

Target apex-seeking in factor analysis of medical image sequences

I Buvat, H Benali, F Frouin, J P Bazin and R Di Paola
U66 INSERM, Institut Gustave Roussy, 94 805 Villejuif Cedex, France

Received 7 February 1992, in final form 15 June 1992

Abstract. The aim of factor analysis of medical image sequences (FAMIS) is to estimate a limited number of physical or physiological fundamental functions. Its oblique rotation stage strongly affects the quality and the interpretation of the resulting estimates (factors and factor images). A new target apex-seeking method which integrates physical or physiological knowledge in this stage is described. This knowledge concerns some of the fundamental functions and reacts on the determination of all the factors. A simulated spectral study illustrates the method. We discuss its properties in comparison with the other approaches using *a priori* physical or physiological information.

1. Introduction

In nuclear medicine, factor analysis of dynamic structures (FADS) is now considered as a powerful tool to process time image sequences (Houston 1990). It gives rise to many investigations, particularly to introduce constraints in order to overcome the main problem of FADS, i.e., the non-uniqueness of the solution (Barber and Nijran 1981), which prevents the method from being a quantitative one (Houston 1984). The method has been adapted to the analysis of scintigraphic energy image sequences in 1982 (Di Paola *et al* 1982b). This so-called factor analysis of spectral studies (FASS) was at that time useful to assess the methodology, but its use for clinical studies was limited until these last years (Cavailloles *et al* 1987, Manil *et al* 1989). Recently, there has been a fresh interest in approaches conceptually identical to FASS to address the problem of Compton scatter correction in scintigraphic imaging (Gagnon *et al* 1989, Mas *et al* 1990), proposed as early as 1987 (Cavailloles *et al* 1987). Here, the problem is to extract unscattered and scattered spatial components from a sequence of images acquired at different energies. It has been shown that such a problem could not be properly solved by factor analysis without taking into account some additional information (Hannequin *et al* 1988). As in dynamic studies, the necessity to introduce *a priori* knowledge to achieve a proper and unambiguous solution clearly appears. A new approach to take advantage of available *a priori* information about the features of the underlying time or energy components is proposed here. Its efficiency is demonstrated on simulated data. The benefits of this approach with respect to the existing ones are discussed (Barber and Nijran 1982, Houston 1986, Samal *et al* 1987, Hannequin *et al* 1988, Nijran and Barber 1988, Buvat *et al* 1991, Mas *et al* 1990, Van Daele *et al* 1991).

2. Method

A medical image sequence can be considered as the combination of a limited number of fundamental functions, $\{f_k\}_{k=1,\dots,q}$, and of their associated spatial distributions, $\{a_k\}_{k=1,\dots,q}$, according to the following additive model:

$$x(i, j) = \sum_{k=1}^q a_k(i) f_k(j) + e(i, j). \quad (1)$$

Here, $x(i, j)$ represents the content of pixel, i ($i = 1, \dots, n$), in the picture, j ($j = 1, \dots, p$), of the initial data set, \mathbf{X} . Each row i of the matrix \mathbf{X} , called a trixel, is a vector describing the time or energy behaviour within the pixel i . Each column j corresponds to the j th image of the sequence. The error matrix, \mathbf{E} , includes both noise and modelling errors.

The goal of factor analysis of medical image sequences (FAMIS) is to estimate the q fundamental functions by factors and the spatial distributions by factor images, assuming q is known. This analysis requires four stages: data preprocessing, orthogonal analysis, oblique analysis, and factor image computation. As the goal of the procedure we proposed in this paper is to include *a priori* knowledge within the oblique analysis, this stage is fully described. The three others will be mentioned only briefly.

2.1. Data preprocessing

To improve signal-to-noise ratio, two data preprocessing stages are performed, which consist of thresholding and clustering: the contents of neighbouring trixels are summed, either according to a rectangular segmentation (4×4 , 8×8 , ...) (Bazin *et al* 1980) or to a stochastic classification (Aurengo 1989). This latter technique takes into account the similarities of time or energy behaviour of the trixels. At the end of this stage, let n be the number of clustered trixels, which are now simply called trixels.

2.2. Orthogonal analysis

In the case of scintigraphic data, taking into account that the counting statistics follow Poisson's law, the optimal orthogonal decomposition is the one of correspondence analysis, which uses a χ^2 metric (Frouin *et al* 1991). A q principal component analysis of the matrix \mathbf{X} , using the χ^2 metric, leads to a set of q orthogonal factors, $\{u_k\}_{k=0,\dots,q-1}$, and orthogonal factor images, $\{v_k\}_{k=0,\dots,q-1}$. They correspond to the best least square approximation of the matrix \mathbf{X} , according to the reconstitution formula

$$\hat{x}(i, j) = \frac{x_i x_j}{x} \left[1 + \sum_{k=1}^{q-1} \sqrt{\lambda_k} v_k(i) u_k(j) \right]$$

with

$$u_0(j) = v_0(i) = 1 \quad \forall (i, j) \text{ and } \lambda_0 = 1$$

$$x_i = \sum_{j=1}^p x(i, j), \quad x_j = \sum_{i=1}^n x(i, j), \quad x = \sum_{i=1}^n \sum_{j=1}^p x(i, j),$$

$$\sum_{j=1}^p \frac{x_j}{x} u_k^2(j) = 1, \quad \sum_{i=1}^n \frac{x_i}{x} v_k^2(i) = 1 \quad \forall k$$

$\lambda_0 \geq \lambda_1 \geq \dots \geq \lambda_{q-1} \geq 0$ are the first q eigenvalues obtained by correspondence analysis. g will denote the centroid of the trixels, i.e. the vector of values x_j/x , $j = 1, \dots, p$.

