Implementation of Segmentation Methods for the Diagnosis and Prognosis of Mild Cognitive Impairment and Alzheimer Disease

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Abstract. Alzheimer's disease (AD) is the most common form of dementia affecting seniors age 65 and over. When AD is suspected, the diagnosis is usually confirmed with behavioural assessments and cognitive tests, often followed by a brain scan. Advanced medical imaging is a good tool to predict conversion from prodromal stages (mild cognitive impairment) to Alzheimer's disease. Since volumetric MRI can detect changes in the size of brain regions, measuring those regions that atrophy during the progress of Alzheimer's disease can help the neurologist in his diagnostic. In the present investigation, we present an automatic tool that reads volumetric MRI and performs 2-dimensional (volume slices) and volumetric segmentation methods in order to segment gray matter, white matter and cerebrospinal fluid (CSF). We used the MRI data sets database from the Open Access Series of Imaging Studies (OASIS).

1. Introduction
AD leads to nerve cell death and tissue loss throughout the brain, resulting in brain tissue shrinking and larger ventricles (chambers within the brain that contain cerebrospinal fluid). When AD is suspected, the diagnosis is usually confirmed with behavioral assessments and cognitive tests, often followed by a brain scan [1]. Advanced medical imaging with computed tomography (CT) or magnetic resonance imaging (MRI), and with single photon emission computed tomography (SPECT) or positron emission tomography (PET) can be used to help exclude other cerebral pathology or subtypes of dementia [1]. Moreover, it may predict conversion from prodromal stages (mild cognitive impairment) to Alzheimer's disease [2].
In this paper, we describe succinctly image segmentation methods that segment the slice brain's neuroimages in order to extract the ventricles' region, as a way to get a first visual assessment.

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Section 2 describes briefly the theory behind the image segmentation. Section 3 describes and discusses the system implementation including the data access, visualization and different segmentation methods while incorporating different algorithms.

2. Theory behind the system implementation

The proposed system is to perform 3D image segmentation of original 3D MRI neuroimage brain data. The theory about 2D segmentation is easily transported into 3D, however the cost of the algorithms is theoretically squared $O(3D) = O(2D)^2$. The 3D segmentation transforms the original voxels in 3D images into 3D regions where each region, identified by a different label, represents meaningful physical behaviors defined by a vector of attributes (average, standard deviation, etc.). There are many existing segmentation techniques applied for medical image segmentation, including statistical methods, thresholding, edge detection, region-based techniques and more recently multi-resolution (using wavelets, ridgelets, etc.) techniques [3], [4]. The choice of the method depends on the type and quality of the image.

2.1. Thresholding

When images contain different contrasting objects, thresholding provides effective means for obtaining segmented images. Thresholding techniques are based on partitioning the intensities using global or local threshold calculations techniques such as Otsu [5] and Niblack methods [6], where each threshold classifies the voxels (or pixels) into different modes using a clustering criterion.

2.1.1. The Otsu Method

The Otsu method [5] is a clustering technique that tends to produce two tight clusters by minimizing their overlap (misclassified pixels). The threshold is adjusted dynamically by increasing the spread of one cluster and decreasing the spread of the other one. The goal then is to select the threshold that minimizes the combined spread. We define the within-class variance as the weighted sum of the variances of each cluster:

$$\sigma_{within}^2 = n_B(T)\sigma_B^2(T) + n_O(T)\sigma_O^2(T)$$  \hspace{1cm} (1)

$$\sigma_{between}^2 = n_B(T)n_O(T)\left(\mu_B^2(T) + \mu_O^2(T)\right)$$  \hspace{1cm} (2)

Where:

$$n_B(T) = \sum_{i=0}^{T-1} p(i)$$: the number of pixels in the first cluster

$$n_O(T) = \sum_{i=T}^{N-1} p(i)$$: the number of pixels in the second cluster

$$\sigma_B^2(T)$$: the variance of the pixels in the background (below threshold)

$$\sigma_O^2(T)$$: the variance of the pixels in the foreground (above threshold)

$$\mu_B(T)$$: the mean of all pixels less than the threshold

$$\mu_O(T)$$: the mean of all pixels greater than the threshold

[0, N-1]: is the range of intensity levels.

