SOLUTION OF THE FORWARD AND INVERSE PROBLEMS
ASSOCIATED WITH THE POTENTIAL FIELD OF A
SINGLE ACTIVE FIBER IN A VOLUME CONDUCTOR

by

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ABSTRACT

A solution of Laplace's equation relating the transmembrane potential
distribution of an active fiber in a volume conductor to its extracellular
field distribution utilizing a Fourier transform method [4] has been reformu-
lated as a one-dimensional linear filtering problem. Formulation of the solu-
tion in this manner allows the application of well-known techniques in linear
system theory and optimal linear filtering thereby facilitating the solution
for both the forward (from transmembrane to field potential distribution) and
inverse (from field to transmembrane potential distribution) problems. The
forward problem is shown to be a simple two-stage filtering process composed
of a membrane and medium filter. In the inverse case the field potential dis-
tribution is considered in the presence of additive measurement noise and the
best estimate in the least-mean-square sense will be obtained for the trans-
membrane potential distribution.

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INTRODUCTION

The relationship existing between the intracellular and extracellular potentials recorded from isolated cells in a volume conductor is a problem of basic interest in electrophysiology. Of special interest are the intra- and extracellular fields of elongated cells possessing circular cylindrical geometry; an excellent review of literature in this area is contained in references [1] and [2]. Applications have been demonstrated for nerve [3-5], skeletal muscle [5,6], and cardiac muscle [7-9]. This paper is concerned with the relationship between the "forward" and "inverse" problems associated with this very fundamental problem in electrophysiology. In the forward problem, one is given transmembrane action potential data (as well as certain additional electrical and geometrical data including the fiber radius conduction velocity and the specific conductivities of the intra- and extracellular media) and is asked to compute the potential at an arbitrary field point in the extracellular medium. This is contrasted with the inverse problem where one is given the potential distribution at an arbitrary radial distance (R) from the fiber and (supplied the same electrical and geometrical information as in the forward problem) is asked to determine the transmembrane action potential within an arbitrary constant, the resting potential.
Modeling Aspects

The approach that will be taken in studying the forward and inverse problem associated with the isolated active fiber in a volume conductor is based on previous studies of Clark and Plonsey [4,10] and Harman, et al. [9] which develop and extend a field theoretic model of the intra- and extracellular fields surrounding the isolated fiber. The model assumes the intra- and extracellular media to be uniform, homogeneous and purely passive (all sources for the potential being assumed to lie within the fiber membrane (Fig. 1)); quasi-stationarity (i.e., propagation effects are neglected (see [11])) and axial symmetry (in cylindrical coordinates $\partial/\partial\phi = 0$.) The scalar potential ($\psi$) as a function of radial ($r$) and axial ($z$) distance in the external ($\psi^0(r,z)$) and internal ($\psi^1(r,z)$) media are obtained by solving Laplace's equation in each of these media subject to appropriate boundary conditions (see [4]). Fourier transform techniques are utilized in solving Laplace's equation in these media and it is these techniques that facilitate the solution of the "inverse" problem as well.

1. The Forward Problem

The expression for extracellular potential ($\psi^0$) at an arbitrary field point from a fiber of radius $a$ is given by [4] as

$$\psi^0(r,z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F_m(k)K_0(|k|r)e^{-jzk}dk$$

where $F_m(k)$ is the Fourier transform of the transmembrane potential distribution $\hat{\psi}_m(z)$, that is
\[ F_m(k) = \int_{-\infty}^{\infty} \Phi_m(z) \exp(\text{j}kz) \, dz \]  

and

\[ \Phi_m(z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F_m(k) \exp(-\text{j}kz) \, dk \]  

The term \( \alpha(|k|a) \) in equation (1) is defined as

\[ \alpha(|k|a) \equiv -[1 + \frac{\sigma_0}{\sigma_i} \frac{K_0(|k|a)I_0(|k|a)}{K_0(|k|a)I_1(|k|a)}] \]  

where \( K_0 \) is the modified Bessel function of the second kind (order 0) and \( I_1 \) is the modified Bessel function of the first kind (order 1). The constants \( \sigma_0 \) and \( \sigma_i \) are the specific conductivities of the extra- and intracellular media, respectively.

