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Automatic segmentation of magnetic resonance images of the brain

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AUTOMATIC SEGMENTATION OF MAGNETIC RESONANCE IMAGES OF THE BRAIN

A Dissertation

Submitted to the Graduate Faculty of the Louisiana State University and Agricultural and Mechanical College in partial fulfillment of the requirements for the degree of Doctor of Philosophy

In

The Department of Computer Science

by

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B.Sc., University of the West Indies (Mona), 1989
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May 2005
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In loving memory of

Monica Eloise Hemmings (Mama),

Thelma Gloria Henriques (Aunt G)

&

Kenneth Henriques (Daddy)
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ABSTRACT

Magnetic resonance imaging (MRI) is a technique used primarily in medical settings to produce high quality images of the human body’s internal anatomy. Each image is of a thin slice through the body, with the typical distance between slices being a few millimeters. Brain segmentation is the delineation of one or more anatomical structures within images of the brain. It promotes greater understanding of spatial relationships to aid in such tasks as surgical planning and clinical diagnoses, particularly when the segmented outlines from each image slice are displayed together as a surface in three-dimensions.

A review of the literature indicates that current brain segmentation methods require a trained human expert to inspect the images and decide appropriate parameters, thresholds, or regions of interest to achieve the proper segmentation. This is a tedious time-consuming task because of the large number of images involved. A truly automatic method is needed to transform brain segmentation into a practical clinical tool.

This dissertation describes a novel pattern classification approach to the problem of automatically segmenting magnetic resonance images of the brain. Based on this approach, algorithms were designed and implemented to automatically segment a number of anatomical structures. These algorithms were applied to several standard image data sets of human subjects obtained from the Internet Brain Segmentation Repository (IBSR). The resulting segmentations of the lateral ventricles and the caudate nuclei were compared to reference manual segmentations done by expert radiologists. The Tanimoto similarity coefficient was very good for the lateral ventricles (0.81) and good for the caudate nuclei (0.67).
1 INTRODUCTION

Brain segmentation is the delineation of neuro-anatomical structures within medical images of the head. For example, an outline of the left lateral ventricle might be drawn on the original images to indicate its extent, with a label placed nearby to identify the structure.

Brain segmentation research has increased in importance over the last decade due in part to funding from the US government’s Human Brain Project initiative. The Human Brain Project was announced in the NIH Guide in 1993 and is sponsored by fifteen federal organizations across four federal agencies. Its goal is to produce an internet-based information management system to be used by neuroscientists, behavioral scientists, clinicians and educators, in a quest to foster greater understanding of the brain’s structure, function, and development. Researchers in this broad-based initiative include neuroscientists, computer scientists, engineers, physicists, radiologists, and mathematicians, collaborating to develop the necessary neurological databases and tools. These tools provide graphical interfaces, querying and data mining, information retrieval, data analysis, visualization and manipulation, software integration, biological modeling and simulation, and electronic collaboration.

Brain segmentation is an important preliminary step in registering different image data sets, such as an MRI and a PET scan of the same patient. The brain segmentation step locates corresponding landmarks so that a geometric transformation can be created that will bring the image data sets into alignment. In elastic registration, the images of an individual are regionally deformed (or “warped”) to match those of another individual or reference atlas.

Brain segmentation is used in research to characterize neurological diseases such as multiple sclerosis [Meier 2003][Quarantelli 2003], schizophrenia [Rujescu 2002], Alzheimer’s disease [Baron 2001][Scheltens 1992][Seab 1988], and others [Jack 1990][Duara 1991][Hynd...
1990, 1991]. Accurate brain segmentation provides volume measurements that can detect the onset of degenerative diseases and also monitor the effectiveness of their treatment regimen [Dumoulin 2003] [Bonilha 2004]. At neighboring Tulane University, A.L. Foundas M.D. takes volumetric measurements of brain regions and correlates those measurements with various diseases [Foundas 1996, 1998, 2001a, 2001b]. In such research, an expert manually locates the anatomical landmarks that define the boundaries of the volume to be measured. This is a tedious task for which an automatic brain segmentation algorithm is desired. By eliminating the tedious work and the need for an expert, an accurate automatic brain segmentation algorithm would allow the migration of the research findings into a clinically acceptable tool that diagnoses diseases from volumetric measurements.

Another important future application for automatic brain segmentation is computer-aided diagnoses. A brain segmentation algorithm could be used to recognize pathologies, such as tumors, by first eliminating the recognizable neuro-anatomical structures. Any remaining unrecognized feature is likely to be pathological. Furthermore, the algorithm could also be used in determining the particular disease from a set of differential diagnoses. Medical textbooks contain differential diagnoses – essentially, “disease-determining” algorithms, which conceivably can be converted into computer programs. These differential diagnoses generally require knowledge of the position of any pathology. Location is very important because the evolution of the disease, its cause, and the available treatment options depend on the affected anatomical structure in which the pathology lies. A differential diagnosis computer program could use a brain segmentation algorithm to identify the surrounding anatomical structure.

This dissertation documents a novel approach to the automatic segmentation of the brain in Magnetic Resonance (MR) images. The approach combines pattern classification and
computational geometry to identify the iso-intense contours that delineate the anatomical structure being segmented. A review of the literature found several semi-automated brain segmentation algorithms, that is, algorithms requiring a user’s input to decide image-specific parameters, thresholds, or regions of interest. However, no truly automatic brain segmentation algorithm was found in the literature, so the completely automatic techniques proposed in this dissertation might be the seeds for further research.

1.1 **NEURO-ANATOMY**

The brain is composed primarily of neurons, with each neuron having a cell body and a long cylindrical axon as illustrated in Figure 1-1. The axon is usually covered with a white lipid sheath, whereas the cell body is uncovered and so appears gray. Signals travel electrically along the axon in one direction only – away from the cell body – and may then be transferred chemically from the end of the axon to the cell bodies of other neurons. Signal connections between neurons are never made along the length of an axon.

![Figure 1-1: A neuron connected to other neurons](image)

Brain tissue is divided into gray matter and white matter because of visual appearances, but there is a deeper significance. Gray matter regions are gray because of the high concentration of cell bodies, and are therefore sites of high neuronal connections and
computational activity. White matter regions are white because of the high concentration of axons, and are therefore major signal pathways. Both tissue types are organized into anatomical structures that are recognizable across individuals. Size and shape may vary a little, but each structure is generally present in roughly the same location and performs the same function. The brain also contains recognizable cavities that are filled with cerebrospinal fluid (CSF). Although liquid, CSF is often considered a third type of brain tissue in the segmentation literature because of its significant presence. It must be noted that a pixel in an MR image represents the signal from a small volume, which might contain more than one type of tissue if the small volume element (voxel) lies on the border of different tissue types. The average signal from such a partial volume (PV) voxel may not even be representative of any of the tissues involved. These PV voxels are usually problematic for many segmentation techniques.

