Parameter Estimation of HRF and Classification of fMRI data using Probabilistic PCA Modeling

R.Srikanth and A.G.Ramakrishnan
Department of Electrical Engineering, Indian Institute of Science, Bangalore, India
(srikanth,ramkiag)@ee.iisc.ernet.in

Abstract

We propose a method for estimating the parameters of Hemodynamic Response Function (HRF) and classifying the different areas of activation of Functional Magnetic Resonance Imaging (fMRI) data. The proposed method can be used in event-related design paradigm. In this method, the probability model for the fMR time-series is obtained by Probabilistic Principal Component Analysis wherein the additive noise component is represented in terms of its dominant principal components. The parameters of the HRF and class labels are estimated using Expectation Maximization algorithm. The class labels are assumed to form a Markov Random Field and the prior is given by Gibbsian distribution. This prior imposes spatial smoothness on class labels. The results are shown for simulated data wherein HRFs with known parameters are added to the real fMR data.

1 Introduction

Functional Magnetic Resonance Imaging (fMRI) is a non-invasive technique allowing the evolution of brain processes to be dynamically followed in various cognitive or behavioral tasks. fMRI attempts to detect brain activity by localized, non-invasive measurements of the change in blood oxygenation called as BOLD (blood oxygenation level dependent) contrast. The brain is imaged at regular intervals when a subject performs specific tasks prompted by some stimulus (e.g., motor or visual task). The aim is to (a) detect the portions of brain that are activated due to the task and (b) characterize the BOLD response. So far research has been focussing in detecting the activated regions [1]. Recently, estimation of Hemodynamic Response Function (HRF) has assumed considerable significance [2],[3], [5]. Knowledge of HRF is useful in understanding the dynamics of brain function and relationship between brain areas. Both parametric [5] and nonparametric models [2], [3] have been used for HRF modeling. In this work, we use gaussian model for HRF. We develop an Expectation Maximization (EM) frame work to find out various regions with different HRFs. In addition to classifying various regions, we also estimate the parameters of those HRFs. This kind of analysis is useful for event-related design paradigms [5].

Generally, the signal recorded during an fMRI experiment consists of the BOLD response buried in colored noise. The noise is due to physiological sources such as pulse, breathing and system sources like scanner and noise drift. The noise also depends upon the acquisition time or repetition time (TR) which decides the aliasing of the above noises and signal power. Generally band pass filtering [5] is used in reducing the noise component. In [1], a subspace based approach is proposed to model noise in a block design paradigm. This approach cannot be used in event related design paradigm where the task is not repeated periodically. We propose a new model for the noise component using Probabilistic Principal Component Analysis (PPCA). Using this model, we estimate the parameters of the HRF and classify the response into different classes. The parameters of the probability model are derived from the data itself.

2 Probabilistic PCA

Principal Component Analysis (PCA) is a widely used tool for data analysis. For a set of $d-$dimensional data vectors $\{t_n\}$, $n = 1, 2, ..., N$, the q principal axes w_j, $j = 1, 2, ..., q$, are those onto which the retained variance under projection is maximal. These principal axes are the q eigenvectors corresponding to the q dominant eigenvalues of the sample covariance matrix of the data $\{t_n\}$. The analysis using PCA does not involve any probability model for the data. Tipping and Bishop [4] showed that PCA can be obtained by assuming a probability model. This approach is very useful because we not only get the principal axes of the data but also a probability model for the data. This model in turn can be used for the tasks like estimation and detection of signals. We use PPCA to model the voxel time-series of fMR data. Using this approach, one can model the noise component in fMR time-series in terms of its significant principal components.

2.1 A Probability Model for PCA

A $d-$dimensional data vector t can be related to $q-$dimensional ($q < d$) latent variables x as:

$$t = \mu_t + Wx + \epsilon \tag{1}$$

where, ϵ and x are independent random processes. μ_t is the mean of the data vectors. By defining a prior pdf to x, the above equation induces a corresponding pdf to t. If we assume

$$x \sim N(0, I_q)$$
$$\epsilon \sim N(0, \sigma_n^2 I)$$

then t is also Gaussian random vector with pdf

$$t \sim N(\mu, WW^t + \sigma_n^2 I) \tag{2}$$

where, I_q and I are $q \times q$ and $d \times d$ identity matrices. With the above pdfs for x and ϵ, we can show that the columns of W are the rotated and scaled principal eigenvectors of the covariance matrix of the data vectors $\{t_n\}$. With the above model, the observed vector t is represented as the sum of systematic component (Wx) and independent noise component (ϵ). It is shown in [4] that the ML estimate of W and σ_n^2 are given by

$$\begin{aligned} W &= U_q(\Lambda_q - \sigma_n^2 I)^{1/2} R \\ \sigma_n^2 &= \frac{1}{d-q} \sum_{j=q+1}^{d} \lambda_j \end{aligned} \tag{3}$$

where the q column vectors in U_q are eigenvectors of the covariance matrix of the data, with the corresponding eigenvalues in the diagonal matrix Λ_q, and R is an arbitrary rotation matrix. The estimate for σ^2 has the interpretation of 'lost' variance in the projection, averaged over the lost dimensions.