Noting that equation (1) for \( \Phi^0(r,z) \) has the form of a Fourier integral for some constant value of radial distance \( r = r^* \), let us define

\[ F^0(kr^*) \equiv H(|k|r^*) \cdot F_m(k) \]  

where

\[ H(|k|r^*) \equiv \frac{K_0(|k|r^*)}{\alpha(|k|a)K_0(|k|a)} \]  

Substituting (5) into equation (1), one obtains the following Fourier transform at radius \( r = r^* \) in the external medium

\[ \Phi^0(r^*,z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F^0(kr^*) \exp(-\text{j}kz) \, dk \]  

\[ F^0(kr^*) = \int_{-\infty}^{\infty} \Phi^0(r^*,z) \exp(\text{j}kz) \, dk \]

At the outer membrane surface of the fiber, the potential \( \Phi_{so}(z) \) is given by
\[ \hat{\Phi}_{so}(z) \equiv \hat{\Phi}^o(a,z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F^o(ka) \exp(-j kz) \, dk \]  

(9)

Defining the Fourier transform of the outer membrane surface potential as

\[ F_{so}^o(k) \equiv F^o(ka) \]  

(10)

we establish via (9) the following Fourier transform pair at the membrane surface

\[ \hat{\Phi}_{so}(z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F_{so}^o(k) \exp(-j kz) \, dk \]  

(11)

\[ F_{so}^o(k) = \int_{-\infty}^{\infty} \hat{\Phi}_{so}(z) \exp(j kz) \, dz \]  

(12)

From (5) at \( r^* = a \), \( F_{so}^o(k) \) is also given by

\[ F_{so}^o(k) = H(|k|a) F_m^o(k) = F_m^o(k) / \alpha(|k|a) \]  

(13)

Thus, equation (5) may also be written as

\[ F^o(kr^*) = H(|k|r^*) \alpha(|k|a) F_{so}^o(k) \]  

(14)

and subsequently, equation (7) may be written as

\[ \hat{\Phi}^o(r^*, z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} W(|k|r^*) F_{so}^o(k) \exp(-j kz) \, dk \]  

(15)

where utilizing equation (6)

\[ W(|k|r^*) = H(|k|r^*) \alpha(|k|a) = \frac{K_0(|k|r^*)}{K_0(|k|a)} \]  

(16)

Thus, from (14) and the Fourier transform of \( \hat{\Phi}^o(r^*, z) \)

\[ F^o(kr^*) = W(|k|r^*) F_{so}^o(k) = \int_{-\infty}^{\infty} \hat{\Phi}^o(r^*, z) \exp(j kz) \, dz \]  

(17)

With regard to the forward problem, the potential distribution in \( z \) at an arbitrary radial distance \( r^* \) from the fiber may be computed by specifi-
cation of the Fourier transforms of either the transmembrane or outer membrane surface potential distributions. That is,

\[
\Phi^O(r^*, z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \mathcal{H}(|k|r^*) F_m(k) \exp(-jkz) dk
\]
or

\[
\Phi^O(r^*, z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \mathcal{W}(|k|r^*) F_{SO}(k) \exp(-jkz) dk
\]

where from (13) and (16) it is recognized that

\[
\mathcal{H}(|k|r^*) = \mathcal{W}(|k|r^*) / \alpha(|k|a)
\]

and

\[
F_{SO}(k) = F_m(k) / \alpha(|k|a)
\]

The Fourier transform of \(\Phi^O(r^*, z)\) is therefore given as

\[
F^O(kr^*) = \alpha^{-1}(|k|a) \mathcal{W}(|k|r^*) F_m(k)
\]

from equations (5) and (16). According to equation (20), the field potential \(\Phi^O(r^*, z)\) may be regarded as the result of a two-stage attenuation of the transmembrane potential \(\Phi_m(z)\); the first being associated with the membrane (i.e., equation (13)) where the filter characteristic is \(\alpha^{-1}(|k|)\) and the second stage being associated with the external medium (i.e., equation (17)) where the filter characteristic is \(\mathcal{W}(|k|r^*)\) [see Fig. 2]. The characteristics of these filters are shown in Figs. 3 and 4. From Fig. 3 one will observe that the forward membrane filter function \(\alpha^{-1}(|k|a)\) goes to zero at \(k = 0\). This implies that the d.c. component of the transmembrane potential \(\phi_m\) is completely attenuated by the membrane filter. As is well known from cable theory [10], the transmembrane action current per unit length \(i_m\) entering the extracellular medium is related to the second spatial derivative of the transmembrane poten-
tial \((d^2 \psi(z)/dz^2)\). Therefore any d.c. offset voltage associated with the \(\hat{\phi}_m(z)\) waveform (i.e., the resting potential) does not contribute to the current \(i_m\) traveling through the membrane or to the outer membrane surface potential distribution \((\phi_{so}(z))\). Thus it is appropriate that the membrane filter function (Figure 3) behaves in this fashion at \(k = 0\); and, as one might expect, the resting potential is not recoverable in the inverse problem.

