SOLVING THE INVERSE PROBLEM OF ELECTROCARDIOGRAPHY USING A DUNCAN AND HORN FORMULATION OF THE KALMAN FILTER

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Abstract

Numeric regularization methods most often used to solve the ill-posed inverse problem of electrocardiography are spatial and ignore the temporal nature of the problem. In this study, a reformulation of

the Kalman filter was used to incorporate temporal information in regularizing the inverse problem. The inverse problem was solved in the left ventricle by reconstructing endocardial surface electrograms based on cavitary electrograms measured by a noncontact, multielectrode probe. The results were validated based on electrograms measured *in situ* at the same endocardial locations using an integrated, multielectrode basket-catheter. A three-dimensional, probe-endocardium model was determined from multiplane fluoroscopic images. The boundary element method was applied to solve the boundary value problem and determine a linear relationship between endocardial and probe potentials. The Duncan and Horn formulation of the Kalman filter was employed and was compared to the commonly used zero- and first-order Tikhonov regularization as well as Twomey regularization. Endocardial electrograms were reconstructed during both sinus and paced rhythms. The Paige and Saunders solution of the Duncan and Horn formulation reconstructed endocardial electrograms at an amplitude relative error of 13% (potential amplitude) which was superior to solutions obtained with zero-order Tikhonov (relative error, 31%), first-order Tikhonov (relative error, 19%), and Twomey regularization (relative error, 44%). Likewise, activation error in the inverse solution using the Duncan and Horn formulation (2.9 ms) was smaller than that of zero-order Tikhonov (4.8 ms), first-order Tikhonov (5.4 ms), and Twomey regularization (5.8 ms). Therefore, temporal regularization based on the Duncan and Horn formulation of the Kalman filter improves the solution of the inverse problem of electrocardiography.

Index Terms — Inverse problem, noncontact mapping, regularization, Kalman filter.

Introduction

The aim of cardiac mapping is to record electrical potentials (electrograms) on the surface of the heart to reveal the underlying myocardial activity leading to an appropriate diagnosis and treatment of abnormal heartbeats. In order to find the endocardial potentials, a noncontact, multielectrode probe is used in the present study to make cavity potential measurements on a beat-by-beat basis,^{[33][20]} and endocardial potentials are computed based on the noncontact measurements (electrocardiographic inverse problem).^[21] This noncontact device avoids some of the limitations found when using the usual roving electrode catheters. However, the ill-posed nature of the underlying continuous problem leads to a discrete, ill-posed approximation.^{[9][14]} The resulting solutions are oscillatory and nonphysiologically large. Many approaches have been taken to provide reasonable solutions of this discrete, ill-posed problem with its inherent difficulties. These methods stabilize (regularize) the solution by limiting the solution or by solving a nearby problem that is better conditioned. These methods are typically spatial in nature and only a few have incorporated temporal information. Recent reviews of the inverse problem of electrocardiography may be found in [22] and [8].

The most common regularization method employed is that of Tikhonov^[34] and Phillips^[28] (appearing in a variety of forms and with different parameter selection schemes). This technique balances the residual with a measure of some undesirable property of the solution such as a large magnitude. Alternatively, rather than the overall magnitude, a spatial regularization can be used where each of the spectral components is considered separately.^[39]

Prior work on the temporal nature of the electrocardiographic inverse problem is limited but does show improved results. Oster and Rudy^{[26][29]} applied Twomey regularization^[37] which balances the residual with an error estimate (with respect to an estimate of the solution). Their studies used estimates calculated from multipoint stencils over time, to possibly include the future. Brooks *et al.*^{[2][3]} used a multiterm Tikhonov-type, spatiotemporal regularization employing a larger linear system built using the Kronicker product. Two regularization parameters were needed in this formulation and were chosen using an *L-surface*.^{[11][12][13]} Greensite and Huiskamp^[7] used the

singular value decomposition of the observations to eliminate measurement noise by subset selection (from the spatial basis of the noisy, augmented observations).^[4]

Kalman (and Bucy) previously described a recursive solution to the discrete-data linear filtering problem.^{[17][18]} Kalman filters have been considered for physiological monitoring^[15] including cardiology.^{[38][42][31][32]} Joly *et al.*^[16] introduced the use of the Kalman filter for the electrocardiographic inverse problem. Their process model was a linear prediction model with a scalar weighting of the immediately previous value. El-Jakl *et al.*^[6] built on this method with a predictor adding information from the four nearest neighbors at the previous instant.

The goal of the present study was to improve on the solution of the electrocardiographic inverse problem through algorithmic changes incorporating temporal information. This is accomplished using the Duncan and Horn formulation of a Kalman filter.

Methods

Animal Model

Preparation. A sternal thorachotomy was performed on a 27 kg mongrel dog that was intubated and anesthetized with sodium pentobarbital. The heart was suspended in a pericardial cradle and a custom probe-basket catheter introduced into the left ventricle through an apical incision and secured by a purse-string suture^[39] (see Figure 1). The procedure was conducted in accordance with institutional guidelines.

