Temporal Resolution Properties of Dynamic PET Reconstructions [1]

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Abstract

We describe methods for computing mean and variance approximations to instantaneous and average rate estimates obtained from continuous-time penalized ML dynamic PET image reconstructions. The derivation is based on writing the likelihood for the list-mode data as the limiting case of the likelihood for binned sinogram data as the temporal bin width goes to zero. We show that approximations of the mean and covariance can then be computed for continuous-time penalized ML estimates by exploiting spatio-temporal separability and the use of Kronecker decompositions. The resulting expressions are tractible forms that provide estimates of the mean and of instantaneous and time-averaged covariance between any two voxels and time instances.

I. Introduction

Maximum a posteriori (MAP) or penalized ML image reconstruction methods combine accurate physical and statistical modeling of the coincidence detection process in positron emission tomography (PET) to produce images with improved resolution and noise performances compared to Þltered-backprojection methods. Spatial resolution and noise properties of MAP reconstructions, as characterized by the mean and variance of the reconstructed images, have previously been investigated, e.g. [1], [2], [6]. However, there is little or no work on the *temporal* resolution properties of MAP images. This is mainly because dynamic imaging is traditionally performed as a series of static reconstructions and temporal resolution is determined by frame length.

In our work on dynamic PET image reconstruction from list-mode data [4] we showed that continuous-time PET image reconstruction was a tractable problem and investigated the mean and variance of reconstructed images through Monte Carlo simulations. In this paper we investigate the temporal behavior of our list-mode penalized ML algorithm through analytic approximations developed in [1] and [2]. We derive computationally efÞcient approximate methods for estimation of the mean and variance of dynamic reconstructions.

II. Methods and Results

A. Log-likelihood Functions

We model the positron emissions in each voxel in the volume as an inhomogeneous Poisson process. We denote the rate function at voxel j by $\eta_j(t)$ and parametrize it using a set of basis functions so that $\eta_j(t) = \sum_l w_{jl} B_l(t)$. It follows that the detection process at detector pair i is also an inhomogeneous Poisson process with rate function $r_i(t) = \sum_l (\sum_j p_{ij} w_{jl}) B_l(t)$ where p_{ij} is the ij^{th} element of the system matrix $\mathbf{P}$ and denotes the probability of an event at voxel j being detected at detector pair i. Using the likelihood function of event arrival times in an inhomogeneous Poisson process, we obtain the log-likelihood function of the arrival times as a function of the coefÞcients as follows [4]:

$$L_{continuous}(\mathbf{w}) = \sum_{i=1}^{n_p} \sum_{k=1}^{x_i} \log\left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} B_\ell(a_{ik}) \right) - \sum_{i=1}^{n_p} \left(\sum_{\ell=1}^{n_b} (\sum_{j=1}^{n_v} p_{ij} w_{j\ell}) \int_0^T B_\ell(t) dt \right) \quad (1)$$

where n_p is the number of detector pairs, n_v is the number of voxels, n_b is the number of temporal basis functions, x_i is the number of events at detector pair i and a_{ik} is the arrival time of the k^{th} event at detector pair i.

Computing the Fisher information matrix using this log-likelihood function from $-E(\frac{\partial^2 L(\mathbf{w})}{\partial^2 (\mathbf{w})})$ leads to an intractable form. To overcome this difÞculty, we divide the scan duration into N time bins and model our observation at each detector pair as the $N \times 1$ vector whose n^{th} element is the number of events observed during time bin n at that detector pair. Therefore our observation at detector pair i is given by $\mathbf{y_i} = [y_i^{(1)}, y_i^{(2)} \dots y_i^{(N)}]^T$. When we concatenate the observation vectors at all detector pairs into a single $n_d \times N$ vector where n_d is the total number of detector pairs, our observation vector becomes $\mathbf{y} = [\mathbf{y_1}^T \mathbf{y_2}^T \dots \mathbf{y_{n_d}}^\mathbf{T}]^\mathbf{T}$.

