Model Considerations for Blind Source Separation of Medical Image Sequences

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Abstract. The problem of functional analysis of medical image sequences is studied. The obtained images are assumed to be a superposition of images of underlying biological organs. This is commonly modeled as a Factor Analysis (FA) model. However, this model alone allows for biologically impossible solutions. Therefore, we seek additional biologically motivated assumptions that can be incorporated into the model to yield better solutions. In this paper, we review additional assumptions such as convolution of time activity, regions of interest selection, and noise analysis. All these assumptions can be incorporated into the FA model and their parameters estimated by the Variation Bayes estimation procedure. We compare these assumptions and discuss their influence on the resulting decomposition from diagnostic point of view. The algorithms are tested and demonstrated on real data from renal scintigraphy; however, the methodology can be used in any other imaging modality.

Keywords: Blind Source Separation, Factor Analysis, Convolution, Regions of Interest, Image Sequence

Abstrakt. V příspěvku je studován problém funkční analýzy obrazových sekvencí v medicíně. Získaný obraz je tvořen superpozicí obrázků jednotlivých orgánů ve snímané oblasti, což je typicky modelováno jako model faktorové analýzy, který však v základním tvaru dovoluje biologicky nesmysluplná řešení. Proto je studována možnost zavést do modelu biologicky motivované předpoklady. V tomto příspěvku je uveden přehled dosavadních předpokladů, konkrétně konvolučního modelu časových křivek, automatický výběr oblastí zájmu a analýza šumu. Tyto předpoklady jsou zabudovány do modelu faktorové analýzy, jehož parametry jsou odhadovány pomocí Variační Bayesovy metody. Jednotlivé modely jsou porovnány a je diskutován vliv předpokladů z hlediska diagnostiky. Algoritmy jsou testovány na reálných scintigrafických datech, nicméně mohou být použity i v jiných zobrazovacích modalitách.

Klíčová slova: Slepá Separace, Faktorová Analýza, Konvoluce, Oblasti Zájmu, Obrazová Sekvence

1 Introduction

In many imaging modalities, the original organs are not observed directly but only via observing the activity of radioactive particles and scan of their superposition. In this paper, we are concerned with modalities, where the images are superposed in all observed

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pictures in the series. The task of source separation is to recover the original images of the biological organs (sources) from the observed images.

One of the first methods of source separation is Factor Analysis (FA). It has been used in functional medical imaging such as scintigraphy, Positron Emission Tomography, or functional Magnetic Resonance Imaging [8]. The factor analysis model is based on a simple assumption that the observed image is a linear combination of the underlying factor image weighted by its time-activity curves. This model is also the basis of other methods, such as the Independent Component Analysis (ICA). The FA and ICA as methods have the same basic model but differ in additional assumptions.

The additional assumptions has potential to change the results significantly. If they are justified for the studied problem, they improve the results of separation. In medical imaging, the additional assumptions are needed to recover biologically meaningful solutions of the separation problem. One of the first additional assumptions was positivity of the images and the time-activity curves [9]. It comes from the physical meaning of measurements of radioactive particles. However, even with this restriction, the model allows for biologically impossible solutions. Therefore, we seek additional assumptions and constraints that restrict the space of possible solutions to those with biological meaning. However, the assumption must be also very general to allow for a great variability that is exhibited by a living body.

All assumptions are translated into parameters of a mathematical model, which needs to be estimated from the data. We are concerned with Bayesian estimation, specifically by an approximate solution provided by the Variational Bayes approximation [12]. It offers a reasonable ratio between possibilities of mathematical modeling and computational difficulties.

2   Mathematical Models

The objective is to analyze a sequence of n images obtained at time $t = 1, \ldots, n$ and stored in vectors $\mathbf{d}_t$ with pixels stacked columnwise. The number of pixels in each image is p, thus $\mathbf{d}_t \in \mathbf{R}^p$. The important assumption is that every observed image is a linear combination of r factor images, stored in vectors $\mathbf{a}_j \in \mathbf{R}^p$, $j = 1, \ldots, r$, using the same order of pixels as in $\mathbf{d}_t$. The dimensions of the problem are typically ordered as $r < n \ll p$. Each factor image has its respective time-activity curve stored in vector $\mathbf{x}_j \in \mathbf{R}^n$, $j = 1, \ldots, r$, $\mathbf{x}_j = [x_{1,j}, \ldots, x_{n,j}]'$, $\mathbf{x}'$ denotes transpose of vector $\mathbf{x}$. With these assumptions, the model of Factor Analysis is:

$$\mathbf{d}_t = \sum_{j=1}^{r} \mathbf{a}_j x_{t,j} + \mathbf{e}_t, \tag{1}$$

where vector $\mathbf{e}_t$ denotes the noise of the t-th observed image. Note that vectors $\mathbf{a}_j$ and $\mathbf{x}_j$, are unknown and must be estimated from measurements $\mathbf{d}_t$ so as the variance of a noise, ω.

