Partial Volume Segmentation of Cerebral MRI Scans with Mixture Model Clustering

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Abstract. A mixture model clustering algorithm is presented for robust MRI brain image segmentation in the presence of partial volume averaging. The method uses additional classes to represent partial volume voxels of mixed tissue type in the data with their probability distributions modeled accordingly. The image model also allows for tissue-dependent variance values and voxel neighborhood information is taken into account in the clustering formulation. The final result is the estimated fractional amount of each tissue type present within a voxel in addition to the label assigned to the voxel. A multi-threaded implementation of the method is evaluated using both synthetic and real MRI data.

1 Introduction

Unsupervised image segmentation is a fundamental task in many applications of medical image analysis, the object of which is to associate with each image voxel a particular class based on its attributes, neighborhood information, or geometric characteristics of objects belonging to the class. This classification is then used by higher-level image analysis and processing algorithms, thus accurate and robust image segmentation is a key element of many medical imaging applications.

In this work, we consider the problem of segmenting magnetic resonance (MR) images, which is made difficult by the existence of partial volume (PV) averaging due to limited spatial resolution of the scanner. MR images are also subject to intensity shading artifacts caused by RF field inhomogeneity. To improve the quantitative precision of our segmentation, we focus on the first factor and develop a method for determining the fractional content of each tissue class for so-called partial volume voxels of mixed tissue type. Of specific interest in the current work are the primary tissue constituents of the brain: gray (GM) and white matter (WM) as well as cerebrospinal fluid (CSF).

Two approaches have been commonly applied to address the problem of partial volume segmentation. In the first, *mixel model*, [1,2], every voxel in an image is assumed to be a PV voxel, consisting of a mixture of pure tissue classes. The object of segmentation in this case is to determine the relative fraction of

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each tissue class present within every image voxel. Because of the number of parameters that must be estimated at each voxel, multi-channel data and/or additional constraints are required to obtain the segmentation solution.

A second approach [3,4] has been to marginalize over the variables describing the fractional portions of each *pure tissue class*. This produces an additional, new set of *partial volume classes*, with which each image voxel may be associated. In this way, PV voxels may be separately identified using existing "binary" segmentation algorithms. In the current work, this method is used to adapt the maximum likelihood mixture model clustering algorithm [5,6,7] for segmentation of PV voxels in MR images of the brain.

2 Image Model

We generalize the image model proposed in [3,4] to account for tissue dependent intensity variations. Experiments on MRI data show that differences in intensity variation across tissue type are not insignificant: intensity values for CSF voxels always having the largest amount of variability, followed by GM and WM.

Let $\mathbf{I}_i = (I_{i,1}, I_{i,2}, \ldots I_{i,M})^T$ be the M-channel observation of the i-th voxel in an input image. Voxels of pure tissue class are described by a particular intensity distribution associated with the image appearance of that tissue type. Partial volume voxels, on the other hand, are represented as a linear combination of the intensity distributions associated with the K possible tissue types that can be found in those voxels:

$$\mathbf{I}_i = \sum_{k=1}^{K} t_{i,k} \mathbf{N}(\boldsymbol{\mu}_k, \Sigma_k), \quad \sum_{k=1}^{K} t_{i,k} = 1\,, \tag{1}$$

where the voxel intensity $\mathbf{I}$ for pure tissue class k is represented as an M-element column vector of random variables, which are distributed according to the multivariate Gaussian distribution $\mathbf{N}$ with $\boldsymbol{\mu}_k = (\mu_{k,1}, \mu_{k,2}, \ldots, \mu_{k,M})^T$, the vector of mean intensity values (M channels) for pure tissue class k, and Σ_k is the associated M by M covariance matrix for the M-channel observation. Term $t_{i,k}$ represents the fraction of pure tissue class k that is present at the i-th voxel. Note that the $\boldsymbol{\mu}_k$ and Σ_k do not change with location i; that is, we assume that shading artifacts in the MRI data are first removed in a preprocessing step.

