TISSUE MIXTURE CHARACTERIZATION IN THE PRESENCE OF MRI INHOMOGENEITY BY THE EM ALGORITHM

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ABSTRACT

This paper presents a model-based approach to correct for both partial volume effect and inhomogeneity in segmenting tissue mixtures inside each voxel of magnetic resonance images. A maximum *a posteriori* probability (MAP) solution is sought. In calculating the solution, the well-known expectation maximization (EM) algorithm is employed. The models of data likelihood and Markov priors for tissue mixture and bias field in establishing this MAP-EM framework are described in details. A preliminary test is presented.

1. INTRODUCTION

Characterizing tissue structures and volumes from magnetic resonance (MR) images plays a very important role in clinical research and diagnosis. A conventional approach usually labels each image voxel by a specific tissue type. This hard segmentation ignores partial volume (PV) effect and, therefore, losses both the detail of the tissue structure and the accuracy in quantifying the tissue volume. An alternative approach has been attempted to find the probability of a specific tissue type inside each voxel [1-5]. While this soft segmentation is theoretically attractive in dealing the PV effect, it usually either has a very complicated model of numerically intractable or an approximated model of less numerical accuracy. A more specific model for PV segmentation was explored by Choi *et al*. [6] by dividing each voxel according to assumed tissue types. Each tissue type inside a voxel was described by a random variable. Choi *et al*. attempted to quantify directly the mean of each random variable for the corresponding tissue type in that voxel. It has been a very challenging task to quantify directly the mean of a random variable because of the incompleteness of measurements. Another more specific model for PV segmentation was explored by Leemput *et al*. [7] by dividing each voxel into sub-voxels and by the use of the EM (expectation-maximization) algorithm [8] to consider the data incompleteness. All the sub-voxels were then labeled by a hard segmentation algorithm. The ratio of the number of a specific tissue label over the total number of the sub-voxels in a voxel reflects the proportion of that tissue type in the voxel. This discrete PV model becomes more accurate when each voxels is divided into a larger number of sub-voxels. We have previously presented a continuous PV model [9] which quantifies the tissue mixtures in each voxel based on the EM algorithm. This work extends that PV model to include inhomogeneity effect in MR images and presents an efficient method to compute the tissue mixtures in each voxel.

2. METHOD

2.1. Partial Volume Model with Inhomogeneity Effect

Let the acquired MR image density distribution $\boldsymbol{Y}$ be represented by a column vector $[y_1, y_2, ..., y_N]^T$, where y_i is the observed density value at voxel i and N is the total number of voxels in the image. (For multi-spectral MR images, y_i becomes a vector). Assume the acquired image $\{y_i\}$ contains K tissue types distributed inside the body. Within each voxel i, there possibly are K tissue types (although frequently one or two tissue types are present in a voxel), where each tissue type has a contribution to the observed density value y_i at that voxel. Let tissue type k contributes x_{ik} to the observation y_i at voxel i, then we have:

$$y_i = \sum_{k=1}^{K} x_{ik} \quad . \tag{1}$$

Assume the unobservable variable x_{ik} follows a Gaussian distribution with mean μ_{ik} and variance σ_k^2. If voxel *i* is fully filled by tissue type *k*, then x_{ik} becomes observable variable, *i.e.*, y_i in this case, with Gaussian probability distribution characterized by tissue parameters (μ_k and σ_k^2). If voxel *i* is partially filled by tissue type *k* and let ω_{ik} be the fraction of tissue type *k* inside that voxel, then we have:

$$\mu_{ik} = \omega_{ik}\mu_k, \quad \sigma_{ik}^2 = \omega_{ik}\sigma_k^2, \quad \sum_{k=1}^{K}\omega_{ik} = 1$$
$$0 \le \omega_{ik} \le 1, \quad (\mu_k, \sigma_k^2, \mu_{ik}, \sigma_{ik}^2) \ge 0. \qquad (2)$$

