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Factor Analysis of Dynamic Myocardial PET Images Based on Kinetic Clustering and -Divergence Measure (Post-print)

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Abstract

Objective: To establish a factor analysis method based on kinetic clustering and -divergence measure for noninvasively extracting blood input function and regional tissue time-activity curves from dynamic myocardial PET images. Methods: The dynamic PET images were preliminarily decomposed by minimizing the -divergence between the dynamic images and the factor model to obtain initial factors and factor images. Then, prior information from PET pixel kinetic clustering was incorporated to address the non-uniqueness problem of solutions in the factor analysis model, and the initial factors and factor images were transformed spatially to generate physiologically meaningful tissue activity curves and tissue spatial distributions. Results: Compared with traditional least squares measure and the model constrained by minimizing overlap between factor images, this model exhibits lower sensitivity to noise and higher accuracy of the extracted results. Conclusion: By selecting the optimal value as the measure for the factor analysis model and introducing kinetic clustering information from PET image pixels, blood input function and regional tissue time-activity curves can be accurately obtained, demonstrating superior performance in both visual and quantitative evaluations.

Full Text

Preamble

Kinetic Cluster and -Divergence-Based Dynamic Myocardial Factorial Analysis of Positron Emission Computed Tomography Images

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Abstract

Objective: We propose a novel factor analysis method based on kinetic clustering and -divergence measure for extracting the blood input function and time-activity curves of regional tissues from dynamic myocardial positron emission tomography (PET) images. **Methods:** Dynamic PET images were decomposed into initial factors and factor images by minimizing the -divergence between the factor model and actual image data. The kinetic clustering prior was then incorporated into the model to solve the non-uniqueness problem, generating tissue time-activity curves and spatial distributions with physiological significance. **Results:** Compared with traditional least squares measures and minimal spatial overlap constraint models, our model exhibits lower noise sensitivity and higher accuracy in extracted results. **Conclusion:** By selecting the optimal value as the measure for the factor analysis model and introducing kinetic clustering information from PET image pixels, we can accurately obtain blood input functions and local tissue time-activity curves, demonstrating superior performance in both visual and quantitative evaluations.

Keywords: factor analysis; -divergence; positron emission computed tomography; kinetic cluster

Introduction

Non-invasive determination of regional myocardial blood flow (RMBF) has long been a clinical cardiology objective. By estimating blood input functions and output functions from dynamic images and applying kinetic models, absolute quantitative parameters (such as substance transport rates, metabolic rates, and receptor binding rates) can be obtained to enable quantitative myocardial blood flow analysis. In kinetic model applications, blood input function estimation is critical, as its accuracy directly affects subsequent quantitative analysis. Currently, the widely used region-of-interest method is simple but heavily relies on manually drawn ROIs, whose accuracy is influenced by physician experience and partial volume effects.

Factor analysis, a statistical technique for extracting common factors from variable groups, has been applied to non-invasively extract blood input functions and tissue time-activity curves from dynamic images. Methods based on principal component analysis, independent component analysis, least squares, and maximum likelihood have been proposed. However, factor analysis results suffer from non-uniqueness, prompting various prior information-based approaches to address this issue. Additionally, Sitek et al. proposed an optimization method based on minimizing overlap between factor images to obtain unique results.

Properly constructing the measure between the factor model and actual data is key to accurate modeling. Current factor analysis models commonly use least squares measures based on Gaussian noise models or maximum likelihood measures based on Poisson noise models. However, noise in clinically acquired dynamic PET images cannot be directly characterized by Gaussian or Pois-

son models. Therefore, we propose an -divergence-based factor analysis model. Introduced by S. Amari, -divergence belongs to the family of information divergences for measuring deviation between data distributions. By selecting different values, it can serve as a measure for data with arbitrary noise models.

To address the non-uniqueness problem in factor analysis models, traditional methods use constraints that minimize overlap between factor images. However, due to PET image resolution and partial volume effects, myocardial signals often contain 10-15% blood signal, which the minimal overlap constraint fails to consider. In dynamic PET studies, each pixel' s temporal behavior can be described by time-activity curves (TACs). We cluster pixels with identical temporal behavior and use this clustering result as a prior constraint to solve the non-uniqueness problem in factor analysis, obtaining physiologically meaningful tissue activity curves. The factor analysis model was applied to simulated ^{82}Rb PET myocardial perfusion data based on the XCAT (Extended Cardiac-Torso) phantom. Experiments demonstrate our method' s superiority over traditional factor analysis models in visual and quantitative evaluations.

