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# Non-parametric Bayesian models of response function in dynamic image sequences



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#### ABSTRACT

Estimation of response functions is an important task in dynamic medical imaging. This task arises for example in dynamic renal scintigraphy, where impulse response or retention functions are estimated, or in functional magnetic resonance imaging where hemodynamic response functions are required. These functions can not be observed directly and their estimation is complicated because the recorded images are subject to superposition of underlying signals. Therefore, the response functions are estimated via blind source separation and deconvolution. Performance of this algorithm heavily depends on the used models of the response functions. Response functions in real image sequences are rather complicated and finding a suitable parametric form is problematic. In this paper, we study estimation of the response functions, such as sparsity or smoothness. These assumptions are used within hierarchical priors of the blind source separation algorithm. Comparison of the resulting algorithms with these priors is performed on synthetic datasets as well as on real datasets from dynamic renal scintigraphy. It is shown that flexible non-parametric priors improve estimation of response functions in both cases. MATLAB implementation of the resulting algorithms is freely available for download.

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#### 1. Introduction

Computer analysis of dynamic image sequences offers an opportunity to obtain information about organ function without invasive intervention. A typical example is replacement of invasive blood sampling by computer analysis of dynamic images [1]. The unknown input function can be obtained by deconvolution of the organ time activity curve and organ response function. Typically, both the input function and the response functions are unknown. Moreover, the time-activity curves are also not directly observed since the recorded images are observed as superposition of multiple signals. The superposition arises e.g. from partial volume effect in dynamic positron emission tomography [2] or dynamic and functional magnetic resonance imaging [3] or from projection of the volume into planar dynamic scintigraphy [4]. Analysis of the dynamic image sequences thus requires to separate the original sources (source images, mean images of active components) and their weights over the time forming the time-activity curves (TACs). The TACs are then decomposed into input function and response functions. Success of the procedure is dependent on the model of the image sequence.

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The common model for dynamic image sequences is the factor analysis model [5], which assumes linear combination of the source images and TACs. Another common model is that TAC arise as a convolution of common input function and source specific kernel [6,7]. The common input function is typically the original signal from the blood and the role of convolution kernels vary from application area: impulse response or retention function in dynamic renal scintigraphy [8] or hemodynamic response function in functional magnetic resonance imaging [9]. In this paper, we will refer to the source kernels as the response functions, however other interpretations are also possible.

Analysis of the dynamic image sequences can be done with supervision of experienced physician or technician, who follows recommended guidelines and uses medical knowledge. However, we aim at fully automated approach where the analysis fully depends on the used model. The most sensitive parameter of the analysis is the model of the response functions (i.e. the convolution kernels). Many parametric models of response functions have been proposed, including the exponential model [10] and the piece-wise linear model [11,12]. An obvious disadvantage of the approach is that the real response function may differ from the assumed parametric models. Therefore, more flexible class of models based on nonparametric ideas were proposed such as averaging over region [13], temporal regularization using finite impulse response filters [14], or free-form response functions using automatic relevance determination principle [15].

#### In this paper, we will study the probabilistic models of response functions using Bayesian methodology within the general blind source separation model [16]. The Bayesian approach was chosen for its inference flexibility and for its ability to incorporate prior information of models [17,18]. We will formulate the prior model for general blind source separation problem with deconvolution [15] where the hierarchical structure of the model allow us to study various versions of prior models of response functions. Specifically, we design different prior models of the response functions with more parameters then the number of points in the unknown response function. The challenge is to regularize the estimation procedure such that all parameters are estimated from the observed data. We will use the approximate Bayesian approach known as the Variational Bayes method [19]. The resulting algorithms are tested on synthetic as well as on real datasets and comparisons with parametric methods are provided.

#### 2. Probabilistic blind source separation with deconvolution

In this Section, we introduce a model of dynamic image sequences. Estimation of the model parameters yields an algorithm for Blind Source Separation and Deconvolution. Prior models of all parameters except for the response functions are described here while the priors for the response functions will be studied in details in the next section.

#### 2.1. Model of observation

Each recorded image is stored as a column vector  $\mathbf{d}_j \in \mathbf{R}^{p \times 1}$ , j = 1, ..., n, where *n* is the total number of recorded images. Each vector  $\mathbf{d}_j$  is supposed to be an observation of a superposition of *r* source images  $\mathbf{a}_k \in \mathbf{R}^{p \times 1}$ , k = 1, ..., r, stored again columnwise. The source images are weighted by their specific activities in time *j* denoted as  $x_{1,j}, ..., x_{r,j} \equiv \overline{\mathbf{x}}_j \in \mathbf{R}^{1 \times r}$ . Formally,

$$\mathbf{d}_j = \mathbf{a}_1 x_{1,j} + \mathbf{a}_2 x_{2,j} + \dots + \mathbf{a}_r x_{r,j} + \mathbf{e}_j = A \overline{\mathbf{x}}_j^T + \mathbf{e}_j, \tag{1}$$