From equation (1), the observed image density value at voxel *i* is expressed as $y_i = \rho_i \sum_{k=1}^{K}\omega_{ik}\mu_k + \varepsilon_i$, where ε_i is a Gaussian noise associated with the observation y_i at voxel *i* with its mean being zero and variance of $\sigma_{y_i}^2 = \sum_{k=1}^{K}\sigma_{ik}^2 = \sum_{k=1}^{K}\omega_{ik}\sigma_k^2$. Notation ρ_i reflects the bias field or inhomogeneity effect at voxel *i* which is a result of non-uniform RF field across the body and tissue response to the local magnetic field [10, 11]. The probability distribution of sampling $\{y_i\}$, given the model parameters $\{\omega_{ik}, \rho_i, \mu_k, \sigma_k^2\}$, assuming that $\{y_i\}$ are statistically dependent from each other, is:

$$\Pr(Y|\boldsymbol{\omega}, \boldsymbol{\rho}, \boldsymbol{\mu}, \boldsymbol{\sigma}) = \prod_{i=1}^{N}\Pr(y_i|\omega_i, \rho, \mu, \sigma) =$$
$$\prod_{i=1}^{N}\frac{1}{\sqrt{2\pi\sum_{k=1}^{K}\omega_{ik}\sigma_k^2}}\exp\left[-\frac{(y_i - \rho_i\sum_{k=1}^{K}\omega_{ik}\mu_k)^2}{2\sum_{k=1}^{K}\omega_{ik}\sigma_k^2}\right] \qquad (3)$$

where $\boldsymbol{\omega}$ represents tissue mixture vector $[\omega_1, \omega_2, ..., \omega_N]^T$ with $\omega_i = [\omega_{i1}, \omega_{i2}, ..., \omega_{iK}]^T$, and the tissue model parameters are $\mu = [\mu_1, \mu_2, ..., \mu_K]^T$ and $\sigma^2 = [\sigma_1^2, \sigma_2^2, ..., \sigma_K^2]^T$. The probability distribution of sampling $\{x_{ik}\}$, given the tissue model parameters $\{\omega_{ik}, \rho_i, \mu_k, \sigma_k^2\}$, is:

$$\Pr(X \mid \omega, \rho, \mu, \sigma) = \prod_{i,k=1}^{N,K}\frac{1}{\sqrt{2\pi\,\omega_{ik}\sigma_k^2}}\exp\left[-\frac{(x_{ik} - \rho_i\omega_{ik}\mu_k)^2}{2\omega_{ik}\sigma_k^2}\right] \qquad (4)$$

where X represents vector $[x_1, x_2, ..., x_N]^T$ with $x_i = [x_{i1}, x_{i2}, ..., x_{iK}]^T$. Equations (3) and (4) describe the same continuous PV model of equation (2) in two different spaces under the connection of equation (1). In the space of observable data $\{y_i\}$, determining the model parameters from incomplete data $\{y_i\}$ via equation (3) can be very complicated [5]. In the space of unobservable complete data $\{x_{ik}\}$, the well-known EM algorithm [8] is readily available to determine the model parameters via equation (4) by conditional expectation under the condition of equation (1). This will be described in detail in Section 2.2 below.

The task of determining the model parameters $\{\omega_{ik}, \rho_i, \mu_k, \sigma_k^2\}$ given the acquired image data $\{y_i\}$ is specified by a *posteriori* probability which requires specification on the *a priori* distribution of $\{\omega_{ik}\}$ and $\{\rho_i\}$.

