectric field problems, its main disadvantage is that it allows elements to overlap interior boundaries. A single element may span two different conductive regions, for example, when part of an element represents muscle tissue (which could be anisotropic) and the other part of the element falls into a region representing fat tissue. It then becomes very difficult to assign unique conductivity parameters to each element and at the same time accurately represent the geometry.

A second method of mesh generation is the Delaunay triangulation strategy. Given a three-dimensional set of points which define the boundaries and interior regions of the domain to be modeled, one tessellates the point cloud into an optimal mesh of tetrahedra. For bioelectric field problems, the advantages and disadvantages tend to be exactly contrary to those arising from the divide and conquer strategy. The primary advantage is that one can create the mesh to fit any predefined geometry, including subsurfaces, by starting with points which define all the necessary surfaces and subsurfaces and then adding additional interior points to minimize the aspect ratio. For tetrahedra, the aspect ratio can be defined as $4\sqrt{\frac{3}{2}}\frac{\rho_k}{h_k}$, where ρ_k denotes the diameter of the sphere circumscribed about the tetrahedron, and h_k is the maximum distance between two vertices. These formulations yield a value of 1 for an equilateral tetrahedron and a value of 0 for a degenerate (flat) element [18]. The closer to the value of 1, the better. The Delaunay criterion is a method for minimizing the occurrence of obtuse angles in the mesh, yielding elements which have aspect ratios as close to 1 as possible, given the available point set. While the ideas behind Delaunay triangulation are straightforward, the programming is nontrivial and is the primary drawback to this method. Fortunately, there exist several public domain, two-dimensional versions, including one from netlib called sweep2.c from the directory Voronoi, as well as at least one three-dimensional package [41]. For more information on mesh generation and various aspects of biomedical modeling, see [19, 20, 21, 22, 23, 24, 25, 26, 27].

4 Numerical Methods

Because of the geometrical complexity of, and numerous inhomogeneities inherent in, anatomical structures in physiological models, solutions of bioelectric field problems are usually tractable (except in the most simplified of models) only when one employs a numerical approximation method such as the Finite Difference (FD), the Finite Element (FE), Boundary Element (BE), or the Multigrid (MG) Method to solve the governing field equation(s).

4.1 Approximation Techniques - The Galerkin Method

The problem posed in (1) can be solved using any of the aforementioned approximation schemes. One technique which addresses three of the previously mentioned techniques (FD, FE, and BE) can be derived by the Galerkin method. The Galerkin method is one of the most widely used methods for discretizing elliptic boundary value problems such as (1) and for treating the spatial portion of time-dependent parabolic problems, which are common in models of cardiac wave propagation. While the Galerkin technique is not essential to the application of any of the techniques, it provides for a unifying bridge between the various numerical methods. To express our problem in a Galerkin form, we begin by rewriting (1) as:

$$A\Phi = -I_v, \tag{9}$$

where A is the differential operator, $A = \nabla \cdot (\sigma\nabla)$. An equivalent statement of (9) is, find Φ such that $(A\Phi + I_v, \overline{\Phi}) = 0$. Here, $\overline{\Phi}$ is an arbitrary *test function*, which can be thought of physically as a virtual potential field, and the notation $(\phi_1, \phi_2) \equiv \int_\Omega \phi_1\phi_2 \, d\Omega$ denotes the inner product in $L_2(\Omega)$. Applying Green's theorem, we can equivalently write,

$$(\sigma\nabla\Phi, \nabla\overline{\Phi}) - \langle\frac{\partial\Phi}{\partial n}, \overline{\Phi}\rangle = -(I_v, \overline{\Phi}), \tag{10}$$

where the notation $\langle \phi_1, \phi_2 \rangle \equiv \int_S \phi_1 \phi_2 \, dS$ denotes the inner product on the boundary S. When the Dirichlet, $\Phi = \Phi_0$, and Neumann, $\sigma \nabla \Phi \cdot \mathbf{n} = 0$, boundary conditions are specified on S, we obtain the *weak form* of (1):

$$(\sigma \nabla \Phi, \nabla \overline{\Phi}) = -(I_v, \overline{\Phi}). \tag{11}$$

It is understood that this equation must hold for all test functions, $\overline{\Phi}$, which must vanish at the boundaries where $\Phi = \Phi_0$. The Galerkin approximation ϕ to the weak form solution Φ in (11) can be expressed as:

$$\phi(\mathbf{x}) = \sum_{i=0}^{N} \phi_i \psi_i(\mathbf{x}) \tag{12}$$

The trial functions $\psi_i, i = 0, 1, \ldots, N$ form a basis for an N+1 dimensional space $\mathcal{S}$. We define the *Galerkin approximation* to be that element $\phi \in \mathcal{S}$ which satisfies

$$(\sigma \nabla \phi, \nabla \psi_j) = -(I_v, \psi_j) \qquad (\forall \psi_j \in \mathcal{S}). \tag{13}$$