3 Probability model of fMRI data using PPCA

3.1 Hemodynamic Response Model

Hemodynamic response (HR) refers to the local change in blood oxygenation as an effect of increased neuronal activity. This change is not immediate but is delayed by 2 to 6 seconds from the stimulus onset. It is observed that this response increases slowly and attains maximum and returns to the base line. In this work, we model HR by a Gaussian function. The advantage of this model is that the parameters give a physiological interpretation [5]. The HR as a function of time can be represented as:

$$h(t) = \eta \exp(-(t.TR - \mu)^2/\sigma^2) \tag{4}$$

where, μ represents the time lag from the onset of the stimuli to the peak of HR; σ reflects the rise and decay time and η denotes the amplitude of the response as shown in Figure 1 and TR is the sampling period. Let $\theta = [\mu, \sigma, \eta]$ denote the unknown parameters of the HRF. The BOLD response of the brain for a given task can be modeled as convolution of the HRF and the input task [2]. The input task can be considered as a binary function of time which has a value of 1 during the period of task and 0 during the rest period.

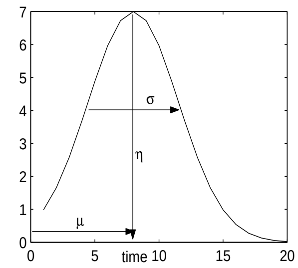

Figure 1: A sample HR function showing physiological significance of the three parameters. μ represents the time lag from the onset of the stimuli to the peak of HR; σ gives the rise and decay time and η denotes the amplitude of the response

3.2 Probability Model

The observed time-series of kth voxel can be modeled as:

$$y_k = Xh(\theta_k) + n \tag{5}$$

where, the $T-$dimensional vectors $y_k, h(\theta_k), n$ are respectively, observed time-series at kth voxel, HRF and noise. X is the convolution matrix. The noise n can be represented using the latent variable model defined in the last section as:

$$n = Wx + \epsilon \tag{6}$$

where x is a $q-$dimensional ($q < T$) latent variable and ϵ is a noise component. Assuming Gaussian pdf models as described in the last section, the columns of W correspond to q principal components of n corresponding to the first q dominant eigenvalues. The pdf of noise is given as

$$n \sim N(0, C) \tag{7}$$

where, $C = WW^t + \sigma^2 I$. Hence the noise vector n is represented as a combination of systematic component (Wx) and a iid component (ϵ). Now, the observed time-series can be represented as a sum of BOLD response, systematic noise component and an iid noise component:

$$y_k = Xh(\theta_k) + Wx + \epsilon \tag{8}$$

Therefore, the probability model for the observed fMRI time-series y_k for a given θ is given by

$$y_k \sim N(Xh(\theta_k), C) \tag{9}$$

Hence, using the PPCA model, we can express the observed fMRI time-series in terms of the convolution model and principal components of noise. The principal components of noise can be computed from the data itself as explained in the later sections.

4 Estimation and Classification Using EM algorithm

In this work, the aim is not only to find the activated voxels but also to find the different kinds (classes) of activation. One can expect the adjacent pixels to have the same class labels. This spatial smoothness can be imposed using Markov Random Fields (MRF) [6]. Since the class labels are not observable, we can model them as Hidden Markov Random Field (HMRF). We assume that there are K different classes (including no activation) in the given fMRI data. The task is to find the K sets of parameters of the HRF and associate each voxel with one of the appropriate classes. Let Z be the random field of the class labels of the fMRI voxels. The key property of MRF is that the distribution of the random variable associated with a pixel k, given the values of pixels in a neighborhood of k, is independent of the values of the rest of the pixels in the image. This can be written as:

$$f(x_k|x_l, k \neq l) = f(x_k|x_l \in N_k) \tag{10}$$

where x_k is the class label of pixel k and N_k is a set of random variables representing the labels for the pixels that are in the neighborhood of k. By Hammersley-Clifford [6] theorem, the distribution over an MRF can be specified in terms of Gibbs distribution