In the case of the filter \(W(|k|r^*)\) associated with the external medium (Figure 4), one will note that as \(r^*\) increases (increasing radial distance from the fiber), the degree of attenuation of the filter \(W(|k|r^*)\) with regard to \(k\) increases. The transfer function \(W(|k|r^*)\) therefore behaves as a low-pass filter, i.e., the further from the fiber the potential distribution is recorded, the more its energy will be concentrated at lower spatial frequencies. The combined filter \(H(|k|r^*)\) plotted as a function of \(k\) is seen in Figure 5.

Thus, in the forward problem, one is given the filter characteristics \(W(|k|r^*)\) and \(\alpha^{-1}(|k|a)\) and the transmembrane potential distribution \(\hat{\phi}_m(z)\). The Fourier transform of \(\hat{\phi}_m(z)\) is \(F_m(k)\) from (2), and equation (20) specifies \(F^O(kr^*)\). The inverse transform of \(F^O(kr^*)\) yields the desired result, the potential distribution \(\hat{\phi}^O(r^*,z)\) at an arbitrary radial distance \(r^*\) from the fiber.

2. The Idealized Inverse Problem

The procedure for solving the inverse problem in the \(k\)-domain is quite analogous to the procedure outlined in the previous section for the forward
problem. One is given the filter characteristics as before and the potential distribution \( \Phi^O(r^*, z) \). The objective is to solve for \( F_m(k) \) via equation (20), i.e.,

\[
F_m(k) = \alpha(|k|a)W^{-1}(|k|r^*)F^O(kr^*)
\]  

(21)

Similarly, to obtain \( F_{so}(k) \), one employs equation (17) such that

\[
F_{so}(k) = W^{-1}(|k|r^*)F^O(kr^*)
\]  

(22)

The validity of these equations, of course, depends on the existence of the operators \( \alpha(|k|a) \) and \( W^{-1}(|k|r^*) \). From definitions (4) and (16) and Figures 3 and 4, it follows that

\[
\alpha(|k|a) \to \infty \text{ as } k \to 0
\]

\[
W^{-1}(|k|r^*) \to \infty \text{ as } k \to \infty
\]

Therefore these inverse filter functions are not defined for all \( k \) in the range \( -\infty \leq k \leq \infty \). In particular, the \( W^{-1}(|k|r^*) \) function is an inverse filter function associated with the extracellular medium and its properties are such that for band-limited signals such as \( \Phi^O(r^*, z) \), the Fourier transform of the surface potential distribution \( F_{so}(k) \) can be obtained via equation (22) for a range of \( r^* \) values of interest.

The membrane inverse filter function \( \alpha(|k|a) \) is well behaved except at \( k = 0 \) and, as previously discussed, this indicates that the d.c. resting potential is unable to be recovered in the inverse filtering process.

**DISCRETE FOURIER METHODS OF SOLUTION**

The continuous domain expressions for the various potentials \( \Phi_m(z), \Phi^O(r^*, z), \Phi_{so}(z) \) and their Fourier transforms \( F_m(k), F^O(kr^*), F_{so}(k) \) can
be reformulated in the discrete k-domain for implementation on a digital computer, by introducing the following Discrete Fourier Transform (DFT)* pair (transmembrane potential is used as an example):

\[
F_m(Pq) = \frac{1}{N} \sum_{n=0}^{N-1} \phi_m(Zn) \exp(j2\pi nq/N) = \text{DFT}(\phi_m(Zn)) \tag{23}
\]

\[
\phi_m(Zn) = \frac{1}{N} \sum_{q=0}^{N-1} F_m(Pq) \exp(-j2\pi nq/N) = \text{IDFT}(F_m(Pq)) \tag{24}
\]

where

\[
P = 2\pi/NZ
\]

Here \(Z\) and \(P\) are the sampling intervals in the \(z\) and \(k\) domains, respectively, and \(n\) and \(q\) are integers. The function \(\phi_m(z)\) is normally limited in both the \(z\) and \(k\) domains, meaning that \(\phi_m(z)\) (see Fig. 9) is nonzero for a small finite range of \(z\) values \((-Z_1 \leq z \leq Z_2\) and is essentially zero outside this range. Similarly, \(\phi_m(z)\) is limited with respect to frequency content and therefore \(F_m(k)\) is nonzero only within a small range \(|k| < M\) (a constant) and zero elsewhere. Thus the discrete functions \(\phi_m(Zn)\) and \(F_m(Pq)\) both approach zero as \(Zn\) and \(Pq\), respectively, become large. The sampling intervals \((Z\) and \(P)\) must, of course, be chosen so that no aliasing occurs in the \(k\)-domain and no folding in the \(z\)-domain [12]. Relationships similar in form to the Discrete Fourier transform pair of equations (23) and (24) exist for \(\phi_{so}(z)\) and \(F_{so}(k)\) as well as \(\phi^0(rk*,z)\) and \(F^0(kr*)\).