Measurements. Simultaneous, *in situ*, unipolar electrograms were recorded over several cycles at 1 ms intervals from the probe and basket electrodes (64 each) during ten protocols: one sinus rhythm protocol and nine artificial pacing protocols. The measuring electrodes were arranged eight to a column in eight columns on the probe and eight electrodes to each of the eight basket spokes (see Figure 1). Artificial stimulation was applied through one of the basket electrodes with a cycle length of 350 ms. The pacing electrodes provided approximately 180° of equatorial coverage from the anterior-lateral to posterior-septal regions with 45° spacing. Also, the anterior lateral region was paced from above the apex towards the base with approximately 5 mm spacing.

FIGURE 1.

Probe-basket catheter system. The probe and basket are arranged coaxially. They are fixed at their proximal ends and a piston arrangement at the distal end permits compression and expansion of the basket. On the right, the catheter is inserted through the mitral valve of a model of the human left ventricle. The insertion was apical for this study.

Geometry. The end-diastolic geometry of the left ventricle was reconstructed from fluoroscopic images of the basket electrodes using a convolution backprojection technique.^{[39][40]} The proximity of the 64 radio-opaque basket electrodes provided the necessary demarcation of the endocardium. This one geometry is used to construct the single transfer matrix that is used in the calculations that follow.

Mathematical Model

The governing equation for the present boundary value problem is Laplace's equation.

$$\nabla^2 (z) = 0 \quad z \quad \text{EQ 1}$$

where the well-behaved^[30] volume conductor, consisting of the cavity blood, is bounded by the probe P and endocardial E surfaces. The probe potentials are measured and the current density normal to the surface of the nonconducting probe is assumed zero.

$$\begin{aligned} u_P &= (z_P) \\ q_P &= -\frac{1}{n} (z_P) = 0 \quad z_P \quad P \end{aligned} \quad \text{EQ 2}$$

The boundary element method^[36] is used to construct the linear system describing the relationship between the probe and endocardial potentials and current densities. An appropriate partitioning, a separation of variables, and assuming that $q_P = 0$, the potentials and

current densities can be determined at the endocardial surface from

$$Au_E = u_P \quad \text{EQ 3}$$

$$Lu_E = q_E \quad \text{EQ 4}$$

Let $x = u_E$ and $b = u_P$ with $X = \{x_1, \dots, x_d\}$ and $B = \{b_1, \dots, b_d\}$. The transfer function $A \in \mathbf{R}^{m \times n}$ relates the endocardial potentials $X \in \mathbf{R}^{n \times d}$ and probe potentials $B \in \mathbf{R}^{m \times d}$ for the d observations of the system $AX = B$. The normal gradient $L \in \mathbf{R}^{n \times n}$ describes the relationship between the endocardial potentials and the normal current density. (In this study, L was used in the 1-order Tikhonov regularization.^[19])

Equation 3 involves only the surface potentials and is the model commonly associated with the electrocardiographic inverse problem. The underlying ill-posedness is manifested in the ill-conditioning of the transfer matrix A . Calculating the endocardial potentials given the probe potentials is the inverse problem. In the unavoidable presence of observation error the inverse solutions are rendered useless, if unmoderated. To stabilize these solutions, regularizing methods are used.

Numerical Methods

Regularization. Regularization can include additional information to stabilize the solution. For example, a state nearly satisfying the system can be sought by minimizing the residual while penalizing a solution's "bad" behavior. This additional information is incorporated as the regularizing term of the objective function.

$$\min_x (\|b - Ax\|^2 + F(x)) \quad \text{EQ 5}$$

The importance of the regularizing term is given by the regularization parameter (weight) $\lambda > 0$. The regularization term $F(x)$ can take many forms.

In the method of Tikhonov^[34] and Phillips^[28] the regularization term incorporates the matrix L . The use of the n -order discrete derivative has led to the term *n-order Tikhonov regularization*.

$$\min_x (\|Ax - b\|^2 + \|Lx\|^2) \quad \text{EQ 6}$$

The familiar solution is

$$x_{Tik} = (A^T A + L^T L)^{-1} A^T b \quad \text{EQ 7}$$

When L is chosen such that $\text{rank}[A^T, L^T]^T = n$ and is sufficiently large, the term to be inverted in EQ 7 is numerically nonsingular (well conditioned). The choices for L include measures of magnitude, smoothness, or proximity to an estimate. This approach is useful since the nonphysiologic behavior is manifested in wildly varying and unreasonably large solutions. For the electrocardiographic inverse problem the identity (zero-order derivative) is the dominant choice for L .^{[23][24]} This limits the solution magnitude. Improvements have been observed using a regularization matrix other than the identity.^{[19][39][25]} In this study the matrix from EQ 4 is used.