Developed algorithm

The optimal threshold is the one that maximizes the between-class variance (or, conversely, minimizes the within-class variance). So, for each potential threshold $T$ we:

1. Separate the pixels into two clusters according to the threshold.
2. Find the mean of each cluster.
3. Square the difference between the means.
4. Multiply by the number of pixels in one cluster times the number in the other.
2.1.2. Niblack method
Niblack’s algorithm [6] calculates a local threshold \( T \) for each pixel. The threshold \( T \) is computed by using the mean \( \mu \) and standard deviation \( \sigma \) of all the pixels in the pixel neighborhood, and is denoted as: \( T = \mu + k*\sigma \), where the parameter \( k \) is a constant, which determines how much of the total object is extracted, and is usually chosen between 0 and 1. The value of \( k \) and the size of the neighborhood influence the result of thresholding.

2.2. Edge detection
Other segmentation methods are based on edge detection techniques such as Canny [7], active contours or snakes using the technique of matching a deformable model to an image by means of energy minimization [8], [9].

2.2.1. Canny edge detection
The Canny edge detection algorithm [7] aims to the following optimal properties:
- Good detection: the algorithm should detect as many real edges in the image as possible.
- Good localization: the edges marked should be as close as possible to the edge in the real image.
- Minimal response: a given edge in the image should only be marked once, and where possible, image noise should not create false edges.

Canny’s algorithm is based on finding an optimal function as the first derivative of a Gaussian, originally described by the sum of four exponential terms. The effectiveness and cost of the algorithm depends on the size of the Gaussian filter and the hysteresis thresholds.

2.2.2. Active contours
The active contour [8], [9] is also sometimes called snake algorithm. Given an approximation of the boundary of an object in an image, an active contour model deforms the initial boundary to lock onto characteristic features within the region of interest. The contour is deformed iteratively until it matches the boundary of the region of interest by looking for the minimum of energy of a given problem. The energy functional is a weighted combination of internal and external forces depending on the shape of the snake and location within the image. It is defined by the following algorithm:

The integral energy functional to be minimized is given by:

\[
E_{\text{snake}}^* = \int_0^1 E_{\text{snake}}(v(s)) \, ds \\
= \int_0^1 (E_{\text{int}}(v(s)) + E_{\text{image}}(v(s)) + E_{\text{con}}(v(s))) \, ds
\]  

Where \( E_{\text{int}} = \alpha(s) \left( \frac{dv}{dx} \right)^2 + \left( \frac{d^2v}{dx^2} \right)^2 \) is the internal spline energy.
\( \alpha(s) \) and \( \beta(s) \) are the elasticity and stiffness of the snake respectively.
\( E_{\text{image}} \) is derived from the image data over which the snake lies and it is modeled as a weighted combination of different functional, and \( E_{\text{con}} \) comes from external constraints that force the snake toward or away from particular features.
The effectiveness of the algorithm depends on the initial choice of the approximate shape and starting position. A priori information is then used to move the snake toward an optimal solution.

2.3. Region-based segmentation
Region-based segmentation uses different techniques such as seeded region-growing [10], split-and-merge [11], watershed [12] and Wavelet-based segmentation [13] which is based on mathematical concepts such as quadrature mirror filtering, sub-band coding, and pyramidal image processing.
2.3.1. Region-growing segmentation:
Region-growing segmentation [10] starts with initial seed points chosen from the target region or without a priori knowledge, taken from the picks of the histogram. It checks the neighborhood pixels and adds them to the region if they are similar to the chosen seeds using a similarity criteria (homogeneity predicates) based on a vector of characteristics (attributes) in the image such as the average, standard deviation, texture, etc.

2.3.2. Split-and-merge segmentation:
Split-and-merge segmentation [11] consists of two different parts. The split process keeps dividing the image into smaller regions that do not respect a criterion of similarity. In the merge process, neighboring regions, resulting from the split process that respects a similarity criterion, using a vector of predicates, are merged into bigger regions.

3. System implementation and discussion

3.1. Data access
Medical images database consist of headers containing the information such as the patient sex and age, the type of radiography, the view and the size of voxels. The data itself is stored as a 3D matrix usually of single type. Each type of data has a different info structure. Matlab was used to access the data.

