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DIRECT RECONSTRUCTION OF DYNAMIC PET PARAMETRIC IMAGES USING SPARSE SPECTRAL REPRESENTATION

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Abstract

To generate parametric images for dynamic PET, direct reconstruction from projection data is statistically more efficient than conventional indirect methods that perform image reconstruction and kinetic modeling in two separate steps. Existing direct reconstruction methods often use nonlinear compartmental models, which require the knowledge of model order. This paper presents a direct reconstruction approach using a linear spectral representation and does not require model order assumption. A Laplacian prior is used to ensure sparsity in the spectral representation. The resultant maximum *a posteriori* (MAP) formulation is solved by an expectation maximization shrinkage algorithm. A bias correction step is developed to improve the MAP estimate. Computer simulations show that the proposed method achieves better bias-variance tradeoff than a conventional indirect method for estimating parametric images from dynamic PET data.

Index Terms

Dynamic PET; spectral analysis; sparse representation; image reconstruction; tracer kinetic modeling

1. INTRODUCTION

Molecular imaging using dynamic positron emission tomography (PET) can provide in vivo parametric images of physiologically or biochemically important parameters. To obtain a parametric image, a conventional approach is to reconstruct a sequence of emission images from measured projection data first, and then to fit the time activity curve (TAC) at each pixel to a linear or nonlinear kinetic model. To obtain an efficient estimate, the noise distribution of the reconstructed activity images should be modeled in the kinetic analysis. However, exact modeling of the noise distribution in emission images reconstructed by iterative methods is difficult because the noise is spatially variant and object-dependent. Usually the space-variant noise variance and correlations between pixels are simply ignored in the kinetic analysis, which leads to sub-optimal results. Direct reconstruction of parametric images from the raw projection data solves this problem by combining kinetic modeling and emission image reconstruction into a single formula. It allows accurate modeling of the Poisson noise statistics in data. It has been shown that the images reconstructed by direct reconstruction methods have better bias-variance tradeoff than those reconstructed by indirect methods for both linear [1,2] and nonlinear kinetic models [3–5].

Many existing direct reconstruction methods [3–5] use compartmental models to describe tracer kinetic behaviors in PET data. The use of compartmental models usually requires the knowledge of model order which is not always available in PET studies, in particular for novel tracers. Moreover, the log-likelihood function is nonconvex with respect to the kinetic parameters, so global convergence can not be achieved by deterministic algorithms. While

using the Patlak model in direct reconstruction [1,2] can avoid these problems, the Patlak model is only applicable to irreversible tracers. An alternative method to analyze dynamic PET data is the spectral analysis that uses a set of linear spectra to represent tracer time activity curves [6]. The spectral analysis does not assume a model order *a priori*. Parameters of interest (e.g. volume of distribution) can also be directly computed from the spectral coefficients, which is an advantage when compared with other type of linear basis functions, e.g. [7]. In this paper we integrate the spectral analysis model into image reconstruction and present a direct approach to reconstruct spectral coefficients from projection data. An independent Laplacian prior is used to encourage sparsity in the overcomplete spectral representation, which improves the robustness of the estimation over the unregularized approach [8].

2. RECONSTRUCTION OF PARAMETRIC IMAGES

2.1. Image Reconstruction

PET data are modeled as a collection of independent Poisson random variables with the expectation $\bar{\mathbf{y}}_m$ in frame m related to the image $\mathbf{x}_m$ through an affine transform

$$\bar{\mathbf{y}}_m = \mathbf{P} \mathbf{x}_m + \mathbf{r}_m, \quad (1)$$

where $\mathbf{P} \in \mathbb{R}^{n_i \times n_j}$ is the detection probability matrix with element (i,j) being the probability of detecting an event originated in voxel j by detector pair i , and $\mathbf{r}_m \in \mathbb{R}^{n_i}$ is the expectation of scattered and random events in the m th frame. The log-likelihood function of a dynamic PET data set, omitting constants that are independent of $\mathbf{x}$, is

$$\mathcal{L}(\mathbf{y}|\mathbf{x}) = \sum_m \sum_i y_{im} \log \bar{y}_{im} - \bar{y}_{im}, \quad (2)$$

where $\mathbf{y} = \{\mathbf{y}_m\}$ denotes the measured dynamic PET data and $\mathbf{x} = \{\mathbf{x}_m\}$ denotes the unknown dynamic image.

The dynamic emission image $\mathbf{x}$ can be estimated by using a maximum *a posteriori* (MAP) method as

$$\hat{\mathbf{x}} = \arg \max_{\mathbf{x} \geq 0} \mathcal{L}(\mathbf{y}|\mathbf{x}) - \beta \mathcal{U}(\mathbf{x}), \quad (3)$$

where $\mathcal{U}(\mathbf{x})$ is the prior energy function for regularizing the noise and β is the hyperparameter that controls the tradeoff between the resolution and noise.