* See reference [12] for an introduction to Discrete Fourier Transform methods.
In order to perform convolution of two sequences utilizing the DFT, it is necessary to modify these sequences by appending an appropriate number of adjacent zeros to each sequence [12]. If these zero values are not included in either or both of the two sequences to be convolved, the convolutional result will differ from the desired result due to the circular or wraparound nature of the DFT operator. Thus, if sequence 1 has \( L \) adjacent nonzero values and sequence 2 has \( M \), then it is necessary that both sequences be of length \( N \), where \( N \geq L+M-1 \), for sequences 1 and 2 to be convolved by DFT techniques. This requirement is discussed in more detail in [12].

The forward solution, as defined previously, can now be written in term of the products of the DFT's. With the transmembrane potential given, \( \hat{\psi}_m(z) \), the DFT of the field potential at a given radius \( r^* \) is

\[
F^0(Pq,r^*) = H(Pq,r^*) \cdot F_m(Pq)
\]

where \( q = 0,1,...,N-1 \) and \( P \) (the sampling interval in the \( k \) domain) is defined by (25). This result, in discrete space, is the analog of (5) in continuous space. The sequence \( \hat{\psi}_m(Zn) \) is defined as follows:

\[
\hat{\psi}_m(Zn) = \{ \hat{\psi}_m(0), \hat{\psi}_m(Z), \hat{\psi}_m(2Z), \ldots, \hat{\psi}_m(\frac{N}{2} - 1)Z), 0, \ldots, 0 \}
\]

where the first \( N/2 \) values are the samples of \( \hat{\psi}_m(z) \) with the sampling interval \( Z \) and the last \( N/2 \) values are zero. The filter \( H(Pq,r^*) \) must have a finite-duration impulse response (FIR) so that the appropriate number of zero values, \( N/2 \), are included in the impulse response sequence, \( \{h(Zn,r^*)\}, n = 0,1,...,N-1 \).

The actual impulse response for the filters described in this paper
(h_{-1}(z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \alpha^{-1}(|k|a) \exp(-jkz) dk) are not, in general, finite. However, both filters (\alpha^{-1} and W) are stable; they have absolutely summable pulse responses. The membrane filter, \alpha^{-1}, is essentially a second derivative function. The central difference approximation to the pulse response is (1,-2,1) for unity step size. The medium filter, W, is essentially a low pass filter; thus its pulse response is a geometrically decreasing sequence. There are several design techniques described in [13] for obtaining finite impulse response (FIR) filter given the "frequency response." The "windowing method" is the easiest to implement and is quite adequate for the filters here. Specifically, the windowing method requires the impulse response be multiplied by a window function, i.e., the window function, \omega(z) = 0 for all \ |z| \geq z^*, where \ omega(0) = 1. The resulting finite duration impulse response can thus be defined as follows

\[ h(Zn,r^*) = (h(0,r^*), h(Z(r^*),\ldots,h(Z(\frac{N}{2}-1),r^*),0,\ldots,0,h(Z(\frac{3N}{4}),r^*),\ldots,h(Z(N-1),r^*)) \]  

(28)

where \ z^* = \frac{N}{4} Z. Now if \ H(Pq,r^*) = \text{DFT}(h(Zn,r^*)) , the product defined in (26) will be the desired result and

\[ \hat{\phi}^O(Zn,r^*) = \text{IDFT}(\hat{F}^O(Pq,r^*)) \]  

(29)

is the discrete analog to \ \hat{\phi}(z,r^*). As expected, the sequence \ \hat{\phi}(Zn,r^*) has in general \ N-1 non-zero values where \ \hat{\phi}(Zn) and \ h(Zn,r^*) have \ \frac{N}{2}. The sequence \ \hat{\phi}(Zn,r^*), truncated to obtain \ h(Zn,r^*), is the set of coefficients from the Fourier series expansion of the filter's "frequency response." Since this expansion cannot be obtained analytically an approximation
can be obtained by sampling the filter's "frequency response" at a much larger number of samples, \( \hat{N} \gg \frac{N}{2} \), than required for the FIR filter.