To determine the fractional amount of specified pure tissue classes within every image voxel, (1) is solved for $t_{i,k}$. Assuming that the class parameters ($\boldsymbol{\mu}_k$ and Σ_k) are known, a solution can be found if $M \geq (K-1)$, as shown in [1]. In practice, we are interested in the three classes: CSF, GM and WM. Multi-echo images of high resolution are generally not available and even these would be partially correlated and noisy, so the problem remains ill posed.

Additional constraints are therefore necessary and as in [3,4], we make the assumption that each partial volume voxel is a mixture of only two tissue types. We define sets $\mathcal{G}_k = \{k_1, k_2\}$ containing indices of pure classes that are present in the k-th PV class. There are K_{PV} PV classes in an image.

For voxels of pure tissue class k and PV voxels consisting of pure classes k_1 and k_2, respectively, (1) reduces to:

$$\mathbf{I}_i = \mathbf{N}(\boldsymbol{\mu}_k, \Sigma_k) \tag{2}$$

and

$$\mathbf{I}_i = t_{i,k_1}\mathbf{N}(\boldsymbol{\mu}_{k_1}, \Sigma_{k_1}) + t_{i,k_2}\mathbf{N}(\boldsymbol{\mu}_{k_2}, \Sigma_{k_2})\,, \quad t_{i,k_1} + t_{i,k_2} = 1\,. \tag{3}$$

To determine the parameters $(\boldsymbol{\mu}_k, \Sigma_k)$ for the pure tissue classes, an extended version of the maximum likelihood mixture model algorithm [5,6,7] is developed below.

3 Mixture Model Clustering

3.1 Probability Density Functions

For brevity, we develop here just the likelihood model for PV voxels containing a mixture of pure tissue classes k_1 and k_2 – see (3):

$$\begin{aligned} P_{PV}(\mathbf{I}_i|k_1,k_2,t) &= \frac{\exp\left(-\frac{1}{2}\left(\mathbf{I}_i-\hat{\boldsymbol{\mu}}_k(t)\right)^T\hat{\Sigma}_k(t)^{-1}\left(\mathbf{I}_i-\hat{\boldsymbol{\mu}}_k(t)\right)\right)}{\sqrt{(2\pi)^M\left|\hat{\Sigma}_k(t)\right|}}\,, \\ \hat{\boldsymbol{\mu}}_k(t) &= t\boldsymbol{\mu}_{k_1} + (1-t)\boldsymbol{\mu}_{k_2}\,, \quad \hat{\Sigma}_k(t) = t^2\Sigma_{k_1} + (1-t)^2\Sigma_{k_2}\,. \end{aligned} \tag{4}$$

As in [3,4], we marginalize the density in (4) over t to obtain the likelihood for PV classes. To generalize the notation, we have numbered the PV classes from $K+1$ to $K+K_{PV}$, so that $P(\mathbf{I}_i|k)$ expresses the conditional density for both pure tissue and PV classes. The integral in (5) does not have a closed form solution and must therefore be evaluated by numerical integration:

$$P(\mathbf{I}_i|k+K) = \int_0^1 P_{PV}(\mathbf{I}_i|k_1,k_2,t)dt\,, \quad k_1,k_2 \in \mathcal{G}_k,\ k = 1\ldots K_{PV}\,. \tag{5}$$

3.2 Weighting Functions

In [5,6] the probability density function (PDF) for class k is weighted by the current estimate of the voxel count for that class. This weighting is used to update the probabilities in a manner similar to that of a Bayesian prior. Here we introduce an alternative weighting function that favors segmentations, which are spatially extended. Specifically, we use the familiar Potts model that is also applied in [4]:

$$P_i(k) = \frac{1}{Z}\exp\left(-\beta\cdot\sum_{j\in\mathcal{N}_i}\frac{\delta(k,k_j)}{d(i,j)}\right)\ ; \quad \begin{aligned} k_j &= \arg\max_{k'}\left(P(\mathbf{I}_j|k')\right)\,, \\ k &= 1\ldots K+K_{PV}\,, \end{aligned} \tag{6}$$

where $\delta(k_1,k_2)$ provides the likelihood of different classes being neighbors as in [4]; k is the class for which the prior probability is being calculated; $\mathcal{N}_i$ is the

set of D18 neighborhood voxels of voxel i; β is a parameter of the distribution, controlling the amount of influence the weighting function should exert on the likelihood function; and Z is a normalizing constant. Function $d(i,j)$ represents the distance between voxels i and j, which limits the influence of distant neighborhood voxels.