Twomey regularization has been used to incorporate temporal information into the solution. The method of Twomey^[37] uses an error with respect to an estimate as the regularizing term.

$$\min_x (\|Ax - b\|^2 + \|x - x_{\text{est}}\|^2) \quad \text{EQ 8}$$

$$x_{\text{Twomey}} = (A^T A + I)^{-1} (A^T b + x_{\text{est}}) \quad \text{EQ 9}$$

Oster and Rudy^[26] employed the Twomey technique with 2-, 3- and 4-point stencils to estimate the value of the solution (and is important because it illustrated the benefit of incorporating temporal information). The state estimates were based on data in the immediate vicinity of the current time, first employing data from their truth model^[26] and subsequently from calculations^[29]. The estimates were formed from the truncated Taylor series (difference formulas). The estimates which were not forward-looking are

$$x_{\text{est}}(t) = \frac{x(t-1) + 2x(t-1) - x(t-2)}{2} \quad \text{EQ 10}$$

These two estimates were examined in this study, the better results, coming from the first, are presented.

Kalman Filter. The *Kalman filter* is another method that takes advantage of the temporal nature of the electrocardiographic inverse problem. Simply, a Kalman^[17] (Kalman-Bucy^[18]) filter uses a recursive scheme that first predicts, then corrects an estimate of the state (potentials) using a process model and a measurement model, respectively. Temporal information is not only incorporated by the predictor but carried by the error variance-covariance matrices as well. A simple formulation is presented to illustrate the predictor-corrector nature of the filter. An alternate formulation,

very different from the recursive schemes, is then presented. The equations for the predictor and corrector are combined into a single linear system as described by Duncan and Horn^[5] (DH) and solved as a weighted least squares problem. This includes a (more) stable solution by Paige and Saunders^[27] (PS).

The two major steps of the recursive Kalman filter *predict* and *update* (correct) the endocardial potentials (state). Predictions are made for the endocardial potentials and error covariance (EQ 13). Updates are then made for the Kalman gain, endocardial potentials, and error covariance (EQ 14). These process and measurement models comprise the state-space model for the problem. In this typical Kalman filter the covariance matrices P are recursed and the filter is a *covariance filter*. (The variance-covariance matrix is simply referred to as the covariance matrix.) The linear estimation (process) model of the predictor is

$$x_k = G_k x_{k-1} + x_k \quad \text{EQ 11}$$

incorporating information from spatiotemporal neighbors where the endocardial potentials at time t_{k+1} are estimated from those at time t_k . The measurement model of the corrector is

$$b_k = A_k x_k + b_k \quad \text{EQ 12}$$

where the transfer function A_k relates the surface potentials: the probe measurements b_k and the endocardial potentials x_k (x^+) at time t_k . The vectors x_k and b_k above are the errors and the corresponding V_k and W_k below are the estimates of the error variance-covariance matrices.

Predictor

$$\begin{aligned} x^- &= Gx^+ \\ P^- &= GP^+G^T + V \end{aligned} \quad \text{EQ 13}$$

Corrector

$$\begin{aligned} K &= P^- A^T (A P^- A^T + W)^{-1} \\ x^+ &= x^- + K(b - A x^-) \\ P^+ &= (I - KA) P^- \end{aligned} \quad \text{EQ 14}$$

The transfer matrix relating the probe and endocardial potentials is used here as the measurement model but the underlying process is not well-defined and a definitive predictor is not available. Fortunately, one of the benefits of using the Kalman filter is that even though the process model (the nature of the underlying system) is uncertain it can still be used.^[41] A scalar multiple of

the identity is used here making the prediction proportional to the previous solution.

Duncan and Horn Formulation. Duncan and Horn describe an alternate formulation of the Kalman filter where the equations from the predictor and corrector are combined into a single linear system.^[5] A block is added for each additional point in time and is solved as a weighted least squares problem using the standard deviation of the errors. (An excellent description is provided by Hammarling.^{[10][11]})

Duncan and Horn formulated the discrete problem such that the state estimates are the solutions to the sequence of weighted linear least squares problems

$$\min \|F^{(k)}x^{(k)} - y^{(k)}\| \quad k = 1, 2, \dots \quad \text{EQ 15}$$

where $F^{(k+1)}$ is $F^{(k)}$ with additional rows and columns. The state and observation vectors gain a corresponding addition of rows. This system is weighted with factors of the error covariance matrices. To construct this system consider the prediction and correction steps through time k .

$$\begin{aligned} x_1 &= x_{init} + x_1 & b_1 &= A_1 x_1 + b_1 \\ x_2 &= G_2 x_1 + x_2 & b_2 &= A_2 x_2 + b_2 \\ &\vdots & &\vdots \\ x_k &= G_k x_{k-1} + x_k & b_k &= A_k x_k + b_k \end{aligned} \quad \text{EQ 16}$$

$$\begin{bmatrix} -S_{x1}^{-1} x_{init} \\ S_{b1}^{-1} b_1 \\ 0 \\ S_{b2}^{-1} b_2 \\ 0 \\ \vdots \\ 0 \\ S_{bk}^{-1} b_k \end{bmatrix} = \begin{bmatrix} -S_{x1}^{-1} & & & & \\ S_{b1}^{-1} A_1 & & & & \\ S_{x2}^{-1} G_2 & -S_{x2}^{-1} & & & \\ & S_{b2}^{-1} A_2 & & & \\ & S_{x3}^{-1} G_3 & -S_{x3}^{-1} & & \\ & & \ddots & \ddots & \\ & & & S_{xk}^{-1} G_k & -S_{xk}^{-1} \\ & & & & S_{bk}^{-1} A_k \end{bmatrix} \begin{bmatrix} x_{1|k} \\ x_{2|k} \\ x_{3|k} \\ \vdots \\ x_{k|k} \end{bmatrix} + \begin{bmatrix} S_{x1}^{-1} x_1 \\ S_{b1}^{-1} b_1 \\ S_{x2}^{-1} x_2 \\ S_{b2}^{-1} b_2 \\ S_{x3}^{-1} x_3 \\ \vdots \\ S_{xk}^{-1} x_k \\ S_{bk}^{-1} b_k \end{bmatrix} \quad \text{EQ 20}$$

