New methods in Brain MR Segmentation with Fuzzy EM algorithm

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***Abstract*—Expectation maximization algorithm has been extensively used in a variety of medical image processing applications, especially for detecting human brain disease. In this paper, an efficient and improved semi-automated Fuzzy EM based techniques for 3-D MR segmentation of human brain images is presented. FEM along with histogram based K-means in initialization step is used for the labeling of individual pixels/voxels of a 3D anatomical MR image (MRI) into the main tissue classes in the brain, Gray matter (GM), White matter (WM), CSF (Celebro-spinal fluid). FEM's membership function were estimated through a histogram-based method. The results show our proposed FEM-KMeans has better performance and convergence speed compare to histogram based EM.**

***Index Terms*—Brain MRI segmentation; fuzzy expected maximization; histogram based k-mean.**

I. INTRODUCTION

Automatic three-dimensional (3-D) segmentation of the magnetic resonance (MR) scans is a challenging problem that has received an enormous amount of attention lately. Quantitative analysis of signal intensity on MRI changes and their correlation with clinical finding provide important information to diagnose of many neurodegenerative and psychiatric diseases. After the enhancement of images and brain extraction, brain segmentation is the next level. As a result, brain segmentation is of great interest to many researches.

In the context of neuro-imaging, 3-D segmentation of white matter (WM), gray matter (GM), and cerebro-spinal fluid (CSF) are extremely important for quantitative analysis such as volume measurements. Data clustering algorithms can be classified as Hierarchical, Partitional and Density-based. Hierarchical algorithms find successive clusters using previously established clusters. These algorithms can be either agglomerative ("bottom-up") or divisive ("top-down"). Agglomerative algorithms begin with each element as a separate cluster and merge them into successively larger clusters. Divisive algorithms begin with the whole set and proceed to divide it into successively smaller clusters. Partitional algorithms typically determine all clusters at once, but can also be used as divisive algorithms in the hierarchical clustering.

Density-based clustering algorithms are devised to discover arbitrary-shaped clusters. In medical imaging, such as PET scans, MRI scans, cluster analysis can be used to differentiate between different types of tissue and blood in a three dimensional image. In this application, actual position does not matter, but the voxel intensity is considered as a vector, with a dimension for each image that was taken over time. This technique allows, for example, accurate measurement of the rate a radioactive tracer is delivered to the area of interest, without a separate sampling of arterial blood, an intrusive technique that is most common today.

An accurate and robust tissue classification is the basis for many applications such as: quantitative measurement of tissue volume in normal and diseased brain, morphological analysis, or visualization. Manual or even semi-automatic, Classification performed by a trained expert is labor-intensive and hence impractical for processing large amounts of data, highly subjective, and non-reproducible [1]. The main difficulties found in the automatic segmentation of MR brain images are due to the fact that image intensities are not necessarily constant for each tissue class. Several methods have been developed for this purpose, Lee and his colleagues not only applied active contours for automatic segmentation [2] but also used another method watershed transform [3]. Besides, Duta developed a fully automated active shape model for segmentation and interpretation of MR images [4]. Watershed transform is another method that have used by some researchers such as Lee and his colleagues [3].In addition to aforementioned methods, atlas-based segmentation and Learning vector quantization (LVQ) models are two other methods applied in brain MR segmentation [5], [6].

Double region based active control is another method that for example In [7] region based segmentation for two regions is formulated as follows

$$E(\emptyset, p1, p2) = -\int_{\varphi} H(\emptyset) logp1dx - \int_{\varphi}\left(1 - H(\emptyset)\right) logp2dx + v\int_{\varphi} |\nabla H(\emptyset)| dx \tag{1}$$

where $\emptyset$ is Level Set Function that is $\emptyset > 0$ for first region and $\emptyset < 0$ for second region and

H is Heaviside function for separating two regions that is, 0 for second region and 1 for first

Region. In [8] $P1$ and $P2$ are determined by nonparametric Parzen density estimates [9] which are computed using smoothed histograms of the regions [10].

Also some research have conducted to compare different type of algorithm and methods.[11] is one of them that have tried to compare three major software SPM, FSL and BrainSuite for MRI segmentations.

Some papers have tried to obtain specified information from Brain MRI images. [12] is one of them that tried to

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evaluate Volume of Hippocampus which is important in diagnosis of some diseases such as Alzheimer.