1.1 PET Image Acquisition

For a dynamic PET image sequence I, the tracer activity x_{jm} at pixel j in frame m can be calculated through the integral:

$$x_{jm} = \int_{t_{m,s}}^{t_{m,e}} c(j,t)e^{-\lambda\tau}dt$$

where $c(j,t)$ represents the tracer activity at pixel location j at time t, and $t_{m,s}$ and $t_{m,e}$ denote the start and end times of frame m, respectively. The dynamic sequence can be represented as:

$$I = \begin{pmatrix} x_{11} & x_{12} & \cdots & x_{1n_m} \\ x_{21} & x_{22} & \cdots & x_{2n_m} \\ \vdots & \vdots & \ddots & \vdots \\ x_{n_j1} & x_{n_j2} & \cdots & x_{n_jn_m} \end{pmatrix}_{n_j \times n_m}$$

where each column represents one image frame and each row represents the time-activity curve of a single pixel.

Dynamic PET sequence images can be decomposed into a limited number of temporal basis vectors F and their corresponding spatial distributions C, expressed as:

$$I = CF + \varepsilon$$

where the dynamic PET image I has dimensions $N \times T$ (N = number of pixels per frame, T = number of frames). The factor matrix F is $K \times T$ and the factor image matrix C is $N \times K$, with K being the number of factors to extract. ε represents residual signals (image noise and minor signals ignored by the model). For practical application, K must satisfy $K \ll N$ and $K \ll T$.

[Figure 1: see original paper] illustrates factor analysis for dynamic sequences. Under ideal conditions, factor matrix F corresponds to time-activity curves of various physiological tissues in the dynamic image, while factor images C correspond to the spatial distributions of these tissues.

1.2 Proposed Factor Analysis Model

Factor analysis model solving involves two main steps: (1) Decomposing the image to obtain initial factors and factor images by minimizing the measure between the model and actual data; (2) Resolving the model' s non-uniqueness problem.

We quantify the deviation between image I and model CF using -divergence. Introduced by S. Amari, -divergence measures the deviation between two data distributions $p(x)$ and $q(x)$:

$$D_\alpha(p,q) = \frac{1}{\alpha(1-\alpha)} \sum_i \left(\alpha p_i + (1-\alpha) q_i - p_i^\alpha q_i^{1-\alpha}\right), \quad \alpha \in \mathbb{R}$$

Leveraging this information divergence property, we propose minimizing the following -divergence-based objective function to estimate factors F and factor images C:

$$f_\alpha(C,F) = \frac{1}{\alpha(1-\alpha)} \sum_i \sum_f \left(\alpha I_{if} + (1-\alpha)(CF)_{if} - I_{if}^\alpha (CF)_{if}^{1-\alpha}\right) \quad (5)$$

The -divergence-based dynamic PET factor analysis model is formulated as the convex optimization problem:

$$(C,F) = \arg \min_{C_{ik} \geq 0, F_{kf} \geq 0} f_\alpha(C,F)$$

We solve this using an iterative algorithm:

i. Initialization: Set elements of C to random numbers between 0-1, then estimate initial F from C.

ii. Iteration: - (a) **C-step:** Estimate C from current I and F - (b) Set negative elements in C to zero - (c) **F-step:** Estimate F from current I and C - (d) Set negative elements in F to zero - (e) Check for convergence; if not converged, return to step (a)

iii. Normalization: Normalize factor images C and scale F accordingly.

In the C-step, setting $\frac{\partial f_\alpha(C,F)}{\partial (FC_m)_{if}} = 0$ yields the update. In the F-step, setting $\frac{\partial f_\alpha(C,F)}{\partial (CF_m)_{if}} = 0$ yields the update.

1.3 Uniqueness Constraints

The factor model described in Equation (1) is mathematically non-unique. The non-uniqueness can be expressed as:

$$I = (CR)(R^{-1}F) = C'F'$$

where C and F represent the true factor image and factor matrices. Through an invertible matrix R, infinite sets of factor images C' and factors F' can theoretically satisfy the model. Therefore, reasonable constraints must be found to ensure unique results.

A. Traditional Method: Minimal Spatial Overlap Constraint

Sitek et al. proposed using minimal structure overlap (MSO) between factor images as the uniqueness constraint. The overlap between factors is calculated as:

$$f_{\text{uni}}(\cdot) = \sum_{p=1}^{K} \sum_{q=p+1}^{K} \frac{\sum_{i=1}^{N} (CR)_{ip}(CR)_{iq}}{\sqrt{\sum_{i=1}^{N} (CR)_{ip}^2 \sum_{i=1}^{N} (CR)_{iq}^2}}$$

The penalty term $f_n(CR, R^{-1}F)$ ensures non-negative values for factors and factor images:

$$f_n(\cdot) = \sum_{i=1}^{N} \sum_{k=1}^{K} H((CR)_{ik}) + \sum_{f=1}^{T} \sum_{k=1}^{K} H((R^{-1}F)_{kf})$$

where $H(x) = \begin{cases} 0 & x \geq 0 \\ x^2 & x < 0 \end{cases}$.