This is the weighted problem of EQ 15.

$$y^{(k)} = F^{(k)}x^{(k)} + \begin{pmatrix} \end{pmatrix}^{(k)} \quad \text{EQ 21}$$

This can be rewritten as the augmented system where x_{ij} is the state at time i calculated using $j-i+1$ observations.

$$\begin{bmatrix} -x_{init} \\ b_1 \\ 0 \\ b_2 \\ 0 \\ \vdots \\ 0 \\ b_k \end{bmatrix} = \begin{bmatrix} -I & & & & \\ A_1 & & & & \\ G_2 & -I & & & \\ & A_2 & & & \\ & G_3 & -I & & \\ & & \ddots & \ddots & \\ & & & G_k & -I \\ & & & & A_k \end{bmatrix} \begin{bmatrix} x_{1|k} \\ x_{2|k} \\ x_{3|k} \\ \vdots \\ x_{k|k} \end{bmatrix} + \begin{bmatrix} x_1 \\ b_1 \\ x_2 \\ b_2 \\ x_3 \\ \vdots \\ x_k \\ b_k \end{bmatrix} \quad \text{EQ 17}$$

The error vectors are assumed to have zero mean with symmetric nonnegative definite covariance matrices. (" $E(\cdot)$ " denotes the *expectation*.)

$$E(x_k) = 0, E(b_k) = 0 \quad \text{EQ 18}$$

$$\begin{aligned} E(x_k^T x_k) &= V_k = S_{xk} S_{xk}^T \\ E(b_k^T b_k) &= W_k = S_{bk} S_{bk}^T \end{aligned} \quad \text{EQ 19}$$

The errors are then equilibrated by premultiplying EQ 17 with the inverse of the "square root" of the covariance matrices.

where the superscript indicates the number of measurements (partitions). The least squares solution is

$$x^{(k)} = \begin{bmatrix} x_{1|k} \\ x_{2|k} \\ x_{3|k} \\ \vdots \\ x_{k|k} \end{bmatrix} \quad \text{argmin} \|F^{(k)}x^{(k)} - y^{(k)}\| \quad k \in \{1, 2, \dots\} \quad \text{EQ 22}$$

where the i^{th} partition $x_{i|j}$ is the state at time i calculated using $j - i + 1$ observations, ($i = j$) *filtered*, and ($i < j$) *smoothed*. That is, there are smoothed solutions in addition to the filtered solutions. The system becomes larger with an increase in the number of smoothed states. The first partition contains the most smoothed and the last contains the filtered. The system can be truncated to the desired number of states.

Paige and Saunders Solution. Paige and Saunders describe the use of QR factorizations in the solution of the DH augmented system.^[27] The transfer matrix can be put into upper triangular form.

$$(Fx = y) \quad (Q^T Fx = Q^T y) \quad \begin{bmatrix} R \\ 0 \end{bmatrix} x = \begin{bmatrix} Q_1^T y \\ Q_2^T y \end{bmatrix} \quad \text{EQ 23}$$

Use the following notation for EQ 20.

$$\begin{bmatrix} \bar{S}_1 \\ \bar{A}_1 \\ \bar{G}_2 \quad \bar{S}_2 \\ \bar{A}_2 \\ \bar{G}_3 \quad \bar{S}_3 \\ \ddots \quad \ddots \\ \bar{G}_k \quad \bar{S}_k \\ \bar{A}_k \end{bmatrix} \begin{bmatrix} x_{1|k} \\ x_{2|k} \\ x_{3|k} \\ \vdots \\ x_{k|k} \end{bmatrix} = \begin{bmatrix} y_{init} \\ y_1 \\ y_2 \\ 0 \\ \vdots \\ 0 \\ y_k \end{bmatrix} \quad \text{EQ 24}$$

The transformation of each block is^[27]

$$\bar{Q}^T \begin{bmatrix} \bar{R}_j & 0 \\ \bar{A}_j & 0 \\ \bar{G}_{j+1} & \bar{S}_{j+1} \end{bmatrix} = \begin{bmatrix} R_j & R_{j,j+1} \\ 0 & 0 \\ 0 & \bar{R}_{j+1} \end{bmatrix} \quad \text{EQ 25}$$

$$P^T \begin{bmatrix} R_j & R_{j,j+1} \\ 0 & 0 \\ 0 & \bar{R}_{j+1} \end{bmatrix} = \begin{bmatrix} R_j & R_{j,j+1} \\ 0 & \bar{R}_{j+1} \\ 0 & 0 \end{bmatrix} \quad \text{EQ 26}$$

$$Q^T = P^T \bar{Q}^T \quad \text{EQ 27}$$

Or, alternatively, the transformation is^[10]

$$Q^T \begin{bmatrix} \bar{R}_j & 0 \\ \bar{G}_{j+1} & \bar{S}_{j+1} \\ 0 & \bar{A}_{j+1} \end{bmatrix} = \begin{bmatrix} R_j & R_{j,j+1} \\ 0 & \bar{R}_{j+1} \\ 0 & 0 \end{bmatrix} \quad \text{EQ 28}$$