2.1.1. A Priori Model on the Mixture Parameters $\{\omega_{ik}\}$

In image processing applications, a Markov random field (MRF) prior or regularization is usually used for a maximum *a posteriori* probability (MAP) solution, where the MRF prior has the following form:

$$\Pr(\omega_i|N_i) = \frac{1}{Z}\exp(-\beta\sum_{k=1, j\in N_i}^{K}\alpha_{ij}(\omega_{ik} - \omega_{jk})^2 \qquad (5)$$

where N_i denotes the neighborhood of voxel *i*, β is a parameter controlling the degree of the penalty on mixtures $\{\omega_{ik}\}$, α_{ij} is a scale factor which depends on the order of the neighbors, and *Z* is the normalization factor for the MRF model. In this study, only the first-order neighborhood system is considered and α_{ij} is the same for the six first-order neighbors if the image has a uniform spatial resolution in three dimensions. When the axial resolution is twice lower than the transverse resolution, then α_{ij} is twice smaller for the two neighbors in the axial direction than the four neighbors in transverse plan.

2.1.2. A Priori Model on the Bias Field Parameters $\{\rho_i\}$

A similar MRF prior can be specified for $\{\rho_i\}$ as [12]:

$$\Pr(\rho_i|N_i) = \frac{1}{Z}\exp[-\gamma_1\sum_{j=1}^{R}(D_j * \rho)_i^2 - \gamma_2\sum_{j,l=1}^{R}(D_j * D_l * \rho)_i^2] \qquad (6)$$

where *R* equals 2 for two-dimensional (2D) slice images and 3 for 3D volume images. Notation *D* is the standard forward finite difference operator along the corresponding directions. Symbol * denotes the 1D discrete convolution operator. The first-order regularization term (associated with γ_1) penalizes a large variation in the bias field and the second-order regularization term (associated with γ_2) penalizes the discontinuities in the bias field. Both

parameters γ_1 and γ_2 play a similar role as β does, controlling the degree of smoothness of the bias field.

2.2. MAP-EM Algorithm for Parameter Estimation

Including the MRF priors (5) and (6) into equation (4) for the *posteriori* cost function and performing the E-step or the conditional expectation of the EM algorithm after an operation of log on the cost function, we have:

$$Q(.)=-\frac{1}{2}\sum_{i=1,k=1}^{N,K}\{[\ln(2\pi\omega_{ik}\sigma_k^2)+\frac{1}{\omega_{ik}\sigma_k^2}(x_{ik}^{2(n)}-2\rho_i\omega_{ik}\mu_k x_{ik}^{(n)}+\rho_i^2\omega_{ik}^2\mu_k^2)]$$
$$+2\beta\sum_{j\in N_i}\alpha_{ij}(\omega_{ik}-\omega_{jk})^2+2[\gamma_1\sum_{j=1}^{R}(D_j*\rho)_i^2+\gamma_2\sum_{j,l=1}^{R}(D_j*D_l*\rho)_i^2]\} \tag{7}$$

where the conditional expectations for x_{ik} and x_{ik}^2 are given by:

$$x_{ik}^{(n)}=\mathrm{E}[x_{ik}\mid y_i,\omega^{(n)},\rho^{(n)},\mu^{(n)},\sigma^{2(n)}]=$$
$$\rho_i^{(n)}\omega_{ik}^{(n)}\mu_k^{(n)}+\frac{\omega_{ik}^{(n)}\sigma_k^{2(n)}}{\sum_{j=1}^{K}\omega_{ij}^{(n)}\sigma_j^{2(n)}}\cdot(y_i-\rho_i^{(n)}\sum_{j=1}^{K}\omega_{ij}^{(n)}\mu_j^{(n)}) \tag{8}$$

$$x_{ik}^{2(n)}=\mathrm{E}[x_{ik}^2\mid y_i,\omega^{(n)},\rho^{(n)},\mu^{(n)},\sigma^{2(n)}]=$$
$$(x_{ik}^{(n)})^2+\omega_{ik}^{(n)}\sigma_k^{2(n)}\frac{\sum_{j\neq k}^{K}\omega_{ij}^{(n)}\sigma_j^{2(n)}}{\sum_{j=1}^{K}\omega_{ij}^{(n)}\sigma_j^{2(n)}} \tag{9}$$