Minimizing the objective function $(f_{\text{uni}} + \beta_1 f_n)$ yields the optimal solution for R, producing final factor images (CR) and physiologically meaningful factors $(R^{-1}F)$ representing tissue activity curves.

B. Novel Method: Kinetic Clustering-Based Constraint

Due to PET image resolution and partial volume effects, myocardial signals often contain 10-15% blood signal, which the minimal overlap constraint fails to

account for. Therefore, we propose a kinetic-based (KB) prior constraint using time-activity curve clustering to solve the non-uniqueness problem in factor analysis.

In dynamic PET studies, each pixel' s temporal behavior can be described by TAC curves. We classify images based on pixel kinetics, ensuring TACs within the same class are homogeneous while being heterogeneous between classes. Assuming dynamic image I has K distinct classes, the fuzzy C-means clustering algorithm minimizes:

$$J = \sum_{j=1}^{N} \sum_{k=1}^{K} u_{kj}^{q} \|I_j - v_k\|^2$$

where $\|\cdot\|$ represents Euclidean distance, I_j denotes the TAC of pixel j in image I, v_k is the TAC of the kth cluster center, u_{kj} represents the membership degree of pixel j to class k, and q ($q > 1$) is the fuzziness parameter.

The solution is obtained iteratively:

i. Set initial class number K and stopping criterion ε
ii. Randomly initialize fuzzy membership matrix $U^{(0)}$ containing individual membership values
iii. Set iteration counter $b = 0$
iv. Compute cluster centers v_k from $U^{(b)}$: $v_k = \frac{\sum_j (u_{kj}^{(b)})^q I_j}{\sum_j (u_{kj}^{(b)})^q}$
v. Compute membership matrix $U^{(b+1)}$: $u_{kj}^{(b+1)} = \frac{1}{\sum_{i=1}^{K} \left(\frac{\|I_j - v_k\|}{\|I_j - v_i\|} \right)^{2/(q-1)}}$
vi. If $\max\{|U^{(b)} - U^{(b+1)}|\} < \varepsilon$, stop; otherwise, set $b = b+1$ and return to step iv.

The cluster centers v_k are applied as pixel kinetic prior information to the factor analysis uniqueness constraint via Equation (11):

$$f_{\mathrm{TAC}}(R) = \sum_{k=1}^{K} \|(R^{-1}F)_k - v_k\|^2$$

The non-uniqueness problem in factor analysis is solved by minimizing the objective function ($f_{\mathrm{TAC}} + \beta_2 f_n$) to obtain the optimal R, yielding final factor images (CR) and physiologically meaningful factors ($R^{-1}F$).

Experimental Setup

Computer Simulation Data

In computer simulation experiments, we used the XCAT digital phantom shown in [Figure 2: see original paper]. The cardiac region consists of blood pool and

myocardial tissue components, which were isolated for this study. The phantom has $64 \times 64 \times 30$ voxels with dimensions $3.27\,\text{mm} \times 3.27\,\text{mm} \times 3.27\,\text{mm}$. We simulated the physiological metabolic imaging process of the cardiac region using a single-compartment model with ^{82}Rb (half-life = 1.27 min). Blood input functions and kinetic parameters were measured from five volunteers at Johns Hopkins University PET Center. Myocardial tissue time-activity curves were generated using the single-compartment model, blood input function, and kinetic parameters ($K_1 = 1.4822\,\text{mL/min/g}$, $k_2 = 0.3159\,\text{min}^{-1}$, blood volume fraction $V_p = 0.3829$). Tissue time-activity curves and spatial distributions are shown in [Figure 3: see original paper]. The dynamic PET scanning protocol consisted of 18 time frames: $12 \times 5\,\text{s}$ and $6 \times 10\,\text{s}$. Dynamic PET images were generated by assigning time-activity values to their corresponding spatial distributions.

Forward projection of the dynamic images yielded noise-free projection data (total photon count = 5×10^6). Poisson noise was added to simulate realistic projection data, which were reconstructed using FBP algorithm. The reconstructed dynamic images were then denoised using a Gaussian filter (FWHM = 4 mm). All simulation experiments were based on this data.

