Chapter 2

Related Works

2.1 Introduction

The important forms of medical image analysis are segmentation, registration, reconstruction, classification, validation, visualization, interaction, simulation, etc. Out of these, image segmentation is the most popular technique. The methodologies used for the detection of brain tumors in this thesis are image segmentation and classification. Medical image segmentation means to divide an image into non-overlapping regions that belong to meaningful objects such as tissues, organs, anatomical structures, cell colonies and so on. Image segmentation is a fundamental process in several image processing and computer vision applications. Brain tumor detection has been a challenge in the field of brain computer-aided diagnosis. A large amount of research effort has been focused on the segmentation of images of the brain in MR images. Segmentation is an important process in most medical image classification and analysis for radiological evaluation or computer-aided [Dhawan 1990] diagnosis. It is the process of separating out mutually exclusive homogeneous regions of interest. The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze [Shapiro and Stockman 2001]. Image segmentation is typically used to locate objects and boundaries (lines, curves, etc.) in images.
The result of image segmentation is a set of segments that collectively cover the entire image, or a set of contours extracted from the image. Each of the pixels in a region is similar with respect to some characteristic or computed property, such as color, intensity, or texture. Adjacent regions are significantly different with respect to the same characteristic(s). This chapter provides a survey of many of the proposed approaches for automatic brain tumor segmentation in MR images. The first two types of methods we examine are unsupervised and supervised methods. These methods do not incorporate spatial registration. The difference between these two is that supervised methods make use of training data that has been manually labeled, while unsupervised methods do not. Figure 2.1 summarizes the main methods of image segmentations under study in this chapter.

2.2 Unsupervised segmentation

In unsupervised segmentation the computer selects natural groupings of pixels based on their spectral properties. An unsupervised classification algorithm still requires user interaction; however, these occur after the classification has been performed. In unsupervised classification the user attempts to assign information classes to the spectral classes the computer has created. Following are the main categories of unsupervised image segmentation:

2.2.1 Thresholding Techniques:

Thresholding [Gonzalez and Woods 1992; Jain et al. 1995] is the simplest image segmentation technique. In its simplest version an image is divided into two segments:
object and background by specifying a threshold. A pixel above the threshold is assigned
to one segment and a pixel below the threshold is assigned to the other segment. For more
sophisticated images multiple thresholds can be used.

2.3.2 Edge-based Techniques

In edge-based techniques [Gonzalez and Woods 1992; Jain et al. 1995; Kwok and
Constantinides 1997], segmentation is achieved by finding the edges of the regions.

2.2.3 Region growing Techniques

In region growing [Gonzalez and Woods 1992; Jain et al. 1995; Fuh et al. 2000], a
set of seed pixels are chosen. Neighboring pixels of a seed are agglomerated if they satisfy
a homogeneity criterion. This is repeated until no more pixels can be added to the region.
This approach has following problems [Turi 2001]:

- The selection of the seed pixels which is not a straightforward task.
- The selection of the homogeneity criterion.

Region splitting and merging divide the image into regions. A region is then split if it
does not satisfy a homogeneity condition. Regions can also be merged if their merging
results in a region that satisfies some condition. This is repeated until no more splitting and
merging can occur [Gonzalez and Woods 1992].
Fig. 2.1. Important methods of Medical Image Segmentation

An unsupervised approach for the segmentation of enhancing tumor pixels from T1-weighted post-contrast images was proposed by Gibbs et al. [1996]. This system first applied an intensity threshold to a manually selected region of interest and then used a region growing algorithm to expand the thresholded regions up to the edges defined by a Sobel edge detection filter. A similar approach was proposed by Zhu and Yan [1997] for the segmentation element of their enhancing tumor boundary detection approach. These methods represent a clearly justified approach for segmenting image objects that are different in intensity than their surroundings. A fully unsupervised approach for tumor segmentation was proposed by Ho et al. [2002]. This system used both the T1-weighted pre-contrast and the T1-weighted post-contrast images as input, and the first step in this system was the coregistration of these two volumes. Coregistration refers to the spatial alignment of two volumes that may not be of the same modality, but that represent a
(potentially unaligned) measurement of the same underlying object. After this alignment step, an image was computed that represented the difference between the T1-weighted images before and after the injection of the contrast agent. A Mixture Model was then applied to the histogram of this difference image. This method was not subject to many of the disadvantages of the earlier methods.