For the purpose of medical image analysis we already imposed restrictions on the elements of the probabilistic model of FA (1): (i) all elements of the observed vectors $\mathbf{d}_{t \in 1, \ldots, n}$ are positive, (ii) all elements of the factor images $\mathbf{a}_{j \in 1, \ldots, r}$ and the factor curves $\mathbf{x}_{j \in 1, \ldots, r}$ are also positive, and (iii) the number of relevant factors, r, is unknown. These

assumptions are translated into probabilistic model as follows [12]: the positivity in (i) and (ii) is imposed using truncation of priors of the parameters, i.e. $\mathbf{d}$, $\mathbf{a}$, and $\mathbf{x}$, to the positive numbers; and (iii) the number of factors is estimated using Automatic Relevance Detection (ARD) procedure via hyper-parameters, see [2].

Additional assumptions that are known about the problem are: (i) The time activity curves represent flow of fluids in the human body. The flow is a result of different pressures on the input and output of a biological organ. The output flow is then modeled as convolution of the input flow and convolution kernel of the biological organ. (ii) The biological organ is covers only an area in the full image. When selected manually, these areas are called regions-of-interest. (iii) The noise within the observed image is not isotropic. Good model of the noise properties is required.

These assumptions will be now described as parameters of mathematical models. Discussion of classical methods for their estimation is also provided.

2.1   Regions of Interest

The FA assumption of linear combination (1) are typically not valid over the full size of the images but only in a limited area. This can be modeled by an indicator variable for each pixel of the factor image. Specifically, each pixel of the jth factor, $\mathbf{a}_{i,j}$, has its indicator variable $\mathbf{i}_{i,j}$ which is 1 if the ith pixel belongs to the jth factor and 0 if the ith pixel does not belong to the jth factor. Once again, the indicator variable is unknown and must be estimated from the data.

This task is also standard and the estimation of the indicator variable is known as selection of Regions of Interest (ROI). This is often done manually and it is considered to be a necessary preprocessing step of factor analysis after which it yields much better results [7]. Several automatic and semi-automatic methods were proposed, however, the ROI selection is almost exclusively done by specialists in clinical practice. The incorrect selection of the ROI has significant impact on the following factor analysis. Often, the ROI must be selected iteratively until an acceptable solution is found. This procedure is very time consuming and strongly depends on the experience of specialists and chosen method [4].

2.2   Convolution Model

The assumption that factor curve is a result of convolution of an input function and a kernel is well established [6]. The kernels are organ-specific and are useful in diagnostic parameters estimation [5]. Illustration of the assumption is displayed in Fig. 1.

Mathematically formulated, the time-activity curve of the fth factor, $\mathbf{x}_f$, is modeled as

$$x_{t,f} = \sum_{m=1}^{t} \mathbf{b}_{t-m+1} u_{m,f}, \tag{2}$$

where $\mathbf{b}$ is the input activity, common to all factors, and $\mathbf{u}_f$ is the convolution kernel of the factor. Following [6], we consider the kernel elements $u_{m,t}$ to be decreasing, hence they are modeled by a sum of non-negative increments.

Organ time activity   Blood time activity   Convolution kernel

=   *

t   t   t
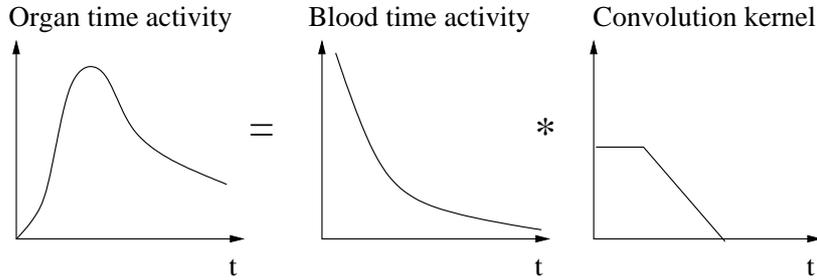
Figure 1: Illustration of assumed shapes of curves in convolution.