3.3 Parameter Estimation

Given the probability density and weighting functions, the conditional probability $P(k|\mathbf{I}_i)$ is calculated, from which an estimate of the parameters $\boldsymbol{\mu}_k$ and Σ_k for each pure tissue class k can then be determined as follows:

$$P(k|\mathbf{I}_i) = \frac{P_i(k)P(\mathbf{I}_i|k)}{\sum_{k'=1}^{K+K_{PV}} P_i(k')P(\mathbf{I}_i|k')}\,, \quad k = 1\ldots K + K_{PV}\,; \tag{7}$$

$$\boldsymbol{\mu}_k = \frac{\sum_{i=1}^{N} P(k|\mathbf{I}_i)\cdot \mathbf{I}_i}{h_k}\,; \qquad \Sigma_k = \frac{\sum_{i=1}^{N} P(k|\mathbf{I}_i)\cdot \mathbf{I_i}\cdot \mathbf{I}_i^T}{h_k} - \boldsymbol{\mu}_k \cdot \boldsymbol{\mu}_k^T\,; \tag{8}$$

$$h_k = \sum_{i=1}^{N} P(k|\mathbf{I}_i)\,, \quad k = 1\ldots K\,.$$

These parameter estimates then yield new PDFs and the process is repeated until the voxel count in each pure tissue class does not change from one iteration to the next.

3.4 Initialization

Based on extensive experimentation on real and simulated MR images, we have found that the clustering algorithm can be made robust to initialization values by specifying a sufficiently large class variance. Therefore, without additional prior information available, initial mean intensity values are equally distributed between the minimum and maximum intensity values found in the image. Diagonal elements of the covariance matrix are all set to the image intensity range divided by the number of pure classes, whereas off-diagonal elements are set to zero.

4 Partial Volume Tissue Classification

The clustering algorithm determines $\boldsymbol{\mu}_k$ and Σ_k by iterating over the estimation of $P(k|\mathbf{I}_i)$, until convergence is achieved. Once the intensity distribution and all class parameters are known for each tissue type, the fractional portion t_{i,k_1} for a PV voxel at location i consisting of tissues k_1 and k_2 can then be obtained by solving (3) for t using maximum likelihood estimation (MLE).

To allow segmentation without the need to specify a threshold for distinguishing between partial volume and pure tissue voxels, we require certain information about the pure tissue classes to be included:

$$t^*_{i,k} = P\left(k\,|\mathbf{I}_i\right) + \sum_{k'} P\left(k' + K\,|\mathbf{I}_i\right) \frac{(\boldsymbol{\mu}_k - \boldsymbol{\mu}_{k_2})^T(\mathbf{I}_i - \boldsymbol{\mu}_{k_2})}{(\boldsymbol{\mu}_k - \boldsymbol{\mu}_{k_2})^T(\boldsymbol{\mu}_k - \boldsymbol{\mu}_{k_2})}\,, \tag{9}$$

where the summation is over all PV classes that contain pure class k (for which $k \in \mathcal{G}_{k'}$ is true) and $k_2 \in \mathcal{G}_{k'}$, $k_2 \neq k$. We must also normalize the fractional portions of pure classes so that they sum to unity over all classes k.

5 Implementation and Experimental Results

Two preprocessing steps must be performed prior to segmentation. First, we extract the brain parenchyma from the MR image of the head using the Brain Extraction Tool—details of the method can be found in [8]. Intensity shading artifacts in the extracted image are then removed with the MNI-N3 method [9].