The maximization or the M-step of the EM algorithm determines the (n+1)-th iterated estimate, which maximizes the conditional expectation of equation (7) respect to the corresponding parameter. For parameters $\{\mu_k\}$, we have $\partial Q(.)/\partial\mu_k\mid_{\mu_k=\mu_k^{(n+1)}}=0$, which leads to

$$\mu_k^{(n+1)}=\frac{\sum_{i=1}^{N}x_{ik}^{(n)}}{\sum_{i=1}^{N}\rho_i^{(n)}\omega_{ik}^{(n)}}. \tag{10}$$

For parameters $\{\sigma_k^2\}$, we obtain:

$$\sigma_k^{2(n+1)}=\frac{1}{N}\sum_{i=1}^{N}\frac{x_{ik}^{2(n)}-2\rho_i^{(n)}\omega_{ik}^{(n)}\mu_k^{(n)}x_{ik}^{(n)}+\rho_i^{(n)}\omega_{ik}^{2(n)}\mu_k^{2(n)}}{\omega_{ik}^{(n)}} \tag{11}$$

For the mixture $\{\omega_{ik}\}$, when only two tissue types are present in a voxel, *i.e.*, $\omega_{i2}=1-\omega_{i1}$, we have:

$$\omega_{i1}^{(n+1)}=\frac{\rho_i^{(n)}(x_{i1}^{(n)}\sigma_{i2}^{2(n)}\mu_1^{(n)}+\sigma_{i1}^{2(n)}\mu_2^{2(n)}-x_{i2}^{(n)}\sigma_{i1}^{2(n)}\mu_2^{(n)})+\phi\sum_{j\in N_i}\alpha_{ij}\omega_{j1}^{(n)}}{\rho_i^{2(n)}(\mu_1^{2(n)}\sigma_{i2}^{2(n)}+\mu_2^{2(n)}\sigma_{i1}^{2(n)})+\phi\sum_{j\in N_i}\alpha_{ij}} \tag{12}$$

where $\sigma_{ik}^2=\omega_{ik}\sigma_k^2$ and $\phi=4\beta\sigma_{i1}^{2(n)}\sigma_{i2}^{2(n)}$. When three tissue types are present in a voxel, the projection strategy of [6] is adapted to determine the mixtures by:

$$\begin{cases}\omega_{i1}+\omega_{i2}+\omega_{i3}=1\\ \omega_{i1}(T_0-T_1)+\omega_{i2}(T_3-T_4)+\omega_{i3}(T_6-T_7)=b_0-b_1\\ \omega_{i1}(T_0-T_2)+\omega_{i2}(T_3-T_5)+\omega_{i3}(T_6-T_8)=b_0-b_2\end{cases} \tag{13}$$

where

$$T_0=\frac{\rho_i^{2(n)}\mu_1^{2(n)}}{\omega_{i1}^{(n)}\sigma_1^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir},\quad T_1=T_2=T_3=0,$$

$$T_4=\frac{\rho_i^{2(n)}\mu_2^{2(n)}}{\omega_{i2}^{(n)}\sigma_2^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir},\ T_5=T_6=T_7=0,$$

$$T_8=\frac{\rho_i^{2(n)}\mu_3^{2(n)}}{\omega_{i3}^{(n)}\sigma_3^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir},$$

$$b_0=\frac{\rho_i^{(n)}x_{i1}^{(n)}\mu_1^{(n)}}{\omega_{i1}^{(n)}\sigma_1^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir}\omega_{r1}^{(n)},$$

$$b_1=\frac{\rho_i^{(n)}x_{i2}^{(n)}\mu_2^{(n)}}{\omega_{i2}^{(n)}\sigma_2^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir}\omega_{r2}^{(n)},$$

$$b_2=\frac{\rho_i^{(n)}x_{i3}^{(n)}\mu_3^{(n)}}{\omega_{i3}^{(n)}\sigma_3^{2(n)}}+2\beta\sum_{r\in\varepsilon_i}\alpha_{ir}\omega_{r3}^{(n)}.$$

In a similar manner, we can determine four and more tissue types in a voxel.