Applying this procedure to (13) and (17), the equivalent discrete convolutions are

\[
F_{S0}(Pq) = H(Pq, a)F_m(Pq)
\]

(30)

and

\[
F^o(Pq, r^*) = W(Pq, r^*)F_{S0}(Pq)
\]

(31)

where the sequences \([\hat{q}_m(Zn)]\) and \([h(Zn, a)]\) from (30) and \([h_w(Zn, r^*)]\) and \([\hat{q}_{S0}(Zn)]\) from (31) have been formed in a manner analogous to (27) and (28).

The discrete surface potential obtained from (30)

\[
\hat{q}_{S0}(Zn) = \text{IDFT}(F_{S0}(Pq))
\]

(32)

must have the appropriate number of zeros appended before including in (31).

In the "inverse problem" in discrete space the field potential at the surface \( \hat{q}_{S0}(z) \), or the field potential at some radius \( r^* \), \( \hat{q}^o(z, r^*) \), is given and the source potential is desired. The source potential is either the transmembrane potential, \( \hat{q}_m(z) \), for a single fiber or the surface potential, \( \hat{q}_{S0}(z) \), for a fiber bundle. The procedure for obtaining the surface or transmembrane potential is essentially that of deconvolution. Thus given \( \hat{q}_{S0}(Zn) \), where now additional zero values are not augmented, the deconvolution is

\[
\hat{F}_m(Pq) = F_{S0}(Pq)/H(Pq, a)
\]

(33)

where \( H(Pq, a) \) is the same transform as in (30). \( \hat{F}_m \) is related to \( F_m \) by a d.c. term. Recall \( H(0) = 0 \), thus the d.c. value of \( F_m \) is not recoverable.
Given \( \hat{\phi}^O(Zn,r^*) \), again no appended zero values, the inverses of (26) and (31) are

\[
\hat{p}_m(Pq) = \frac{F^O(Pq,r^*)}{H(Pq,r^*)} \tag{34}
\]

and

\[
\hat{p}_{SO}(Pq) = \frac{F^O(Pq,r^*)}{W(Pq,r^*)} \tag{35}
\]

respectively.

**NOISE CONSIDERATIONS -- DEVELOPMENT OF AN OPTIMAL INVERSE FILTER FOR PREDICTION OF \( \hat{\phi}_m(z) \)**

With extracellular potential decaying with increasing radial distance from the active fiber and in the presence of an additive measurement noise, the signal to noise ratio (S/N) diminishes and a question arises as to the influence of measurement noise on the ability of an inverse algorithm to reconstruct the waveshape of the transmembrane potential. As one might expect, the presence of even small amounts of additive random noise seriously influences the recovery process as will be demonstrated in the results section. The situation is far from hopeless, however, since standard optimal linear filtering techniques can be employed to yield a best approximation to the transmembrane potential (or outer membrane surface potential) given the extracellular potential in the presence of additive noise, i.e.,

\[
Y^O(r^*,z) = \hat{\phi}^O(r^*,z) + n(z) \tag{36}
\]

where \( n(z) \) = random noise function and \( Y(r^*,z) \) is the measured potential waveform at \( r^* \geq a \) assumed to be corrupted by additive noise.
The potential \( \Psi^O(r^*,z) \) as described by equation (1) satisfies a second-order linear differential equation* and therefore, well-known techniques from linear estimation theory are readily applicable to this problem. Specifically, Wiener-Hopf least-squares estimation theory for the case of additive white noise will be utilized in this study. The general scheme is shown in Figure 6.

With measured extracellular potential \( \Psi^O(r^*,z) \) given according to (36), the mean squared error between the actual extracellular potential \( \Psi^O(r^*,z) \) and an optimally-filtered version of \( \Psi^O(r^*,z) \) [designated as \( \Phi^O(r^*,z) \)], is

\[
I = E[|\Phi^O(r^*,z) - \Psi^O(r^*,z)|^2]
\]  

(37)

where \( E \) is the expectation operator. Thus, \( \Psi^O(r^*,z) \) is assumed to be a stationary random process that is filtered in such a manner as to minimize the functional \( I \). Therefore,

\[
\Phi^O(r^*,z) = \int_{-\infty}^{\infty} g(r^*,z-z')\Psi^O(r^*,z')dz'
\]  

(38)

where the solution for the filter \( g(r^*,z) \) minimizing \( I \) is given in the \( k \)-domain [14] as

\[
G(kr^*) = \frac{S_{\Psi^O}(kr^*)}{S_{\Psi^O}(kr^*)}
\]  