A multi-threaded version of the clustering algorithm was implemented by subdividing the image into a number of segments, which are then processed in separate threads, one for each processor available. All threads are synchronized at 3 time points: before and after the calculation of the weighting values and before the estimation of the new class parameters. The algorithm is outlined below:

1. Initialization - set K, K_{PV}, $\mathcal{G}_k$ and initial estimates of class parameters ($\boldsymbol{\mu}_k$,Σ_k)
2. Calculate the PDFs for all classes using multivatiate Gaussian's and (5) in multiple threads. Wait until all threads complete their processing before proceeding.
3. Calculate the weighting values in multiple threads using (6). Wait until all threads complete their processing before proceeding.
4. Calculate the updated probabilities using (7) for each class k and the new estimates for the class parameters using (8). Wait until all threads complete their processing before proceeding.
5. Terminate the loop when the change in $\Sigma_{k=1}^{K} h_k$ between iterations is less than 1 or number of iterations is 50; otherwise return to step 2.
6. Determinine the fractional amount of each tissue type within every image voxel using (9).

The segmentation algorithm was evaluated using both synthetic and real data. In each of the reported experiments, β was set to 0.3 and algorithm convergence usually occurred after 10–20 iterations.

5.1 Synthetic Image

We constructed a square, 100 by 100, image and subdivided the image into 3 vertically separated regions. The regions to the far left and right were considered pure "tissues" and their image values were drawn from normal distributions with the following mean and variance values, respectively: $\mu_1 = 70$, $\Sigma_1 = 100$ and $\mu_2 = 150$, $\Sigma_2 = 400$. The middle strip of the image, 30 pixels wide, contained partial volume pixels, which modeled a smooth linear transition between the two pure classes. The synthetic image and its segmentation is shown in Fig. 1.

The following are the estimated mean and variances for the tissue classes: $\mu_1 = 70.35$, $\Sigma_1 = 101$; $\mu_2 = 148.34$, $\Sigma_2 = 369.41$. Fig. 1 also shows the squared error between the ideal and estimated t values for the class—the total error was $E_1 = 26.65$, where $E_{i,k} = (t_{i,k} - t_{i,k}^{ideal})^2$, $E_k = \sum_{i=1}^{N} E_{i,k}$.

We can see that the errors occur only at the boundaries where the region with PV voxels meets the regions containing pure classes. We contribute this error largely to noise because it decreases when we reduce the amount of noise variance for the pure classes. This also explains the smaller amount of error in the segmentation of the left half of the image, where the noise variance for the first pure class was smaller.

Fig. 1. Synthetic data with segmentation results. (Left) Image to be segmented. (Center) Fractional values t for the first class at each voxel plotted as an 8-bit gray-scale image with intensity = 0 corresponding to $t = 0.0$ and intensity = 255 to $t = 1.0$. (Right) Pointwise squared error between estimated and ideal t values for the first class.

5.2 Simulated T1-Weighted Brain Volume

A second, more realistic synthetic dataset of an MRI head scan was created using the Brain-Web simulator [10,11,12]. Each simulation was a 1mm^3 isotropic MRI volume with dimensions $181 \times 217 \times 181$. Three datasets incorporating different amounts of noise were segmented and the mean absolute error between the ideal and estimated t values over all voxels were as follows:

- 9% noise: GM: 0.08458 (σ=0.11885); WM: 0.04399 (σ=0.08759); CSF: 0.04157 (σ=0.09795)
- 3% noise: GM: 0.05435 (σ=0.08597); WM: 0.02923 (σ=0.06414); CSF: 0.02585 (σ=0.06517)
- 0% noise: GM: 0.03874 (σ=0.06301); WM: 0.01936 (σ=0.03755); CSF: 0.02077 (σ=0.05612)

Although there appears to be minimal partial volume averaging in the results, the segmentation obtained without the use of PV classes ($K_{PV} = 0$) had errors about 2 times larger and the algorithm took much longer to converge (> 50 iterations).

5.3 Manually Segmented Real T1 MR Images of the Brain

Twenty normal brain MRI datasets and their manual segmentations were obtained from the Center for Morphometric Analysis at Massachusetts General Hospital—these IBSR datasets are publicly available on the Internet [13]. The volumes were preprocessed to extract brain parenchyma and corrected for intensity inhomogeneities. However, 7 of the preprocessed volumes exhibited strong shading artifacts of relatively high frequency that the MNI-N3 method [9] was unable to remove. These volumes were excluded from further processing.

Table 1. Jaccard similarity between estimated and *true* segmentation of IBSR images.