An important step in any clustering is to select a distance measure, which will determine how the similarity of two elements is calculated/determined. This will influence the shape of the clusters, as some elements may be close to one another according to one distance and farther away according to another. For example, in a 2-dimensional space, the distance between the point ($x = 1$, $y = 0$) and the origin ($x = 0$, $y = 0$) is always 1 according to the usual norms, but the distance between the point ($x = 1$, $y = 1$) and the origin can be 2, $\sqrt{2}$ or 1 if you take respectively the 1-norm, 2-norm or infinity-norm distance. Common distance functions: The Euclidean distance (also called distance as the crow flies or 2-norm distance). The Manhattan distance (aka taxicab norm or 1-norm). The maximum norm (aka infinity norm). The Mahalanobis distance corrects data for different scales and correlations in the variables. The angle between two vectors can be used as a distance measure when clustering high dimensional data. The Hamming distance measures the minimum number of substitutions required to change one member into another.

As the most natural framework for the design of such methods is statistical/ probabilistic, Bayesian approach is more suitable for such applications with anatomical/geometric constraints about the location of each class which may be specified as prior probabilities, The resulting estimation procedure is EM algorithm which is iterative; in general, it contains two steps that are repeated until convergence as follows: Estimating the segmentation (class label), given the intensity models (GMM) for each class and Estimating the intensity models (probability density function), given segmentation with an appropriate initialization step.

The EM algorithm has been used by a number of medical image processing researchers for different kinds of studies [13], [11].

Yongyue improved EM by using hidden Markov random field (HMRF) model in which state sequence estimated through observations [12] .

Mounira suggested another approach on building statistical model from data itself, for normal brain MRI and including clustering tissue type [14]. Gu proposed another improvement on EM algorithm to estimate parameters of the prior probabilities and likelihood probabilities and the Segmentation is carried out by means of a MAP estimator [15]. Also, Quost proposed a fuzzy EM algorithm in clustering imprecise data using finite mixtures of Gaussians [16].

In this paper we applied Quost’s proposed fuzzy EM model to 3d brain MR images along with improvement on initialization phase done by a histogram based on k-means algorithm and a histogram based membership function**.**

II. MATERIALS AND METHODS

A. *Data*

The Internet Brain Segmentation Repository (IBSR),operated by CMA (Center for Morphometric Analysis) at MGH (Massachusetts General Hospital) , contains MR images with manually-guided segmentations that has been considered during this paper. IBSR provided T1-weighted coronal MRI data with gray/white/cerebral spinal fluid/other expert segmentations for twenty normal subjects. The data sets had an intensity range of 0-216 .

B. *Methods*

In statistics, a mixture model is a probabilistic model for density estimation using mixture distributions. A mixture model can be regarded as a type of unsupervised learning or clustering. Mixture model is a statistical technique which models the data by using a number of distributions. It assumes the data as a set of observations from a mixture of different probability distributions. Each distribution corresponds to a cluster and the parameters of each distribution (also known as component) provide a description of the corresponding cluster in terms of mean and variance. Gaussian mixture models consider Gaussian distribution in mixture models. The maximum likelihood principle is applied to estimate the parameters of statistical distributions from the data and is known as maximum likelihood estimation (MLE).An expectation-maximization algorithm is used in statistics for finding maximumlikelihood estimate of parameters in probabilistic models, where the model depends on unobserved hidden variables.

During the normalization phase images can be aligned with each other, warp them (normalize) so that each subject's anatomy is roughly the same shape, correct them for differences in slice time acquisition, and smooth them spatially [17] .

These steps are used for a couple of reasons. Registration and normalization aim to line images from a single subject up (since subjects' heads move slightly during the experiment) and normalization aims to stretch and squeeze the shape of the images so that their anatomy roughly matches a standard template; both of these aim to make localizing your activations easier and more meaningful, by making individual voxels' locations in a given image file match up in a standard way to a particular anatomical location. Slice timing correction and smoothing both enable SPM to make certain assumptions about the data images - that each whole image occurred at a particular point in time (as opposed to slices being taken over the course of an image acquisition, or TR), and that noise in an image is distributed in a relatively random and independent fashion (as opposed to being localized) [18].

EM is an iterative method which alternates between performing an expectation (E) step, which computes an expectation of the log likelihood with respect to the current estimate of the distribution for the hidden variables, and a maximization (M) step, which computes the parameters which maximize the expected log likelihood found on the E-step. The EM algorithm is an efficient iterative procedure to compute the Maximum Likelihood (M) estimate in the presence of missing or hidden data. In ML Estimation, the model parameter(s) are estimated for which the observed data are the most likely.