Parameters of the model $\mathbf{u}_{j \in 1,...,r}$ and input curve $\mathbf{b}$ are unknown and must be estimated.

Traditional methods of deconvolution are well established method in analysis of dynamic medical image sequences analysis [6]. However, these methods require to know the input curve $\mathbf{b}$ which must be done manually.

2.3   Noise Model

Properties of the noise e_t in (1) determine the quality of separation of the signal. Estimation of the noise properties and its elimination is a crucial step in medical imaging, [3].

The noise may vary across pixels, as well as in time. The noise e_t is assumed to be generated from a Gaussian distribution with zero mean and variance $\sigma_{i,t}$ which may be different for each pixel i and time t. The typical assumption of isotropic noise is $\sigma_{i,t} = \omega^{-1}$, where ω is known as precision. However, it is unrealistic in many modalities. In general, the noise variance is also unknown and should be estimated from the observed data.

Classical methods estimate the noise properties using asymptotic analysis. An example is the correspondence analysis approach [1], where

$$\sigma_{i,t} = \omega^{-1} \sqrt{\sum_{\tau=1}^{n} d_{i,\tau} \sum_{j=1}^{p} d_{j,t}} \tag{3}$$

with unknown precision ω. Correspondence analysis can be interpreted as preprocessing of the data before the factor analysis algorithm.

3   Variational Source Separation

Estimation of parameters of the models described above can be achieved using Bayesian approach. The main advantage of this approach is its ability to determine also the number of relevant factors, r. In such a case, probabilistic formulation of the measurement model (1) must be complemented by prior probabilities of all model parameters. The estimates are obtained by application of the Bayes rule. Exact evaluation of the posterior distribution is however intractable. Therefore, we use an approximate technique known as the Variational Bayes method [12].

We will illustrate the method on the basic model of the factor analysis (1). This model can be written in matrix form $D = AX' + E$, where $D = [\mathbf{d}_1, \ldots, \mathbf{d}_n]$, $A = [\mathbf{a}_1, \ldots, \mathbf{a}_r]$, and $X = [\mathbf{x}_1, \ldots, \mathbf{x}_r]$. The unknown parameters are matrices A, X and scalar ω. The intractable posterior distribution is

$$f(A, X, \omega | D) = \frac{f(D|A, X, \omega) f(A, X, \omega)}{f(D)}. \tag{4}$$

where $f(A, X, \omega)$ is the prior distribution.

The Variational Bayes approximation is based on restriction of the posterior density to the class of conditionally independent distributions:

$$f(A, X, \omega | D) \equiv f(A|D) f(X|D) f(\omega|D). \tag{5}$$

Under this assumption, necessary conditions for approximate posterior distributions $f(A|D)$, $f(X|D)$, and $f(\omega|D)$ minimizing Kullback-Leibler divergence to the true posterior can be found analytically [12]. The posterior distributions are solutions of a set of implicit equations, typically obtained by an iterative algorithm.

The Variational Bayes method has been applied to the FA model with positivity restrictions in [12], and also extended for unknown noise properties. Extension of the method using the convolution kernels is published in [11]. The Variational solution for the FA model with unknown ROI is presented in [10]. These methods will be now compared on real data and their results will be discussed from diagnostic point of view.

4 Results

The methods will be tested on representative clinical data sets from renal scintigraphy. At first, we briefly describe scintigraphy and biological aspects of dynamics of kidneys. Then, we will discuss the results of the proposed models.

4.1 Renal Scintigraphy

Scintigraphy is a well established and important diagnostic method in nuclear medicine. We are concerned with planar dynamic scintigraphy where the measurements are in the form of a sequence of images of the same scanned region of a body. Each pixel in the sequence is a summation of radioactive particles coming from a whole part of the body under the detector. Therefore, each pixel accumulates activity from potentially many factors. The factors has to be separated using a source separation method such as factor analysis.