Image	100_23	110_3	111_2	112_2	11_3	13_3	16_3	17_3	191_3	202_3	205_3	7_8	8_4
GM	0.833	0.821	0.811	0.756	0.798	0.845	0.720	0.734	0.819	0.842	0.823	0.776	0.739
WM	0.752	0.707	0.739	0.679	0.723	0.777	0.640	0.628	0.740	0.763	0.768	0.684	0.665

Since the manual segmentations for this set of images do not contain any information about fractional tissue content, we calculated a similarity index for each class by thresholding our partial volume segmentation results. Specifically,

in table 1 we report the values for the Jaccard similarity $= |S_e \cap S_{ideal}|/|S_e \cup S_{ideal}|$, where S_e and S_{ideal} are the estimated and "true" sets of voxels, respectively, for a given tissue class. The mean Jaccard index was 0.783 and 0.698 for GM and WM, respectively. These results are superior to those reported in the recent literature [4,14].

6 Conclusion

We have presented an algorithm for partial volume segmentation of MR images of the brain. Experimental results are comparable or superior to other published algorithms. Our method is an extension of a probabilistic clustering algorithm, [5,6], to accommodate partial volume voxels and to allow class-dependent model values for the intensity variance. In the current work, the weighting function was augmented to favor spatially contiguous regions in the segmentation but other possibilities are being examined, including the use of prior anatomic information as in [7]. Another, more important feature that is under implementation is the simultaneous correction of intensity inhomogeneities to not only obviate the need for this preprocessing step but to improve on existing techniques.

References

1. H. S. Choi, D. R. Haynor, and Y. Kim, "Partial volume tissue classification of multichannel magnetic resonance images - a mixel model," in *IEEE Transactions on Medical Imaging*, vol. 10, pp. 395–407, Sept. 1991.
2. L. Nocera and J. C. Gee, "Robust partial volume tissue classification of cerebral MRI scans," in *SPIE Medical Imaging* (K. M. Hanson, ed.), vol. 3034, pp. 312–322, Feb. 1997.
3. D. H. Laidlaw, K. W. Flescher, and A. H. Barr, "Partial-volume Bayesian classification of material mixtures in MR volume data using voxel histograms," in *IEEE Transactions on Medical Imaging*, vol. 17, pp. 74–86, Feb. 1998.
4. D. W. Shattuck, S. R. Sandor-Leahy, K. A. Schaper, D. A. Rottenberg, and R. M. Leahy, "Magnetic resonance image tissue classification using a partial voume model," 2000. Submitted.
5. J. A. Hartigan, *Clustering algorithms*. New York: John Wiley & Sons, Inc., 1975.
6. R. O. Duda and P. E. Hart, *Pattern classification and scene analysis*. New York: John Wiley & Sons, Inc., 1973.
7. J. Ashburner and K. Friston, "Multimodal image coregistration and partitioning - a unified framework," in *Neuroimage*, vol. 6, pp. 209–217, Oct. 1997.
8. S. M. Smith, "Robust automated brain extraction," in *Sixth Int. Conf. on Functional Mapping of the Human Brain*, p. 625, 1998.
9. J. G. Sled, A. P. Zijdenbos, and A. C. Evans, "A nonparametric method for automatic correction of intensity nonuniformity in MRI data," in *IEEE Transactions on Medical Imaging*, vol. 17, pp. 87–97, Feb. 1998.
10. `http://www.bic.mni.mcgill.ca/brainweb/`.
11. R.-S. Kwan, A. Evans, and G. B. Pike, *An Extensible MRI Simulator for Post-Processing Evaluation*, vol. 1131 of *Lecture Notes in Computer Science*, pp. 135–140. Springer-Verlag, May 1996.

12. D. L. Collins, A. Zijdenbos, V. Kollokian, J. Sled, N. Kabani, C. Holmes, and A. Evans, "Design and construction of a realistic digital brain phantom," in *IEEE Transactions on Medical Imaging*, vol. 17, pp. 463–468, June 1998.
13. `http://neuro-www.mgh.harvard.edu/cma/ibsr`.
14. J. C. Rajapakse and F. Kruggel, "Segmentation of MR images with intensity inhomogeneities," in *Image and Vision Computing*, vol. 16, pp. 165–180, 1998.