The log-likelihood for the binned data is:

$$L_{bin}(\mathbf{w}) = \sum_{i=1}^{n_p} \sum_{n=1}^{N} y_i^{(n)} \log\left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} \int_{t_{n-1}}^{t_n} B_\ell(t) dt \right) - \sum_{i=1}^{n_p} \left(\sum_{\ell=1}^{n_b} (\sum_{j=1}^{n_v} p_{ij} w_{j\ell}) \int_0^T B_\ell(t) dt \right) \quad (2)$$

As bin-width approaches zero, the bin-mode log-likelihood function given by (2), and therefore its maximizer, approach the continuous-time log-likelihood and its maximizer respectively. Therefore we can work with bin-mode data and extend these results to the continous time case by making the bin width approach zero.

The $(i,n)^{th}$ element of our observation vector $\mathbf{y}$, (i.e. $y_i^{(n)}$) has a Poisson distribution with mean $\int_{t_{n-1}}^{t_n} r_i(t) dt$ where t_{n-1} and t_n are the end points of time bin n. By substituting

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$\sum_l (\sum_j p_{ij} w_{jl}) B_l(t)$ for the rate function $r_i(t)$ we can relate the mean number of events at each spatiotemporal bin $\bar{y}_i^{(n)}$ to the parameters to be estimated as follows:

$$\bar{y}_i^{(n)} = \sum_{j=1}^{n_v} \sum_{l=1}^{n_b} p_{ij} \left[\int_{t_{n-1}}^{t_n} B_l(t) dt \right] w_{jl} \tag{3}$$

Note the space-time separability in (3) which allows us to write the mean of our observation vector in terms of the control vertex vector $\mathbf{w}$ as follows:

$$\bar{\mathbf{y}} = (\mathbf{P} \otimes \mathbf{B}) \mathbf{w} \tag{4}$$

Here $\mathbf{w}$ is the large vector containing the control vertex vectors of all voxels. i.e. $\mathbf{w} = (\mathbf{w_1}^T \mathbf{w_2}^T \ldots \mathbf{w_{n_p}}^T)^T$. $\mathbf{B}$ is the temporal sensitivity matrix whose $(n,l)^{th}$ element is given by $\int_{t_{n-1}}^{t_n} B_l(t) dt$ and $\otimes$ denotes the left Kronecker product.

B. Mean Estimation

A simple but reasonably accurate method for estimating the mean in static (i.e. single frame) reconstructions is to reconstruct noise-free data [1]. Even if the means are non-integers, they can be formally substituted into the static objective function and the optimization of that objective function will give an estimate for the reconstruction mean.

The same approach in the dynamic case is not possible with the continuous-time log-likelihood function because it is based on the event arrival times rather than the total number of events at each detector pair. However, the bin-mode approach allows for a similar substitution in which the $y_i^{(n)}$Õs are replaced by (possibly non-integer) $\bar{y}_i^{(n)} = \int_{t_{n-1}}^{t_n} r_i(t) dt$. Substitution of this into (3) together with the use of the mean value theorem, allowing bin width to approach zero and removing terms not dependent on $\mathbf{w}$ gives the following objective function whose maximization results in a Þrst order estimate for the mean of the reconstructed control vertices:

$$L(\mathbf{r}(t), \mathbf{w}) = \sum_{i=1}^{n_d} \int_0^T r_i(t) \log \left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} B_\ell(t) dt \right) - \sum_{i=1}^{n_p} \left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} \int_0^T B_\ell(t) dt \right) \tag{5}$$

Unlike the static case, in which the rate functions are integrated over disjoint intervals for each bin, here the values of the rate functions at each time instant contribute to multiple control vertices through weighting by the basis functions $B_l(t)$. A comparison with (1) reveals that maximization of the continuous-time objective function falls into the general category of maximizing an objective function of the form:

$$L(\mathbf{f}(t), \mathbf{w}) = \sum_{i=1}^{n_d} \int_0^T f_i(t) \log \left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} B_\ell(t) dt \right) - \sum_{i=1}^{n_p} \left(\sum_{\ell=1}^{n_b} \sum_{j=1}^{n_v} p_{ij} w_{j\ell} \int_0^T B_\ell(t) dt \right) \tag{6}$$

where $\mathbf{f}(t)$ is a vector valued function of time whose i^{th} element is given by $f_i(t) = r_i(t)$ in the noiseless case and $f_i(t) = \sum_{k=1}^{x_i} \delta(t - a_{ik})$ in the noisy case. This result is intuitive in the sense that when the rate functions at detector pairs are known, a reconstruction using those rate functions gives a Þrst order estimate for the mean. On the other hand, we can think of the noisy situation (i.e. when we have a realization of the inhomogeneous Poisson process instead of its rate function) as one in which the rate functions are replaced by their estimates $\sum_{k=1}^{x_i} \delta(t - a_{ik})$ corresponding to an impulse train at event arrival times.