The advantages of this system are a) use of a Mixture Model allows the technique to adaptively find the enhancing area and is thus more robust to differences in intensity between images and b) non-enhancing areas surrounded by enhancing areas will be included in the segmentation through the use of the active contour. Some more systems based on the similar approach were presented by Yoon et al. [1999], Gosche et al. [1999], Fletcher-Heath et al. [2001] etc.

2.3 Supervised Segmentation

The classification problem formulation is a popular method to perform image segmentation using a supervised approach. The task in classification is to assign a class, from a finite set of classes, to an entity based on a set of features. Supervised classification involves a training phase that uses labeled data to learn a model that maps from features to labels, and a testing phase that is used to assign labels to unlabeled data based on the measured features. While many unsupervised approaches also use these two phases, the use of labeled data in the training phase of supervised approaches forces the model to focus on making discriminations in the feature space that correspond to the desired semantic discriminations.
Labels, as normal or tumor are used as classes in the segmentation task. The training phase under this formulation would consist of learning a model that uses the MR image intensities to discriminate between normal and tumor pixels. The testing phase would consist of the use of this model to classify unlabeled pixels into one of the two classes based on their intensities. A major advantage of using a supervised formulation is that supervised methods can perform different tasks simply by changing the training set. The supervised approaches that have been used in medical imaging include kNN, Artificial Neural Networks (ANN), Maximum Likelihood classifier (ML), Decision Tree Classifier, Support Vector Machines (SVM) etc. Figure 2.2 shows the basic outline of a supervised learning framework.

A comparison between Maximum Likelihood (ML) and Artificial Neural Network (ANN) was done by Clarke [1991] for brain tumor segmentation in MR images. It was found that the ANN performed better than the ML approach. Training ML classifiers consists of optimizing the parameters of an assumed model of the features (often assuming a parametric model such a univariate or multivariate Gaussian) and assigning pixels to the class that they are statistically most likely to belong to, based on these models. On the other hand, ANN approaches ‘feed’ the features through a series of nodes, where mathematical operations are applied to the input values at each node and a classification is made at the final output nodes.
**Fig.2.2.** Supervised Learning Framework: In the training phase labeled data is used to make a model for classification, whereas in testing phase this model is used to predict labels of unlabelled images.

**Fig.2.3.** Architecture of a Neural Network: Multi-spectral intensities represent the input to this network, linear combinations of the intensities, the output node values are formed from linear combinations of the results of the hidden layer transformations.

Figure 2.3 shows the overall architecture of ANN. Training for these models consists of determining the values of the parameters for the mathematical operations such
that the error in the predictions made by the output nodes is minimized. ANN approaches are non-parametric techniques and, with the use of ‘hidden’ layers of nodes, allow the modeling of non-linear dependencies in the features. In another system developed by Ozkan et al. [1993] pixel intensities were used in the different channels and patient-specific training was done. This work also confirmed that Neural Networks outperformed Maximum Likelihood methods.

In a different work by Schad et al. [1993] a Decision Tree classifier was used based on first-order and second-order texture features, that is statistical moments and spatial co-occurrence features, respectively. Decision Trees are a popular classification technique due to their ability to model non-linear dependencies in the features, and their intuitive graphical representation of the learned model (as opposed to, for example, ANNs). Decision Trees perform classification by making a set of decisions based on the features, beginning from a root ‘node’ and following decision made to other nodes in the tree where new decisions are made, leading finally to a ‘leaf’ where a classification is made. There are many methods of automatic Decision Tree learning, including the popular C4.5 classifier [Quinlan, 1993].