A healthy kidney is composed of two main structures, parenchyma and pelvis. There are two important specific properties of a structure and dynamic of these structures: (i) the parenchyma is typically surrounding the whole kidney including the pelvis, and (ii) only the parenchyma is active at the first $100 - 180$ seconds (depending on the patient's state) [5]; this time is called uptake. After the uptake time, the activity passes from parenchyma through pelvis to urinary bladder. Diagnostic parameters related to the uptake time are:

PTT Parenchymal Transit Time (PTT) is the time from the beginning of the sequence to that when pelves are activated.

RRF Relative Renal Function (RRF) can be estimated from an activity in the left (L) and in the right (R) parenchyma as $rel_L = \frac{L}{R+L} \times 100$. Historically, the activity is taken only from the uptake time.

If the assumptions (i) and (ii) are not satisfied, the factor separation is incomplete and could cause significant error in diagnostics. There could be some exceptions in case of abnormal or harmed kidney, this case must be carefully considered by physicians.

4.2   Factor Analysis

The basic model of factor analysis from section 2 was applied to a selected clinical data set from dynamic renal scintigraphy. The sequence is composed of 180 images taken after each 10 seconds. The size of each image is 128×128 pixels.

Four factors were found to be relevant using ARD; however, we shown six factors for following comparison. The results are shown in Fig. 2, on the left side.

The estimates of blood and tissue background, the first and the third factors, are reasonable. The main issue of these results is in a bad separation of parenchyma and pelves, the second factor. There are pelves, dark structures in the inner bound of parenchyma, mixed with the whole parenchyma covering the whole kidneys. Consequently, factor curves of parenchyma and pelves are superposed in this factor too.

Due to the bad separation of the most important structures in our task, we are not able to estimate the PTT.

4.3   Factor Analysis with Regions of Interest

The factor analysis with integrated estimation of regions of interest (FAROI), section 2.1, is applied to the same sequence as in the previous section. The results are shown in Fig. 2, right. The factors are displayed in the same order as in case of the FA.

The main difference between the FA and FAROI algorithms is in separation of parenchyma and pelves. In contrast to the FA algorithm, the FAROI algorithm separated pelves as an independent factor. The assumption of the zero plateau in the beginning of the curve is well satisfied; hence, the diagnostic coefficient PTT could be easily estimated from this result. In this case, $PTT = 130$ seconds.

The second factor, parenchyma, is well separated from pelves; however, the resulting factor image suffer from bad separation from the tissue background. This fact is due to the similar shape of activities of the structures. The sixth factor seems to be an artifact, a residual activity of the urinal process.

We stress that FAROI algorithm, in general, provides comparable or better result then the basic FA algorithm without additional assumptions.