The only practical way to get a good view of inside the brain is to slice it, so three-dimensional anatomical structures are traditionally displayed in two-dimensional cross-sections. Interpreting the contents of an individual cross-section, as displayed by an MR image, is difficult without prior knowledge of the three-dimensional shape and location of the brain’s internal anatomical structures [Brinkley 1997]. A physician will scan back and forth through a set of MR images (Figure 1-3) to create a three-dimensional mental picture like Figure 1-2.

![Figure 1-2: 3D view of some anatomical structures in the human brain [Sundsten 1994]](image-url)
Each pixel within an MR image represents the magnitude of an electromagnetic signal emitted from a small volume of space. One must understand the nature of this signal to understand the wide variety of MR images and the type of errors to be expected.

The source of the electromagnetic signal is the hydrogen nuclei that are abundantly present within the human body as water and fat molecules. Like all subatomic particles, the hydrogen nucleus possesses a quantum mechanical property called “spin”. The spin $j$ of a hydrogen nucleus has two possible values, either $+1/2$ or $-1/2$. The hydrogen nucleus also possesses an angular momentum $\mathbf{a} = j\hbar/2\pi$, just like rotating bodies. It also possesses a small electrical charge and, like actual rotating charges, the hydrogen nucleus generates a small magnetic moment $\mu$ along its spin axis. The constant ratio $\mu/\mathbf{a}$ is called the gyro-magnetic ratio $\gamma$. If a hydrogen nucleus is placed in a strong magnetic field $\mathbf{B}_0$, its tiny magnetic moment will either be parallel with the direction of $\mathbf{B}_0$ or anti-parallel with it, corresponding to spin
values of \( +1/2 \) (up) or \( -1/2 \) (down). Less energy is required for alignment with the magnetic field than against it. By convention, the direction of \( B_0 \) is considered to be along the \( z \)-axis.

A small volume of space, such as that represented by a pixel within an MR image, can contain a large number of hydrogen nuclei. The individual spins within a large ensemble of hydrogen nuclei will be randomly up or down. In the absence of a magnetic field, there will be equal numbers of both spin states so that the overall magnetic moment will be zero. If the strong magnetic field \( B_0 \) is now applied, the proportion of up spins will increase. Consequently, the resultant magnetic moment of the ensemble will increase gradually from zero until a thermal equilibrium is reached. Likewise, the resultant angular momentum of the ensemble increases from zero to an equilibrium value. The ensemble therefore possesses both a magnetic moment and an angular momentum, like a gigantic hydrogen nucleus. However, unlike a hydrogen nucleus, the direction of the ensemble’s magnetic moment is not restricted to only two states, so an ensemble is like a spinning top with a magnet through its rotational axis. Like a top, the ensemble can be manipulated into displaying the peculiar wobbling motion called precession.

If the magnetic moment of the ensemble is somehow displaced at an angle to \( B_0 \), it will eventually realign itself with \( B_0 \), much like a compass needle realigning itself with the earth’s magnetic field. However, instead of taking a direct path, the magnetic moment describes a cone about the direction of \( B_0 \) because of the angular momentum. A spinning top also displays this wobbling motion for the same reason. The natural frequency of precession, the Larmor frequency \( f_0 \), is proportional to the magnitude of \( B_0 \) and is given by the equation

\[
f_0 = \left(\gamma / 2\pi\right) B_0.
\]

Gradually, the conical angle decreases until the magnetic moment is again aligned with \( B_0 \). It is the precession of the ensemble’s magnetic moment that generates the
electromagnetic signal measured by MR equipment. Figure 1-4 illustrates the steps leading to precession. As the precession subsides, the signal strength decays in a manner characteristic of the tissue type. The relative strength of the signal over time is governed by three characteristic values for the tissue – the proton density, the T1 relaxation time, and the T2 relaxation time.

Proton density (PD) is the number of mobile hydrogen nuclei per unit volume. For example, cerebrospinal fluid (CSF), being practically pure water, has the highest proton density. PD is directly proportional to the magnitude of the magnetic moment $M_0$ at the thermal equilibrium temperature $T$, according to the equation

$$M_0 = PD \left( \frac{\mu^2}{kT} \right) B_0$$

T1 is the time it takes for the $z$ component of the magnetic moment, $M_z$, to go from zero to sixty-three percent of the equilibrium value, $M_0$, according to the equation

$$M_z(t) = M_0 \{1 - \exp\left(-t/T1\right)\}$$

T2 is the time it takes for the transverse component of the magnetic moment, $M_{xy}$, to drop to thirty-seven percent of its initial value according to the equation

$$M_{xy}(t) = M_0 \exp\left(-t/T2\right)$$

Figure 1-4: A Magnetic Field $B_0$ induces a magnetic field $M_0$ in the ensemble (left). $M_0$ is forced $90^\circ$ from its equilibrium position and begins precession (center). The vertical $M_z$ and horizontal $M_{xy}$ components change as precession decays (right).
Each type of tissue has characteristic values for PD, T1, and T2 [Bottomley 1984]. There are many kinds of MR images, with each being optimal in contrasting particular tissue types. A physician gets better information by examining several kinds of MR images. Three commonly encountered kinds of MR images are PD-weighted, T1-weighted, and T2-weighted images (Figure 1-5).

![Figure 1-5: PD-weighted (left), T1-weighted (center) and T2-weighted (right) images showing the different contrast and relative intensities for tissues in the head](image)

### 1.3 PACS

A picture archiving and communication system (PACS) stores and distributes digital images received from a wide variety of medical imaging systems such as MRI, computed tomography, ultrasound, and mammography systems. PACS technology was introduced in the mid 1980s to replace the more cumbersome and costly analog film technology. Being digital, the images stored by a PACS can be processed readily with increasingly sophisticated software tools. Over time, the integration of these software tools has broadened the scope and increased the effectiveness of PACS. Tools for aiding manual segmentation of medical images are now standard in most modern PACS.
As time passes, the resolution of imaging technologies improves, the technologies proliferate, and the cost to the patient goes down. All of these factors have lead to the huge increase in the number of images that the medical professional must handle. Segmentation reduces this vast amount of information and allows the radiologist to view an easy to understand graphical surface of a three-dimensional anatomical structure. Unfortunately, even with good software tools, manual segmentation is still time-consuming.