The augmented system is then transformed

$$\begin{bmatrix} R_1 & R_{1,2} & & & & \\ & R_2 & R_{2,3} & & & \\ & & R_3 & \ddots & & \\ & & & \ddots & R_{k-2,k-1} & \\ & & & & R_{k-1} & R_{k-1,k} \\ & & & & & \bar{R}_k \end{bmatrix} \begin{bmatrix} x_{1|k} \\ x_{2|k} \\ x_{3|k} \\ \vdots \\ x_{k-1|k} \\ x_{k|k} \end{bmatrix} = \begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ \vdots \\ y_{k-1} \\ y_k \end{bmatrix} \quad \text{EQ 29}$$

With the addition of new measurements only the submatrix $\bar{R}_k$ is altered by the update of the factorization. When the transfer function, predictor, and error covariance matrices remain constant, then further simplifications may be applied, eliminating the need for recurring factorizations, reducing storage requirements and allowing for a more efficient (sparse) solver. These simplifications were not implemented in the present study.

Metrics. The total relative error (RE), activation time (act) and average activation error (AE_{act}) are defined as follows. The total relative error is defined

$$RE(X) = \frac{\|X_{meas} - X\|_F}{\|X_{meas}\|_F} \quad \text{EQ 30}$$

Activation time $act(y_i(t))$ is the instant of the minimum of the first derivative of the electrogram between the first

negative potential and the minimum of the QRS. The average activation error is defined

$$AE_{act}(v_i(t)) = \frac{1}{n} \sum_{i=1}^n |act(v_i) - act(v_{meas,i})| \quad \text{EQ 31}$$

where $v_{meas,i}$ and v_i are the measured and calculated potentials (electrograms), respectively, for a range of times, for the i^{th} electrode. That is, v is from a row of X . The pacing electrode is not included in the calculation of the average.

Results

Endocardial electrograms were computed from the *in situ* measurements made in the canine left ventricle. This was done for ten protocols using Tikhonov regularization, Twomey regularization and Kalman filtering. A post-stimulus 100 ms segment of a single cycle was used for each protocol.

The optimal regularization parameter (within 0.01 $\log_{10}$) was determined at each time step for the 0- and 1-order Tikhonov methods (0-Tik and 1-Tik, respectively) as well as for the Twomey method. (The parameter resulting in the minimum relative error is referred to as the *optimal regularization parameter*.) This was done to illustrate the best possible performance for the methods but requires the use of the measured values constituting the truth model. The regularization matrix for 1-Tik (EQ 6) came from EQ 4. For Twomey (EQ 8) the estimate was the first item in EQ 10 (the immediately previous value).

The Duncan & Horn formulation was solved using the Paige & Saunders method to provide smoothed potentials (PS_S). As with the Tikhonov solutions the truth model was used, but for the Kalman solutions the truth model was used to calculate the *measurement error covariance* matrix. A single matrix was used for all times within a protocol. The *process error covariance* matrix was of the form I with chosen (within 0.1 $\log_{10}$) to optimize the total relative error.

The total relative error for all of the methods are summarized in Table 1. The activation times were also calculated and the average error appears in Table 2.

TABLE 1. Total Relative Error (%).

protocol	Tikhonov		Twomey	Kalman
	0-Tik	1-Tik		PS_S
*1	28.4	15.5	34.9	12.6
2	29.8	17.6	43.9	15.2
3	28.9	18.5	42.0	13.2
4	30.5	17.7	48.0	12.9
5	30.4	19.0	47.4	12.2
6	31.5	19.7	59.3	12.8
7	30.4	18.0	43.2	12.5
8	31.9	20.3	40.9	13.5
9	32.6	20.7	41.8	13.1
10	35.4	23.4	38.5	17.1
mean	31.0	19.0	44.0	13.5
Asterisk indicates sinus rhythm.				

TABLE 2. Average Activation Error (ms).

protocol	Tikhonov		Twomey	Kalman
	0-Tik	1-Tik		PS_S
*1	3.0	2.9	3.5	1.4
2	5.3	7.8	6.7	4.7
3	4.8	5.6	5.2	4.2
4	5.4	6.3	7.3	4.7
5	5.9	6.8	6.4	3.0
6	4.9	6.1	8.7	3.1
7	5.0	5.3	5.7	2.5
8	5.3	6.1	6.4	2.5
9	5.1	3.6	4.4	1.4
10	3.7	3.8	3.7	1.7
mean	4.8	5.4	5.8	2.9
Asterisk indicates sinus rhythm.				

FIGURE 2.