2.2. Spectral Analysis

Spectral analysis models a tracer time activity curve as a linear combination of a set of basis functions [6],

$$c(t) = \sum_{k=0}^{n_k} \theta_k b_k(t) \quad (4)$$

where $b_k(t)$ is the k th spectrum and θ_k is the corresponding spectral coefficient. A common choice of the basis functions is a set of exponential functions convoluted with the blood input function $C_p(t)$:

$$b_k(t) = \exp(-\phi_k t) \otimes C_p(t) \quad (5)$$

where ϕ_k denotes the rate constant of the k th spectrum.

The advantage of using exponential bases is that they are consistent with compartmental models and many parameters of interest can be directly computed from the spectral coefficients. For example, the volume of distribution (VD) is given by

$$VD = \sum_k \frac{\theta_k}{\phi_k}. \quad (6)$$

To estimate the spectral coefficients, a least squares method can be used. Gunn *et al* proposed a basis pursuit method that includes a sparsity regularization in the least squares formulation as [9]:

$$\hat{\theta} = \arg \min_{\theta} \frac{1}{2} \sum_m w_m \left(c_m - \sum_k b_{mk} \theta_k \right)^2 + \alpha \sum_k |\theta_k|, \quad (7)$$

where w_m is a weighting factor, c_m is the measured activity in time frame m , and b_{mk} is the average value of $b_k(t)$ in frame m . The ℓ_1 regularization encourages the solution to be sparse and the sparsity can be controlled by the regularization parameter α .

2.3. Direct Reconstruction

This paper presents a method to reconstruct images of spectral coefficients directly from projection data by combining the spectral analysis model and imaging model into a single formula. Considering the spectral coefficient images θ as the unknowns, the log-likelihood function of the dynamic PET data becomes

$$\mathcal{L}(\mathbf{y}|\theta) = \sum_{m=1}^{n_m} \sum_{i=1}^{n_i} y_{im} \log \bar{y}_{im}(\theta) - \bar{y}_{im}(\theta) \quad (8)$$

where the expectation of PET data is related to the spectral coefficients through

$$\bar{y}_{im}(\theta) = \sum_{j=1}^{n_j} \sum_{k=0}^{n_k} b_{mk} p_{ij} \theta_{jk} + r_{im}. \quad (9)$$

The MAP estimate of θ can be obtained by

$$\hat{\theta}_{\text{MAP}} = \arg \max_{\theta \geq 0} \mathcal{L}(\mathbf{y}|\theta) - \alpha \|\theta\|_1, \quad (10)$$

where $\|\theta\|_1$ is the energy function of an independent Laplacian prior used to encourage sparse solutions and α is the hyperparameter. When α is 0, the solution becomes the traditional maximum likelihood (ML) reconstruction which imposes sparsity constraints implicitly through the nonnegativity constraint [10]. The effect of the Laplacian prior is

similar to the sparsity regularization used in the basis pursuit method. Recently a similar form of ℓ_1 -regularized Poisson-likelihood estimation was also used for Compton imaging [11].

2.4. Bias Correction

One problem that we have observed when using (10) directly was that the Laplacian prior introduced noticeable bias to the MAP estimate (see figure 1 for example). Here we present a method to reduce the bias.

Instead of using the MAP estimate obtained in (10) directly, we consider the MAP estimation as a basis learning process to find a set of sparse bases to represent tracer time activity curves. Let us denote the MAP solution given by (10) as a function of the spectral basis matrix $\mathbf{B} \equiv \{b^{mk}\}$ and the sparsity regularization parameter α

$$\hat{\theta}_{\text{MAP}} = F(\mathbf{B}, \alpha). \quad (11)$$

After the initial MAP estimate, the basis functions with insignificant spectral coefficients (less than a preset threshold) will be removed from the spectral basis matrix $\mathbf{B}$. We denote the resulting new basis matrix as $\mathbf{B}^*$. Note that $\mathbf{B}^*$ has different basis functions for different pixels. Then a ML estimate is performed using (10) with $\mathbf{B}^*$ and $\alpha = 0$,

$$\hat{\theta} = F(\mathbf{B}^*, 0). \quad (12)$$

Because $\mathbf{B}^*$ contains only the spectral bases that have nonzero coefficients, sparsity regularization is unnecessary. The ML estimate obtained in (12) has significantly reduced bias compared to the MAP estimate in (10).