3.2. Segmentation
The resulting 3D data shows slices of images that can be visualized into different views (coronal, transversal or longitudinal). Since the cost is very important, we noticed that some of the upfront or down-front slices, spatially low positioned (below brain mass), show very low intensity values which leads to the choice of thresholding values that remove those slices in order to decrease the cost of the algorithms. Before segmenting the reduced slices, we noticed that the area of interest that corresponds to the most visible ventricle is located in the middle slices, which correspond to the transversal slices numbers beyond 40 and less than 200; figure 1, shows the grey view of the slices numbered from 121 to 135. In order to get the initial threshold value that segments the slices into different regions, we generate the histograms of the slices (grey level images). The histograms of the different slices (figure 2) show that the origin that corresponds to the extreme dark regions has a peak (many data) however; we ignored low level intensities because it is due to the background air, cerebrospinal fluid (CSF) and other soft tissues which correspond to the intensities 0 to 21. We also ignored the high level intensities that correspond to the skull and other hard tissues which correspond to the intensities above 1995 (table 1). The resulting preprocessed images are shown in figure 3 after ignoring the low and high intensities.
Figure 1. Grey view of the transversal middle slices (numbers 121 to 135)

Figure 2. Histograms of the transversal middle slices (numbers 121 to 135)
The first performed segmentation method was the Otsu global thresholding by selecting initial threshold level values using the histograms of figure 2 and performing an adaptive thresholding based on the iterative threshold and the in-between variances. The resulting image gives the entire area of the brain based on the intensity value (figure 4). The result could be used for selecting some markers as initial points to more sophisticated segmentation methods but is insufficient by itself. The Niblack adaptive (local) thresholding depends on the choice of the parameter $k$ and the size of the filter. Increased size values ($N \geq 11$) showed better results by using smoothing filters (figure 5).

The edge detection using Canny gave correct output edges with less noise compared to Marr-and-Hildreth or Sobel, the ventricle region is well detected and stable however some noise is introduced outside the region itself that must be thresholded a second time (figure 6). The active contour gave much better results (figure 7) than Canny's, however the initialization is not automatic and is based on the central slice. The cost has been reduced by initializing the edge to the same contour for every slice.

One of the best results has been given by the region growing algorithm, however the choice of the initial seed has to be more automatic and less prone to errors, the cost is 10 times bigger since the seed is chosen for every slide; figure 8 shows the resulting segmented image for a distance=0.01 and an initial seed point of coordinates $x=80$ and $y=85$. Finally the watershed method extracted the ventricle region but over-segmented the live tissue of the brain (figure 9).

To decrease the cost, we calculated the singular value decomposition (SVD) of each slice, with $n (= \text{rank}(\text{Slice})-5)$ as the number of decomposed images, the image is well reconstructed (figure 10) with an average error of $10^{-2}$.

Figure 3. Results of preprocessing after removing low and high intensities of the transversal middle slices (numbers 121 to 135)
**Figure 4.** Results of using global Otsu thresholding of the transversal middle slices (numbers 121 to 135)

**Table 1.** Cost (number of pixels) of removing low (less than the 21 intensity value) and high (above the 1995 intensity value) level intensities.

| Slice number | lower intensities | higher intensities |
|--------------|-------------------|--------------------|
| 121          | 228               | 404                |
| 122          | 227               | 369                |
| 123          | 209               | 381                |
| 124          | 223               | 336                |
| 125          | 229               | 371                |
| 126          | 203               | 398                |
| 127          | 234               | 407                |
| 128          | 210               | 434                |
| 129          | 229               | 357                |
| 130          | 229               | 308                |
| 131          | 217               | 285                |
| 132          | 193               | 276                |
| 133          | 212               | 286                |
| 134          | 241               | 275                |
| 135          | 219               | 243                |
Figure 5. Results of using Niblack local thresholding on the middle slice with different values of the coefficient $k$ and the size of the filter $N$, where $ULk$, $URk$, $BLk$ and $BRk$ correspond respectively to the $k$ value respectively for the upper left, upper right, bottom left and bottom right images.
Figure 6. Results of using Canny edge detector of the transversal middle slices (numbers 121 to 135)
**Figure 7.** Results of using the active contour of the transversal middle slices (numbers 121 to 135)

**Figure 8.** Segmentation of the middle slice using region growing method

**Figure 9.** Segmentation of the middle slice using Watershed method.

**Figure 10.** Singular value decomposition (SVD) of the middle slice
4. Conclusion

Image segmentation is very useful for MRI medical images, to detect regions of interest for radiotherapy planning and brain damage diagnostic. Several segmentation methods have been adapted and applied on 2D and 3D medical images. The developed algorithms have been tested on real medical data from OASIS database. The system was used to extract the ventricles from each slice, and these results were visually inspected and compared to the real images. Thresholding was applied to remove unnecessary regions and edge detection techniques in addition to region segmentations were used to extract the ventricles. Ongoing research is focusing on reducing the cost and improving the precision of the algorithms by using more intelligent algorithms including the SVD decomposition and more adaptive seeds initialization.

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