Since our differential operator A is positive definite and self adjoint (i.e., $(A\Phi, \Phi) \geq \alpha(\Phi, \Phi) > 0$ for some non-zero positive constant α and $(A\Phi, \overline{\Phi}) = (\Phi, A\overline{\Phi})$, respectively), then we can define a space E with an inner product defined as $(\Phi, \overline{\Phi})_E = (A\Phi, \overline{\Phi}) \equiv a(\Phi, \overline{\Phi})$ and norm (the so-called energy norm) equal to:

$$\|\Phi\|_E = \{\int_\Omega (\nabla \Phi)^2 d\,\Omega\}^{\frac{1}{2}} = (\Phi, \Phi)_E^{\frac{1}{2}}. \tag{14}$$

The solution Φ of (9) satisfies

$$(A\Phi, \psi_i) = -(I_v, \psi_i) \qquad (\forall \psi_i \in \mathcal{S}) \tag{15}$$

and the approximate Galerkin solution obtained by solving (13) satisfies

$$(A\phi, \psi_i) = -(I_v, \psi_i) \qquad (\forall \psi_i \in \mathcal{S}). \tag{16}$$

Subtracting (15) from (16) yields

$$(A(\phi - \Phi), \psi_i) = (\phi - \Phi, \psi_i)_E = 0 \qquad (\forall \psi_i \in \mathcal{S}). \tag{17}$$

The difference $\phi - \Phi$ denotes the error between the solution in the infinite dimensional space V and the $N+1$ dimensional space $\mathcal{S}$. Equation (17) states that the error is orthogonal to all basis functions spanning the space of possible Galerkin solutions. Consequently, the error is orthogonal to all elements in $\mathcal{S}$ and must therefore be the minimum error. Thus the Galerkin approximation is an orthogonal projection of the true solution Φ onto the given finite dimensional space of possible approximate solutions. Therefore, the Galerkin approximation is the best approximation in the energy space E. Since the operator is positive definite, the approximate solution is unique. Assume for a moment there are two solutions, ϕ_1 and ϕ_2, satisfying

$$(A\phi_1, \psi_i) = -(I_v, \psi_i) \quad (A\phi_2, \psi_i) = -(I_v, \psi_i) \qquad (\forall \psi_i \in \mathcal{S}) \tag{18}$$

respectively. Then, the difference yields

$$(A(\phi_1 - \phi_2), \psi_i) = 0 \quad (\forall \psi_i \in \mathcal{S}). \tag{19}$$

The function arising from subtracting one member from another member in $\mathcal{S}$ also belongs in $\mathcal{S}$; hence, the difference function can be expressed by the set of A orthogonal basis functions spanning $\mathcal{S}$:

$$\sum_{j=0}^{N} \Delta\phi_j (A(\psi_j, \psi_i)) = 0 \quad (\forall \psi_i \in) \tag{20}$$

When $i \neq j$, the terms vanish due to the basis functions being orthogonal with respect to A. Since A is positive definite:

$$(A\Phi_i, \Phi_i) > 0 \quad i = 0, \ldots, N. \tag{21}$$

Thus, $\Delta\phi_i = 0$, $i = 0, \ldots, N$, and by virtue of (20), $\delta\phi = 0$, such that $\phi_1 = \phi_2$. The identity contradicts the assumption of two distinct Galerkin solutions. This proves the solution is unique [28].

4.2 The Finite Difference Method

Perhaps the most traditional way to solve (1) utilizes the finite difference approach by discretizing the solution domain Ω using a grid of uniform hexahedral elements. The coordinates of a typical grid point are $x = lh, y = mh, z = nh$ (l,m,n=integers), and the value of $\Phi(x, y, z)$ at a grid point is denoted by $\Phi_{l,m,n}$. Taylor's theorem can then be utilized to provide the difference equations. For example:

$$\Phi_{l+1,m,n} = (\Phi + h\frac{\partial\Phi}{\partial x} + \frac{1}{2}h^2\frac{\partial^2\Phi}{\partial x^2} + \frac{1}{6}h^3\frac{\partial^3\Phi}{\partial x^3} + \ldots)_{l,m,n} \tag{22}$$

with similar equations for $\Phi_{l-1,m,n}$, $\Phi_{l,m+1,n}$, $\Phi_{l,m-1,n,\ldots}$. The finite difference representation of (1) is

$$\frac{\Phi_{l+1,m,n} - 2\Phi_{l,m,n} + \Phi_{l-1,m,n}}{h^2} + \frac{\Phi_{l,m+1,n} - 2\Phi_{l,m,n} + \Phi_{l,m-1,n}}{h^2} + \frac{\Phi_{l,m,n+1} - 2\Phi_{l,m,n} + \Phi_{l,m,n-1}}{h^2} = -I_{l,m,n}(v) \tag{23}$$

or, equivalently,

$$\Phi_{l+1,m,n} + \Phi_{l-1,m,n} + \Phi_{l,m+1,n} + \Phi_{l,m-1,n} + \Phi_{l,m,n+1} + \Phi_{l,m,n-1} - 6\Phi_{l,m,n} = -h^2 I_{l,m,n}(v). \tag{24}$$