2.3. Oblique analysis

The components $\{u_k\}_{k=1, \dots, q-1}$ resulting from the orthogonal analysis define a $(q-1)$ dimensional subspace, \mathcal{U} , called 'study subspace' (Barber and Nijran 1982), from which the initial data \mathbf{X} may be reconstituted with a minimum loss of information in the least square sense. However, the orthogonal factors and the corresponding orthogonal factor images have no physiological or physical meaning, since they include negative values. The oblique analysis is based on the hypothesis that the fundamental functions $\{f_k\}_{k=1, \dots, q}$ of equation (1) lie within the subspace generated by \mathcal{U} and g . In fact, if $\{f_k\}_{k=1, \dots, q}$ are normalized such that $\sum_{j=1}^p f_k(j) = 1$, it can be shown that f_k can be written as

$$f_k = g + \sum_{i=1}^{q-1} b_{ki} u_i. \quad (2)$$

Consequently, the oblique analysis consists in searching the set of $\{f_k - g\}_{k=1, \dots, q}$, denoted by $\{\tilde{f}_k\}_{k=1, \dots, q}$, within the study subspace \mathcal{U} , to obtain the factors $\{f_k\}_{k=1, \dots, q}$. Such a search, called an 'apex-seeking' procedure, requires some criteria to determine automatically and without ambiguity the set of $\{f_k\}_{k=1, \dots, q}$. The first and most commonly used approach is based on non-negativity constraints of both factors and factor images (Barber 1980, Di Paola *et al* 1982a). Since scintigraphic images result from counting detected events, the spatial distributions $\{a_k\}_{k=1, \dots, q}$ of the decomposition (1), as well as the fundamental functions $\{f_k\}_{k=1, \dots, q}$ are non-negative. However, the range of possible solutions satisfying these constraints may be quite extensive (Barber and Nijran 1981). The final solution will then be one among many possible solutions.

This non-uniqueness problem is better addressed by taking into account some *a priori* knowledge about underlying fundamental functions (Nijran and Barber 1985, Mas *et al* 1990) or spatial distributions (Houston 1986, Samal *et al* 1987, Nijran and Barber 1988, Van Daele *et al* 1990). Our approach constrains the apex-seeking routine using the available information related to the fundamental functions. It includes two steps: first, the target apex-seeking procedure determines the r target factors, $\{f_k^0\}_{k=1, \dots, r}$, for which there is an *a priori* knowledge. Then, the $q - r$ remaining functions are estimated by taking advantage of the correct localization of the first r ones.

2.3.1. Target apex-seeking (TAS) procedure. The basic idea of the proposed procedure is to scan the subspace \mathcal{U} to search the point corresponding to a function which best

fits the expected factor. The matching between one function and the known features, such as the position of a maximum, or the range wherein the expected factor is equal to zero, must be quantified. Consequently, it requires that the *a priori* information, θ , can be formalized to define a criterion, $h(S, \theta)$, measuring the deviation between the function corresponding to a point, S , of \mathcal{U} and θ . Any point S with coordinates, $(b_{s1}, \dots, b_{s(q-1)})$, defines a profile, i.e., a normalized function

$$s = g + \sum_{t=1}^{q-1} b_{st} u_t$$

which is similar to equation (2).

The appropriate definition of $h(S, \theta)$, which depends on the mathematical description of the available knowledge, is a prerequisite to the use of the proposed target apex-seeking procedure. This knowledge is not necessarily related to the whole function, but can concern only a part of it, provided it is sufficient to identify in \mathcal{U} the corresponding factor.

Starting from any point of \mathcal{U} , an iterative procedure scans this subspace to find the point corresponding to the minimization of h . The orthogonal subspace \mathcal{U} is a structured one, i.e. the movement in a parallel direction to a basis vector u_k involves a continuous distortion of the corresponding function. Consequently, the scanning of \mathcal{U} is performed according to the following algorithm (figure 1).

(i) Initialization: $m = 0$ (iteration index). Start from any point S of \mathcal{U} and compute $h(S, \theta)$.

(ii) $m = m + 1$. For $k = 1$ to $q - 1$, move in a parallel direction to u_k with a step δ_k such that $\delta_k = \frac{1}{n} [\max_i b_{ik} - \min_i b_{ik}]$, until h reaches a minimum value: $h(S^m, \theta)$. The displacement direction (left or right, up or down) is the one which makes h decrease.

(iii) If $h(S^m, \theta) \neq h(S^{m-1}, \theta)$, go to (ii) from $h(S^m, \theta)$, else take the function corresponding to S^{m-1} as the searched factor. This procedure is repeated to compute the r target factors $\{f_k^0\}_{k=1, \dots, r}$, using for each one an adapted h criterion.

2.3.2. *Search for the remaining factors.* The determination of the $q - r > 1$ remaining factors comprises three steps, each including specific constraints.