4.4   Factor Analysis with Convolution

The assumption of the convolution model from section 2.2 is not valid for the whole sequence but well satisfied for the uptake part of a sequence, where only blood, parenchyma,
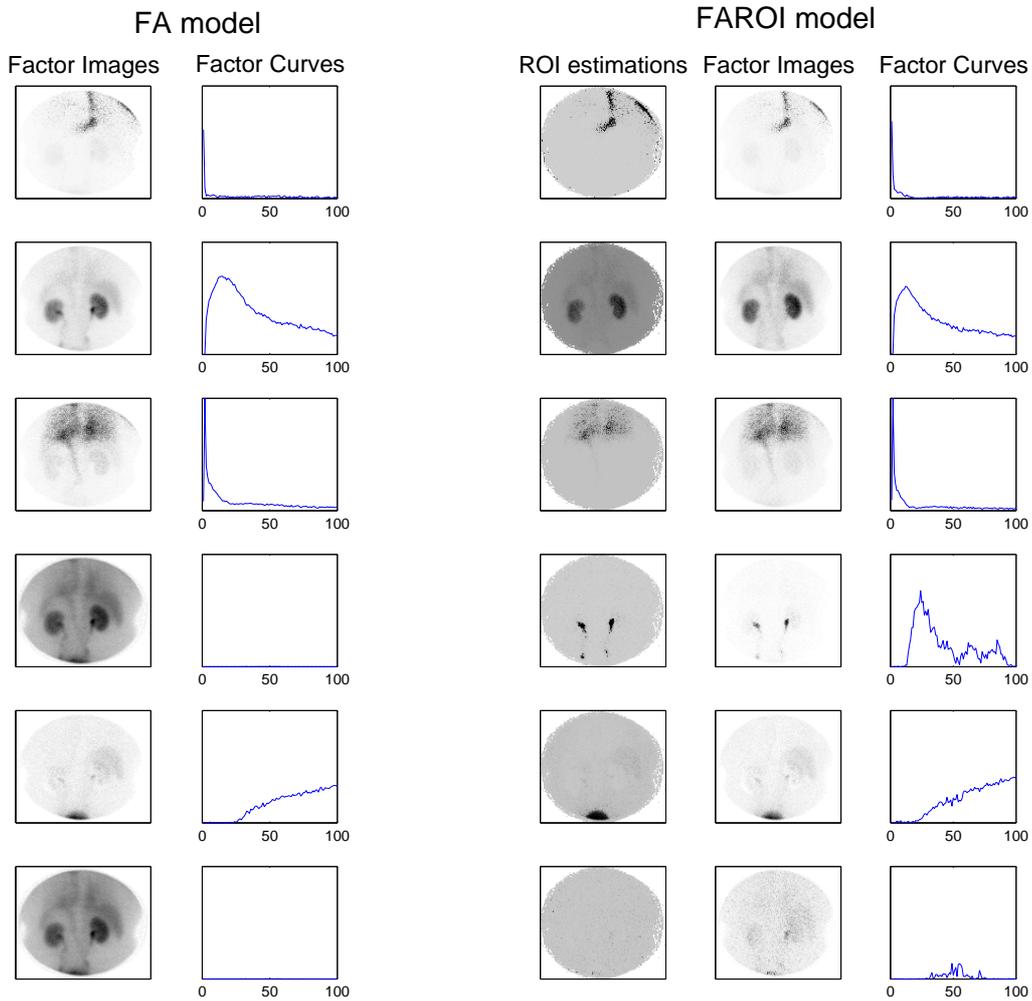
Figure 2: Results from the FA (left) and FAROI (right) models. In the case of FA model, there are (from the top): heart, parenchyma mixed with pelves, lungs and tissue background, dummy factor, urinary bladder, and dummy factor. Estimated factor images are in the first column and estimated factor curves are in the second column. Results from the FAROI algorithm, section II.A., are in the right. There are (from the top): heart, parenchyma, lungs and tissue background, pelves, urinary bladder, and tissue artifact. Estimated parameters are: ROI in the left column, factor images in the middle column, and factor curves in the right column.

and tissue background are activated. This limitation is due to the assumed shape of the convolution kernel of biological structures. The shape in Fig. 1, right, is valid only for structures activated from the beginning of the sequence, e.g. not for the pelves and urinary bladder. Hence, we applied the FA combined with convolution model of factor curves (CFA) only on uptake part of the sequence. The number of images in the up-take part can be estimated using FA or FAROI algorithms automatically. This task is very important part of diagnosis. Here, the parenchyma should be separated from the blood and the tissue backgrounds. After that, the Relative Renal Function (RRF) can be estimated, see section 4.1.
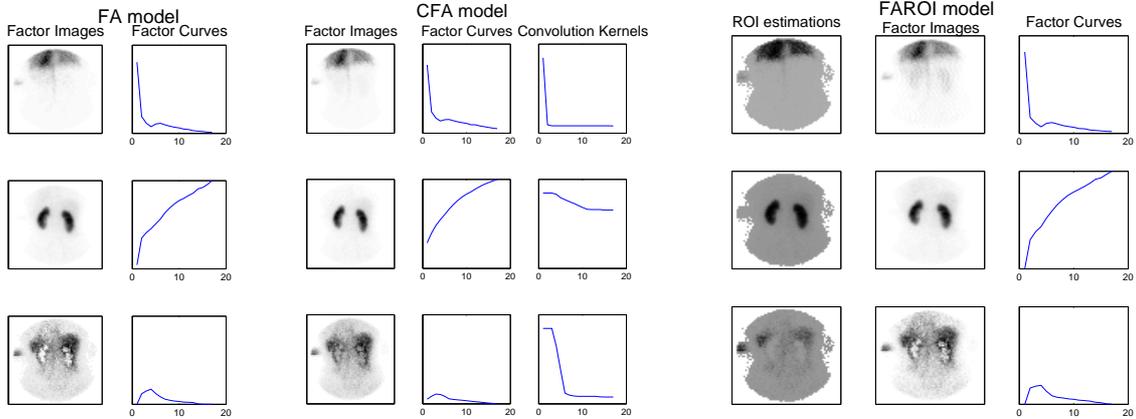
Figure 3: Results from the FA (left), CFA (middle), and FAROI (left) models are shown on the uptake part of the sequence (data set IM3). Estimative procedures estimated in each case three factors (from the top): blood background, parenchyma, and tissue background. In columns are shown (from the left to the right): FA: factor images and factor curves; CFA: factor images, factor curves, and estimated convolution kernels; FAROI: estimated ROI, factor images, and factor curves.