If we define the vector $\mathbf{\Phi}$ to be $[\Phi_{1,1,1} \ldots \Phi_{1,1,N-1}; \ldots \Phi_{1,N-1,1} \ldots \Phi_{N-1,N-1,N-1}]^T$ to designate the $(N-1)^3$ unknown grid values, and pull out all the known information from (24), we can reformulate (1) by its finite difference approximation in the form of the matrix equation $A\mathbf{\Phi} = \mathbf{b}$, where $\mathbf{b}$ is a vector which contains the sources and modifications due to the Dirichlet boundary condition.

Unlike the traditional Taylor's series expansion method, the Galerkin approach utilizes basis functions, such as linear piecewise polynomials, to approximate the true solution. For example, the

Galerkin approximation to the sample problem (1) would require evaluating (13) for the specific grid formation and specific choice of basis function:

$$\int_\Omega (\sigma_x \frac{\partial \phi}{\partial x}\frac{\partial \psi_i}{\partial x} + \sigma_y \frac{\partial \phi}{\partial y}\frac{\partial \psi_i}{\partial y} + \sigma_z \frac{\partial \phi}{\partial z}\frac{\partial \psi_i}{\partial z}) d\Omega = -\int_\Omega I_v \psi_i d\Omega \tag{25}$$

Difference quotients are then used to approximate the derivatives in (25). We note that if linear basis functions are utilized in (25), one obtains a formulation which corresponds exactly with the standard finite difference operator. Regardless of the difference scheme or order of basis function, the approximation results in a linear system of equations of the form $A\mathbf{\Phi} = \mathbf{b}$, subject to the appropriate boundary conditions.

4.3 The Finite Element Method

As we have seen above, in the classical numerical treatment for partial differential equations - the finite difference method - the solution domain is approximated by a grid of uniformly spaced nodes. At each node, the governing differential equation is approximated by an algebraic expression which references adjacent grid points. A system of equations is obtained by evaluating the previous algebraic approximations for each node in the domain. Finally, the system is solved for each value of the dependent variable at each node. In the Finite Element Method, the solution domain can be discretized into a number of uniform or non-uniform finite elements that are connected via nodes. The change of the dependent variable with regard to location is approximated within each element by an interpolation function. The interpolation function is defined relative to the values of the variable at the nodes associated with each element. The original boundary value problem is then replaced with an equivalent integral formulation (such as (13)). The interpolation functions are then substituted into the integral equation, integrated, and combined with the results from all other elements in the solution domain. The results of this procedure can be reformulated into a matrix equation of the form $A\mathbf{\Phi} = \mathbf{b}$, which is subsequently solved for the unknown variable [29, 20].

The formulation of the finite element approximation starts with the Galerkin approximation, $(\sigma\nabla\Phi, \nabla\overline{\Phi}) = -(I_v, \overline{\Phi})$, where $\overline{\Phi}$ is our test function. We now use the finite element method to turn the continuous problems into a discrete formulation. First we discretize the solution domain, $\Omega = \cup_{e=1}^{E}\Omega_e$, and define a finite dimensional subspace, $V_h \subset V = \{\overline{\Phi} : \overline{\Phi}$ is continuous on Ω, $\nabla\overline{\Phi}$ is piecewise continuous on $\Omega\}$. One usually defines parameters of the function $\overline{\Phi} \in V_h$ at node points $\alpha_i = \overline{\Phi}(x_i)$, i = 0, 1, ..., N. If we now define the basis functions, $\psi_i \in V_h$, as linear continuous piecewise functions that take the value 1 at node points and zero at other node points, then we can represent the function $\overline{\Phi} \in V_h$ as

$$\overline{\Phi}(x) = \sum_{i=0}^{N} \alpha_i \Psi_i(x) \tag{26}$$

such that each $\overline{\Phi} \in V_h$ can be written in a unique way as a linear combination of the basis functions $\Psi_i \in V_h$. Now the finite element approximation of the original boundary value problem can be stated as

$$\text{Find } \Phi_h \in V_h \text{ such that } (\sigma\nabla\Phi_h, \nabla\overline{\Phi}) = -(I_v, \overline{\Phi}). \tag{27}$$