2.3.2.1. *Bootstrap.* Using the previous estimate of the r target factors, generating a r -dimensional subspace, \mathcal{R} , the $q - r$ remaining factors are first characterized by the data analysis in a $q - r - 1$ dimensional space \mathcal{R}' orthogonal to \mathcal{R} such that

$$\mathcal{R}' \oplus \mathcal{R} = \mathcal{U}$$

where \oplus represents the direct sum. The projection onto the subspace \mathcal{R}' of the data $x(i, j)$, using the χ^2 metric, leads to a matrix, \mathbf{Y} , which is submitted to a correspondence analysis. Considering the first $q - r$ principal components, the reconstitution formula gives the following $\hat{y}(i, j)$ estimates (Escofier and Pages 1988):

$$\hat{y}(i, j) = \frac{x_i x_j}{x} \left[1 + \sum_{k=1}^{q-r-1} \sqrt{\mu_k} z_k(i) w_k(j) \right]$$

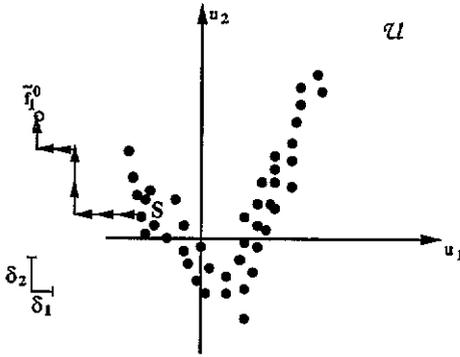


Figure 1. Hypothetic three factor study: the trixels (●) are projected in the subspace \mathcal{U} defined by the two first orthogonal factors u_1 and u_2 . From any starting point S , the scanning procedure leads to the target factor \tilde{f}_1^0 . For one direction u_i ($i = 1, 2$), displacement is performed with a step δ_i as long as the minimization criterion h decreases. Then, the other direction is scanned until a minimum with respect to all the directions is reached. As \tilde{f}_1^0 estimates a fundamental function, which cannot always be represented by any trixel, it may lie outside the cloud of trixel projections.

where

$$z_0(i) = w_0(j) = 1 \quad \forall(i, j) \text{ and } \mu_0 = 1,$$

$$\sum_{j=1}^p \frac{x_j}{x} w_k^2(j) = 1, \quad \sum_{i=1}^n \frac{x_i}{x} z_k^2(i) = 1 \quad \forall k.$$

$\mu_0 \geq \mu_1 \geq \dots \geq \mu_{q-r-1} \geq 0$ are the first $q - r$ eigenvalues resulting from the correspondence analysis.

The $q - r - 1$ principal components, $\{w_k\}_{k=1, \dots, q-r-1}$ explain the variance of the subspace \mathcal{R}' . They generate the subspace \mathcal{W} of \mathcal{U} which contains the information not included in \mathcal{R} . The initial estimation of the $q - r$ factors, $\tilde{f}_{r+1}^0, \dots, \tilde{f}_q^0$, in \mathcal{W} is performed using the initialization procedure described by Di Paola *et al* (1982a).

- (i) \tilde{f}_{r+1}^0 corresponds to the trixel projection, W_1 , in \mathcal{W} farthest from g , which is also the centroid of the set of $\hat{y}(i, j)$;
- (ii) \tilde{f}_{r+2}^0 corresponds to the trixel projection, W_2 , in \mathcal{W} farthest from W_1 ; . . . ;
- (iii) \tilde{f}_{r+t}^0 corresponds to the trixel projection, W_t , in \mathcal{W} for which the sum of the distances to W_1, W_2, \dots, W_{t-1} , is maximum; . . . ; (iv) \tilde{f}_q^0 corresponds to the trixel projection, W_{q-r} , in \mathcal{W} for which the sum of the distances to $W_1, W_2, \dots, W_{q-r-1}$, is maximum. As these $\tilde{f}_{r+1}^0, \tilde{f}_{r+2}^0, \dots, \tilde{f}_q^0$ estimates are included in \mathcal{R}' , which is orthogonal to \mathcal{R} , they have no physical or physiological meaning.

2.3.2.2. *Translation.* This second step consists in the addition of an \mathcal{R} component to the estimates $\{f_k^0\}_{k=r+1, \dots, q}$, to give them a physical or physiological meaning, using the non-negativity constraint on factor images. This constraint can be geometrically expressed as follows (Barber 1980): the points representing trixels are all inside a convex polytope whose q apices are the q points $\{f_k^0\}_{k=1, \dots, q}$. As the estimates $\{f_k^0\}_{k=r+1, \dots, q}$ do not allow us to include all these points, the new estimates