Convergence is assured since the algorithm is guaranteed to increase the likelihood at each iteration.

These parameters are then used to determine the distribution of the hidden variables in the next E step .The EM algorithm is an efficient iterative procedure to compute the Maximum Likelihood (M) estimate in the presence of missing or hidden data. In ML Estimation, the model parameter(s) are estimated for which the observed data are the most likely. Each iteration of the EM algorithm consists of two processes: The E-step, and the M-step. In the expectation, or E-step, the missing data are estimated given the observed data and current estimate of the model parameters. This is achieved using the conditional expectation, explaining the choice of terminology. In the M-step, the likelihood function is maximized under the assumption that the missing data are known. The estimate of the missing data from the E-step is used in lieu of the actual missing data. Convergence is assured since the algorithm is guaranteed to increase the likelihood at each iteration. An atlas is a composite image formed from segmented, co-registered images of several subjects. A 3D mapping is determined between the atlas and an image with unknown segmentation and the atlas supplies prior probabilities for statistical pattern recognition. In many cases, the use of an atlas requires distinct steps for registration and for segmentation. A method for jointly performing these steps has been reported. Although fully automatic registration is desirable, semiautomatic registration is also used where manually defined, landmark points constrain the deformation and improve segmentation accuracy especially in cortical regions where substantial inter-subject variability exists. Many kind of computerized analyses can be used to extract information from three dimensional MRI data of the human head such as atlas based and mathematical morphological method. Another categorization is manual, semi-automatic and automatic categories. Manual segmentation is possible but is time-consuming task and subject to operator variability .In this section, first we explain our preprocessing phase, and will mention our Fuzzy EM method and our histogram-based EM initialization procedure. During the preprocessing phase, the brain images are aligned with each other and in the normalizing each subject's anatomy becomes roughly the same shape, we corrected them for differences in slice time acquisition, and smooth them spatially. Data is combined across individuals and use standard coordinate system. In order to compare different data from different scans and research subjects, all the brain images have to be in the same 3D space. In the normalization step we stretch and squeeze the shape of the images so that their anatomy roughly matches a standard template and also makes localizing our activations easier and more meaningful, by making individual voxels' locations in a given image file match up in a standard way to a particular anatomical location.

An EM algorithm is used in statistics for finding maximum Likelihood estimate of parameters in probabilistic models, where the model depends on unobserved hidden variables [19]. EM is an iterative method which alternates between performing an expectation (E) step, which computes an expectation of the log likelihood with respect to the current estimate of the distribution for the hidden variables, and a maximization (M) step, which computes the parameters which maximize the expected log likelihood found on the E-step. These parameters are then used to determine the distribution of the hidden variables in the next E step .The Classic EM algorithm is an iterative procedure to compute the Maximum Likelihood (ML) estimate in the presence of missing or hidden data. In ML Estimation, the model parameter(s) are estimated for which the observed data are the most likely. In the expectation, or E-step, the missing data are estimated given the observed data and current estimate of the model parameters. The result is achieved using the conditional expectation, explaining the choice of terminology. In the M-step, the likelihood function is maximized under the assumption that the missing data are known. Convergence is assured since the algorithm is guaranteed to increase the likelihood at each iteration [20].

A fuzzy EM algorithm can be considered as follows [21]:

The value can be interpreted as the degree of possibility in which the real value is taken by the random variable is x.

We suppose that the membership function of a multidimensional fuzzy number produced by the membership functions of its components. The complete data sample is

Also, the probability of a fuzzy event definition may be applied to measure the observed data log-likelihood [22]:

$$L(\psi) = \sum_{z} p(z;\psi) \int g(y|z;\psi)dy. \tag{2}$$

Therefore, the E-step consists in calculating

$$Q(\psi,\psi^{q}) = E_{\psi^{q}}[log l_{c}(\psi)|\tilde{y},z]. \tag{3}$$

The conditional density of a continuous random variable X with respect to a fuzzy event with fuzzy membership function is:

$$(gx(x|\tilde{x}) = \frac{\mu_{\tilde{x}}(x)gx}{\int \mu_{\tilde{x}}(x)gxdx} \tag{4}$$