Furthermore, if $\Phi_h \in V_h$ satisfies (27), then we have $(\sigma\nabla\Phi_h, \nabla\Psi_i) = -(I_v, \Psi_i)$ [30]. Finally, since Φ_h itself can be expressed as the linear combination

$$\Phi_h = \sum_{i=0}^{N} \xi_i \Psi_i(x) \qquad \xi_i = \Phi_h(x_i), \tag{28}$$

we can then write (27) as

$$\sum_{i=0}^{N} \xi_i(\sigma_{ij}\nabla\Psi_i, \nabla\Psi_j) = -(I_v, \Psi_j) \qquad j = 0, \ldots, N, \tag{29}$$

subject to the Dirichlet boundary condition. Then the finite element approximation of (1) can equivalently be expressed as a system of N equations with N unknowns $\xi_i, \ldots, \xi_N$ (the electrostatic potentials, for example). In matrix form, the above system can be written as $A\xi = b$, where $A = (a_{ij})$ is called the global stiffness matrix and has elements $(a_{ij}) = (\sigma_{ij}\nabla\Psi_i, \nabla\Psi_j)$, while $b_i = -(I_v, \Psi_i)$ and is usually termed the load vector.

For volume conductor problems, A contains all of the geometry and conductivity information of the model. The matrix A is symmetric and positive definite; thus, it is nonsingular and has a unique solution. Because the basis function differs from zero for only a few intervals, A is sparse - (only a few of its entries are nonzero).

4.3.1 Application of the FE Method for 3-D Domains

We now illustrate the concepts of the Finite Element Method by considering the solution of (1) using linear three-dimensional elements. We start with a 3D domain Ω which represents the geometry of our volume conductor and break it up into discrete elements to form a finite dimensional subspace, Ω_h. For 3D domains we have the choice of representing our function as either tetrahedra,

$$\tilde{\Phi} = \alpha_1 + \alpha_2 x + \alpha_3 y + \alpha_4 z, \tag{30}$$

or hexahedra,

$$\tilde{\Phi} = \alpha_1 + \alpha_2 x + \alpha_3 y + \alpha_4 z + \alpha_5 xy + \alpha_6 yz + \alpha_7 xz + \alpha_8 xyz. \tag{31}$$

Because of space limitations we restrict our development to tetrahera, knowing that it is easy to modify our formulae for hexahedra. We take out a specific tetrahedra from our finite dimensional subspace and apply the previous formulations for the four vertices,

$$\begin{pmatrix} \tilde{\Phi}_1 \\ \tilde{\Phi}_2 \\ \tilde{\Phi}_3 \\ \tilde{\Phi}_4 \end{pmatrix} = \begin{pmatrix} 1 & x_1 & y_1 & z_1 \\ 1 & x_2 & y_2 & z_2 \\ 1 & x_3 & y_3 & z_3 \\ 1 & x_4 & y_4 & z_4 \end{pmatrix} \begin{pmatrix} \alpha_1 \\ \alpha_2 \\ \alpha_3 \\ \alpha_4 \end{pmatrix}, \tag{32}$$

or

$$\tilde{\mathbf{\Phi}}_{\mathbf{i}} = \mathbf{C}\alpha, \tag{33}$$

which define the coordinate vertices, and

$$\alpha = \mathbf{C}^{-1}\tilde{\mathbf{\Phi}}_{\mathbf{i}} \tag{34}$$

which defines the coefficients. From equations (30) and (34) we can express $\tilde{\Phi}$ at any point within the tetrahedra,

$$\tilde{\Phi} = [1, x, y, z]\alpha = \mathbf{S}\alpha = \mathbf{S}\mathbf{C}^{-1}\tilde{\mathbf{\Phi}}_{\mathbf{i}} \tag{35}$$

or, most succintly,

$$\tilde{\Phi} = \sum_i N_i \tilde{\Phi}_i. \tag{36}$$

$\tilde{\Phi}_i$ is the solution value at node i, and $\mathbf{N} = \mathbf{S}\mathbf{C}^{-1}$ is the local *shape function* or *basis function.* This can be expressed in a variety of ways in the literature (depending, usually, on whether you are reading engineering or mathematical treatments of finite element analysis):

$$\Phi_j(N_i) = N_i(x, y, z) = f_i(x, y, z) \equiv \frac{a_i + b_i x + c_i y + d_i z}{6V} \tag{37}$$

where

$$6V = \begin{vmatrix} 1 & x_1 & y_1 & z_1 \\ 1 & x_2 & y_2 & z_2 \\ 1 & x_3 & y_3 & z_3 \\ 1 & x_3 & y_3 & z_4 \end{vmatrix} \tag{38}$$

defines the volume of the tetrahedra, V.