In summary, our procedure for estimating the mean is to maximize (6) (or its penalized ML version with appropriate penalties) and to use the resulting control vertex estimates $\hat{\mathbf{w}}$ in $\hat{\eta}_j(t) = \sum_{l=1}^{n_b} \hat{w}_{jl} B_l(t)$.

C. Variance Estimation

1) Variances of Instantaneous and Average Rate Estimates

The objective of instantaneous rate estimation is to estimate average activity at a given voxel at a Þxed point in time - i.e. the desired expression is $\eta_j(t)$. In average rate estimation, the objective is to estimate average activity at a given voxel over a period of time i.e. the desired expression is $\frac{1}{(t_2 - t_1)} \int_{t_1}^{t_2} \eta_j(t) dt$. Under our parametrized inhomogeneous Poisson process model, the covariance between rate function estimates at any two voxels j and k at any two time points t_m and t_n (instantaneous) or averaged from t_1 to t_2 (average) can be obtained via

$$\begin{aligned} cov\left(\hat{\eta}_j(t_m), \hat{\eta}_k(t_n)\right) &= cov\left(\sum_{l=1}^{n_b} w_{jl} B_l(t_m), \sum_{l=1}^{n_b} w_{kl} B_l(t_n) \right) \\ &= \mathbf{b}(t_m)^T \mathbf{C}_{w_j, w_k} \mathbf{b}(t_n) \end{aligned} \tag{7}$$

$$\begin{aligned} &cov\left(\frac{\int_{t_1}^{t_2} \hat{\eta}_j(t) dt}{(t_2 - t_1)}, \frac{\int_{t_1}^{t_2} \hat{\eta}_k(t) dt}{(t_2 - t_1)} \right) \\ &= \frac{1}{(t_2 - t_1)^2} \left(\int_{t_1}^{t_2} \mathbf{b}(t) \right)^T \mathbf{C}_{w_j, w_k} \left(\int_{t_1}^{t_2} \mathbf{b}(t) \right) \end{aligned} \tag{8}$$

where $\mathbf{b}(t) \equiv (B_1(t) \ldots B_{n_b}(t))^T$ and $\mathbf{C}_{w_j, w_k}$ is the jk^{th} block submatrix of $\mathbf{C_w} \equiv cov(\mathbf{w})$.

From these expressions, or by simply observing that rate function estimates are related to control vertices deterministically, we conclude that an estimate of $\mathbf{C_w}$ is necessary and sufÞcient for estimating the variances/covariances of instantaneous or average rate estimates at any pair of voxels at any pair of time points. Once $\mathbf{C_w}$ is estimated, it can be used in (7) or (8) to obtain the desired expressions.

2) Penalized ML Control Vertex Covariance Matrix Estimation

In this subsection we will derive an approximation to $\mathbf{C_w}$ in the context of penalized ML estimation. In our reconstruction work [4] we added spatial and temporal roughness penalty terms to the log-likelihood in order to enforce spatial and temporal smoothness.

We used a spatial smoothing function equivalent to the pair-wise quadratic penalty used previously in penalized ML [8] and Bayesian estimation [5] of static PET images. Our temporal roughness penalty was in the form of integrated squared curvature. For voxel j this is $\int \left\{ \frac{\partial^2}{\partial u^2} \eta_j(u) \right\}^2 du$. Fortunately, for cubic splines this quantity is a quadratic form of the control vertices ([7], pg. 238). We denote the symmetric banded matrix of this quadratic form $\mathbf{Q}$. Thus our spatial and temporal smoothness penalties are

$$\phi(\mathbf{w}) = \sum_{\ell} \sum_{j} \sum_{j' \in \mathcal{N}_j, j' > j} \kappa_{jj'} (w_{j\ell} - w_{j'\ell})^2 \tag{9}$$

$$\rho(\mathbf{w}) = \sum_{j} \sum_{\ell_1} \sum_{\ell_2} w_{j\ell_1} Q_{\ell_1 \ell_2} w_{j\ell_2} \tag{10}$$