Vinitski et al. [1997] also presented a supervised method that addressed several issues previously ignored in most automatic systems for tumor segmentation. This method used several preprocessing steps before the classification in order to improve results. These steps were step coregistration, anisotropic diffusion filter and intensity inhomogeneity correction. The classifier used was a k-Nearest Neighbors (kNN) classifier, that assigns labels to pixels based on the most frequent label among the k closest training points under
a distance metric applied to the features (referred to as ‘lazy’ learning, since no explicit model is learned). The kNN algorithm is a simple and effective method for multi-class classification that is able to model non-linear distributions. Disadvantages of the kNN algorithm include the dependence on the parameter k, large storage requirements (the model consists of all training points), sensitivity to noise in the training data, and the undesirable behavior that can occur in cases where a class is underrepresented in the training data.

To overcome the need of patient-specific training in supervised methods, a method was proposed by Dickson and Thomas [1997] which used a set of 50 hand-labeled MR slices from the same area of the head of different patients with brain tumors, and learned to automatically label this without patient specific training. The features used in this system included not only the pixel intensities, but the intensities of neighboring pixels and the pixel’s location within the image. This work compared the use of a kNN classifier, a Learning Vector Quantization (LVQ) classifier, and an ANN. The comparative studies done in this work have provided valuable insights into the problem. These results indicated that a) the ANN outperformed the other two methods, b) pixel neighborhood intensities increase classification performance, c) the combination of intensity and texture information performed better than either individually, and d) 1 hidden layer in the network topology outperformed 0 or 2 hidden layers. After pixel classification with the ANN, this system performed an unsupervised segmentation to divide the image into homogeneous regions. These regions were assigned a label based on the results of the classifier, and were
processed with morphological operations. A second ANN was used to determine whether the resulting regions represented tumors based on a feature set.

One more method was presented by [Busch, 1997] that did not require patient-specific training. This work focused on the segmentation of a specific type of non-enhancing homogeneous tumor (low-grade astrocytomas) from T1-weighted, T2-weighted, and coregistered CT (X-ray) images. Recently, a method was proposed by Zhang et al. [2004] for automatic tumor segmentation in MR images. This approach used Support Vector Machines (SVMs), which are currently an extremely popular method for performing binary classification.

In addition to the supervised learning methods discussed above, many methods have been proposed that use Supervised Segmentation with Advanced Image Modalities. The advantages of these methods are that they may facilitate an easier automatic segmentation task and that they may more appropriately characterize the extent of the tumor infiltration. The disadvantages of these approaches are that they require additional acquisition time and that the additional modalities are not available for historical data. A method to segment tumors was evaluated by Soltanian-Zadeh et al. [1998]. The system presented to segment this large combination of images used patient specific training, and consisted of coregistration, brain masking, anisotropic filtering, intensity non-uniformity correction, and finally an eigenimage analysis.
2.4 Registration-Based Segmentation

Registration-based methods, also known as atlas based method make use of a segmented image (deformable atlas) which is elastically warped to a new image and tissue labels are simply transferred. A deformable atlas is usually obtained using one or several manual segmentations. The main advantage of these methods is possibility to propagate any brain structure available in the atlas without any additional cost.

The aim of registration of image X to image Y is to find a transformation which maps any point x in image X to its corresponding point y in image Y. First, the global 12-parameter affine transformation $A(X \rightarrow Y)$ is calculated to perform translation, rotation, scaling and skewing so that the best possible alignment of the images is achieved [Hajnal et al. 2001]. Affine registration is often not sufficient due to natural variability in shape and size of normal healthy brains. One of the ways to model the local component is using uniform tensor-product 3D cubic B-splines [Rueckert et al. 1999]. During the iteration step in both affine and non-rigid registration, Normalized Mutual Information NMI [Studholme et al. 1998] is used as the similarity metric of the two images, given as follows:

$$NMI(X,Y) = \frac{H(X) + H(Y)}{H(X,Y)}$$

where, $H()$ denotes the entropy of normalized image histogram. A cost function consisting of similarity term and in case of B-spline registration also of regularization term to ensure smoothness is then minimized using gradient descent. The B-spline registration is performed in multi-resolution framework. The resolution is refined by halving the spacing
between the B-spline control points and consequently inserting new B-spline control points. Affine registration is always performed before B-spline registration so we can write

\[ N_{X \rightarrow R}(X) = A_{X \rightarrow R}(X) + B_{X \rightarrow R}(X) \]  

(2.1)

Let \( R \) be the reference image and \( M \) corresponding manual segmentation of image \( R \). A new image \( I \) can be segmented by transferring the manual segmentation using non-rigid registration. Let \( \text{Seg}_{\text{m}}(I) \) denote registration-based segmentation of \( I \). Then,

\[ \text{Seg}_{\text{m}}(I) = N_{R \rightarrow I}(M) \]  

(2.2)

where, transformation of the image means that the transformation is applied to every pixel of the image. Segmentation approaches based on this idea typically first align a labeled template (or atlas) image with the image to be segmented, and infer the labels for the new image by assuming that they correspond to the labels of the aligned template.

The advantage of this type of method is that spatial information is encoded through the use of the template, as opposed to pixel classification based methods that encode limited spatial information. The major disadvantage of this method is that the registration may not be perfect, and that there may be anatomical differences between the template and the image to be segmented. These disadvantages make template registration methods inappropriate to apply directly for tumor segmentation, since the template does not have a tumor, nor is its anatomy affected by the presence of a tumor. However, the ability to use spatial information derived from the spatial alignment of a template is appealing, and there has been considerable recent effort focusing on the incorporation of template registration into methods for tumor segmentation.
The major work using this approach include those of Kaus et al. (2001). This model is shown in Figure 2.3. They employed a kNN classification algorithm with patient-specific training, used a label-based registration algorithm based on principles of optical flow, and preprocessed images with an anisotropic diffusion filter before analysis. After preprocessing, the segmentation consisted of performing kNN classifications.

![Diagram of tumor segmentation scheme](image)

**Fig.2.4.** Diagram of the tumor segmentation scheme proposed by [Kaus et al. 2001]

Gering [2003] proposed a system that used template registration in segmentation. This method used a database of normal brains as training data. Each normal brain would be registered with the image to be segmented, and a simple multi-resolution statistic would be computed for each pixel to determine how significantly it differed from the most similar normal brain at that location. One of its limitations is that it does not account for the intensity non-standardization effects that would be present in a large database of normal brains, while another weakness is the lack of availability of a database of completely normal brains. In a hybrid approach, Murgasova et al. [2006] combined intensity based
and registration based approaches to obtain a robust segmentation method which is successfully used on healthy and diseased brain MRI of 2-year-old children.

2.5 EM-based segmentation

The expectation-maximization algorithm (EM) [Dempster et al. 1977] is a general technique for finding missing data based on observed data and maximum likelihood parameters estimates. [Leemput et al. 1999a] presented a model in which observed data are the image intensities, the missing data are the labels and the parameters are the means and variances of the Gaussian distribution which is assumed for the intensity distribution of each tissue class. This is an iterative process which interleaves the calculation of posterior probabilities of each voxel belonging to each tissue class (usually white matter, gray matter, cerebrospinal fluid, other) - the expectation step, with maximum likelihood estimation of the Gaussian distribution parameters the maximization step.