1-Tikhonov, Kalman PS_S and Measured Electrograms. The calculated electrograms (thin) for 1-Tik (A) and PS_S (B) are each coplotted with the *in situ* measurements (thick) for protocol 7. Each electrogram is 100 ms in length and spaced vertically 30 mv. The

electrograms are arranged approximately as in the isopotential maps of Figure 4: posterior, septal, anterior to lateral (left to right) and base to apex (top to bottom). The forth row was near mid ventricle. The pacing electrode ('X') was anterior.

A. Endocardial Electrograms: 1-Tikhonov (thin), Measured (thick).

B. Endocardial Electrograms: Kalman PS_S (thin), Measured (thick).

Example endocardial electrograms are provided in Figure 2 for protocol 7 for the measured, 1-Tik, and PS_S potentials. Many of the electrograms are matched well by both methods. The corresponding endocardial potentials are also depicted spatially in isopotential maps. The three-dimensional maps in Figure 3 are for a time instant of 30 ms. The isopotentials are more easily examined in the corresponding two-dimensional maps, though the anatomic landmarks are lost. Sequences of these two-dimensional maps are provided in Figure 4 for times from 5 to 65 ms at 5 ms intervals. Activation isochrones for protocol 7 are provided for the measured, 1-Tik and PS_S in Figure 5.

FIGURE 3.

Three-dimensional isopotential maps at $t = 30$ ms for protocol 7 are plotted as isopotentials with the nodes positioned in 3-space. The views are posterior, septal, anterior and lateral (left to right). Each map is scaled similarly.

FIGURE 4.

Two-dimensional isopotential map sequence for protocol 7 using 1-Tik and PS_S are plotted as isopotentials. The potentials are from 5 ms to 65 ms at 5 ms intervals. Each map is arranged posterior, septal, anterior to lateral (left to right) and base to apex (top to bottom). Each map is scaled similarly. The early depolarization occurs in the mid to apical anterior region consistent with the location of the pacing site. The potentials for $t = 30$ ms are also plotted in Figure 3.

FIGURE 5.

The activation times for the measured and calculated (1-Tik and PS_S) potentials for protocol 7 are plotted as isochrones. Each map is laid out from left to right: posterior, septal, anterior to lateral; and top to bottom: base to apex. Each map is scaled similarly. The activation begins in the mid to apical anterior region, ending in the basal septum.

Discussion

Measurement errors are inevitable and, when solving the discrete ill-posed inverse problem of electrocardiography, these errors render simple, unmoderated solutions useless. Of the numerical methods examined in this study the most reasonable results were obtained by the smoothed Paige and Saunders (PS_S) and 1-order Tikhonov (1-Tik) methods. The lowest total relative error, averaging 13.5%, was consistently provided by the PS_S solution of the Duncan and Horn (DH) formulation. By comparison, the 1-Tik averaged 19.0%. (In results not presented, even the simple DH solutions and filtered PS solutions had lower relative errors than the 1-Tik solutions, with the exception of one protocol.) As for the activation errors, all were lower for the PS_S solutions. The average for PS_S was 2.9 ms, nearly a 40% improvement over the 0-Tik (4.8 ms) and a 46% improvement over the 1-Tik (5.4 ms). The activation times for Twomey had very large errors in a few electrodes. If the protocols associated with the worst of these are removed from the average Twomey performs on par with 1-Tik.

For the 0-Tik and 1-Tik methods, as well as the PS method, the measured electrograms were used. The former used them to obtain optimal regularization parameters and the latter for determining the measurement error covariances. The problems associated with parameter selection (error estimation) were not addressed here. Rather, an attempt was made in the present study to show the *best possible performance* for each method.

An overall (and objective) sense of the quality of the solutions is provided by the total relative error (and holds for smaller errors of distinctly different size). In

addition to the size of the errors, the shape of the solutions is important. The correlation coefficients were not presented since they provided little differentiation. However, temporal and spatial views of the solutions were useful. These were provided in the form of electrograms and isopotential maps (for protocol 7). The shapes of the curves and contours and how much they look like the measured potentials are a good measure of the quality of the solutions. Many of the calculated electrograms for 1-Tik and PS_S (Figure 2) followed the measured values well. A closer examination of the posterior and septal regions (second through fourth columns) of the electrograms reveals an amplitude mismatch in the midst of the QRS by both solution methods. However, the PS_S potentials match the measured values more closely as there is an obvious lag in the 1-Tik potentials. Other examples are found in the mid-ventricular, anterior-septal region (third row, fourth and fifth columns); the features apparent in the measured potentials are more closely matched by PS_S .

The 1-Tik solutions matched the measured values fairly well and, in particular, were smoother than filtered PS solutions. This was addressed, first, by using the smoothed rather than filtered potentials. Second, a point-wise averaging was applied. This averaging did not affect the 1-Tik or PS_S solutions enough to warrant their inclusion. (The averaging was useful when examining filtered solutions.)

The isopotential maps of Figure 4 illustrate that the potentials calculated through PS_S better portray the sequence of activation. This is more easily seen in the shape of the isochrones of Figure 5, where PS_S more closely matches the measured values than do those for 1-Tik. The improvement in the average activation error for PS_S over 1-Tik was over 46%.