Both of these penalty terms are quadratic in the control vertices and therefore can be put in the standard quadratic form:

$$\phi(\mathbf{w}) = \frac{1}{2} \mathbf{w}^T \mathbf{R}_s \mathbf{w} \tag{11}$$

$$\rho(\mathbf{w}) = \frac{1}{2} \mathbf{w}^T \mathbf{R}_t \mathbf{w} \tag{12}$$

We will show and use the special factorization properties of $\mathbf{R}_s$ and $\mathbf{R}_t$ later in the derivation. At this point we take advantage of the Þxed observation vector size due to the bin-mode approach in (2) and quadratic forms of both penalties which allow us to adopt approximations similar to those in [1]:

$$\mathbf{C_w} \approx (\mathbf{F} + \beta \mathbf{R}_s + \gamma \mathbf{R}_t)^{-1} \mathbf{F} (\mathbf{F} + \beta \mathbf{R}_s + \gamma \mathbf{R}_t)^{-1} \tag{13}$$

where $\mathbf{F}$ is the Fisher Information Matrix (FIM) given by $\mathbf{F} \equiv (\mathbf{P} \otimes \mathbf{B})^T diag\{\frac{1}{\bar{y}_i^{(n)}}\} (\mathbf{P} \otimes \mathbf{B})$. The difÞculty in evaluating the covariance matrix is in the matrix inversions and we will use Fourier transform arguments as in [3] and [6] together with properties of Kronecker products [9] to obtain an approximation to $\mathbf{C_w}$.

First we introduce the double index notation (j,l) to denote $((j-1)n_b + l)$ and note that the $(k,l)(m,s)^{th}$ element of the $n_b n_v \times n_b n_v$ FIM is given by

$$F_{(k,l)(m,s)} = \sum_{i=1}^{n_d} \sum_{n=1}^{N} \frac{p_{ik} p_{im} A_l^{(n)} A_s^{(n)}}{\bar{y}_i^{(n)}} \tag{14}$$

where $A_l^{(n)} \equiv \int_{t_{n-1}}^{t_n} B_l(t) dt$. Using this exact form of the FIM together with the penalty terms in (13) makes the computation of $(\mathbf{F} + \beta \mathbf{R}_s + \gamma \mathbf{R}_t)^{-1}$ very difÞcult. Therefore we proceed by making an approximation to the FIM very similar to that in [1]:

$$\begin{aligned} \mathbf{F} \approx\ & D\{\kappa_{(j,l)}\} D\{v_{(j,l)}\}^{-1} (\mathbf{P} \otimes \mathbf{B})^T \\ & (\mathbf{P} \otimes \mathbf{B}) D\{v_{(j,l)}\}^{-1} D\{\kappa_{(j,l)}\} \end{aligned} \tag{15}$$

where $D\{\cdot\}$ denotes a diagonal matrix and $\kappa_{(j,l)}$ and $v_{(j,l)}$ are given by

$$\kappa_{(j,l)} = \sqrt{\sum_{i=1}^{n_d} p_{ij}^2 \left(\int_0^T \frac{B_l^2(t) dt}{r_i(t)} \right)} \tag{16}$$

$$v_{(j,l)} = \sqrt{\sum_{i=1}^{n_d} p_{ij}^2 \left(\int_0^T B_l(t) dt \right)^2} \tag{17}$$