(39)

where \( G(kr^*) \) is the Fourier transform of \( g(kr^*) \), \( S_{\Psi^O}(kr^*) \) is the cross-spectral density of \( \Psi^O \) and \( \Psi^O \), and \( S_{\Psi^O}(kr^*) \) is the spectral density of \( \Psi^O(kr^*) \). Assuming further that the signal \( \Psi^O \) and noise \( n(z) \) are statistically independent, one obtains [14]

* At \( r = r^* \), Laplace's equation for constant \( r \) is simply \( \frac{d^2\Psi}{dz^2} + kr^2\Psi = 0 \).
\[ G(kr^*) = \frac{S_{mm}(k)H^*(|k|r^*)}{|H(|k|r^*)|^2 S_{mm}(k) + S_{nn}(k)} \] (40)

where \( S_{mm}(k) \) is the spectral density function of the transmembrane potential* and \( H^*(|k|r^*) \) is the complex conjugate of the filter function defined by (6).

In regions of the \( k \)-domain where the noise spectral density \( S_{nn}(k) \) can be neglected

\[ G(kr^*) = 1/H(|k|r^*) \] (41)

which is to be expected from previous discussion of the idealized inverse problem. For regions of the \( k \)-domain where \( S_{nn} \) is significant, the attenuation of the optimal filter is greater than that of the idealized inverse filter. Here one will recall that the forward filter function (equation (19)) has a zero at \( k = 0 \). Thus from (40) the optimum inverse filter function \( G(kr^*) \) with a nonzero noise spectral density also has a zero at \( k = 0 \).† Thus, \( G(0) \equiv 0 \) as in the idealized inverse case discussed previously.

In this study one is dealing with band-limited signals, e.g., \( S_{mm}(k) = 0 \) for \( k > M \). In general, \( S_{mm}(k) \) can be expected to decay exponentially with \( k \) whereas \( H(|k|a) = \alpha^{-1}(|k|a) \) (see Figure 3) increases in an approximately linear fashion for large \( k \). Thus in equation (40), \(|H|^2 S_{mm} \to 0 \) as \( k \to M \). Also, the larger the noise spectral density function \( S_{nn} \), the faster \( G(k) \) falls off with increasing \( k \) (see Figures 7 and 8).

* The spectral density function \( S_{ss} \) may be substituted for \( S_{mm} \) in (38) and \( W(|k|r) \) for \( H(|k|r^*) \) if the surface potential distribution is desired instead of \( \varphi_m \).

† Thus, with this filter as well, one is unable to recover the d.c. term.
Since the idealized inverse filter \( H^{-1}(|k|r^*) \) approaches \( \infty \) for large \( k \), the optimal inverse filter \( G(|k|r^*) \) which approaches zero for large \( k \) (Figure 8), intuitively provides a distinct improvement in the capability of the algorithm to reconstruct the transmembrane potential. The behavior of the optimal \( G(|k|r^*) \) filter at large \( k \) is important in that numerical errors generated in the digital computation of the inverse problem using the idealized inverse filter function \( H^{-1}(|k|r^*) \) can possibly cause the solution to go unstable (this will be discussed in greater detail when the effects of noise on the reconstructive capabilities of the algorithm are discussed in the results section).

With any noise present in the signal the idealized inverse applied to the signal produces a larger mean square error than does the optimal filter. Evaluation of the functional \( I \) for the idealized inverse filter results in

\[
I_{\text{ideal}} = \int_{-\infty}^{\infty} S_{nn}(k)/|H(k)|^2 dk
\]

(42)

whereas for the optimal inverse filter

\[
I_{\text{optimum}} = \int_{-\infty}^{\infty} S_{nn}(k)/(|H(k)|^2 + [S_{nn}(k)/S_{mm}(k)]) dk
\]

(43)

and from Franks [14], \( I_{\text{optimum}} < I_{\text{ideal}} \).

The implementation of the optimal filter is accomplished in a manner similar to the idealized filter described previously. Thus the optimal estimate of \( F_m \) is

\[
\hat{f}_m(Pq) = G_{\alpha}(Pqa)G_r(Pqr^*)F^0(Pq) = G_{\alpha}(Pqa)F_{so}(Pq)
\]

(44)
where
\[ G_\alpha(Pqa) = \frac{S_{mm}(Pq) / |\alpha(Pqa)|^2}{S_{mm}(Pq) + S_{nn}(Pq)} \] (45)

and
\[ G_w(Pqr^*) = \frac{S_{mm}(Pq)W(Pqr^*)}{S_{mm}(Pq)|W(Pqr^*)|^2 + S_{nn}(Pq)} \] (46)

and \( W(Pqr^*) \) and \( \alpha(Pqa) \) are real functions described previously. The estimates of the spectral densities are obtained as follows:
\[ S_{mm}(Pq) = \frac{Z}{N} |F_m(Pq)|^2 \] (47)

where \( Z \) is the sampling interval and
\[ S_{nn} = Z\sigma^2 \]

where \( \sigma^2 \) is the variance of the noise. We have assumed the noise is white Gaussian. The estimate of the power spectral density of \( \xi_m \), i.e., \( S_{mm} \) given above assumes that \( \xi_m \) is a deterministic signal. Non-deterministic signal power spectral densities estimates can be obtained from a procedure described by Welch [15].