The DH methods improved upon not only the methods presented but also the recursive Kalman filter. The results for the recursive Kalman filter were not presented as the covariance selections used were only able to achieve a total relative error of 49%, at best. This may not speak to the best performance of the recursive formulation so much as the difficulty in selecting the appropriate error covariance estimates.

Conclusion

The Duncan & Horn formulation of the Kalman filter produced results superior to the commonly used Tikhonov method even when the 1-order regularization was used. The use of laboratory data here was significant since there is little doubt that improvements, similar to those presented here, will be possible with clinical data, given that suitable means are found for estimating the measurement error covariance.

References

- 1 M. Belge, M.E. Kilmer and E.L. Miller, "Efficient Determination of Multiple Regularization Parameters in a Generalized L-Curve Framework," *Inverse Problems*, vol. 18(4), pp. 1161-1183, August 2002.
- 2 D.H. Brooks, G.M. Maratos, G. Ahmad, and R.S. MacLeod, "The augmented inverse problem of electrocardiography: combined time and space regularization," *Proc. 15th Ann. Int. Conf. IEEE EMBS*, pp. 773-774, San Diego, CA, October 1993.
- 3 D.H. Brooks, G.F. Ahmad, R.S. MacLeod and G.M. Maratos, "Inverse electrocardiography by simultaneous imposition of multiple constraints," *IEEE Transactions on Biomedical Engineering*, vol. 46, pp. 3-18, 1999.
- 4 A.A. Damen and J. van der Kam, "The use of the singular value decomposition in electrocardiography," *Medical and Biological Engineering and Computing*, vol. 20, pp. 473-482, July 1982.
- 5 D.B. Duncan and S.D. Horn, "Linear Dynamic Recursive Estimation from the Viewpoint of Regression Analysis," *J. Am. Stat. Assoc.*, vol. 67, pp. 815-821, 1972.
- 6 J. El-Jakl, F. Champagnat and Y. Goussard, "Time-space regularization of the inverse problem of electrocardiography," *Proc. Annual IEEE-EMBS Conf.*, (Montréal, Québec, Canada), pp. 213-214, 1995.
- 7 F. Greensite and G. Huiskamp, "An improved method for estimating epicardial potentials from the body surface," *IEEE Transactions on Biomedical Engineering*, vol. 45, pp. 98-104, 1998.
- 8 R.M. Gulrajani, "The forward and inverse problems of electrocardiography," *IEEE Eng. Med. Biol.*, vol. 17(5), pp. 84-122, 1998.
- 9 J. Hadamard, *Lectures on Cauchy's Problem in Linear Partial Differential Equations*, Yale University Press, New Haven, 1923 (Dover, New York, 1952).
- 10 S.J. Hammarling, "The Numerical Solution of the Kalman Filtering Problem," *Numerical Algorithms Group Inc.*, 1101 31st St. #100, Downers Grove, IL, 60515-1263, USA.
- 11 *Computational and Combinatorial Methods in Systems Theory*. C.I. Byrnes and A. Lindquist eds. Elsevier Science Publishers B.V. (North-Holland), 1986.
- 12 S. Hammarling, "The Numerical Solution of the Kalman Filtering Problem," pp. 23-36.
- 12 P.C. Hansen, "Analysis of discrete ill-posed problems by means of the L-curve," *SIAM Review*, 34(4):561-580, 1992.
- 13 P.C. Hansen, "The use of L-curve in the regularization of ill-posed problems," *SIAM J. Sci. Comput.*, 14(6):1487-1503, 1993.
- 14 P.C. Hansen, *Rank-Deficient and Discrete Ill-Posed Problems: numerical aspects of linear inversion*, Society for Industrial and Applied Mathematics, Philadelphia, 1997.
- 15 R.A. Heath, "Detection of change in physiological measures using an adaptive Kalman filter algorithm," *Psychol Bull.*, vol. 96, pp. 581-588, 1984.
- 16 D. Joly, Y. Goussard and P. Savard, "Time-recursive solution to the inverse problem of electrocardiography: a model-based approach," *Proc. Annual IEEE-EMBS Conf.*, (San Diego, CA), pp. 767-768, 1993.