3. SIMULATION STUDIES

3.1. Two-Pixel Dynamic Imaging

We first simulated a simplified PET system with only two pixels to demonstrate the advantage of the MAP reconstruction with bias correction over the traditional ML direct reconstruction. One pixel has a two-tissue compartment kinetics with $VD = 0.8250$. The other pixel has a one-tissue compartment kinetics with $VD = 0.3333$. The dynamic PET data consists of 22 time frames over 30 minutes: 4×0.25 min, 4×0.5 min, 7×1 min, 5×2 mins and 2×5 mins. The time activity curves were integrated for each frame and forward projected using an imaging system matrix

$$\mathbf{P} = \begin{pmatrix} 1 & 0.5 \\ 0.5 & 1 \\ 1 & 1 \end{pmatrix}.$$

Three direct reconstruction methods (the traditional ML, MAP without bias correction, and MAP with bias correction) were applied to reconstruct TACs from the projection data. The spectral basis functions were 100 exponential functions with rate constants range from 0.01 to 1.0 convolved with the blood function. All methods used 50000 iterations to guarantee convergence. The sparsity regularization parameter in MAP reconstructions was set to 1.0.

Fig. 1 shows the reconstructed TACs with comparison to the true TACs. While both the ML (top row) and MAP with bias correction (bottom row) provide good fit to the true TAC

within the scan duration (0–30 mins), only the MAP reconstruction with bias correction provides good prediction of TACs beyond the scan time (60–90 mins). For the pixel with one tissue compartment kinetics, the VD estimated from the three re-construction methods are 0.3336, 0.3275 and 0.3349, all with high accuracy. For the pixel with two tissue compartment kinetics, the VD estimates are 0.9149 and 0.7573 for the ML and MAP with no bias correction, respectively. Both have a relative error around 10%. The VD estimated using MAP with bias correction is 0.8185. The relative error is less than 1%.

3.2. Brain Receptor Imaging

A phantom shown in Fig. 2 was used to simulate a ^{11}C -labeled ligand-receptor binding kinetics in brain. The phantom consists of gray matter, white matter and a small tumor inside the white matter. The TACs of the gray matter and tumor region were generated using a two-tissue compartment model. The TAC of the white matter was generated using a one-tissue compartment model. The scanning schedule is same as that in the two-pixel simulation. The TACs were integrated for each frame and forward projected to generate noise-free dynamic sinograms. Poisson noise was then generated, which resulted in about 9 millions total number of events over the 30-minute scan. One hundred independent and identically-distributed noisy datasets were generated and processed independently by the MAP reconstruction with bias correction and an indirect method to estimate the spectral coefficients and VD.

The sparsity regularization parameter in the MAP direct reconstruction was set to 1.0. For the indirect method, ML reconstruction was used to reconstruct dynamic images. The basis pursuit method was applied to pixel-wise TAC to generate parametric images. The weighting factors in (7) were chosen to be inversely proportional to the data variance in each frame. The regularization parameter α in (7) was set to 2×10^{-4} , which was selected from a range of values, 1×10^{-5} , 2×10^{-5} , 5×10^{-5} , 1×10^{-4} , 2×10^{-4} , 5×10^{-4} , and 1×10^{-3} , to give a good bias-variance performance for VD estimation. The value is much smaller than that used in the direct reconstruction because the weighting factors are of small values (about 1×10^{-5}). We found that the optimum α value is insensitive to the number of iterations used in the ML reconstruction.

Fig. 3 shows VD images reconstructed by the indirect method and the proposed direct method, respectively. In comparison, the image reconstructed by the direct reconstruction is less noisy. To quantitatively compare the two reconstruction methods, we plot in Fig. 4 the average bias versus standard deviation tradeoff curves of VD estimated by the direct and indirect methods for different regions in the brain phantom. Different points on each curve were obtained by varying the iteration number from 50 to 300 with an increment of 25 in each reconstruction. For all the regions, the proposed direct reconstruction results in less variance at any given bias level than the indirect method. To take into account of spatial correlation, we also calculated the bias versus standard deviation tradeoff curve for region of interest (ROI) quantification. The tumor was chosen as the ROI. The bias versus standard deviation tradeoff curves are plotted in Fig. 4(d). Again, the proposed direct reconstruction achieves better bias-variance performance than the indirect approach.

4. CONCLUSIONS

This paper proposes a direct reconstruction approach using sparse spectral representation to reconstruct parametric images for dynamic PET. Computer simulations have shown that the proposed MAP reconstruction with bias correction achieves better quantification performance than the traditional ML direct reconstruction and the indirect method.

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Fig. 1.

Comparisons of direct reconstruction methods using a two-pixel dynamic imaging system. Left column: true and reconstructed TACs over the scan duration (0–30 min); Right: true and estimated TACs between 60 and 90 minutes. Top row: the traditional ML reconstruction; middle row: MAP without bias correction; bottom row: MAP with bias correction. Circles denote the true TACs and the solid lines denote the reconstructed TACs.

Fig. 2.
The brain phantom (left) and regional time activity curves (right) used in the simulation.

(a) Indirect

(b) Direct

Fig. 3.
VD images reconstructed using (a) the indirect method and (b) the proposed direct method.

Fig. 4. Bias versus standard deviation tradeoff curves of the VD estimated using the direct and indirect approaches. (a)–(c) Average bias and standard deviation of pixel-wise quantification; (d) bias and standard deviation of ROI quantification.