The PACS market includes full-featured systems such as the commercial BIRPacs from the Mayo Clinic and the non-commercial CDMEDIC PACS from the Open Source Technology Group. There are also several excellent standalone medical imaging programs such as the freely available AMIDE [Loening 2003]. [Shattuck 2002] describes BrainSuite, an image analysis tool that produces cortical surface representations with spherical topology from MR images of the human brain. BrainSuite provides tools for skull and scalp removal, image non-uniformity compensation, voxel-based tissue classification, topological correction, rendering, and editing functions. A new product that includes reliable automatic segmentation software will differentiate itself in the market and be of significant benefit to the radiologist and others.

1.4 IMAGE SEGMENTATION TECHNIQUES

A review of the literature yields a wide range of brain segmentation algorithms. Some of the techniques used in these algorithms will be described.

1.4.1 THRESHOLDING

Segmentation methods based on thresholding attempt to determine intensity values, called thresholds, which separate the pixels’ intensities into ranges that correspond to the tissue types. One approach to determining an appropriate threshold value is to iteratively try each possible value and evaluate its resulting segmentation for features that indicate the segmentation
is satisfactory. [Lee 1998] and [Suzuki 1991] both use this approach. Another approach to determining appropriate threshold values is to examine the image’s histogram of pixel intensities. Since each tissue type has a characteristic MR signal intensity as shown by [Bottomley 1984], it is assumed that the histogram of pixel intensities should display a discernable peak for each tissue type, with the valleys between these peaks occurring at the desired thresholds. The problem of segmenting the brain into tissue types is therefore transformed into the presumably simpler problem of finding peaks in a histogram. For example, [Momenan 1997] uses the K-means nonparametric clustering algorithm to partition the histogram of each image into K peaks (e.g., into 2 peaks corresponding to CSF and brain). The algorithm iteratively adjusts each cluster’s central intensity value to minimize the sum-of-squared difference between each pixel in the cluster and the central intensity value, and adjusts the membership of pixels in each cluster according to this new central intensity value. The algorithm repeats until there is no change in the clusters. A different approach used by [Shan 2002] and [Kovacevic 2002] is to fit Gaussian distributions to the intensity histogram. [Shan 2002] uses the Levenberg-Marquardt method of [Marquardt 1963] to fit an equation consisting of three Gaussian distributions. This equation of nine parameters is

\[ N(I) = \sum_{k=1}^{3} N_k^{(p)} \exp \left[ -\frac{1}{2} \left( \frac{I - \mu_k}{\sigma_k} \right)^2 \right] \]  

where \( I \) is image intensity and \( N(I) \) is the number of pixels at intensity value \( I \). [Kovacevic 2002] uses the Expectation Maximization (EM) algorithm of [Hartley 1958] to fit four Gaussians. Other examples of brain segmentation by using peak detection in histograms are to be found in [O’Donell 1986] and [Worth 1997]. Instead of explicitly searching for peaks in the histogram, a simpler approach is to assume the relative position of the peaks. [Suzuki 1991] uses the 70th percentile point of the image’s
histogram as the upper range of the peak for air, since the black air background is usually about seventy percent of an image’s area.

Except for the peak corresponding to the background air, the peaks in the histogram for a typical MR image are generally not well defined (see figure 1-6). Random noise broadens the peaks while simultaneously reducing their height. Non-brain tissues, such as muscle, are also present in every image and have a broad range of intensity values that overlap that of brain tissues. Even brain tissues have a broad range of intensity values, since gray and white matter are both composed of cell bodies and axons, but in different proportions that can vary widely. Partial volume pixels also contribute significantly to the poor definition of peaks, but their effect can be reduced if pixels within regions of high intensity changes are not included in the histogram as done in [Worth 1998]. Even if the peaks can be discerned, the overlapping region between peaks usually shows no clear division to set a definite threshold. The most fundamental limitation of histogram methods in image segmentation is described by [Jain 1995] as follows:

“The most basic limitation of the histogram-based approaches is due to the fact that a histogram throws away spatial information about the intensity values in an image. The histogram describes the global intensity distribution. Several images with very different spatial distributions of gray values may have similar histograms. For example, one cannot distinguish between a random distribution of black and white points, a binary checkerboard, and an image that is half black and half white just on the basis of their histograms. The global nature of a histogram limits its applicability to complex scenes. It does not exploit the important fact that points from the same object are usually spatially close due to surface coherence.” [Jain 1995, page 86]
1.4.2 Clustering

When a patient undergoes an MR exam, several kinds of MR images are normally acquired simultaneously. Multi-spectral techniques combine the pixel intensity information from these different kinds of images, so that each “pixel” has an ordered set of intensities instead of just one. For example, [Li 1993] combines PD-weighted, T1-weighted, and T2-weighted images of a patient. A point is plotted for each “pixel” in a three-dimensional (PD, T1, T2)-intensity space. A clustering algorithm then finds clusters of points in this space – equivalent to finding intensity peaks in a one-dimensional histogram. Each “pixel” cluster is assumed to belong to only one type of tissue, but since the clustering algorithm over-segments by finding ten clusters,
one type of tissue is composed of a few clusters. Further knowledge-based classification rules are then applied to associate the clusters to the appropriate tissue.

### 1.4.3 Deformable Surface Models

Segmentation methods based on deformable surface models pose segmentation as an optimization problem. A large number of deformable models are derived from “Snakes” as originally described in [Kass 1987]. Deformable surface segmentation methods start with an approximate boundary and deform this initial boundary into a better fit around the anatomical structure. This initial boundary is modeled as a physical object subject to internal forces such as elasticity and bending moments that promote smoothness in the boundary, and to external forces from the image data such as intensity gradients that promote a close fit to the anatomical structure. Finding the final boundary configuration is reduced to a physics problem in energy minimization while simultaneously balancing the internal and external forces. [Davatzikos 1995] uses a deformable boundary technique in which the boundary has a thickness, much like the brain’s cortical surface that it represents. The final result is found to be sensitive to a user determined constant, which must be chosen carefully.