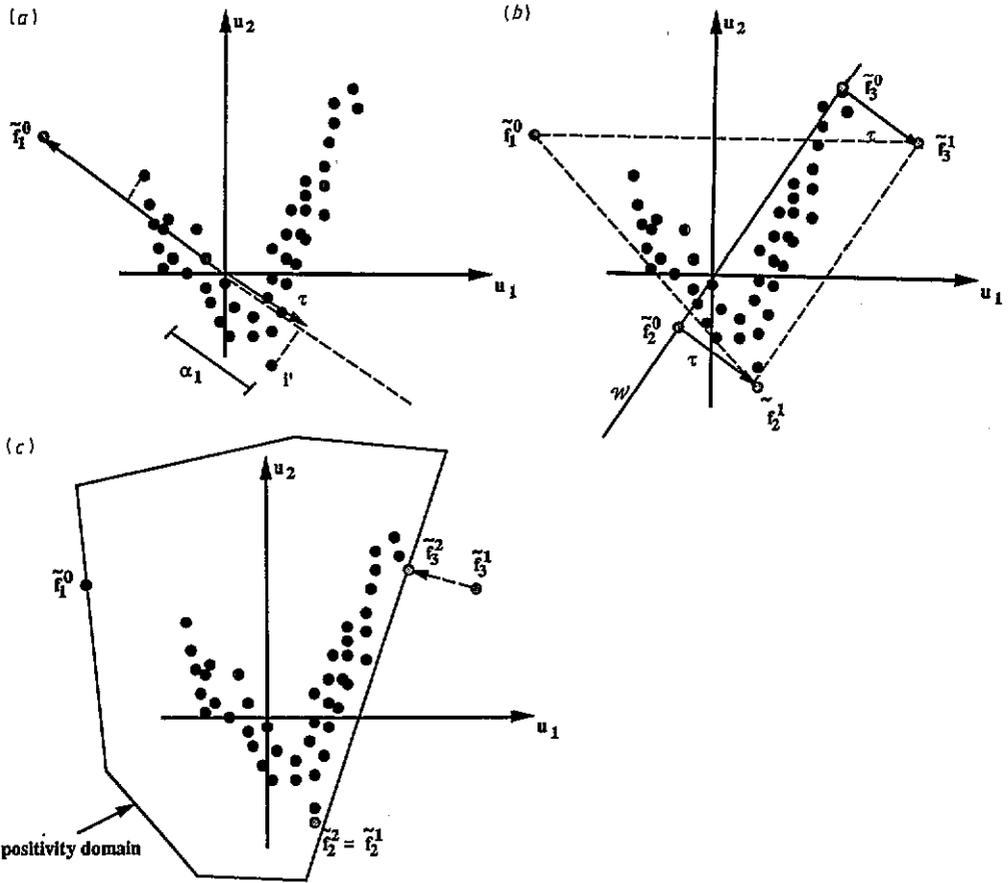


Figure 2. Different stages of the search for the two remaining factors of the same study as in figure 1. (a) Determination of translation vector: all the trixels are projected onto the vector represented by \tilde{f}_1^0 . i' is the trixel the projection of which is the farthest from \tilde{f}_1^0 and determines the weighting coefficient α_1 , and consequently the translation vector τ . (b) Translation: \tilde{f}_2^0 and \tilde{f}_3^0 , which have been initialized in the one-dimensional space \mathcal{W} , are translated by the vector τ , leading to \tilde{f}_2^1 and \tilde{f}_3^1 . More trixel projections are then included in the polytope, whose apices are \tilde{f}_1^0 , \tilde{f}_2^1 and \tilde{f}_3^1 . (c) Non-negativity constraints on factors: as \tilde{f}_3^1 leaves the positivity domain, it is replaced by the nearest point lying on the boundary of this domain \tilde{f}_3^2 . \tilde{f}_2^1 , included in the positivity domain, is unchanged.

$\{\tilde{f}_k^1\}_{k=r+1, \dots, q}$ are obtained by translating the $q - r$ factors $\{\tilde{f}_k^0\}_{k=r+1, \dots, q}$ by a vector τ belonging to \mathcal{U} , such that

$$\tau = \alpha_1 \tilde{f}_1^0 + \alpha_2 \tilde{f}_2^0 + \dots + \alpha_r \tilde{f}_r^0.$$

All the trixels i are projected onto the vector represented by \tilde{f}_c^0 ($c = 1, \dots, r$). Let i' be the trixel the projection of which is the farthest from \tilde{f}_c^0 , i.e.

$$\left(\frac{\sum_{m=1}^{q-1} \lambda_m b_{im} b_{cm} - 1}{\sum_{m=1}^{q-1} \lambda_m b_{cm}^2} \right)^2$$

is maximum (figure 2(a)).

Each weighting coefficient, α_c , is the projection value of the trixel i' onto the vector represented by f_c^0 , which is equivalent to

$$\alpha_c = \frac{\sum_{m=1}^{q-1} \lambda_m b_{i'm} b_{cm}}{\sum_{m=1}^{q-1} \lambda_m b_{cm}^2}$$

If this translation ensures that more trixel projections are included in the polytope (figure 2(b)), the last $q - r$ factors $\{\tilde{f}_k^1\}_{k=r+1, \dots, q}$ can contain negative values. Thus, if \tilde{f}_k^1 , $k = r + 1, \dots, q$, leaves the positivity domain resulting from the non-negativity constraint on factors (Di Paola *et al* 1982a), it is replaced by the nearest point, \tilde{f}_k^2 , lying on the boundary of this domain (figure 2(c)).

2.3.2.3. Constrained iterations. To achieve the final estimation of the fundamental functions complying at best with non-negativity constraints and *a priori* knowledge, an apex-seeking procedure was performed. It includes the following steps.

- (i) Initialization: $m = 2$.
- (ii) Compute $\{c_k^m(i)\}_{k=1, \dots, q}$ using the following oblique reconstitution formula with the χ^2 metric: $\frac{\hat{x}(i, j)}{x_i} = \sum_{k=1}^r c_k^m(i) f_k^0(j) + \sum_{k=r+1}^q c_k^m(i) f_k^m(j)$, with $\sum_{k=1}^q c_k^m(i) = 1$.
- (iii) Compute the number η^m of negative $c_k^m(i)$.
- (iv) If $\eta^m \leq \eta^{m-1}$, set the η^m negative $c_k^m(i)$ to $c_k^m(i)/2 + \epsilon$, where ϵ is a small positive value, else take $\{f_k^0\}_{k=1, \dots, r}$ and $\{f_k^{m-1}\}_{k=r+1, \dots, q}$ as final factors and exit.
- (v) Compute the resulting $\{f_k^{m+1}\}_{k=1, \dots, q}$.
- (vi) For $k = 1, \dots, r$ replace f_k^{m+1} by f_k^0 (target factors). For $k = r + 1, \dots, q$, if f_k^{m+1} leaves the positivity domain, replace it by the nearest point of the boundary of this domain. For each k' , $k' = 1, \dots, r$, if the absolute value of the correlation between f_k^{m+1} and $f_{k'}^0$ increases, replace f_k^{m+1} by $f_{k'}^m$.
- (vii) If $\{f_k^{m+1}\}_{k=r+1, \dots, q} \neq \{f_k^m\}_{k=r+1, \dots, q}$ return to (ii), else take $\{f_k^0\}_{k=1, \dots, r}$ and $\{f_k^m\}_{k=r+1, \dots, q}$ as final factors and exit. If these steps have the same objects as those described by Barber (Barber 1980) and Di Paola (Di Paola *et al* 1982a), steps (ii), (iv) and (vi) differ. The changes we introduced concern the metric, the target factors, the non-negativity constraint, and the stopping criteria. A particular case is if only one factor remains to determine ($q - r = 1$) after the target apex-seeking; its first estimation is directly performed in \mathcal{U} , according to the conventional initialization (Di Paola *et al* 1982a) and is followed by the above described iterative procedure.