With the following notations:

$$p\,^{(q)}_{i} = p_{\psi^{(q)}}(\tilde{x}_i) = \sum_{k=1}^{r} \pi_k^{(q)} \int \mu_{\tilde{x}_i}(x) g_k\left(x;\psi^{(q)}\right).dx; \tag{5}$$

$$\pi_{ijk\,(q)} = E_{\psi^{(q)}}[x|\tilde{x}, z_{ik} = 1] = \frac{\int x_j \mu_{\tilde{x}_{ij}}(x_j) g_{jk}\left(x_j;\psi_k{}^{(q)}\right).dx;}{\gamma_{ijk\,(q)}} \tag{6}$$

$$\varepsilon_{ijk\,(q)} = E_{\psi^{(q)}}\left[x_{ij}^{2}\middle|\tilde{x}_i, z_{ik} = 1\right] = \frac{\int x_j^2 \mu_{\tilde{x}_{ij}}(x_j) g_{jk}\left(x;\psi^{(q)}\right).dx;}{\gamma_{ijk\,(q)}} \tag{7}$$

$$\gamma\,^{(q)}_{ik} = p_{\psi^{(q)}}(x^{\sim}{}_{i}|z_{ik} = 1) = \int \mu_{\tilde{x}_i}(x) g_k\left(x;\psi^{(q)}\right).dx; \tag{8}$$

And using Bayes’ theorem, we have:

$$t\,^{(q)}_{ik} = E_{\psi^{(q)}}(z_{ik}|x^{\sim}{}_{i}) = \frac{p_{\psi^{(q)}}(x^{\sim}{}_{i}|z_{ik}=1)}{p_{\psi^{(q)}}(x^{\sim}{}_{i})} = \frac{\gamma_{i,k}^{(q)}\pi_k^{(q)}}{p_i^{(q)}} \tag{9}$$

The E-step now consists in computing [23]:

$$Q(\psi, \psi^{q}) = \sum_{k=1}^{g} \log\pi_k \sum_{i=1}^{n} t_{ik}^{(q)} - \frac{np}{2\log(2\pi)}$$

$$-\sum_{k=1}^{g} \sum_{j=1}^{p} log\sigma_{jk}^{(q)} \sum_{i=1}^{n} t_{ik}^{(q)}$$

$$-1/2 \sum_{i=1}^{n} \sum_{k=1}^{g} t_{ik}^{(q)} (\sum_{j=1}^{p} \frac{1}{{\sigma_{jk}^{(q)}}^2} \varepsilon_{i,j,k}^{(q)}$$

$$-2 \sum_{j=1}^{p} \frac{m_{jk}^{(q)}}{{\sigma_{jk}^{(q)}}^2} \pi_{ijk}^{(q)}$$

$$+ \sum_{j=1}^{p} \frac{{m_{jk}^{(q)}}^2}{{\sigma_{jk}^{(q)}}^2} \tag{10}$$

M-step:

$$\pi_k^{(q+1)} = \frac{1}{n} = \sum_{k=0}^{n} t_{ik}^{(q)}. \tag{11}$$

$$m_{jk}^{(q+1)} = \frac{\sum_{i=1}^{n} t_{ik}^{(q)} \mu_{ijk}{}^{(q)}}{\sum_{i=1}^{n} t_{ik}^{(q)}} \tag{12}$$

$$\sigma_k^{(q+1)} = \sqrt{\frac{\sum_{i=1}^{n} t_{ik}^{(q)} \sum_{j=1}^{p} \left(\varepsilon_{ijk}^{(q)} - 2m_{jk}^{(q)} \pi_{ijk}^{(q)} + m_{jk}^{(q)2}\right) + \lambda_k}{p \sum_{i=1}^{n} t_{ik}^{(q)} + p(m_0 + p + 1)}} \tag{13}$$

Q Stands for iteration. Initial value for *q* = 1.

Comparing class EM with crisp data shows that the crisp quantities and are replaced with the conditional expectations and of the fuzzy variables and , respectively [21].

To calculate the membership function in the previous equations we used a simple model of Dou's method for the MR images [24]. For simplicity we applied Dou's proposed steps: calculating the histogram of whole MRI sequence and transforming the histogram into membership function by selecting some feature values such as peaks and valleys of the histogram.