Like most optimization problems, deformable boundary techniques need the initial guess to be reasonably close to the true solution to avoid being trapped in a local minimum. Choosing the initial boundary, whether automatically or manually, can be a non-trivial problem. To find a suitable initial boundary, [Chakraborty 1996] first performs an intensity-based segmentation to get regions of similar pixel intensities. The border around one of these regions then becomes the initial boundary for the deformable boundary segmentation that follows. [Smith 2002] first performs an intensity-based segmentation to get a rough head/background separation. The center-of-gravity of the head region and its approximate size is then found and used to generate
the initial boundary, a triangular tessellation of a sphere’s surface, inside the brain. This surface is allowed to deform one vertex at a time by following forces that keep the surface smooth and the vertices well spaced in a gradual expansion towards the brain’s true surface.

1.4.4 ATLAS-BASED SEGMENTATION

Atlas-based segmentation methods compute an anatomically correct coordinate transformation, i.e. a registration, between the image to be segmented and an already segmented atlas image. This coordinate transformation is then used to map the desired segmented region from the atlas onto the image, thereby segmenting the image, since the location and extent of anatomic structures in the target image is assumed to be the same as that in the transformed atlas. Registration often begins with finding anatomical landmarks in the image to be segmented. The transformation that maps between these landmarks and the identical landmarks in the atlas is used to map the remainder of the image. For example, [Cuadra 2001] starts with identifying the cortical surface and ventricular system in the image, and then applies a global affine transformation between the image and a digital atlas from the Harvard Medical School described in [Kikinis 1996]. Local non-rigid deformations are then used to get a better match. Another approach to registration is to maximize the intensity similarity between both images, without any need for finding landmarks. [D’Agostino 2003] uses this approach in which an image is modeled as a viscous fluid deforming under the influence of forces derived from differences between the images until the best match between their pixel intensities is found. [Rohlfing 2004] describes and evaluates four different ways of using an atlas in brain segmentation of bees – registration to an individual atlas image, registration to an average-shape atlas image, registration to the most similar atlas image, and registration to all images with subsequent decision fusion.
The most well-known brain atlases are the printed books by Schaltenbrand and Wahren [Schaltenbrand 1977] and Talairach and Tournoux [Talairach 1988]. These consist of two-dimensional photographs of slices through the brain and, being on paper, are unsuitable for atlas-based segmentation, but they are the acknowledged foundation of today’s digital atlases. For example, [Ganser 2004] develops a digital version of the Talairach and Tournoux atlas. The advantages of a digital atlas over a paper atlas are that it allows three-dimensional representations, it can be warped to match an image data set, and it can easily integrate new sources of neuro-anatomical knowledge.

1.4.5 SHAPE-BASED SEGMENTATION

An interesting approach to brain segmentation is to use the general shape of the anatomical structure as the primary means for precisely locating it within the image. For example, [Hinshaw 2002] uses a semi-automated shape-based segmentation method for a skull-stripping step. The method takes advantage of the brain’s round shape. In this method, equally spaced radial lines are drawn emanating from a central point within the brain. On one of these lines, the user manually selects the point where the line crosses the brain’s surface. The algorithm then automatically locates where the other radial lines cross the surface of the brain. Since the brain is somewhat round in shape, the distance from center to surface is roughly the same for adjacent radial lines. The algorithm therefore searches along each radial line for an intersecting edge such that the distance of the intersection from the center is roughly the same as the previously determined surface-to-center distance for an adjacent radial line. Since more than one edge might meet this criterion, the most likely candidate edge is selected by additional criteria, such as its intensity gradient. Having found where the brain’s surface intersects all the radial lines, the algorithm removes everything outside of the polygon formed by these
intersection points. This model for representing shape is called the Radial Surface Model (RSM). It is a specific example of the more general Geometric Constraint Network (GCN) described in [Brinkley 1992]. Another model for representing shape is described by [Davies 2002] in which a vector of points \( x_i \) sampled from the boundary of the \( i^{th} \) shape, is expressed using a linear model \( x_i = \bar{x} + P \cdot b_i = \bar{x} + \sum_m p^m b_i^m \) where \( \bar{x} \) is the mean shape vector, \( P = \{p^m\} \) are the eigenvectors of the covariance matrix that describe a set of orthogonal modes of shape variation, and \( b = \{b^m\} \) are shape parameters that control the modes of variation.

1.4.6 Watershed Segmentation

The watershed segmentation algorithm is best understood by considering an image as a topographical surface in which height represents intensity. Within this intensity surface, the algorithm finds crest lines, like the rim of a volcano, that separate valley regions. These segmented valley regions are considered to be distinct objects in the image. The watershed algorithm can also be used to segment hill regions because a hill is nothing more than an inverted valley. [Caron 1996] gives a good explanation of how the watershed algorithm works as follows:

“Every edge is enhanced and is seen as an intensity crestline. The watershed transformation finds these crestlines by flooding simulations. The concept stems from the analogy between an image and a topographic surface. We assume that holes have been punched through every minimum of the surface. The surface is then slowly immersed. Starting from the minima at the lowest altitude, the water will flood the catchment basin of each minimum in the image. As the flooding proceeds, some catchment basins will merge. This is prevented by erecting a dam at the merging location. At the end, only dams remain. These are the watershed divides.”

[Segonne 2004] uses the watershed algorithm to get an approximate boundary of the brain. The watershed algorithm tends to segment too much because real images contain many
small local minima. Implementations of the watershed algorithm usually smooth the image first, or use some other method to remove or ignore these local minima. The watershed algorithm is used for separating objects that are just touching.

1.4.7 COMBINATION OF SEVERAL METHODS

Every segmentation method has some shortcoming. Since two methods might work better than one, techniques for combining several methods merit investigation. Segmentation methods can be combined in parallel. For example, [Rehm 2004] describes the Minneapolis Consensus Strip (McStrip) brain segmentation algorithm that combines three approaches – atlas-based extraction via nonlinear warping, intensity-threshold masking with connectivity constraints, and edge-based masking with morphological operations. The results of each method are combined via a vote-based rule. Since each of the three approaches exhibits different characteristic errors, combining their individual results with a vote-based rule tends to eliminate the errors of any one approach. Segmentation methods can also be combined sequentially as in the brain segmentation algorithm of [Segonne 2004] that combines an initial watershed transform approach with a subsequent deformable surface model approach. Non-linear optimization algorithms, which include deformable surface models, require initialization that is close to the global minimum being sought. The goal of the watershed algorithm therefore is to extract an initial brain volume that is used to initialize the boundary surface for the deformable model.