2.4. Factor image computation

Factor images are computed by projecting each trixel of the original spatial sampling onto the set of factors (Di Paola *et al* 1982a). The contribution of each factor image is computed as

$$\text{Contr}(k) = \frac{\sum_{i=1}^n \max[a_k(i), 0]}{\sum_{k=1}^q \sum_{i=1}^n \max[a_k(i), 0]}$$

3. Numerical experiment

A computer-simulated phantom consisting of three homogeneous rectangular overlapping spatial distributions, a_1 , a_2 and a_3 , was used to compare the results obtained by a conventional FAMIS algorithm and by FAMIS-TAS. The fundamental functions associated with each of the three spatial distributions are chosen to represent spectra (figure 3), as is the case for Compton scatter correction using FASS (Buvat *et al* 1991): a gaussian photopeak spectrum, f_1 , and two realistic scatter spectra, f_2 and f_3 . The contributions of f_1 , f_2 and f_3 were 30%, 50% and 20%, respectively. From the outer product $\sum_{i=1}^3 a_i \otimes f_i$, a sequence of 26 images 64×64 was computed. Poisson noise was added and the resulting image sequence included about five million events. This simulated study was processed (i) by factor analysis using the algorithm of Barber (Barber 1980) as modified by Di Paola *et al* (1982a), taking into account non-negativity constraints related to both factors and factor images, referred to as conventional FAMIS, and (ii) by FAMIS-TAS. In both cases, a 4×4 spatial sampling was used and all the trixels different from zero were included in the analysis.

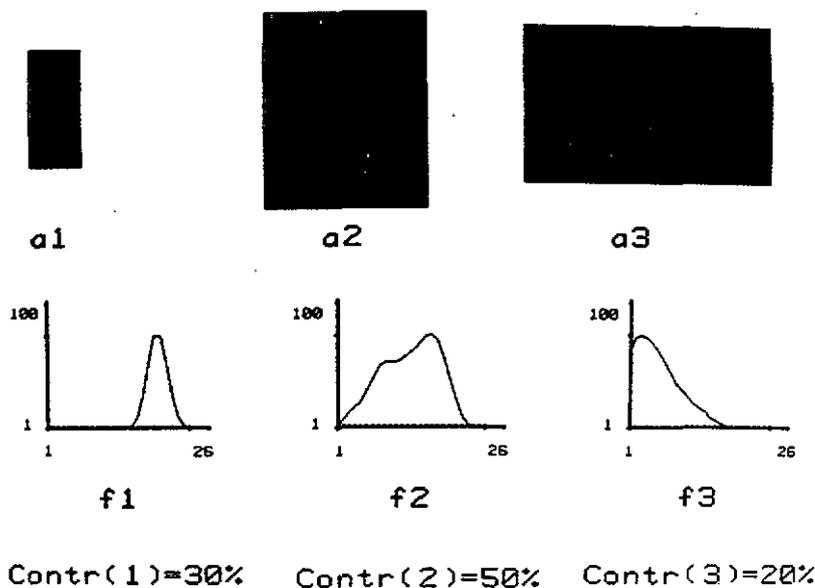


Figure 3. Computer simulation of three homogeneous rectangular overlapping spatial distributions a_1 , a_2 and a_3 and associated fundamental functions f_1 , f_2 and f_3 , with $\text{contr}(1) = 30\%$, $\text{contr}(2) = 50\%$, $\text{contr}(3) = 20\%$.

4. Results

4.1. Conventional FAMIS

Figure 4 shows the projections of the retained trixels onto the U subspace for a 3

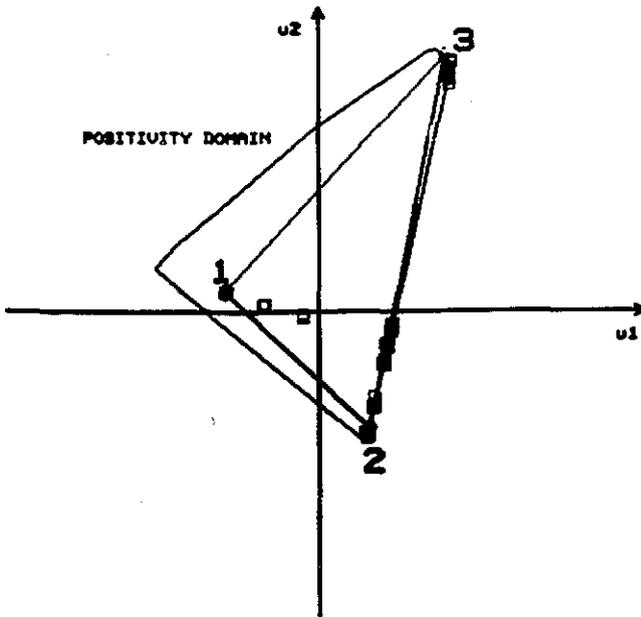


Figure 4. Projections of the 158 trixels (\square) onto the \mathcal{U} subspace, defined by the two first orthogonal factors, and conventional FAMIS factor estimates (1 for \hat{f}_1 , 2 for \hat{f}_2 and 3 for \hat{f}_3). The positivity domain is also visualized.