$$f(z) = \frac{1}{Q}\exp(-\sum_c U_c(z)) \tag{11}$$

where z is vector of class labels for all the pixels in the image; U_c is the potential function for clique c in the lattice of pixels; Q is the normalization constant. A clique is an ordered set of pixels which are all in the neighborhoods of each other. The sum in the above equation runs over all the cliques as defined by our choice of neighborhood. The potential function gives a potential, or cost, for the particular combination of labels in cliques. We use first order neighborhood where the distance between two pixels is one and each clique contain a pair of pixels. The potential function is defined as

$$\begin{aligned} U(z_k, z_l) &= \beta/2, if z_k = z_l \\ &= -\beta/2, otherwise \end{aligned} \tag{12}$$

Hence, the cost for two pixels in a neighborhood to be of different classes increases and is dependent on the parameter β. This will have a smoothing effect on the class label map.

4.1 fMR signal model

We use PPCA to model the observed time-series of each voxel. Let there be K different regions (classes) and let $\Theta = [\theta_1, ..., \theta_K]$ denote the parameters of the K HRFs. The observed time-series at mth voxel assuming that it belongs to kth class can be modeled as

$$y_m = Xh(\theta_k) + Wx + \epsilon, m = 1, ..., M \tag{13}$$

where, M is total number of voxels. Therefore given the class label, the pdf of y_m can be written as

$$p(y_m|Z_m = k, \Theta) \sim N(Xh(\theta_k), C) \tag{14}$$

Assuming y_m's are independent given their class labels (conditional independence), we have

$$p(y|Z, \Theta) = \prod_{m=1}^{M} p(y_m|Z_m = k, \Theta) \tag{15}$$

The above equation can be maximized wrt θ_k to estimate θ_k. But the class labels $Z_n = k$ are unknown. Hence the class labels are to be found before the estimation of θ_k. We estimate both class labels and unknown parameters Θ in an iterative fashion. We first estimate class labels for a given initial Θ^i and using these class labels new Θ^{i+1} is estimated. We repeat this until convergence.

4.2 Estimation of Class Labels

The class label map $Z = z$ can be estimated by maximizing the posteriori probability

$$\begin{aligned} f(Z|y, \Theta^i) &\propto f(y|Z, \Theta^i)f(Z) \\ Z = argmax_Z &\ln f(y|Z, \Theta^i) + \ln f(Z) \end{aligned} \tag{16}$$

where, Θ^i is an initial value of Θ. The above equation is to be maximized over all possible configurations of Z and hence intractable. It can be approximated using Iterated Conditional Modes (ICM) algorithm [7].

$$z_m = argmax_{z_m} \ln f(y_m/z_m, \Theta^i) + \ln f(z_m/N_m) \tag{17}$$

$$f(z_m|N_m) = \frac{1}{Q_m}\exp(-\sum_{j=1}^{4} U(z_m, z_j))$$

where, N_m is I order neighborhood of the voxel m and Q_m is the normalizing constant.

4.3 Parameter Estimation

Using the above estimate of class labels, the parameter Θ^{i+1} can be estimated by maximizing the conditional expectation of the log of posteriori probability $f(\Theta|y, z)$ $(E\{\ln f(\Theta|y, z)|y, \Theta^i\})$. Using Baye's rule, $f(\Theta|y, z)$ can be simplified as:

$$\begin{aligned} f(\Theta|y, z) &\propto f(y, z|\Theta)f(\Theta) \\ &= f(y|z, \Theta)f(z)f(\Theta) \end{aligned}$$

since z is independent of Θ and $f(\Theta)$ is prior probability of Θ ($\Theta \sim N(m_\theta, V_\theta)$). Using the above equation, the required conditional expectation can be written as:

$$E\{\ln f(\Theta|y,z)|y,\Theta^i\} \propto E\{\ln f(y|z,\Theta)|y,\Theta^i\} + E\{\ln f(z)|y,\Theta^i\} + E\{\ln f(\Theta)|y,\Theta^i\} \quad (18)$$

The second term in the above equation is independent of Θ and does not influence the maximization of the required conditional expectation. The third term can be simplified, by taking the conditional expectation wrt $f(l|y,\Theta^i)$, as follows:

$$\begin{aligned} E\{\ln f(\Theta)|y,\Theta^i\} &= \ln f(\Theta)\sum_{l=1}^{K} f(l|y,\Theta^i) \\ &= \ln f(\Theta) \end{aligned}$$

Using the above equation, the required conditional expectation can be written as:

$$E\{\ln f(y,z,\Theta)|y,\Theta^i\} \propto \sum_{l=1}^{K} \ln f(y|z,\Theta) f(l|y,\Theta^i) + \ln f(\Theta) \quad (19)$$