1.5 EVALUATING IMAGE SEGMENTATION ALGORITHMS

An objective method is needed to evaluate the performance of image segmentation algorithms so that different algorithms can be compared. The most important performance criterion is accuracy, that is, the degree to which an algorithm’s segmentation matches some reference “gold standard” segmentation.
The source of the reference segmentation might be a computer model, a physical model, a cadaver, or a clinical patient. In choosing from this list, there is a tradeoff between determining the true segmentation accurately and generating realistic test images. With computer models, the true segmentation is known exactly but the images tend to lack realistic anatomical variability and characteristics introduced by the imaging system. [Kwan 1999] describes BrainWeb, a computer-simulation program that generates magnetic resonance images of the brain. Compared to computer models, the true segmentation from a physical model (called a phantom) is slightly less accurately known. The images from physical phantoms also lack realistic anatomical variability, but do possess realistic characteristics of the imaging system. Cadavers provide very realistic models. The true segmentation from cadavers must be estimated but can be guided by dissection. Clinical patients produce the most realistic images, but there is no practical way of determining the true segmentation accurately.

There are a number of ways to combine the manual segmentations of several human experts to obtain an objective reference. For example, [Warfield 1995] uses a voting rule that selects all voxels where a majority of experts agree that the structure to be segmented is present. Another method is given by [Warfield 2004], which uses an expectation-maximization algorithm that computes a probabilistic estimate of the true segmentation from a collection of segmentations.

A number of similarity coefficients are used to specify how well a given segmentation \( A \) matches a reference segmentation \( B \), where \( A \) and \( B \) are sets of segmented pixels. The Tanimoto coefficient [Duda 1973], which is also known as the Jaccard coefficient, is used by [Rajapakse 1998] to assess their algorithm’s segmentation of the gray and white matter in the brain. The Tanimoto coefficient is defined as
The Dice coefficient [Dice 1945], which is also known as the Sorenson coefficient, is used by [Zijdenbos 1994] to assess the accuracy of their semiautomatic segmentation of white matter lesions because, when compared to the Tanimoto coefficient, it reflects “the intuitive feeling that two regions, of which one fully encompasses the other, are more similar than two partially overlapping regions”. [Atkins 1998] and [Lemieux 1999] also use the Dice coefficient. The Dice coefficient is defined as

\[
\text{Dice coefficient} = \frac{2 \times n(A \cap B)}{n(A) + n(B)}
\]

Another similarity coefficient is the Simpson coefficient [Simpson 1960] defined as

\[
\text{Simpson coefficient} = \frac{n(A \cap B)}{\min(n(A), n(B))}
\]

The Tanimoto, Dice, and Simpson coefficients range between 0 and 1, where 0 indicates that the segmentations have no pixels in common and 1 indicates that the segmentations are identical.

1.6 **MARR’S PRIMAL SKETCH**

Most image processing methods begin with the detection of natural features, such as edges and lines, in gray-scale images. This approach is motivated by Hubel and Wiesel’s discovery of striate cortical cells in the brain that respond selectively to stimuli from edges or lines [Hubel 1959]. David Marr’s posthumous treatise “Vision” [Marr 1982] is influential in promoting this approach to image processing. As part of his primal sketch [Marr 1976], Marr proposes four primitive features: edges, lines, blobs, and terminations (Figure 1-6). The inclusion of terminations might at first seem unwarranted, but consider that in the image of a three-dimensional scene, the abrupt termination of a line could indicate the presence of an object.
blocking the full view of the line. Hence, a termination can hold important information by marking the location of an edge.

Of the four primitive features proposed by Marr, edges have received the most attention in algorithm research. “An edge in an image is an image contour across which the brightness of the image changes abruptly – perhaps in magnitude or in the rate of change of magnitude” [Nalwa 1993]. Canny’s edge detection algorithm [Canny 1986] smoothes images with a Gaussian filter, before marking edges at points where the magnitude of the intensity gradient is a local maximum. In this seminal work, Canny treats an image as a continuous function of two dimensions. However, a computer image is not continuous. It is a two-dimensional array of pixels, so a discrete approximation to the algorithm is used.

Figure 1-6: Examples of Marr’s primitives in an MR image
1.7 Pattern Classification

Pattern classification is the assignment of a physical object or event to one of several pre-specified categories. A typical pattern classification system consists of a transducer, a feature extractor, and a classifier (Figure 1-7). The transducer converts the signals from the physical object or event into raw data. The feature extractor reduces these data by measuring certain features or properties that the system designer believes is relevant. The classifier then evaluates the measured values of these features and outputs a decision regarding the category to which the input object or event should be assigned. The better the feature extractor, the simpler the classifier, and vice-versa. From a theoretical standpoint, the demarcation between feature extractor and classifier is arbitrary. The significance of the distinction is in the practical implementation. The design of a feature extractor tends to be more problem dependent than that of a classifier, so the classifier is often reusable while the feature extractor is often developed anew for each problem.

Classification can be viewed as a problem of partitioning a feature space into regions, where one region corresponds to one and only one category. In an ideal classifier, the partitioning is such that none of the decisions on category assignment is wrong. However, if this is not possible, a good classifier aims to minimize the average cost of errors, which is the same
as the probability of error in the case where all errors are equally costly. Designing such a classifier is a problem in statistical decision theory.

Bayes’ decision theory assumes that the decision problem is posed in probabilistic terms, and that all of the relevant probability values are known. If the output of the feature extractor is a vector $\mathbf{x}$ with each component representing a discrete measurement of some feature, and if $\omega_j$ denotes the $j^{th}$ state of nature or category, then Bayes’ rule determines the \textit{a posteriori} probability that $\omega_j$ is the true state of nature given an observation $\mathbf{x}$, as follows:

$$P(\omega_j | \mathbf{x}) = \frac{P(\mathbf{x} | \omega_j)P(\omega_j)}{P(\mathbf{x})},$$

where

$$P(\mathbf{x}) = \sum_k P(\mathbf{x} | \omega_k)P(\omega_k).$$

Bayes’ rule assigns each possible state of nature a certain probability of being the true state. A classifier must decide which is the true state. In situations where decision errors are equally costly, the usual decision rule is to pick the state of nature that is most probable. This decision rule is called the \textit{maximum a posteriori} or MAP decision rule. The Bayes MAP decision rule is to decide $\omega_1$ if $P(\omega_1 | \mathbf{x}) > P(\omega_2 | \mathbf{x})$; otherwise, decide $\omega_2$. The function $P(\omega_k | \mathbf{x})$ plays the role of a discriminant function, which is often represented generically by $g_k(\mathbf{x})$. Since the denominator $P(\mathbf{x})$ is the same for all states of nature, the discriminant function in Bayes MAP decision rule is sometimes given as

$$g_k(\mathbf{x}) = P(\mathbf{x} | \omega_k)P(\omega_k)$$

or, if it is more convenient as

$$g_k(\mathbf{x}) = \log P(\mathbf{x} | \omega_k) + \log P(\omega_k)$$
since a transformation by a monotonically increasing function does not change the output of the decision rule.