Now that we have a suitable set of basis functions, we can find the finite element approximation to our 3D problem. Our orginal problem can be formulated as

$$a(u, v) = (I_v, v) \quad \forall v \in \Omega, \tag{39}$$

where

$$a(u, v) = \int_\Omega \nabla u \cdot \nabla v d\Omega \tag{40}$$

and

$$(I_v, v) = \int_\Omega I_v \cdot v d\Omega. \tag{41}$$

The finite element approximation to the original boundary value problem is

$$a(u_h, v) = (I_v, v) \quad \forall v \in \Omega_h, \tag{42}$$

which has the equivalent form

$$\sum_{i=1}^{N} \xi_i a(\Phi_i, \Phi_j) = (I_v, \Phi_j), \tag{43}$$

where

$$a(\Phi_i, \Phi_j) = a(\Phi_i(N_j), \Phi_j(N_i)), \tag{44}$$

which can be expressed by the matrix and vector elements

$$(a_{ij}) = \int_{\Omega_E} (\frac{\partial N_i}{\partial x}\frac{\partial N_j}{\partial x} + \frac{\partial N_i}{\partial y}\frac{\partial N_j}{\partial y} + \frac{\partial N_i}{\partial z}\frac{\partial N_j}{\partial z}) d\Omega \tag{45}$$

and

$$I_i = \int_{\Omega_E} N_i I_v \, d\Omega. \tag{46}$$

Fortunately, the above quantities are easy to evaluate for linear tetrahedra. As a matter of fact, there are closed form solutions for the matrix elements (a_{ij}):

$$\int_{\Omega_h} N_1^a N_2^b N_3^c N_4^d \, d\Omega = 6V \frac{a!b!c!d!}{(a+b+c+d+3)!}. \tag{47}$$

Therefore,

$$(a_{ij}) = \int_{\Omega_E} \frac{b_i b_j + c_i c_j + d_i d_j}{6V^2} \, d\Omega = \frac{b_i b_j + c_i c_j + d_i d_j}{6V}, \tag{48}$$

and, for the right hand side, we have, assuming constant sources,

$$I_i = \int_{\Omega_E} \frac{a_i + b_i x + c_i y + d_i z}{6V} I_v \, d\Omega = \frac{V I_v}{4}. \tag{49}$$

which have the compact forms

$$a_{ij}^{(n)} = \frac{1}{6V}(b_i^{(n)} b_j^{(n)} + c_i^{(n)} c_j^{(n)} + d_i^{(n)} d_j^{(n)}) \tag{50}$$

and

$$I_i^{(n)} = \frac{V I_v}{4} \quad \text{for constant sources.} \tag{51}$$

Now we add up all the contributions from each element into a global matrix and global vector.

$$\sum_{n=1}^{Nel} (a_{ij}^{(n)})(\xi_i) = (I_i^{(n)}) \tag{52}$$

where Nel is equal to the total number of elements in the discretized solution domain and i represents the node numbers (vertices). This yields a linear sytem of equations of the form $\mathbf{A\Phi} = \mathbf{b}$, where $\mathbf{\Phi}$ is our solution vector of voltages, $\mathbf{A}$ represents the geometry and conductivity of our volume conductor, and $\mathbf{b}$ represents the contributions from the current sources and boundary conditions.

For the finite difference method, it turns out that the Dirichlet boundary condition is easy to apply while the Neumann condition takes a little extra effort. For the finite element method it is just the opposite. The Neumann boundary condition

$$\nabla \Phi \cdot \mathbf{n} = 0 \tag{53}$$

is satisfied automatically within the Galerkin and variational formulations. This can be seen by using Green's divergence theorem,

$$\int_\Omega \nabla \cdot \mathbf{A} dx = \int_\Gamma \mathbf{A} \cdot \mathbf{n} \, dS, \tag{54}$$

and applying it to the left hand side of the Galerkin finite element formulation:

$$\begin{aligned} \int_\Omega \nabla v \cdot \nabla w \, d\Omega &\equiv \int_\Omega [\frac{\partial v}{\partial x_1}\frac{\partial w}{\partial x_1} + \frac{\partial v}{\partial x_2}\frac{\partial w}{\partial x_2}] \, d\Omega \\ = \int_\Gamma [v \frac{\partial w}{\partial x_1} n_1 + v \frac{\partial w}{\partial x_2} n_2] \, dS &- \int_\Omega v [\frac{\partial^2 w}{\partial x_1^2} + \frac{\partial^2 w}{\partial x_2^2}] \, d\Omega \\ &= \int_\Gamma v \frac{\partial w}{\partial n} \, dS - \int_\Omega v \nabla^2 w \, d\Omega. \end{aligned} \tag{55}$$

If we multiply our original differential equation, $\nabla^2\Phi = -I_v$, by an arbitrary test function and integrate, we obtain

$$(I_v, v) = -\int_\Omega (\nabla^2\Phi) v \, d\Omega = -\int_\Gamma \frac{\partial\Phi}{\partial n} v \, dS + \int_\Omega \nabla\Phi \cdot \nabla v \, d\Omega = a(\Phi, v), \tag{56}$$

where the boundary integral term, $\frac{\partial\Phi}{\partial n}$ vanishes and we obtain the standard Galerkin finite element formulation.