For the task of segmenting head MR images into the three normal brain classes (gray matter, white matter, and cerebrospinal fluid), Expectation Maximization approaches have become a popular framework, since they have shown to be robust to both intensity inhomogeneity and intensity non-standardization. Wells et al. [1996] was the first group to formulate the task of normal brain segmentation as an Expectation Maximization problem. Some other works using this approach are those by Leemput et al. [1999a, 1999b], Evans and Collins [1993] etc.
2.6 Image Segmentation using Clustering

In one more category of unsupervised methods, rather than dividing the image along anatomically meaningful distinctions, images are divided into homogeneous regions using image-based features such as intensities and/or textures. Clustering is one method to this. The main disadvantages of this approach are a) the number of regions often needs to be pre-specified, b) tumors can be divided into multiple regions, and c) tumors may not have clearly defined intensity or textural boundaries. These disadvantages limit the use of this approach. Some significant works done using these methods are by Capelle et al. [2000] and Sammouda et al. [1996].

Image segmentation can be treated as a clustering problem where features describing each pixel correspond to a pattern and an image region (i.e. segment) corresponds to a cluster [Jain et al. 1999]. It can be inferred from the definitions of the clustering problem and the image segmentation problem that both the problems are similar in nature. Therefore, clustering algorithms have been widely used to solve the problem of image segmentation (e.g. K-Means [Tou and Gonzalez 1974], FCM [Trivedi and Bezdek 1986], ISODATA [Tou and Gonzalez 1974] etc. But since the number of clusters is usually not known a priori in image segmentation, clustering algorithms that do not require the user to specify the number of clusters are usually preferred.

In this thesis, the clustering problem and the image segmentation problem are considered to be similar. Thus, algorithms are proposed for both problems interchangeably. Image segmentation is a fundamental process in several image processing and computer
vision applications. It can be considered as the first low-level processing step in image processing and pattern recognition [Cheng et al. 2001]. Image segmentation is defined as the process of dividing an image into disjoint homogenous regions. These homogenous regions should represent objects or parts of them [Lucchese and Mitra 2001]. The homogeneity of the regions is measured using some image property (e.g. pixel intensity) [Jain et al. 1999]. Image segmentation can be formally defined as follows:

Given an image \( I \) and a homogeneity predicate \( P \). The segmentation of image \( I \) is the partitioning of \( I \) into \( K \) regions, \( \{R_1, R_2, \ldots, R_K\} \), satisfying the following conditions:

- Each pixel in the image should be assigned to a region.
- Each pixel is assigned to one and only one region.
- Each region satisfies homogeneity predicate \( P \).
- Two different regions cannot satisfy the same predicate \( P \).

In this work, the various classification techniques used for the detection of anomalies in brain MRI are a) Hybrid of Genetic Algorithms and Artificial Neural Networks b) Adaboost c) Support Vector Machine. As the research interest of this work is to explore the applicability of Particle Swarm Optimization, in chapter 6 the same has been used for a) segmentation using clustering and b) optimization of feature sets to be input to existing classifier such as KNN and clustering algorithm K-Means. The supervised classification stage has two components, a training phase and a testing phase. In the training phase, pixel features and their corresponding manual labels represent the input, and the output is a model that uses the features to predict the corresponding label.
2.7 Conclusion

Several methods of segmentation of brain tumors were discussed. These included supervised and unsupervised methods, registration and EM based methods. Advantages and limitations of all the approaches were presented. It can be concluded that the current state of the art methods for automatic brain tumor segmentation are Expectation Maximization approaches that use outlier detection due to the robustness to intensity non-standardization, along with the registration-based method of [Kaus et al., 2001], due to the use of non-linear registration and the more extensive use of spatial information to enhance discrimination and the neural network based methods of [Dickson and Thomas, 1997; Busch, 1997], due to the use of textural information and more powerful classification techniques. Many methods make use of two or more of the previously discussed approaches. These are termed as Hybrid methods, which has been used in the upcoming chapters. In this work, the use of textural and spatial information has been integrated with some classification techniques which have not yet been used in brain tumor segmentation. Particle Swarm Optimization is one such method. Other methods include Support Vector Machine, kNN, $K$-Means, Genetic Algorithms etc.