For the bias field parameter $\{\rho_i\}$, we have:

$$\sum_{k=1}^{K}\frac{\mu_k^{(n)}x_{ik}^{(n)}}{\sigma_k^{2(n)}}=\rho_i\cdot\sum_{k=1}^{K}\frac{\omega_{ik}^{(n)}\mu_k^{2(n)}}{\sigma_k^{2(n)}}\omega_{ik}^{(n)}\mu_k^{2(n)}+\gamma_1(H_1*\rho)_i+\gamma_2(H_2*\rho)_i \tag{14}$$

where

$$H_1=\begin{bmatrix}0&-1&0\\-1&4&-1\\0&-1&0\end{bmatrix}\qquad H_2=\begin{bmatrix}0&0&1&0&0\\0&2&-8&2&0\\1&-8&20&-8&1\\0&2&-8&2&0\\0&0&1&0&0\end{bmatrix}.$$

Solving equation (14) for $\{\rho_i\}$ can be performed by the Jacobi iterative scheme [12].

3. RESULTS

A set of brain MR images (*i.e.*, Figure 1(a) T_1- and Figure 1(b) T2-weighted scans) was used to test the above presented method. For reference, a hard segmentation using method of [1] is shown by Figure 1(c). Other pictures are the segmented tissue mixture images of white matter-Figure

1(d), gray matter-Figure 1(e) and cerebrospinal fluid-Figure 1(f). Figure 1(g) is the estimated result of the bias field.

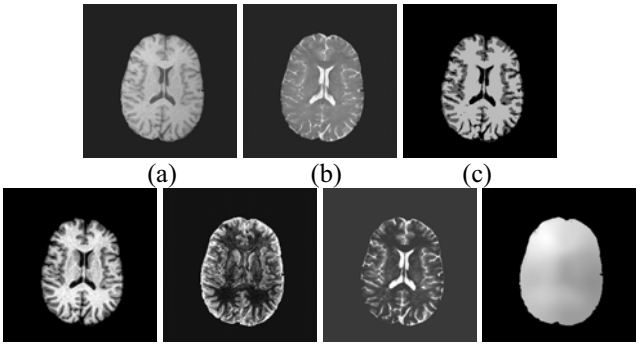

Figure 1: Tested results from a set of images of (a) T_1 - and (b) T_2 - weighted scans. Hard segmentation (c) is shown as a reference for comparison purpose. Pictures (d), (e) and (f) are the segmented white matter, gray matter, and cerebrospinal fluid tissue mixture distributions, respectively. Picture (g) is the estimated bias field.

4. DISCUSSION

Modeling the tissue mixtures in a continuous space in terms of unobservable variables, via the EM algorithm, is a new attempt of this work, compared to the previous research in the field. The statistical distribution of the unobservable variables is consistent with that of the observable data, i.e., a Gaussian distribution, which has been widely accepted in segmentation of MR images. The conditional expectation of the unobservable variables given the observed image data is very useful for estimation of the tissue mixture and model parameters from incomplete data. This conditional expectation is especially useful when the number of the underline tissue types in a voxel is small, such as less than five. In such case, the conditional expectation, given the measured datum, can have a significant impact on the estimation of the parameters of these five variables. At the maximization step of the EM algorithm, all the tissue mixture and model parameters are updated simultaneously under the conditional expectation. This ensures a monotonic increase of the *posteriori* probability [8]. Further optimization of the calculations in the maximization step is currently under progress. The presented solution to the PV effect is theoretically attractive and its usefulness in practical applications needs more extensive investigation, especially by phantom and patient data evaluation.

5. ACKNOWLEDGMENT

This work was partly supported by NIH Grant #CA82402 of the National Cancer Institute. Dr. H. Lu was supported by the National Nature Science Foundation of China under Grant 30470490.

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