To apply the Dirichlet condition, we have to work a bit harder. To apply the Dirichlet boundary condition directly, one usually modifies the (a_{ij}) matrix and b_i vector such that one can use standard linear system solvers. This is accomplished by implementing the following steps.

Assuming we know the ith value of u_i,

1. Subtract from the ith member of the r.h.s. the product of a_{ij} and the known value of Φ_i (call it $\bar{\Phi}_i$, this yields the new right hand side, $\hat{b}_i = b_i - a_{ij}\bar{\Phi}_j$.
2. Zero the ith row and column of A: $\hat{a}_{ij} = \hat{a}_{ji} = 0$.
3. Assign $\hat{a}_{ii} = 1$.
4. Set the jth member of the r.h.s. equal to $\bar{\Phi}_i$.
5. Continue for each Dirichlet condition.
6. Solve the augmented system, $\hat{A}\Phi = \hat{b_v}$.

4.4 The Boundary Element Method

For bioelectric field problems with isotropic domains (and few inhomogeneities), another technique, called the boundary element method, may be utilized. This technique utilizes information only upon the boundaries of interest, and thus reduces the dimension of any field problem by one. For differential operators, the response at any given point to sources and boundary conditions depends only on the response at neighboring points. The FD and FE methods approximate differential operators defined on subregions (volume elements) in the domain; hence, direct mutual influence (connectivity) exists only between neighboring elements, and the coefficient matrices generated by these methods have relatively few non-zero coefficients in any given matrix row. As is demonstrated by Maxwell's laws [?], equations in differential forms can often be replaced by equations in integral forms; e.g. the potential distribution in a domain is uniquely defined by the volume sources and the potential and current density on the boundary. The boundary element method utilizes this fact by transforming the differential operator defined in the domain to integral operators defined on the boundary. In the boundary element method [31, 32, 33], only the boundary is discretized; hence, the mesh generation is considerably simpler for this method than for the volume methods. Boundary solutions are obtained directly by solving the set of linear equations; however, potentials and gradients in the domain can be evaluated only after the boundary solutions have been obtained. As this method has a rich history in bioelectric field problems, the reader is referred to some of the classic references for further information regarding the application of the BE method to bioelectric field problems, [42, 6, 43, 44].

4.5 Solution Methods and Computational Considerations

Application of each of the previous approximation methods to (1) yields a system of linear equations of the form $\mathbf{A\Phi} = \mathbf{b}$, which must be solved to obtain the final solution. There are a plethora of available techniques for the solutions of such systems. The solution techniques can be broadly catagorized as *direct* and *iterative* solvers. Direct solvers include Gaussian Elimination and LU Decomposition, while iterative methods include Jacobi, Gauss-Seidel, Successive Overrelaxation (SOR),and Conjugate Gradient (CG) methods, among others. The choice of the particular solution method is highly dependent upon the approximation technique employed to obtain the linear system, upon the size of the resulting system, and upon accessible computational resources. For example, the linear system resulting from the application of the FD or FE method will yield a matrix $\mathbf{A}$ that is symmetric, positive definite, and sparse. The matrix resulting from the FD method will have a specific band-diagonal structure which is dependent on the order of difference equations one uses to approximate the governing equation. The matrix resulting from the FE method will be exceedingly sparse that only a few of the off diagonal elements will be non-zero. The application of the BE method, on the other hand, will yield a matrix $\mathbf{A}$ that is dense and non-symmetric and thus requires a different choice of solver.

The choice of the optimal solver is further complicated by the size of the system versus access to computational resources. Sequential direct methods are usually confined to single workstations and thus the size of the system should fit in memory for optimal performance. Sequential iterative methods can be employed when the size of the system exceeds the memory of the machine; however, one pays a price in terms of performance as direct methods are usually much faster than iterative methods. In many cases, the size of the system exceeds the computational capability of a single workstation and one must resort to the use of clusters of workstations and/or parallel computers.

While new and improved methods continue to appear in the numerical analysis literature, the author's studies comparing various solution techniques for direct and inverse bioelectric field problems have resulted in the conclusion that the Preconditioned Conjugate Gradient methods and Multigrid methods are the best overall performers for volume conductor problems computed on single workstations. Specifically, the Incomplete Choleski Conjugate Gradient (ICCG) method works well for the FE method* and the Preconditioned Bi-Conjugate Gradient (BCG) methods are often utilized for BE methods. When clusters of workstations and/or parallel architectures are considered, the choice is less clear. For use with some high performance architectures that contain large amounts of memory, parallel direct methods such as LU decomposition become attractive; however, preconditioned conjugate gradient methods still perform well.