factor FAMIS. Let \hat{a}_k and \hat{f}_k be the estimates of a_k and f_k . As there is no point corresponding to pure f_1 , the position of \hat{f}_1 cannot be correctly determined by the iterative process of the conventional FAMIS: \hat{f}_1 is clearly contaminated by f_2 and f_3 (figure 5). Conversely, f_2 and f_3 are properly estimated since some trixels correspond to pure f_2 or f_3 ; \hat{f}_2 and \hat{f}_3 are only slightly distorted, due to noise and initial spatial sampling. \hat{a}_1 is qualitatively a good estimate of a_1 but the error in the factor \hat{f}_1 generates artefacts in \hat{a}_2 and \hat{a}_3 which are underestimated in the region wherein a_1 is present. This is in agreement with Houston's results (Houston 1984). The contribution of \hat{a}_1 , \hat{a}_2 and \hat{a}_3 are equal to 43.0%, 41.3% and 15.7%, respectively, which are far from the correct ones.

4.2. FAMIS-TAS

The superimposition of original fundamental functions and factors obtained by conventional FAMIS and FAMIS-TAS are displayed in figure 8. It demonstrates clearly the better agreement between original and FAMIS-TAS resulting functions.

As a consequence of the physical knowledge which generally concerns the photopeak spectrum, it was realistic to assume that the factor \hat{f}_1 could be reduced to zero in some spectral range. Here, it includes the first 15 images. The criterion h was then defined by

$$h(S, \theta) = \sum_{j=1}^{15} s^2(j).$$

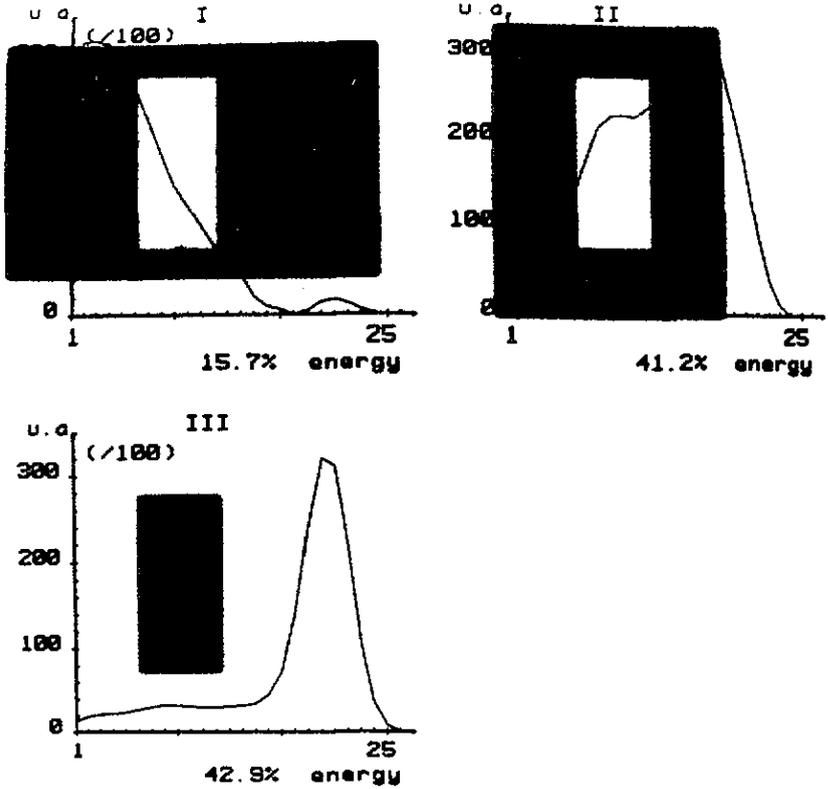


Figure 5. Conventional FAMIS results: factor images, factors and associated contributions: I, \hat{a}_3, \hat{f}_3 ; II, \hat{a}_2, \hat{f}_2 ; III, \hat{a}_1, \hat{f}_1 .

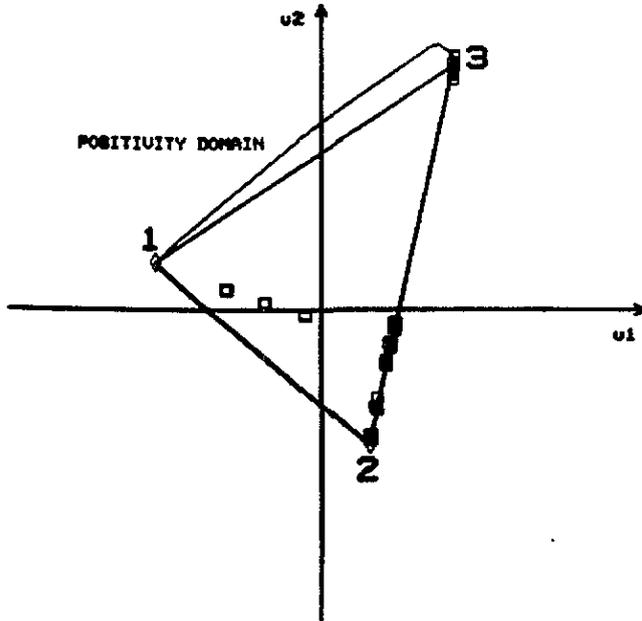


Figure 6. Projections of the 158 trixels (\square) onto the \mathcal{U} subspace, defined by the two first orthogonal factors, and FAMIS-TAS factor estimates (1 for \hat{f}_1 , 2 for \hat{f}_2 and 3 for \hat{f}_3).