Comparison Methods and Evaluation Metrics

In the first step of model solving, we introduced -divergence to quantify the distance between the model and true images, comparing it with traditional least squares measures. Normalized error δ_1 evaluates residual signal ε per frame, while δ_2 evaluates residual signal across all frames:

$$\delta_1 = \frac{\sum_i |I_{if} - (CF)_{if}|}{\sum_i I_{if}}, \quad \delta_2 = \frac{\sum_{i,f} |I_{if} - (CF)_{if}|}{\sum_{i,f} I_{if}}$$

To validate the accuracy of kinetic clustering in solving non-uniqueness, we compared our KB-constrained factor analysis model with the traditional minimal spatial overlap (MSO) model. In addition to visual evaluation, we used RMSE for quantitative comparison between extracted factors and simulated tissue activity curves:

$$\text{RMSE} = \frac{\sum_f |\text{norm}(F) - \text{norm}(F_{\text{ref}})|}{W \cdot \text{norm}(F_{\text{ref}})} \times 100\%$$

where F represents the factor curve, F_{ref} represents the tissue activity curve, W represents time interval per frame, and $\text{norm}(F)$ normalizes F.

Results

3.1 Comparison of Modeling Accuracy Between -Divergence and Least Squares Measures

After obtaining initial factors and factor images by minimizing the measure between model and true images, residual signals can evaluate measure performance. [Figure 4: see original paper] shows normalized error δ_1 per frame for least squares and -divergence measures ($\alpha = 1, 10, 20, 30, 40, 50$). [Figure 5: see original paper] shows δ_2 across all frames versus α. When $\alpha = 1$, -divergence equals least squares error; for other α values, -divergence yields lower normalized errors.

3.2 Uniqueness Constraints

3.3 Selection of Values

After obtaining initial factors, we solved the non-uniqueness problem using both MSO and KB constraints. [Figure 6: see original paper] and [Figure 7: see original paper] show factors and factor images obtained from a dynamic sequence (SNR = 10) using both methods (-divergence measure, $\alpha = 25$). Both methods yield Factor 1 corresponding to blood pool TAC and Factor 2 to myocardial TAC, with factor images matching blood pool and myocardial tissue distributions (14th transverse slice shown). While blood pool factor accuracy is similar between methods, the KB constraint produces more accurate myocardial factors than MSO.

To further validate -divergence effectiveness and select the optimal α, we performed factor analysis across different α values under both constraints. To avoid random noise effects, each method was run 30 times and averaged. [Figure 8: see original paper] shows RMSE for each factor under different α values. With KB constraint, myocardial factor RMSE remains stable, while blood factor RMSE is minimized at $\alpha = 5$, which we selected as optimal. With MSO constraint, both factors stabilize when $\alpha > 12$.

Using the optimal values, compares -divergence ($\alpha = 5$) with least squares under both constraints. -divergence yields lower RMSE, indicating more accurate extraction. [Figure 8: see original paper] also shows that for any α, the average RMSE curves from KB constraint lie below those from MSO constraint, demonstrating KB' s superiority.

3.4 Model Noise Sensitivity

To evaluate noise effects, we added varying noise levels to projection data and reconstructed images with different SNRs. shows factor RMSE under different SNRs using both constraints. RMSE increases with noise, with blood pool TACs estimated more accurately than myocardial TACs.

The purpose of -divergence measure is preliminary decomposition. Due to non-

uniqueness, we use cluster centers as prior information to linearly transform one solution into physiologically meaningful TACs. Notably, when applying kinetic clustering to uniqueness constraints, we introduce penalty term f_n to ensure non-negative results. For regularization parameters β_1 and β_2, experiments show no significant differences when $\beta_1, \beta_2 \in [10, 500]$. We set both to 100 in this study; for different data, appropriate β values can be selected by increasing β if negative values appear.

Results from this cardiac phantom show that blood pool TACs are estimated more accurately than myocardial tissue TACs at the same noise level, primarily because blood pools contain more voxels and are less affected by partial volume effects and noise. Some myocardial wall regions are only 2-3 voxels thick, making them highly susceptible to these effects and reducing accuracy.

Discussion and Conclusion

This study proposes a dynamic 3D cardiac PET image factor analysis model based on kinetic clustering and -divergence measure, enabling accurate extraction of tissue time-activity curves. Traditional factor analysis uses least squares models with minimal factor image overlap constraints to address non-uniqueness. Our approach minimizes -divergence between dynamic images and the factor model, allowing selection of more suitable measures than least squares through different values to obtain initial factors and factor images. When rotating factors, we incorporate kinetic clustering prior information from PET image pixels. Applied to XCAT-based simulation data, experiments show that both -divergence measure and kinetic clustering prior constraints improve tissue activity curve extraction accuracy, maintaining precise extraction even under high noise (SNR = 5) with advantages in visual and quantitative evaluations. However, our method' s regularization parameters cannot be adaptively selected during factor rotation, which will be addressed in future work.

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Note: MSO represents the Minimal Spatial Overlap constraint method and KB represents the Kinetic-Based constraint method.

Note: Figure translations are in progress. See original paper for figures.

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