A discussion of parallel computing methods for the solution of biomedical field problems could fill an entire text. Thus, the reader is directed to the following references on parallel scientific

*This is specifically for the FE method applied to elliptic problems. Such problems yield a matrix which is symmetric and positive definite. The Choleski decomposition only exists for symmetric, positive definite matrices.

computing, [45, 46, 47].

4.6 Comparison of Methods

Since we don't have space to give a detailed, quantitative description of each of the previously mentioned methods, we give an abbreviated summary of the applicability of each method in solving different types of bioelectric field problems.

As outlined above, the FD, FE, and BE methods can all be used to approximate the boundary value problems which arise in biomedical research problems. The choice depends on the nature of the problem. The FE and FD methods are similar in that the entire solution domain must be discretized, while with the BE method only the bounding surfaces must be discretized. For regular domains, the FD method is generally the easiest method to code and implement, but the FD method usually requires special modifications to define irregular boundaries, abrupt changes in material properties, and complex boundary conditions. While typically more difficult to implement, the BE and FE methods are preferred for problems with irregular, inhomogeneous domains and mixed boundary conditions. The FE method is superior to the BE method for representing nonlinearity and true anisotropy, while the BE method is superior to FE method for problems where only the boundary solution is of interest or where solutions are wanted in a set of highly irregularly spaced points in the domain. Because the computational mesh is simpler for the BE method than for the FE method, the BE program requires less book-keeping than a FE program. For this reason BE programs are often considered easier to develop than FE programs; however, the difficulties associated with singular integrals in the BE method are often highly underestimated. In general, the FE method is preferred for problems where the domain is highly heterogeneous, whereas the BE method is preferred for highly homogeneous domains.

5 Adaptive Methods

Thus far we have discussed how one formulates the problem, discretizes the geometry, and finds an approximate solution. We are now faced with answering the difficult question pertaining to the accuracy of our solution. Without reference to experimental data, how can we judge the validity of our solutions? To give yourself an intuitive feel for the problem (and possible solution), consider the approximation of a two-dimensional region discretized into triangular elements. We'll apply the finite element method to solve Laplace's equation in the region.

First, consider the approximation of the potential field $\Phi(x, y)$ by a two dimensional Taylor's series expansion about a point (x, y):

$$\Phi(x+h, y+k) = \Phi(x,y) + [h\frac{\partial\Phi(x,y)}{\partial x} + k\frac{\partial\Phi(x,y)}{\partial y}] + \frac{1}{2!}[h^2\frac{\partial^2\Phi(x,y)}{\partial^2 x} + 2hk\frac{\partial^2\Phi(x,y)}{\partial x\partial y} + k^2\frac{\partial^2\Phi(x,y)}{\partial^2 y}] + \dots \quad (57)$$

where h and k are the maximum x and y distances within an element. Using the first two terms (up to first order terms) in the above Taylor's expansion, we can obtain the standard linear interpolation function for a triangle:

$$\frac{\partial \Phi(x_i, y_i)}{\partial x} = \frac{1}{2A}[\Phi_i(y_j - y_m) + \Phi_m(y_i - y_j) + \Phi_j(y_m - y_i)], \tag{58}$$

where A is the area of the triangle. Likewise, one could calculate the interpolant for the other two nodes and discover that

$$\frac{\partial \Phi(x_i, y_i)}{\partial x} = \frac{\partial \Phi(x_j, y_j)}{\partial x} = \frac{\partial \Phi(x_m, y_m)}{\partial x} \tag{59}$$

is constant over the triangle (and thus so is the gradient in y as well). Thus, we can derive the standard linear interpolation formulas on a triangle which represent the first two terms of the Taylor's series expansion. This means that the error due to discretization (from using linear elements) is proportional to the third term of the Taylor's expansion:

$$\epsilon \approx \frac{1}{2!}[h^2 \frac{\partial^2 \Phi(x, y)}{\partial^2 x} + 2hk \frac{\partial^2 \Phi(x, y)}{\partial x \partial y} + k^2 \frac{\partial^2 \Phi(x, y)}{\partial^2 y}], \tag{60}$$

where Φ is the exact solution. We can conjecture, then, that the error due to discretization for first order linear elements is proportional to the second derivative. If Φ is a linear function over the element, then the first derivative is a constant and the second derivative is zero and there is no error due to discretization. This implies that the gradient must be constant over each element. If the function is not linear, or the gradient is not constant over an element, the second derivative will not be zero and is proportional to the error incurred due to "improper" discretization. Examining (60) we can easily see that one way to decrease the error is to decrease the size of h and k. As h and k go to zero, the error tends to zero as well. Thus, decreasing the mesh size in places of high errors due to high gradients decreases the error. As an aside, we note that if one divides equation (9) by hk, one can also express the error in terms of the elemental aspect ratio $\frac{h}{k}$, which is a measure of the relative shape of the element. It is easy to see that one must be careful to maintain an aspect ratio as close to unity as possible.