**SIMULATED ACTION POTENTIAL DATA**

A simulated test case has been chosen to illustrate the utility of this discrete Fourier method for obtaining numerical solutions to the forward and inverse problems associated with the single active fiber in a volume conductor. The simulated invertebrate neural action potential distributions (from Clark and Plonsey [4]).
\[
\hat{\psi}_m(z) = \sum_{i=1}^{3} A_i \exp\left(-B_i^2(z-c_i)^2\right)
\] (48)

where the coefficients are

\[
\begin{align*}
A_1 &= 51.0 \text{ mv} & B_1 &= 8.00 \text{ cm}^{-1} & C_1 &= 1.34 \text{ cm} \\
A_2 &= 72.0 \text{ mv} & B_2 &= 5.33 \text{ cm}^{-1} & C_2 &= 1.46 \text{ cm} \\
A_3 &= 18.0 \text{ mv} & B_3 &= 3.33 \text{ cm}^{-1} & C_3 &= 1.66 \text{ cm}
\end{align*}
\]

Figure 9 depicts the waveshape of this simulated action potential and the calculated field potential distributions for \( r^* = a, a, \) and 7a.

RESULTS

The forward solution results are shown in Figure 9. These extracellular potential distributions (for \( r^* = a, 4a, \) and 7a) are triphasic in nature and are quite consistent with the results reported in [4] and [9].

The extracellular potential distribution for \( r^* = 7a \) (in the presence of additive white Gaussian noise, \( \Psi^0(z,r^*) \)) was taken as the input to the inverse filter \( G(kr^*) \). The best estimate (in the least-mean-square sense) of the surface potential \( \hat{\Psi}_{so}(z) \) and transmembrane potential \( \hat{\psi}_m(z) \) distributions are shown in Figure 10, for signal-to-noise (S/N) ratio of 800, and in Figure 11, for S/N = 8 The shape of these estimated surface and transmembrane potential distributions compare quite favorably with the original potentials (for both S/N ratios). However as expected, the d.c. potential of the transmembrane potential distribution was not completely recovered by the inverse procedure. Thus the baseline values of the estimated transmembrane potential distributions are not zero as in the original potential.

The d.c. potentials for these estimated transmembrane potential distri-
butions are not exactly zero either, as predicted in the earlier development. The filter design technique used to obtain finite impulse response (FIR) filters for the membrane filter resulted in a nonzero d.c. value \( \frac{1}{\alpha(P_q,a)} \neq 0 \) for \( q = 0 \), thus \( G(P_q,r) \neq 0 \) for \( q = 0 \). This windowing design technique induces the well-known Gibbs phenomenon [12] (a ringing at discontinuities) which is present in these results as a slight distortion of the low frequency terms. This is due to the sharp peak in the \( W(P_qr^*) \) filter. Other design techniques for FIR filters, such as the Chebyshev design technique, could be used to produce less noticeable distortion than that caused by windowing; however, the added complexity of these other design techniques was not considered essential to the results.

In Figure 12, the estimated transmembrane potential distributions for each S/N ratio are compared to the original transmembrane potential distribution. There is an excellent agreement in the high S/N case and only slightly less for the low S/N case.

**DISCUSSION**

A solution of Laplace's equation has been formulated in such a manner as to allow it to be interpreted as a linear, two-stage filtering problem. This formulation of the solution lends itself to the application of some rather well-known and powerful techniques of linear systems, i.e., the DFT for convolution and least-mean-square (Wiener) filtering for optimal prediction of a signal in additive random noise. The forward and inverse solutions have been obtained from a simulation of an action potential to test these techniques. These techniques and the procedure utilized to determine the forward and the
inverse solutions are in no way dependent on the particular action potential chosen. The only restrictions to the transmembrane potential are that it be time and frequency limited. Of course all physiological signals fill these requirements.