At this point we Þrst note that $(\mathbf{P} \otimes \mathbf{B})^T (\mathbf{P} \otimes \mathbf{B}) = (\mathbf{P}^T \mathbf{P} \otimes \mathbf{B}^T \mathbf{B})$ and observe that $v_{(j,l)}$ is separable into $v_{(j,l)} = v_j^{(s)} v_l^{(t)}$ where $v_j^{(s)} = \sqrt{\sum_{i=1}^{n_d} p_{ij}^2}$ and $v_l^{(t)} = \sqrt{\left(\sum_{n=1}^{N} (\int_{t_{n-1}}^{t_n} B_l(t) dt)^2 \right)}$. Superscripts (s) and (t) are used to emphasize the fact that they are spatial and temporal terms respectively. Hence our FIM approximation becomes

$$\begin{aligned} \mathbf{F} \approx\ & D\{\kappa_{(j,l)}\} \left(D\{v_j^{(s)}\} \otimes D\{v_l^{(t)}\} \right)^{-1} \\ & (\mathbf{P}^T \mathbf{P} \otimes \mathbf{B}^T \mathbf{B}) \\ & \left(D\{v_j^{(s)}\} \otimes D\{v_l^{(t)}\} \right)^{-1} D\{\kappa_{(j,l)}\} \\ =\ & D\{\kappa_{(j,l)}\} \Big[[(D\{v_j^{(s)}\}^{-1} \mathbf{P}^T \mathbf{P} D\{v_j^{(s)}\}^{-1})] \otimes \\ & [D\{v_l^{(t)}\} \mathbf{B}^T \mathbf{B} D\{v_l^{(t)}\}^{-1})] \Big] D\{\kappa_{(j,l)}\} \end{aligned} \tag{18}$$

where we again used the properties of the Kronecker product to write the second part of the above equation.

Now we turn our attention to the other two terms in the covariance matrix (13), $\beta \mathbf{R}_s$ and $\gamma \mathbf{R}_t$. It follows from (9)-(12) that we can rewrite $\mathbf{R}_s$ and $\mathbf{R}_t$ as

$$\mathbf{R}_s = \mathbf{S} \otimes \mathbf{I} \tag{19}$$

$$\mathbf{R}_t = \mathbf{I} \otimes \mathbf{T} \tag{20}$$

where $S_{l'l''} \equiv 2Q_{l'l''}$ and $T_{j'j''} \equiv 2\sum_{j \in N_j} \kappa_{jj'}$ if $j' = j''$ and $-2\kappa_{j'j''}$ if $j' \neq j''$. The identity matrix in (19) is $n_b \times n_b$ and the identity matrix in (20) is $n_v \times n_v$.

We proceed by expressing $\beta \mathbf{R}_s$ and $\gamma \mathbf{R}_t$ as follows

$$\beta \mathbf{R}_s = D\{\kappa_{(j,l)}\} D\{\eta_{(j,l)}\} (\mathbf{S} \otimes \mathbf{I}) D\{\eta_{(j,l)}\} D\{\kappa_{(j,l)}\} \tag{21}$$

$$\gamma \mathbf{R}_t = D\{\kappa_{(j,l)}\} D\{\psi_{(j,l)}\} (\mathbf{I} \otimes \mathbf{T}) D\{\psi_{(j,l)}\} D\{\kappa_{(j,l)}\} \tag{22}$$

where

$$\eta_{(j,l)} = \sqrt{\beta} / \kappa_{(j,l)} \tag{23}$$

$$\psi_{(j,l)} = \sqrt{\gamma} / \kappa_{(j,l)} \tag{24}$$

We can now express $\mathbf{C_w}$ in the following form:

$$\begin{aligned}\mathbf{C_w} \approx & [\mathbf{F} + D\{\kappa_{(j,l)}\}D\{\eta_{(j,l)}\}(\mathbf{S}\otimes\mathbf{I})D\{\eta_{(j,l)}\}D\{\kappa_{(j,l)}\} \\ & + D\{\kappa_{(j,l)}\}D\{\psi_{(j,l)}\}(\mathbf{I}\otimes\mathbf{T})D\{\psi_{(j,l)}\}D\{\kappa_{(j,l)}\}]^{-1} \\ & \mathbf{F} \quad [\mathbf{F} + D\{\kappa_{(j,l)}\}D\{\eta_{(j,l)}\}(\mathbf{S}\otimes\mathbf{I})D\{\eta_{(j,l)}\}D\{\kappa_{(j,l)}\} \\ & + D\{\kappa_{(j,l)}\}D\{\psi_{(j,l)}\}(\mathbf{I}\otimes\mathbf{T})D\{\psi_{(j,l)}\}D\{\kappa_{(j,l)}\}]^{-1} \end{aligned} \quad (25)$$