To maximize the above equation, we need the posteriori probability $f(l|y,\Theta^i)$ which can be written as

$$f(l|y,\Theta^i) = \frac{f(y|z=l,\Theta^i)f(l)}{f(y)} \quad (20)$$

The total probability $f(y)$ of voxels is difficult to evaluate. By MRF property, we know the class label of a given voxel is dependent on its neighborhood. Using this, the above posteriori probability can be approximated as

$$\begin{aligned} f(l|y,\Theta^i) &\approx f(l|y_m,\Theta^i,N_m) \\ &= \frac{f(y_m|z_m=l,\Theta^i,N_m)f(l|N_m)}{f(y_m)} \\ f(y_m) &= \sum_{l=1}^{K} f(y_m|z_m=l,N_m)f(z_m|N_m) \end{aligned} \quad (21)$$

The conditional expectation can now be written as:

$$E\{\ln f(y,z,\Theta)|y,\Theta^i\} \propto \sum_{l}^{K}\sum_{m=1}^{M} f(l|y_m,\Theta^i,N_m) \ln f(y_m|z_m=l,\Theta^i) \quad (22)$$

This is maximized wrt Θ. With this new estimate of Θ, the class labels are estimated. This procedure is repeated until convergence. The procedure can be summarized as follows:

1. Initialize $\Theta_o, i = 0$
2. Find the activation map using (17).
3. Using these class labels find new Θ^{i+1} using (22).
4. Go to step 2 until convergence.

5 Simulation Results

5.1 Data

The dataset was acquired at NIMHANS, Bangalore on a 1.5 tesla Siemens MR machine. The scanning sequence was a 3-D echo EPI with 66ms echo time and 90 degrees flip angle. The images were acquired with a matrix size of $128 \times 128 \times 16$ pixels with a slice thickness of 8mm. The time-series of fMRI volume is acquired every 1sec (TR=1). The motor experiment was conducted on a volunteer. The experiment started with a rest period of 20 seconds followed by activation period of 20 seconds during which the subject had to move his figure followed by rest period of 80 seconds. The experiment is not repeated in order to study the intrinsic response for one session.

5.2 Preprocessing

The time-series of each slice is corrected for subject motion. The time-series of frames are registered with the first frame of the time-series. At each voxel, the mean value of the time-series of the voxel is removed from the time-series. This amounts to removing the anatomical structure in the MR images since we are interested only in analyzing the BOLD response.

5.3 Simulations

To verify the performance of the above method, we choose a patch of 16×16 from a slice where there is no activation with the help of an expert. We add the convolution of two Gaussian HRFs of parameters $\theta_1 = [5.5, 2.2, 4.2]$ and $\theta_2 = [7.5, 2.5, 5.5]$ with input stimulation signal (boxcar function = 1 from $t = 20$ to 40) to the time-series of voxels at known locations as shown in Fig 2. Now the task is to find out the class label of each pixel and estimate the parameters of the HR function. We do not consider the first four samples in every voxel time-series to account for the scanner saturation effects. The parameter β is fixed as 1. The parameters of the prior m_θ, V_θ are taken as in [5]. We estimate the matrix W by choosing "noise only" pixels from the same slice but at the location far from the above patch. The sample covariance matrix is estimated and W is found out by the eigenvalue decomposition of the sample covariance matrix. The algorithm is initialized by generating a sample for Θ from the prior distibution $N(m_\theta, V_\theta)$. This initial value for Θ is then used to estimate the class labels for each voxel using Maximum Likelihood (ML) classification. Further refinement in classification of voxels and estimation of parameters of HRFs is carried out using the algorithm described in the earlier section. Fig 3 shows the detection performance of EM algorithm for the above activation pattern. As shown in the figure, the algorithm converges in 5-6 iterations. Fig 4 compares the estimated HRFs with actual HRFs.

6 Conclusions

We proposed a method for estimation of the parameters of Hemodynamic Response Function (HRF) and classification of the different areas of activation in Functional Magnetic Resonance Imaging (fMRI) data. This method can be used in event related design paradigm. The noise in voxel time-series is modeled using Probabilistic Principal Component Analisis (PPCA) and a probability model is derived for the voxel-time series. A Gibbsian prior model is used to impose spatial smoothness of the class labels. The class labels and Hemodynamic Response Function (HRF) parameters are then estimated using an Expectation Maximization (EM) algorithm. The prior information for HRF parameters is incorporated in the EM algorithm. The issue that needs to be addressed in this work is choosing the smoothing parameter β. Also, the algorithm needs to be tested for an event-related fMR experiment.