A classifier may be viewed as a machine that calculates several discriminant functions and selects the category corresponding to the largest discriminant (Figure 1-8).

![Figure 1-8: A general pattern classifier](image)

In the special case where there are only two categories, one discriminant function $g(x) = g_1(x) - g_2(x)$ is often used instead of two. The Bayes MAP decision rule is then stated as: decide $\omega_1$ if $g(x) > 0$; otherwise decide $\omega_2$. A two-category classifier can be viewed as a machine that calculates a single discriminant function and classifies according to the sign of the result (Figure 1-9).

![Figure 1-9: A two-category pattern classifier](image)
2 METHODS AND MATERIALS

2.1 TEST DATA

The images and manual segmentations were obtained from the Internet Brain Segmentation Repository (IBSR). Strict privacy rules governing the distribution of medical information impedes the widespread availability of test images. As part of its mission, the IBSR provides standard test image data sets, thereby allowing a standardized mechanism for evaluating new segmentation algorithms over a wide range of signal to noise ratios, contrast to noise ratios, shape complexity, degree of partial volume effect, etc. Such a repository is necessary since many published algorithms tend to only operate successfully under a narrow range of conditions, which is not realistic in a clinical setting.

The IBSR images used to test the algorithms in this dissertation were T1-weighted images oriented in the coronal plane. The dimension of each image was 256 by 256 pixels. The distance between pixels varied between data sets, but was approximately 1mm. The term “pixel unit” is used in this dissertation to refer to this approximate distance between pixels in the IBSR test images.

2.2 THE INTENSITY SURFACE MODEL AND ISO-INTENSE CONTOURS

An image is an array of discrete pixels, with \( I_{i,j} \) denoting the integer-valued intensity of a pixel at row \( i \) and column \( j \). However, the geometric computations in this dissertation favor modeling the intensity of an image as a continuous function of position. So the intensity at a point \((x, y)\in \mathbb{R}^2\) within the image is given by a piecewise linear interpolation as follows:
\[ I(x, y) = \begin{cases} 
I_A(x, y) & \text{if } x' + y' < 1 \text{ and } x' \geq y' \\
I_B(x, y) & \text{if } x' + y' \geq 1 \text{ and } x' \geq y' \\
I_C(x, y) & \text{if } x' + y' \geq 1 \text{ and } x' < y' \\
I_D(x, y) & \text{if } x' + y' < 1 \text{ and } x' < y' 
\end{cases} \]

where

\[ x' = x - \lfloor x \rfloor \]
\[ y' = y - \lfloor y \rfloor \]

The notation \( \lfloor n \rfloor \) refers to the largest integer less than or equal to \( n \).

The linear interpolation functions \( I_A, I_B, I_C, \) and \( I_D \) above are specified below in terms of the intensities for the four nearest pixels:

\[
I_A(x, y) = 2y' \cdot I_0 + (1 - x' - y') \cdot I_1 + (x' - y') \cdot I_2 \\
I_B(x, y) = 2(1 - x') \cdot I_0 + (x' - y') \cdot I_2 + (x' + y' - 1) \cdot I_3 \\
I_C(x, y) = 2(1 - y') \cdot I_0 + (x' + y' - 1) \cdot I_3 + (y' - x') \cdot I_4 \\
I_D(x, y) = 2x' \cdot I_0 + (y' - x') \cdot I_4 + (1 - x' - y') \cdot I_1
\]

where

\[
I_1 = I_{i,j} \\
I_2 = I_{i,j+1} \\
I_3 = I_{i+1,j+1} \\
I_4 = I_{i+1,j} \\
I_0 = \frac{I_1 + I_2 + I_3 + I_4}{4}
\]

\( i = \lfloor y \rfloor \) and \( j = \lfloor x \rfloor \)

This interpolation scheme is used because it makes computing iso-intense contours simple in comparison to other more popular schemes such as bilinear interpolation. Iso-intense contours are computed only for non-integer intensity thresholds to avoid the complications of saddle points in the intensity surface.
An image’s contour map at an intensity threshold $z$ is the set of points with the same intensity, that is, $\{(x, y) : I(x, y) = z\}$. An iso-intense contour $C_z$ is a connected set of points from the contour map. Since the intensity surface model produces contours that are piecewise linear, i.e. polygons, a contour is represented compactly as an ordered sequence of points, where each point is a vertex of the polygon.

2.3 **SOME PROPERTIES OF CONTOURS**

Each contour has a number of intrinsic properties that are used repeatedly in the algorithms in this dissertation. Some of these properties, and the methods used for measuring them, are described below for convenience. It should be noted that the computational complexity of measuring each of these is $O(n)$ where $n$ is the number of points used to represent the contour.

The area $A$ of a contour $C$ is computed by using the same formula on which the operation of a mechanical planimeter is based. The formula is as follows:

$$A = \frac{1}{2} \left| \oint_C (x \, dy - y \, dx) \right|$$

In general, area is used as a measure of feature size. Large contours are likely to correspond to real objects, whereas very small contours are more likely to be the result of noise.

The perimeter $P$ is computed as the integral of the linear element $ds$ of a contour $C$ as follows:

$$P = \oint_C ds$$

where

$$ds^2 = dx^2 + dy^2$$

The perimeter is sometimes used as an alternate measure of feature size.
The center of gravity \((\bar{x}, \bar{y})\) of the region \(R\) bounded by a contour \(C\) is computed as

\[
\bar{x} = \frac{1}{M} \int_R x \, dx \, dy
\]

\[
\bar{y} = \frac{1}{M} \int_R y \, dx \, dy
\]

where

\[
M = \int_R dx \, dy
\]

The center of gravity is sometimes used as a measure of position.

To determine if an iso-intense contour \(C_1\) is inside another iso-intense contour \(C_2\) of the same image, it is sufficient to determine that any single point \((x, y) \in C_1\) is inside \(C_2\), because iso-intense contours do not intersect. To determine if a point \((x, y)\) is inside a contour \(C\), the following procedure is used:

- If \((x, y) \in C\), decide that \((x, y)\) is inside and exit.
- Construct a ray with \((x, y)\) as its origin.
- Count the number of times the ray crosses \(C\).
- If the number of crossings is odd, decide that \((x, y)\) is inside.
- Otherwise, decide that \((x, y)\) is not inside.