The type of noise chosen to corrupt the field potential distribution measurement is white Gaussian, i.e., it has a uniform power spectral density, $S_{nn}$, for all frequencies. $S_{nn}(k)$ is not necessarily restricted to be white Gaussian noise. It is possible to treat "colored" additive noise, noise which does not have a uniform power spectral density, with this procedure. The only restrictions on the noise are that it be wide-sense stationary and statistically independent of the field potential distribution. If the signal and noise are not statistically independent, the Wiener filter defined by (40) is not valid; however, the more general filter (39) can be applied. Since the optimal filter, $G(k)$, was to be applied to spatial signals, there was no need to restrict $G(k)$ to be a causal filter.

Additive measurement noise was chosen as the most predominant random noise which would occur in experimental extracellular measurements at low signal levels ($\sim 30 \mu V$ peak). It may also be necessary to explore other methods for improvement of the S/N ratio in empirical data before applying Wiener filtering; ensemble averaging time sequence records is one example.

The techniques of DFT (via FFT) convolution and Wiener filtering for noise suppression utilized in the inverse determination of the transmembrane or surface potential distribution given the field potential distribution are not only easily implemented, they are computationally efficient. Computer run
time for the forward determination of the surface and a field potential distribution, and also the inverse estimation of the transmembrane and surface potential distributions, took less than 30 seconds on an IBM 370/155.
REFERENCES


FIGURE CAPTIONS

FIG. 1  Fiber geometry. The specific conductivities of the external and internal medium are denoted $\sigma_o$ and $\sigma_i$, respectively. The fiber radius is $a$ and the radius to the field point is $r$. The axial dimension is $z$.

FIG. 2  Two-stage filter. $F_m(k)$, $F_{so}(k)$, and $F^O(k,r)$ are the Fourier transforms of the transmembrane, surface, and field potential distributions, respectively. The membrane filter is $1/\alpha(|k|a)$ and $W(|k|r)$ is the medium filter. See (13) and (20).

FIG. 3  The membrane filter vs $k$ for two specific conductivity ratios. The fiber radius is $60\mu$.

FIG. 4  The medium filter vs $k$ for three field point radii. The fiber radius is $60\mu$.

FIG. 5  The combined filter ($H = \frac{1}{\alpha \cdot W}$) vs $k$ for three separate field point radii. The fiber radius is $60\mu$ and specific conductivity ratio is 5.0.

FIG. 6  Optimal Wiener filtering scheme. The transmembrane potential distribution, $\Phi_m(z)$, is filtered by the combined filter, $H(|k|r*)$, resulting in a field potential distribution, $\Phi^O(z,r*)$. The observed field potential distribution, $\Phi^O(z,r*)$, is corrupted with additive random noise, $n(z)$, and filtered by the inverse Wiener filter, $G(|k|r*)$, producing an estimate, $\Phi_m(z)$, of the transmembrane potential distribution.
FIG. 7 The inverse medium filter vs k for the idealize inverse, \( W^{-1} \), and inverse Wiener filter for two signal-to-noise (S/N) ratios, at \( r^* = 7a \).

FIG. 8 The inverse combined filter vs k for the idealized inverse, \( H^{-1} \), and the inverse Wiener filter at two signal-to-noise (S/N) ratios, at \( r^* = 7a \).

FIG. 9 Forward solution. \( \hat{g}_m(z) \) is the simulated action potential distribution. \( \hat{g}_m(z, r^*) \) at \( r^* = a, 4a, \) and \( 7a \) are the calculated field potential distributions.

FIG. 10 Inverse solution. \( \psi^o(z, 7a) \) is the field potential with additive white Gaussian noise (S/N = 800). \( \hat{g}_m(z, a) \) and \( \hat{g}_m(z) \) are the reconstructed surface and transmembrane potential distributions utilizing Wiener filtering.

FIG. 11 Inverse solution. \( \psi^o(z, 7a) \) is the field potential with additive white Gaussian noise (S/N = 8). \( \hat{g}_m(z, a) \) and \( \hat{g}_m(z) \) are the reconstructed surface and transmembrane potential distribution utilizing Wiener filtering.

FIG. 12 The reconstructed (dots) are compared with the original (solid line) transmembrane potential distribution. The reconstructed potential is obtained from the field potential distribution at \( r^* = 7a \), with two signal-to-noise ratios (800 and 8).
Figure 2
$W(\kappa \kappa r)$
$a = 60 \text{u}$

$k \text{ (rad/cm)}$

$r = 3a$
$r = 5a$
$r = 7a$
$G_H(\|k\|r)$

$r = 7a$

$H^{-1}$

$\|k\|r$ (rad/cm)
$\Psi^0(z,a)$

$S/N = 8$

$\hat{\Phi}^0(z,a)$

$\hat{\Phi}_m(z)$

Fig 11