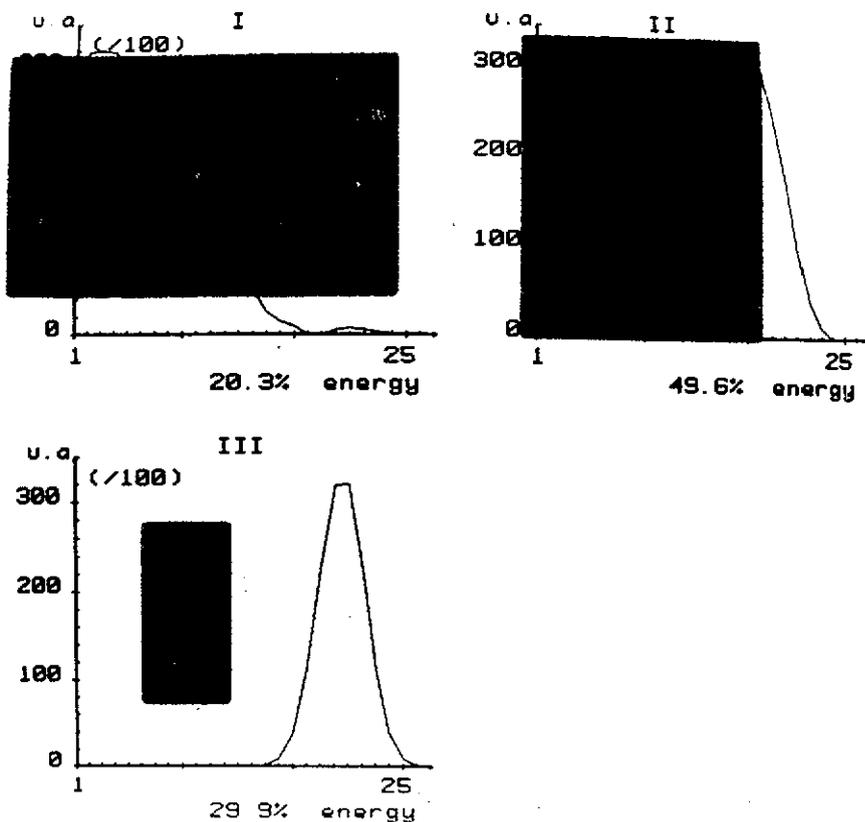


Figure 7. FAMIS-TAS results: factor images, factors, and associated contributions: I, \hat{a}_3 , \hat{f}_3 ; II, \hat{a}_2 , \hat{f}_2 ; III, \hat{a}_1 , \hat{f}_1 .

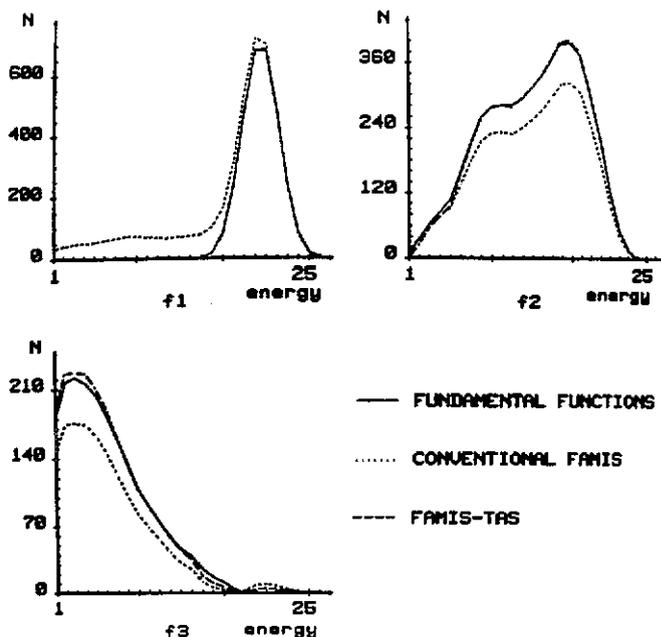


Figure 8. Superimposition of orthogonal fundamental functions (—), conventional FAMIS factors (.....) and FAMIS-TAS factors (----).

\mathcal{U} is scanned as described in section 2.3.1 to search for the point minimizing h and find out a good estimate of f_1 . This point lies on the non-negativity boundary, outside the cloud of trixels. f_2 and f_3 are estimated first in \mathcal{W} , which is a one-dimensional space ($q - r - 1 = 1$), and then they are translated by a vector τ (cf section 2.3.2.2) and projected in the positivity domain; two iterations are sufficient to achieve the final configuration (figure 6). The corresponding factors and factor images are shown in figure 7; they are very similar to the original model. The slight differences are due to noise. The estimated contributions of \hat{a}_1 , \hat{a}_2 and \hat{a}_3 , are equal to 30%, 49.7% and 20.3%, respectively, which are quite correct.

5. Discussion

Several modifications of factor analysis of medical image sequences have already been suggested to improve the oblique rotation step, since the accuracy of the determination of the oblique factors strongly affects the final qualitative and quantitative results. The aim of these investigations is to find the unique physical or physiological data decomposition which could not be obtained using only the non-negativity criteria. Two kinds of approach to rotate the orthogonal factors were reported. The first one deals with the optimization of a more or less complex criterion, which is independent of the processed study. The second one aims at taking into account specific hypotheses by using physical or physiological constraints. FAMIS-TAS belongs to the latter class of methods.

5.1. Criterion optimization methods

The search of the physical or physiological data decomposition, after the orthogonal analysis, may be considered as an optimization problem (Bazin *et al* 1980). To restrict the set of solutions and tend towards the appropriate result, the criterion to minimize must include not only terms taking into account non-negativity of factors and factor images (Bazin *et al* 1980), but also other penalty terms. So, Nakamura *et al* (1989) introduce entropy terms, related to both factors and factor images, whereas Van Daele *et al* (1991) add to non-negativity terms a term corresponding to the Ferguson criterion and another related to the volume defined by the apices. This kind of approach has the advantage of being general but the criteria used are not directly related to a physical or physiological underlying model.