Acknowledgements

We thank Prof.P.N.Jayakumar of NIMHANS for providing the fMRI data. We also thank Dr.Bapiraju, Pammi Chandrasekhar and K.Prasad of University of Hyderabad for their help and discussion.

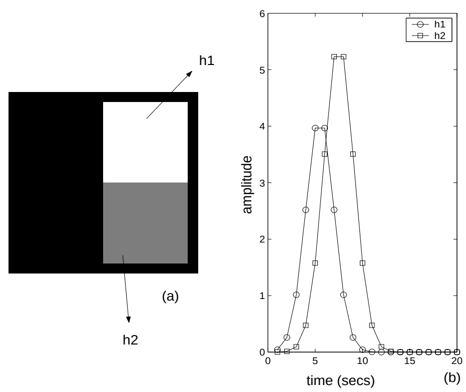

Figure 2: (a)Different Regions (Classes) of Activation. Region with dark pixels indicate no activation. Region with gray pixel values indicates activated region with HRF h_1 (with paramter θ_1) and Region with white pixels indicates activated region with HRF h_2 (with paramter θ_2) (b) Actual simulated HRFs h_1 and h_2 with respective parameters θ_1 and θ_2.

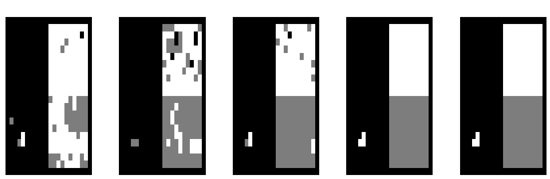

Figure 3: Figures shows the convergence and detection performance of the proposed EM algorithm. The EM algorithm converges in 4-5 iterations.

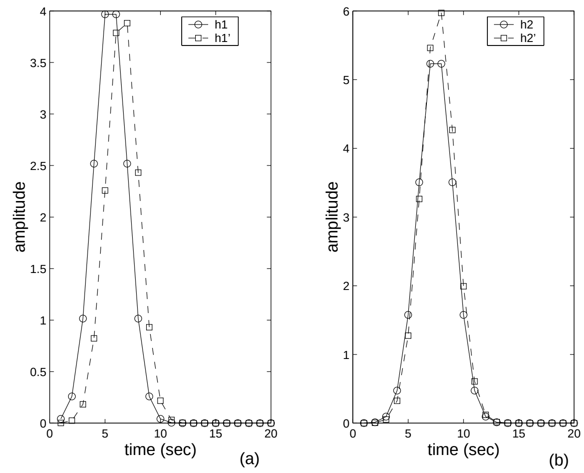

Figure 4: Comparison of Estimated and Actual HRFs. Solid curve shows actual HRF and dashed curve shows estimated HRF of (a) h1 (b) h2.

References

[1] Babak A.Ardekani, Jeff Kershaw, Kenichi Kashikura and Iwao Kanno, ”Activation Detection in Functional MRI Using Subspace Modeling and Maximum Likelihood Estimation”, *IEEE trans. Medical Imaging*, vol.18, no.2, pp.101-114, 1999.

[2] Cyril Goutte, Finn Arup Nielsen and Lars Kai Hansen, ”Modeling the Haemodynamic Response in fMRI Using Smooth FIR filters”, *IEEE trans. Medical Imaging*, vol.19, no.12, pp.1188-1201, 2000.

[3] G.Marrelec, H.Benali, P.Ciuliu and J.B.Pioline, ”Bayesian Estimation of the Hemodynamic Response Function in Functional MRI”, *21st International Workshop, American Institute of Physics*, pp. 229-247, 2002.

[4] Michael E.Tipping and Christopher M.Bishop, ”Probabilistic Principal Component Analysis”, *Neural Computing Research Group (NCRG), Technical Report NCRG/97/010*.

[5] Markus Svensen, Frithjof Kruggel and D.Yves von Cramon, ”Probabilistic Modeling of Single-trial fMRI Data”, *IEEE trans. Medical Imaging*, vol.19, no.1, pp.25-35, 2000.

[6] S.Geman and D.Geman, ”Stochastic Relaxation, Gibbs Distribution, and the Bayesian Restoration of Images”, *IEEE trans. PAMI*, no.PAMI-6, pp.721-741, june’84.

[7] Yongyue Zhang, Michael Brady and Stephen Smith, ”Segmentation of MR Images Through a Hidden Markov Random Field and the Expectation-Maximization Algorithm”, *IEEE trans. Medical Imaging*, vol.20, no.1, Jan-2001.