- 17 R.E. Kalman, "A New Approach to Linear Filtering and Prediction Problems," Transactions of the ASME - Journal of Basic Engineering, pp. 35-45, 1960.
- 18 R.E. Kalman and R.S. Bucy, "New results in linear filtering and prediction theory," Transactions of the ASME, Series D, Journal of Basic Engineering, vol. 83, pp. 95-108, March 1961.
- 19 D.S. Khoury, "Use of current density in the regularization of the inverse problem of electrocardiography," Proceedings of the 16th International Conference on IEEE Eng. Med. Biol., Baltimore, MD, 3-6, pp. 133-134, November 1994.
- 20 D.S. Khoury, B. Taccardi, R.L. Lux, P.R. Ershler and Y. Rudy, "Reconstruction of endocardial potentials and activation sequences from intracavitary probe measurements. Localization of pacing sites and effects of myocardial structure," Circulation, vol. 91, pp. 845-863, 1995.
- 21 D.S. Khoury, K.L. Berrier, S.M. Badruddin and W.A. Zoghbi, "Three-dimensional electrophysiological imaging of the intact canine left ventricle using a noncontact multielectrode cavitary probe: study of sinus, paced, and spontaneous premature beats," Circulation, vol. 97, pp. 399-409, 1998.
- 22 R.S. MacLeod and D.H. Brooks, "Recent progress in inverse problems in electrocardiology," IEEE Eng. Med. Biol., vol. 17(1), pp. 73-83, 1998.
- 23 B.J. Messenger-Rapport and Y. Rudy, "Regularization of the Inverse Problem in Electrocardiography: A Model Study, Mathematical Biosciences," vol. 89, pp. 79-118, 1988.
- 24 B.J. Messenger-Rapport and Y. Rudy, "Computational issues of importance to the inverse recovery of epicardial potentials in a realistic heart-torso geometry," Math Biosci, vol. 97, pp. 85-120, 1989.
[published erratum appears in Math Biosci vol. 99(1):141, April 1990]
- 25 L.G. Olson and R.D. Throne, "A comparison of five methods for construction of regularization operators for higher-order Tikhonov regularization," Proc. Comput. Cardiol., Cleveland, OH, New York: IEEE Press, 357-360, 1998.
- 26 H.S. Oster and Y. Rudy, "The use of temporal information in the regularization of the inverse problem of electrocardiography," IEEE Transactions on Biomedical Engineering, vol. 39, pp. 65-75, 1992.
- 27 C.C. Paige and M.A. Saunders, "Least Squares Estimation of Discrete Linear Dynamic Systems using Orthogonal Transformations," SIAM J. Numer. Anal., vol. 14(2), pp. 180-193, April 1977.
- 28 D.L. Phillips, "A technique for the numerical solution of certain integral equations of the first kind," Journal of the ACM, pp. 84-97, 1962.
- 29 High-Performance Computing in Biomedical Research, Ed. T.C. Pilkington, B. Loftis, J.F. Thompson, S.L.Y. Woo, T.C. Palmer, T.F. Budinger, CRC Press, 1993.
Chapter 6: Y. Rudy and H.S. Oster, "The Electrocardiographic Inverse Problem," pp. 135-155
- 30 R. Plonsey and D.B. Heppner, "Considerations of quasi-stationarity in electrophysiological systems, Bulletin of Mathematical Biophysics," 29(4), pp. 657-664, 1967.
- 31 D.F. Sittig and M. Factor, "Physiologic trend detection and artifact rejection: a parallel implementation of a multi-state Kalman filtering algorithm," Comput Methods Programs Biomed, 31, pp. 1-10, 1990.
- 32 D.F. Sittig and K.H. Cheung, "A parallel implementation of a multi-state Kalman filtering algorithm to detect ECG arrhythmias," Int J Clin Monit Comput, 9, pp. 13-22, 1992.
- 33 B. Taccardi, G. Arisi, E. Macchi, S. Baruffi and S. Spaggiari, "A new intracavitary probe for detecting the site of origin of ectopic ventricular beats during one cardiac cycle," Circulation, vol. 75, pp. 272-281, 1987.
- 34 A.N. Tikhonov and V.Y. Arsenin, "Solutions of ill-posed problems," W. H. Winston, Washington, D.C., 1977.
- 35 A.N. Tikhonov and V.Y. Arsenin, "Solution of ill-posed problems and the regularization method," Soviet Math. Dokl., 4:1035-1038, 1963.
- 36 J. Trevelyan, Boundary Elements for Engineers: Theory and Applications, Computational Mechanics Inc., Boston, MA, 1994.

-
- 37 S. Twomey, "On the numerical solution of Fredholm integral equations of the first kind by the inversion of the linear system produced by quadrature," *J. Assoc. Comput. Mach.*, vol.10, pp. 97-101, 1963.
- 38 M. Vauhkonen, P.A. Karjalainen and J.P. Kaipio, "A Kalman filter approach to track fast impedance changes in electrical impedance tomography," *IEEE Transactions on Biomedical Engineering*, vol. 45, pp. 486-493, 1998.
- 39 E.O. Velipasaoglu, H. Sun, F. Zhang, K.L. Berrier and D.S. Khoury, "Spatial Regularization of the Electrocardiographic Inverse Problem and its Application to Endocardial Mapping," *IEEE Transactions on Biomedical Engineering*, vol. 47(3), pp. 327-337, March 2000.
- 40 E.O. Velipasaoglu, K.L. Berrier, H. Sun H and D.S. Khoury. "Determining locations of intracardiac basket and probe electrodes from multiplane fluoroscopic images," *Proc. Computers in Cardiology*, pp. 465-468, 1998.
- 41 G. Welch and G. Bishop, *An Introduction to the Kalman Filter*, University of North Carolina at Chapel Hill, Department of Computer Science, Chapel Hill, NC, pp. 1-16, 1997.
- 42 M.S. Woolfson, "Study of cardiac arrhythmia using the Kalman filter," *Med Biol Eng Comput*, 29, pp. 398-405, 1991.