where  $\mathbf{e}_j$  is the noise of the observation,  $A \in \mathbf{R}^{p \times r}$  is the matrix composed from source images as its columns  $A = [\mathbf{a}_1, \ldots, \mathbf{a}_r]$ , and symbol  $()^T$  denotes transposition of a vector or a matrix in the whole paper. The Eq. (1) can be rewritten in the matrix form. Suppose the observation matrix  $D = [\mathbf{d}_1, \ldots, \mathbf{d}_n] \in \mathbf{R}^{p \times n}$  and the matrix with TACs in its columns,  $X = [\mathbf{x}_1^T, \ldots, \mathbf{x}_n^T]^T \in \mathbf{R}^{n \times r}$ . Note that we will use the bar symbol,  $\mathbf{x}_k$ , to distinguish the *k*th row of matrix *X*, while  $\mathbf{x}_k$  will be used to denote the *k*the column. Then, the Eq. (1) can be rewritten into the matrix form as

$$D = AX^T + E. (2)$$

The tracer dynamics in each source is commonly described as convolution of common input function, vector  $\mathbf{b} \in \mathbf{R}^{n \times 1}$ , and source specific response function (convolution kernel, mathematically), vector  $\mathbf{u}_k \in \mathbf{R}^{n \times 1}$ , k = 1, ..., r [10,11,20]. Using convolution assumption, each weight  $\mathbf{x}_k$  can be rewritten as

$$\mathbf{x}_k = B\mathbf{u}_k, \ \forall k = 1, \dots, r, \tag{3}$$

where the matrix  $B \in \mathbb{R}^{n \times n}$  is composed from elements of input function **b** as

$$B = \begin{pmatrix} b_1 & 0 & 0 & 0 \\ b_2 & b_1 & 0 & 0 \\ \dots & b_2 & b_1 & 0 \\ b_n & \dots & b_2 & b_1 \end{pmatrix}.$$
 (4)

Suppose the aggregation of response functions  $U = [\mathbf{u}_1, \dots, \mathbf{u}_r] \in \mathbf{R}^{n \times r}$ . Then, X = BU and the model (2) can be rewritten as

$$D = AU^{T}B^{T} + E. (5)$$

The task of subsequent analysis is to estimate the matrices A and U and the vector **b** from the data matrix D.

#### 2.1.1. Noise model

We assume that the noise has homogeneous Gaussian distribution with zero mean and unknown precision parameter  $\omega$ ,  $e_{i,j} = \mathcal{N}(0, \omega^{-1})$ . Then, the data model (2) can be rewritten as

$$f(D|A, X, \omega) = \prod_{j=1}^{n} \mathcal{N}(A\overline{\mathbf{x}}_{j}, \omega^{-1}I_{p}),$$
(6)

where symbol N denotes Gaussian distribution and  $I_p$  is identity matrix of the size given in its subscript. Since all unknown parameters must have their prior distribution in the Variational Bayes methodology, the precision parameter  $\omega$  has a conjugate prior in the form of the Gamma distribution

$$f(\omega) = \mathcal{G}(\vartheta_0, \rho_0),\tag{7}$$

with chosen constants  $\vartheta_0$ ,  $\rho_0$ .

#### 2.2. Probabilistic model of source images

The only assumption on source images is that they are sparse, i.e. only some pixels of source images are non-zeros. The sparsity is achieved using prior model that favors sparse solution depending on data [21]. We will employ the automatic relevance determination (ARD) principle [22] based on joint estimation of the parameter of interest together with its unknown precision. Specifically, each pixel  $a_{i,k}$  of each source image has Gaussian prior truncated to positive values (see A.1, denoted as tN in this paper) with unknown precision parameter  $\xi_{i,k}$  which is supposed to have conjugate Gamma prior as

$$f(a_{i,k}|\xi_{i,k}) = t\mathcal{N}(0,\xi_{i,k}^{-1}),$$
(8)

$$f(\xi_{i,k}) = \mathcal{G}(\phi_0, \psi_0), \tag{9}$$

for  $\forall i = 1, ..., p$ ,  $\forall k = 1, ..., r$ , and  $\phi_0$ ,  $\psi_0$  are chosen constants. The precisions  $\xi_{i,k}$  form the matrix  $\Xi$  of the same size as *A*.

#### 2.3. Probabilistic model of input function

The input function **b** is assumed to be a positive vector; hence, it will be modeled as truncated Gaussian distribution to positive values with scaling parameter  $\zeta \in \mathbf{R}$  as

$$f(\mathbf{b}|\varsigma) = t\mathcal{N}(\mathbf{0}_{n,1}, \varsigma^{-1}I_n), \tag{10}$$

$$f(\varsigma) = \mathcal{G}(\zeta_0, \eta_0), \tag{11}$$

where  $\mathbf{0}_{n,1}$  denotes zeros matrix of the given size and  $\zeta_0$ ,  $\eta_0$  are chosen constants.

#### 2.4. Models of response functions

So far, we have formulated the prior models for source images A and input function **b** from decomposition of the matrix D. The task of this paper is to propose and study prior models for response functions U as illustrated in Fig. 1. Different choices of the priors on the response functions have strong influence on the results of the analysis which will be studied in the next section.

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