The problem with the preceding heuristic argument is that one has to know the exact solution *a priori* before one can estimate the error. This is certainly a drawback considering we are trying to accurately approximate Φ.

5.0.1 Convergence of a Sequence of Approximate Solutions

Let's try to quantitfy our error a bit further. When we consider the preceding example, it seems to make sense that if we increase the number of degrees of freedom we used to approximate our function, the accuracy must approach the true solution. That is, we would hope that the sequence of approximate solutions will *converge* to the exact solution as the number of degrees of freedom (DOF) increases indefinitely:

$$\|\Phi(x) - \tilde{\Phi}_n(x)\| \to 0 \quad \text{as } N \to \infty. \tag{61}$$

This is a statement of *pointwise convergence*. It describes the approximate solution as approaching arbitrarily close to the exact solution at each point in the domain as the number of DOF increases.

Measures of convergence often depend on how the *closeness* of measuring the distance between functions is defined. Another common description of measuring convergence is *uniform convergence*, which requires that the maximum value of $||\Phi(x) - \tilde{\Phi}_n(x)||$ in the domain vanish as $N \to \infty$. This is stronger than pointwise convergence as it requires a unform rate of convergence at every point in the domain. Two other commonly used measures are *convergence in energy* and *convergence in mean*, which involve measuring an *average* of a function of the pointwise error over the domain [40].

In general, proving pointwise convergence is very difficult except in the simplest cases, while proving the convergence of an averged value, such as energy, is often easier. Of course, scientists and engineers are often much more interested in assuring that their answers are accurate in a pointwise sense than in an energy sense because they typically want to know values of the solution $\Phi(x)$ and gradients, $\nabla\Phi(x)$ at specific places.

One intermediate form of convergence is called the *Cauchy convergence*. Here, we require the sequences of two different approximate solutions to approach arbitrarily close to each other:

$$||\Phi_m(x) - \tilde{\Phi}_n(x)|| \to 0 \quad \text{as } M, N \to \infty. \tag{62}$$

While the pointwise convergence expression would imply the previous equation, it is important to note that the Cauchy convergence does not imply pointwise convergence, as the functions could converge to an answer other than the true solution.

While we cannot be assured pointwise convergence of these functions for all but the simplist cases, there do exist theorems that ensure that a sequence of approximate solutions must converge to the exact solution (assuming no computational errors) if the basis functions satisfy certain conditions. The theorems can only ensure convergence in an average sense over the entire domain, but it is usually the case that if the solution converges in an averge sense (energy, etc.), then it will converge in the pointwise sense as well.

5.0.2 Energy Norms

The error in energy, measured by the *energy norm*, is defined in general as [37, 38, 39]

$$||e|| = (\int_\Omega e^T L e \, d\Omega)^{\frac{1}{2}}, \tag{63}$$

where $e = \Phi(x) - \tilde{\Phi}_n(x)$ and L is the differential operator for the governing differential equation (i.e. it contains the derivatives operating on $\Phi(x)$ and any function multiplying $\Phi(x)$). For physical problems this is often associated with the energy density.

Another common measure of convergence utilizes the L_2 norm. This can be termed the average error and can be associated with errors in any quantity. The L_2 norm is defined as

$$||e||_{L_2} = (\int_\Omega e^T e \, d\Omega)^{\frac{1}{2}}. \tag{64}$$

While the norms given above are defined on the whole domain, one can note that the square of each can be obtained by summing element contributions,

$$||e||^2 = \sum_{i=1}^{M} ||e||_i^2, \tag{65}$$

where i represents an element contribution and m the total element number. Often for an *optimal* finite element mesh, one tries to make the contributions to this square of the norm equal for all elements.

While the absolute values given by the energy or L_2 norms have little value, one can construct a relative percentage error that can be more readily interpreted:

$$\eta = \frac{||e||}{||\Phi||} \times 100. \tag{66}$$

This quantity, in effect, represents a weighted RMS error. The analysis can be determined for the whole domain or for element subdomains. One can use it in an adaptive algorithm by checking element errors against some predefined tolerance, η_0, and increasing the DOF only of those areas above the predefined tolerance.

Two other methods, the p and the hp methods, have been found, in most cases, to converge faster than the h method. The p method of refinement requires that one increase the order of the basis function that was used to represent the interpolation (i.e. linear to quadratic to cubic, etc.). The hp method is a combination of the h and p methods and has recently been shown to converge the fastest of the three methods (but, as you might imagine, it is the hardest to implement). To find out more about adaptive refinement methods, see [40, 30, 34, 35, 37, 27].

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