where $\mathbf{F}$ is given by (18). In order to be able to diagonalize the remaining terms after factoring out $D\{\kappa_{(j,l)}\}$ we make the following approximation, similar to its static counterpart in [6]:

$$\begin{aligned} & [(D\{v_j^{(s)}\}^{-1}\mathbf{P}^T\mathbf{P}D\{v_j^{(s)}\}^{-1}) \otimes (D\{v_l^{(t)}\}\mathbf{B}^T\mathbf{B}D\{v_l^{(t)}\}^{-1}) + \\ & D\{\eta_{(j,l)}\}(\mathbf{S}\otimes\mathbf{I})D\{\eta_{(j,l)}\} + D\{\psi_{(j,l)}\}(\mathbf{I}\otimes\mathbf{T})D\{\psi_{(j,l)}\}]\mathbf{e}_{(j,l)} \\ & \approx \\ & [(D\{v_j^{(s)}\}^{-1}\mathbf{P}^T\mathbf{P}D\{v_j^{(s)}\}^{-1}) \otimes (D\{v_l^{(t)}\}\mathbf{B}^T\mathbf{B}D\{v_l^{(t)}\}^{-1}) + \\ & \eta^2_{(j,l)}(\mathbf{S}\otimes\mathbf{I}) + \psi^2_{(j,l)}(\mathbf{I}\otimes\mathbf{T})]\mathbf{e}_{(j,l)} \end{aligned} \quad (26)$$

where $\mathbf{e}_{(j,l)}$ is the unit vector in the $(j,l)^{th}$ control vertex. Now we approximately diagonalize $\mathbf{P}^T\mathbf{P}$ and $\mathbf{S} \equiv \mathbf{C}^T\mathbf{C}$ (since we use pairwise quadratic penalties such a decomposition of $\mathbf{R}_s$ is possible) using 2D-DFTs based on the assumption that they are approximately block circulant. We will also diagonalize $\mathbf{B}^T\mathbf{B}$ and $\mathbf{T} \equiv 2\mathbf{Q}$ using 1D-DFTs assuming that they are approximately circulant. Any $n_b \times n_b$ unitary matrix which can approximately diagonalize both $\mathbf{B}^T\mathbf{B}$ and $\mathbf{Q}$ can also be used. Approximate diagonalization leads to the following expressions:

$$D\{v_j^{(s)}\}^{-1}\mathbf{P}^T\mathbf{P}D\{v_j^{(s)}\} \approx \mathbf{Q}_{n_v}^T D\{\lambda_j^{(s)}\}\mathbf{Q}_{n_v} \quad (27)$$

$$D\{v_l^{(t)}\}^{-1}\mathbf{B}^T\mathbf{B}D\{v_l^{(t)}\} \approx \mathbf{Q}_{n_b}^T D\{\lambda_l^{(t)}\}\mathbf{Q}_{n_b} \quad (28)$$

$$\mathbf{S} \approx \mathbf{Q}_{n_v}^T D\{\mu_j\}\mathbf{Q}_{n_v} \quad (29)$$

$$\mathbf{T} \approx \mathbf{Q}_{n_b}^T D\{\delta_l\}\mathbf{Q}_{n_b} \quad (30)$$

where $\mathbf{Q}_{n_v}$ denotes the Kronecker form of the $n_v \times n_v$ 2D-DFT matrix and $\mathbf{Q}_{n_b}$ denotes the 1D-DFT matrix. Note that the $\lambda_j^{(s)}$ are exactly the same 2D-DFT coefÞcients used in the static case [6]. Substitution of these diagonalizations together with the approximations in (26) into (25) gives the following result for the covariances of the control vertices (which form the entries of $\mathbf{C_w}$):

$$var(w_{j'l'}) = \frac{\kappa^{-2}_{(j',l')}}{n_b n_v}\sum_{j=1}^{n_v}\sum_{l=1}^{n_b}\frac{\lambda_j^{(s)}\lambda_l^{(t)}}{(\lambda_j^{(s)}\lambda_l^{(t)} + \kappa^{-2}_{(j,l)}(\beta\mu_j + \gamma\delta_l))^2} \quad (31)$$