Table 1: Comparison of estimates of RRF coefficient of the left kidney obtained by expert, FA, CFA and FAROI algorithms.

data	expert	FA	CFA	FAROI
IM1	28%-31%	34%	29%	30%
IM2	69%-76%	93%	75%	81%
IM3	48%-51%	48%	49%	49%

The RRF determination is typically performed by an expert using various sets of tools including manually ROI selection, deconvolution, or FA. For our experiment, we roughly selected rectangular ROI around the kidneys and then ran the FA, CFA, and FAROI algorithms on this narrow sequences.

We applied the CFA model on three selected clinical data sets from renal scintigraphy: one set with healthy kidneys (IM3) and two data sets with pathological kidneys (IM1 and IM2). The sequences are composed of images taken after every 10 seconds. Here, the size of each image is 64×64 pixels.

Results of the methods are shown in Tab. 1. For the healthy kidneys (data set IM3), all methods provide comparable estimates corresponding to expert values. Results are different in the case of pathological kidneys (data sets IM1 and IM2). Here, the CFA algorithm provides more reasonable results then the FA and FAROI algorithms due to better background separation from parenchyma, especially for very harmed kidneys (e.g. data set IM2).

An example of results of the algorithms is shown in Fig. 3. For illustration, there are shown results from the whole images, not only for rectangular parts. The ARD procedures estimated in each case three factors. Factor curves are slightly different and

as we can see on comparison of the second factor, the activity of parenchyma by the CFA algorithm suffer from the non-zero start. It is caused by inaccurate parametrization of the convolution kernels, Fig. 1. Factor images are comparable; however, a difference is in separation of parenchyma from tissue backgrounds. The background activity is well estimated by the CFA algorithm in contrast to the FA or FAROI algorithms where the activity is slightly oversubstracted.

A comparison of the FA and CFA algorithms was given in [11]. Generaly, the CFA algorithm provides more relevant estimations of the RRF coefficient then the FA algorithm due to the better separation of parenchyma and blood background. The FAROI algorithm gives promising results, the estimates of the RRF is close to that from an expert; however, the issue with background separation is still not corrected. Note that the difference between the algorithms is more significant especially by harmed kidneys.

4.5   Notes on Noise Estimation

Correspondence analysis from section 2.3 is used in presented algorithms as a preprocessing step. Without this step, there are incorrectness of the background separation.

Various method for online noise-parameters estimation were studied [12]; however, the results are not so different from the used correspondence analysis on typical data sets. Hence, we recommend it for its reasonable results and computational low cost.

5   Conclusion

In this contribution, we summarize various extensions of the model of the factor analysis (FA) for medical image sequences analysis. The extensions of noise, the convolution assumption, and the regions of interest estimation were studied. It is shown that factor analysis provides more physiologically reasonable results with additional, biologically-motivated, extensions.

We discussed the estimation of two diagnostic parameters: parenchymal transit time (PTT) and relative renal function (RRF). For the purpose of PTT estimation, we compared the basic model of FA and the model of FA with regions of interest estimation (FAROI). The FAROI algorithm provides more biologically reasonable results then the FA algorithm. The main difference can be seen on separation of parenchyma and pelves where the FAROI outperforms the FA algorithm. In the case of RRF estimation, we compared FA, FA with convolution (CFA), and FAROI algorithms with estimates provided by an expert. It is shown that the results are similar for healthy kidneys; however, the CFA algorithm provides better results then the other methods on harmed kidneys. Note that all proposed algorithms exploit correspondence analysis as a preprocessing step and automatic relevance determination for significant factors selection. Moreover, we stress that all proposed procedures provide results automatically, without excessive intervention of an expert.

The models were tested on the data from renal scintigraphy; however, the resulting algorithms can be applied in other imaging modalities.

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