5.2. Constrained methods using a priori knowledge

Barber and Nijran (1981) were the first to explicitly introduce additional *a priori* knowledge different from non-negativity to improve FAMIS performances. Then, different approaches were described to take into account some additional information, related either to spatial distributions or to fundamental functions. Most of them were based on specific hypotheses, and then only adapted to a class of studies. This explains the ever-increasing number of proposed methods with the increasing number of studies processed by FAMIS.

5.2.1. Information about spatial distributions. Different hypotheses about spatial distributions have already been considered to deal with dynamic renal, hepatic or gated cardiac studies. Houston (1986, 1988) assumes that the present combinations of overlapping spatial distributions are known and performs cluster analysis to individualize them. The reliability of this method depends on the clustering process, and on the definition of the geometrical configuration of the clusters. It also requires some knowledge concerning the background spatial distribution to complete the analysis.

The method of simple structure proposed by Samal *et al* (1987, 1988, 1989) assumes the spatial uniformity of the background in factor images. After the manual selection of a single reference area of pure background, a constrained rotation is performed, such that no factor image contains pixel values less than the mean value of the reference area. If the presence of a pure homogeneous background area is sometimes adequate, the quality of the results can be affected by its accurate location, which is subject to operator variability. Nijran and Barber (1988) make the suggestion of manually defining, when possible, regions of interest (ROIS) in which one of the searched spatial distributions is missing, and to use this knowledge as constraints. As a consequence, this method may be sensitive to the choice of ROIS. Moreover, the structures, such as background, which are in the whole field of view, need to be modelled.

Van Daele *et al* (1990) estimate the background component, assuming its local homogeneity, to correct the position of the apices estimated by the conventional FAMIS. As the authors notice, the proposed background searching method is not necessarily the best one. Nevertheless, the solution totally depends on this estimation.

5.2.2. Information about fundamental functions. In the case of dynamic studies, the intersection method suggested by Barber and Nijran (1982, 1985, 1986) necessitates a theoretical model to describe one or several fundamental functions. For each modelled function, the intersection of the so-called theory and study spaces provides the corresponding factor. Unfortunately, the theory vector space generated by monoexponential functions (e.g., Barber and Nijran 1982) not only contains monoexponential but also multiexponential functions. Therefore, the factor provided by the intersection method is not necessarily monoexponential. The determination of the factors for which there is no model does not take advantage of constraints other than non-negativity. A further method proposes to introduce *a priori* knowledge related to all the fundamental functions present in the dynamic study, using a compartmental model (Frouin *et al* 1989). All these approaches are strongly dependent on the description of a model and of its complexity.

In the case of energy-indexed studies, the use of known physical information about fundamental spectra is attractive. Hannequin *et al* (1988) and Mas *et al* (1990) make the suggestion of substituting the theoretical photopeak factor for the photopeak factor estimated by conventional factor analysis, just before factor image computation. Such a procedure prevents any comparison of the *a priori* knowledge with the experimental data. Moreover, the used theoretical factor is a rough approximation of the physical spectrum due to coarse energy sampling. We have proposed (Buvat *et al* 1991) to introduce into the experimental data before FAMIS a theoretical trixel corresponding to the known fundamental function. As in the previous method, the relevance of the theoretical trixel cannot be verified prior to the analysis, and the inclusion of a wrong trixel may result in an inappropriate

orthogonal space. Furthermore, an accurate modelling of the theoretical trixel is necessary. The technique introduced here to overcome these difficulties consists in the search, in the study space, for the function which best looks like the expected factor, by referring to known specific features of the corresponding fundamental function.

A main advantage of our approach is that the knowledge about the function can be only partial, provided it is sufficiently specific to unambiguously characterize it. In the example presented in section 3, a slight change of the boundaries of the spectral range, wherein the function must be reduced to zero, yields factors not significantly different from the previous ones. This is a consequence of the presence of many zero values in the photopeak curve.

TAS results are independent of the initial point of the scanning procedure. Unlike conventional FAMIS, this approach identifies the fundamental functions corresponding to totally overlapped spatial distributions. The determination of the remaining factors, for which no *a priori* knowledge is available, takes indirect advantage of the information introduced concerning the other factor(s) in the bootstrap, translation and iteration procedures. According to Houston's results (Houston 1984), it must be emphasized that a correct estimation of all the fundamental functions is essential to obtain a set of consistent images, even if one does not take an interest in some of them.

FAMIS-TAS is fully automatic, which is very advantageous to clinical routine applications. As for previous cases, FAMIS-TAS remains a specific method, since it is based on knowledge about fundamental functions. However, it includes this knowledge directly in the experimental data subspace.

6. Conclusion

A new method to improve the results provided by factor analysis of medical image sequences is described. It is based on a target apex-seeking technique which performs a convenient integration of *a priori* information related to some fundamental functions. It requires a specific but not exhaustive knowledge about some of the functions to define the corresponding suitable criteria. It allows an optimal estimation of the factors corresponding to fully overlapped spatial distributions. The method was applied here on a simulated spectral study as some information about spectra was directly accessible. The evaluation of FAMIS-TAS using real dynamic and spectral data is currently under investigation. It must be underlined that FAMIS-TAS is particularly well adapted to the processing of scintigraphic image sequences for Compton scatter correction.

Acknowledgments

I Buvat thanks the IFSBM (Institut de Formation Supérieure Biomédicale, Villejuif, France) and Sopha Medical (Buc, France) for supporting her PhD.

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