If presents k_{th} gray level, and the total number of gray level is L, k= 0, 1. . . $L-1$, the histogram gives us estimation of the probability of

$$P^{GL_K} = \frac{n_K}{N} \tag{14}$$

n_k *refers* to the total number of pixel which their gray level is equal to .

are noted as peaks as the features points for transformation and their valleys, considered as. Let *F* denote one of transformation Operation, the membership function is presented as equation 16.

$$\mu_{Tiss}^{SI} = F\{(GL_{SI}, P(GL_{SI})), p(GL_{SI}^{pk}), p(GL_{SI}^{vl})\} \tag{15}$$

Where

$$GL_{SI} = \{GL_{T1}, GL_{T2}\} \tag{16}$$

For example, can be obtained with the properties ranking in T1,

and

$$(\mu_{WM}^{T1} \propto GL_{T1}; \text{ and } \quad \mu_{CSF}^{T1} \propto \frac{1}{GL_{T1}} \tag{17}$$

$$\mu_{GM}^{T1} \propto \begin{cases} GL_{T1}, IF\ GL_{T1} \leq GL_{T1}^{P^K} \\ \frac{1}{GL_{T1}}, IF\ GL_{T1}^{P^K} < GL_{T1} \end{cases}; \tag{18}$$

Example of histogram and membership function for one sample MRI image is given in the Fig. 1.

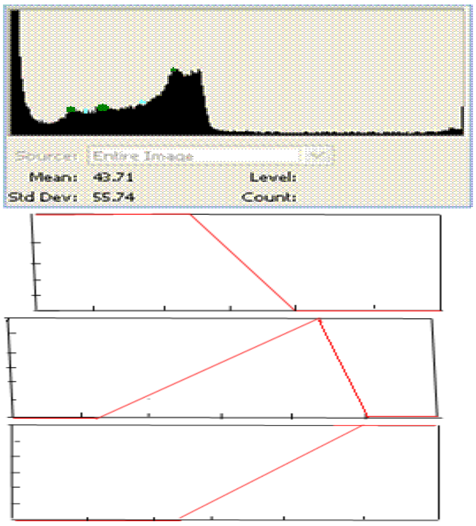

Fig. 1. Histogram of a sample MRI image (left) and continuous membership function (Right)

Another improvement in our proposed algorithm was in initialization phase. EM algorithm can be initiated with different methods. Initialization means finding mixture model parameters (μ_i , σ_i , c_i) in classic notation). These parameters can be obtained using various techniques such as: a) guess or experience, b) Histogram (with plotting histogram), c) K-means clustering algorithm.

We ran algorithm with two different initialization methods: classic histogram and a histogram-based k-means. Based on results, histogram based k-means shows better performance.

K-means is a partitional clustering algorithm.

The Classic K-means algorithm assigns each point to the cluster whose center (also called centroid) is nearest. The center is the average of all the points in the cluster that is, its coordinates are the arithmetic mean for each dimension separately over all the points in the cluster. The K-means algorithm steps are: Choose the number of clusters, *k*

Initialization: Randomly generate *k* clusters and determine the cluster centers, or directly generate *k* random points as cluster centers. Assign each point to the nearest cluster center and then Recompute the new cluster centers. Repeat the two previous steps until some convergence criterion is met (usually that the assignment hasn't changed). The main advantages of this algorithm are its simplicity and speed which allows it to run on large datasets.

III. RESULTS

This section provides simulation results on MRI human brain data set. It also provides some performance analysis of EM algorithm with and without K-means initialization. Computational steps are explained through examples.

A MRI scan is selected for pre-processing from IBSR T1-weighted coronal MRI data with gray/white/cerebral spinal fluid/other expert segmentations from twenty normal subjects. The data sets had an intensity range of 0-2^{16} and each slice had 256x256 pixels. The voxel dimensions are $1.17\times1.17\times3.1$ mm^3.

Synthetic One dimensional data set and Gaussian Mixture Model using EM algorithm Data Analysis results using histogram, K-Means and EM algorithms on Real MR image data set from Harvard University (Massachusetts General Hospital, Center for Morphmetric Analysis Internet Brain Segmentation Repository) (IBSR) which has MRI data base for doing scientific study on human brain on different subjects and has been considered during this project. Data set consists twenty Normal Subjects, T1-Weighted Scans with Segmentations: 16-bit MR data files or 16-bit MR data files or first half 16-bit MR data files or 8-bit MR data files or 8-bit brain-only MR data files and CSF/gray/white/other manual segmentation files OR 8-bit that can analyze format raw images and segmentations .An example of the implementation of the method is shown in the following figures. Fig. 2 presents three representative slice of a normal T1 MR image of a brain, Fig. 3 display the White matter after segmentation and Fig. 4 shows grey matter after FEM-KMeans segmentation process. Besides the classic EM algorithm segmented MR image has been shown at Fig. 5.In the mentioned classic EM algorithm initialized to random, to identity matrix and to .The comparison show a significant correspondence. Segmented images by our proposed FEM-KMeans are more accurate in comparison with classic EM algorithm. Evaluation of the statistical differences of results was performed by a Wilcoxon signed rank test for paired data with manual ground truth. The result indicates that our FEM k-means method has better performance and statistically less difference with manual ground compare to classic EM.