$$\begin{aligned} & cov(w_{j'l'}, w_{j''l''}) = \\ & \kappa^{-1}_{(j',l')}\kappa^{-1}_{(j'',l'')}\mathbf{e}^T_{(j',l')}[\mathbf{Q}_{n_v}\otimes\mathbf{Q}_{n_b}]^T\mathbf{L}[\mathbf{Q}_{n_v}\otimes\mathbf{Q}_{n_b}]\mathbf{e}_{(j'',l'')} \end{aligned} \quad (32)$$

where we used the unitary properties of $\mathbf{Q}_{n_v}$ and $\mathbf{Q}_{n_b}$ in (31) and $\mathbf{L}$ is a diagonal matrix whose $(j,l)^{th}$ diagonal entry is given by:

$$\begin{aligned} & \mathbf{L}_{(j,l)(j,l)} = \\ & \frac{\lambda_j\lambda_l}{[\lambda_j\lambda_l + \kappa^{-2}_{(j',l')}(\beta\mu_j + \gamma\delta_l)][\lambda_j\lambda_l + \kappa^{-2}_{(j'',l'')}(\beta\mu_j + \gamma\delta_l)]} \end{aligned} \quad (33)$$

These last two equations indicate the procedure for computing instantaneous or average activity estimate covariances. We compute $\mathbf{C}_{w_{j'},w_{j''}}$ using (32) (or (31) for the diagonal terms when $j' = j''$), then substitute the result in (7) or (8) to obtain the desired expression. The total computational cost is 2 n_v-point 2D-DFTs and 2 n_b-point 1D-DFTs.

III. Discussion

In order to evaluate the performance of our continuous-time dynamic PET reconstruction algorithm [4], we derived procedures for approximating means and variances of dynamic average and instantaneous rate estimates. We used DFT based diagonalizations as in [3], [6] to perform the matrix inversions which would otherwise not be feasible except for one-dimensional cases. This performance analysis allows us to evaluate the performances of all dynamic reconstructions in which the rate functions are parametrized by continuous basis functions and penalty terms are quadratic and separable in control vertices. This efÞcient analysis can be used in comparing different dynamic reconstruction alogrithms as well as comparing dynamic reconstructions versus static ones without extensive Monte Carlo simulations.

IV. References

[1] J.A. Fessler : Mean and Variance of Implicitly DeÞned Biased Estimators (Such as Penalized Maximum Likelihood): Applications to Tomography. *IEEE Trans. Image Processing* vol. 5, pp. 493-506, Mar. 1996

[2] J.A. Fessler and W.L. Rogers : Spatial Resolution Properties of Penalized-likelihood Image Reconstruction: Spatial-invariant Tomographs. *IEEE Trans. Image Processing* , vol. 9, pp. 1346-1358, Sept. 1996

[3] J.A. Fessler and S.D. Booth : Conjugate-gradient Preconditioning Methods for Shift-variant PET Image Reconstruction *IEEE Trans. Image Processing* vol. 8, pp. 688-699, May 1999

[4] T.E. Nichols, J.Qi, E. Asma and R.M. Leahy : Spatiotemporal Reconstruction of List-Mode PET Data, *IEEE Trans. Medical Imaging* , Vol 21, No. 4, pp. 396-405

[5] J. Qi, R. Leahy, S. Cherry, A. Chatziioannou, and T. Farquhar : ÒHigh resolution 3D Bayesian Image Reconstruction Using the microPET Small Animal Scanner,Ó*Physics in Medicine and Biology*, vol. 43, no. 4, pp. 1001Ð1013,1998.

[6] J. Qi and R.M. Leahy : Resolution and Noise Properties of MAP Reconstruction for Fully 3-D PET. *IEEE Trans. Medical Imaging* , vol. 19, pp. 493-506, May 2000

[7] Carl de Boor : *A Practical Guide to Splines*, volume 27 of Applied Mathematical Sciences. Springer-Verlag, New York, 1978.

[8] J. Fessler : Penalized Weighted Least-Squares Image Reconstruction for PET, *IEEE Trans. Medical Imaging*, vol. 13, no. 2, pp. 290Ð300,June 1994.

[9] P. Lancaster and M. Tismenetsky : *The Theory of Matrices*, Academic Press Inc., Orlando, 1985.

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