The above procedure works regardless of the direction of the ray. However, the computation for detecting crossings is simplest if the ray is directed in the \(x\) or in the \(y\) direction. A detailed explanation of this procedure (and an alternative procedure) can be found in the section entitled “Point in Polygon” on page 233 of [O’Rourke 1994]. A visual explanation is given below in Figure 2-1.
The terms hyper-intense and hypo-intense are used frequently in the clinical radiology literature to describe the apparent brightness of anatomical structures in medical images relative to their surroundings. In this dissertation work, the term hyper-intense is used in a similar sense to label the contours of “mountains” in the intensity surface, and the term hypo-intense is used to label contours of “valleys”. A contour \( C \) is hyper-intense if the intensity gradient \( \nabla I(x, y) \) at a point \((x, y)\in C\) is directed inside the contour. Otherwise, the contour is hypo-intense.

The average gradient \( G \) of a contour \( C \) is computed by the following formula:

\[
G = \frac{\int_C \| \nabla I(x(s), y(s)) \| ds}{\int_C ds}
\]

Since intensity, and hence the intensity gradient, is somewhat arbitrary in MR images, the value of the average gradient itself is not considered significant in this work. Instead, the average gradient is used for “edge detection”, that is for finding the contour with the maximum average gradient within a local region of the image.

A contour has an implicit orientation because it is represented by an ordered sequence of points. Knowing the orientation is important to correctly implement some of the algorithms in
this research. A contour \( C \) has a clockwise orientation if the line integral \( \int_C (x \, dy - y \, dx) \) is positive; otherwise it has a counterclockwise orientation. Note that the coordinate system is assumed to be left-handed as is the convention for computer images.

### 2.4 Feature Extractor

Contours are evaluated for a set of features that depend on the object being segmented. Each feature \( x_i \) is binary-valued, that is, either the contour has the feature \( (x_i = 1) \) or it does not \( (x_i = 0) \). For example, a contour is either large or not large depending on whether or not its area is greater than some predefined size threshold. The exact value of this threshold is not critical, but it is always generously set such that the desired contour will always have the feature. In other words, the feature threshold is set so that conditional probabilities \( P(x_i = 1| \omega_1) = 1.0 \) and \( P(x_i = 0| \omega_1) = 0.0 \). Other contours may or may not have the feature \( x_i \), so \( P(x_i = 1| \omega_2) < 1.0 \) and \( 0.0 < P(x_i = 0| \omega_2) \leq 1.0 \). However, the feature threshold should not be too generous since it is preferable that \( P(x_i = 1| \omega_2) \) be much less than 1.0 while simultaneously ensuring that \( P(x_i = 1| \omega_1) \) is 1.0. Computational geometry is used in the measurement of contour features.

### 2.5 Pattern Classifier

If there are \( d > 2 \) features, and if they are conditionally independent, then

\[
P(x|\omega_1) = \prod_{i=1}^{d} P(x_i|\omega_1) = \begin{cases} 1.0 & \text{if } x_i = 1, \forall i \\ 0.0 & \text{otherwise} \end{cases}
\]

and

\[
P(x|\omega_2) = \prod_{i=1}^{d} P(x_i|\omega_2)
\]

\[
= 0.0 & \text{if } x_i = 1, \forall i \\
\leq 1.0 & \text{otherwise}
\]
Substituting in Bayes’ equation gives

\[
P(\omega_1 | x) = \frac{P(x | \omega_1)P(\omega_1)}{P(x | \omega_1)P(\omega_1) + P(x | \omega_2)P(\omega_2)} = \begin{cases} 
1.0 & \text{if } x_i = 1, \forall i \\
0.0 & \text{otherwise}
\end{cases}
\]

and

\[
P(\omega_2 | x) = \frac{P(x | \omega_2)P(\omega_2)}{P(x | \omega_1)P(\omega_1) + P(x | \omega_2)P(\omega_2)} = \begin{cases} 
0.0 & \text{if } x_i = 1, \forall i \\
1.0 & \text{otherwise}
\end{cases}
\]

That is, the \textit{a posteriori} probabilities are binary.

The above equations support the intuitive idea that an object can be described uniquely by a large enough set of features. Although there is no guarantee that enough features can be found to uniquely describe a particular object, there are still a number of reasons to be optimistic. The relative positions of most anatomic structures are predictable, therefore position relative to a known landmark is generally a very distinguishing feature. Textbooks rigorously describe anatomical structures, and so provide valuable sources of ideas for appropriate features. Depending on the application, one might be satisfied with describing only the easily recognizable objects, and not all objects. Since there is no restriction on what can be a feature, the chance of finding appropriate features is probably good.

The discriminant calculator \( g(x) \) in the resulting classifier is a simple logical-AND function, that is

\[
g(x) = x_1 \cdot x_2 \cdot \ldots \cdot x_d
\]

Since the evaluation of \( g(x) \) can be short-circuited, all features need not be measured for every contour. To take advantage of this fact, feature measurements are ordered from the simplest to the most complicated. This strategy saves a significant amount of computation time. It also makes the use of very complicated features practical, since the measurement of such features will
rarely be executed. Unlike many pattern classification systems, the implementation of the feature detector and the pattern classifier are closely intertwined.

The classifier as described so far will identify several contours for the object being segmented. These contours are at different intensity thresholds, and one is chosen as the best representative of the object being segmented. The best contour $C_{obj}$ is the one having the maximum value for an additional non-binary feature $x_{d+1}$, such as “threshold intensity” or “average intensity gradient”, so that

$$C_{obj} = \arg \max_c \left( f(C) \cdot g(x) \right)$$

where $f(C)$ is the value of the $x_{d+1}$ feature of contour $C$.

The $x_{d+1}$ component of the feature vector is the only non-binary feature used in the pattern classification system. This restriction avoids a fundamental issue of measurement theory that occurs when comparing two feature vectors. The comparison of two vectors invariably involves creating a distance function. This distance function takes, as its input, a vector’s components, and then combines them to produce a single real number as its output. However, in many pattern recognition applications, the components of a feature vector cannot be combined in a meaningful way, especially when their independence is a fundamental assumption. To illustrate the problem, how does one determine if a basket with two apples and four oranges is better than one with say four apples and two oranges? We avoid the problem of meaningfully combining the components of a vector by having only one component to compare.