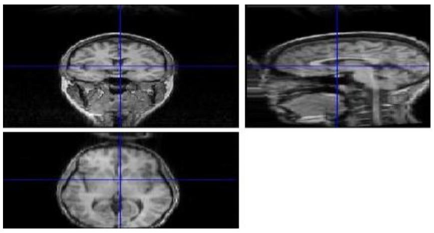

Fig. 2. Normal T1 MR image

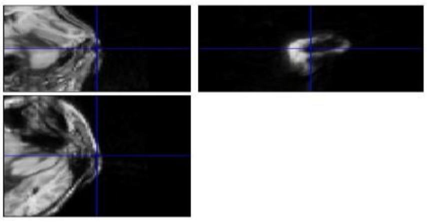

Fig. 3. MR image after preproseccing

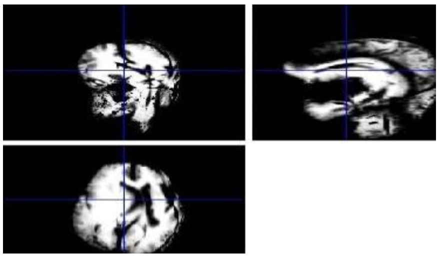

Fig. 4. White matter

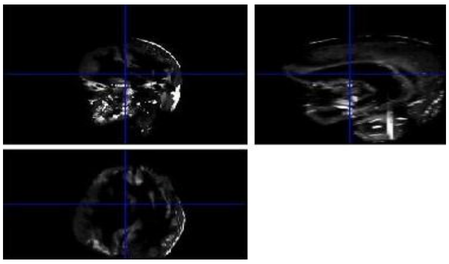

Fig. 5 . Gray matter

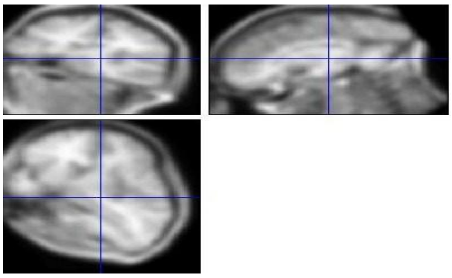

Fig. 6. Cerebrospinal fluid

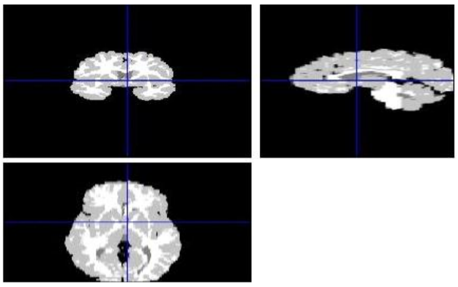

Fig. 7. MR Segmentation by classic EM method

Furthermore our results shows using histogram in finding initial centroids in K-means algorithm in initialization phase of developed FEM algorithm makes faster convergence in compare to other previously used methods. The entire implementation of segmentation has been done using Matlab version 7.0 beside Image processing toolbox and MRIcro software version 1.2.The MR image format was DICOM and the resolutions were 256*256.

IV. CONCLUSION AND FUTURE WORK

Quantitative analysis of signal intensity on MRI changes and their correlation with clinical finding provides important information to diagnose, and brain segmentation is of great interest to many researches. In this paper, a fuzzy expectation maximization method along with histogram based K-means is used for the labeling of individual pixels/voxels of a 3D anatomical MR image with the help of mixture models. A histogram-based method is employed for estimating the membership function. The results indicate that our proposed FEM-KMeans has better performance and convergence speed compare to classic EM and EM-histogram.

In this study, Fuzzy logic is used to cluster MR images, other Fuzzy based methods will be applied in the segmentation of MR images. Furthermore, augmenting Fuzzy-k-means in initialization step along with Fuzzy-EM and employing better Fuzzy membership function scan improve results. These are the issues that future research may assist.

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