### 2.6 Segmentation of the Head

The segmentation of the head from the background is the first step in the automatic segmentation method since the head’s outline provides a very good indication of the location and
extent of the brain within the image. The key feature used in identifying the head’s outline is the shape of the scalp, which is uncommonly smooth. Although, the inner and outer surfaces of the skull also have this shape, only the scalp borders on air. Therefore, the overall method of segmenting the head is to generate contours at every intensity threshold and find the contour that has a curve segment that is

1) wide,

2) smooth,

3) and borders on air.

For simplicity, we are assuming that the entire scalp is framed within the image. This is the typical case, and it affords a simple illustration of the general approach to anatomical segmentation used throughout this research. The case where the scalp is clipped by the top edge of the image into two curves can be solved with the same general approach and will be discussed later. Although the scalp might have other distinctive features, such as a convex shape, the few features listed above are sufficient to reliably differentiate the scalp from other curve segments in unconstrained head images. However, in addition to imparting a greater sense of robustness, the use of additional redundant features might speed up practical implementations by significantly reducing the search space. In general, the set of features used to identify an anatomical object is not unique, and a particular set is chosen because the method of measuring each feature in the set is simple to implement. The method of measuring the three features for the scalp’s curve segment is described below.

A curve segment is considered to be wide if the horizontal distance between its two end points is at least one-third the width of the image. This size threshold is conservative enough to guarantee that all scalp curve segments in relevant image slices will be identified as wide.
Generally speaking, size (i.e. length or area) is an important characteristic because most objects are restricted to a specific size range. In this segmentation research, size is one of the first features measured since the measurement is quick and drastically reduces the number of contours that need to be examined by more time-consuming feature measurements.

A curve segment is smooth if each short section is approximately straight. A short section, $ab$, is straight if its length is almost the same as the distance between its end points, that is

$$\frac{\int_a^b \sqrt{r' \cdot r'} \, dt}{{|r_b - r_a|}} < 0.5$$

Here, a smoothness feature threshold of fifty-percent is used, which is generous enough to guarantee that all smooth curve segments will be identified. An arbitrary length of ten pixel units is used for each short section. The smoothness of a curve is a strong indication that the curve corresponds to the boundary of a real object and is not the product of random noise.

Since the region of background air has not been segmented previously, it is not possible to determine directly if the curve segment borders on it. However, since air always has the lowest intensity in MR images, one can infer that, of all the wide and smooth curve segments, the one with the lowest intensity threshold will border on the background air. Consequently, this curve is selected to represent the scalp.

After segmenting the head by identifying the contour containing the scalp, the center of the head and the range of pixel intensity values for air are determined for use in subsequent brain segmentation steps. The center of the head is taken to be the point that is equidistant from three points on the scalp’s curve segment – the two endpoints and a point halfway between them. This choice is based on a model of the head as a circle, the center of which can always be determined
from any three points on its circumference (Figure 2-2). The maximum pixel value for air is
taken to be the intensity threshold that produced the scalp’s curve segment. This value can also
be used to locate the air cavities within the head, such as the mouth, which lie immediately
below the brain and so give a lower boundary for the brain’s location.

/* find the centre of a circle, given three points on its circumference */
int findcentre3(x1, y1, x2, y2, x3, y3, x, y)
float x1, y1, x2, y2, x3, y3, *x, *y;
{
    float a1, a2, b1, b2, c1, c2;
    a1 = 2 * (x1 - x3);
    a2 = 2 * (x2 - x3);
    b1 = 2 * (y1 - y3);
    b2 = 2 * (y2 - y3);
    c1 = (x1 + x3)*(x1 - x3) + (y1 + y3)*(y1 - y3);
    c2 = (x2 + x3)*(x2 - x3) + (y2 + y3)*(y2 - y3);
    if (a1*b2 == b1*a2) return(0);
    *x = (c1*b2 - b1*c2) / (a1*b2 - b1*a2);
    *y = (a1*c2 - c1*a2) / (a1*b2 - b1*a2);
    return(1);
}

Figure 2-2: C code for calculating the center of a circle

The outline that results from the above segmentation method accurately represents the
actual outline of the head in most image slices. In a few slices, the outline may depart slightly
and include some noisy pixels from the background. This departure does not occur near the
scalp, which is the important reference landmark for locating the brain. Using additional features
would ensure an accurate head outline in all image slices, but since the segmentation of the head
is not the primary goal, the resulting segmentation is more than adequate for subsequent brain
segmentation steps.

Since this approach to segmentation requires a brute force search, some strategies are
employed to speed up the actual implementation. The first strategy is to order the feature
measurements such that the most time-consuming ones are done last, since they might not need
to be done at all if the measured value of another feature precludes the object being sought. This
strategy takes advantage of the customary short-circuit evaluation of the AND logic function. A
second strategy is to plan the search order to facilitate pruning the search space. For example, since the outline of the head is the outermost significant contour in an image, the image area is searched, at each intensity threshold, from the upper left corner toward the center. The first contour that is encountered will be considered the outermost contour at that threshold intensity, and if it does not contain the features of the scalp then the search at that intensity level is halted and restarted at the next intensity threshold. Another strategy for speeding-up the program implementation is to employ additional redundant features to significantly reduce the search space. For example, the scalp in one image slice is in roughly the same position as in an adjacent image slice. This suggests another feature of the scalp: that it passes within three pixel units of an arbitrarily selected point on the scalp in the adjacent and previously segmented image. The search space is now reduced significantly to a line of just seven pixels – three on either side of the given point.

As mentioned before, segmenting the head from the background is based on finding a contour that contains the uniquely shaped scalp. However, the possibility exists that the entire scalp might not be visible in a few images that contain the largest cross-sections of the head. This situation occurs infrequently in routine scans, but in eighteen of the IBSR volumes, the images are intentionally cropped so that the top portion of the scalp is missing in several images within each of these volumes. Instead of a single curve, the scalp’s outline is divided into a pair of curve segments terminating at the top edge of the images. Consequently, the overall method of segmenting the head in this situation is to generate contours at every intensity threshold and find the contours that contain a pair of curve segments that

1) terminate at the top edge of the image,

2) are smooth,
3) are close to the previously segmented scalp in an adjacent image,

4) and borders on air.

A curve terminates at the top edge of the image if there is a point on the curve with a zero y-coordinate (by convention, the y-axis increases downward in computer images). The method of measuring the smoothness feature is the same as described previously. A curve segment is close to the previously segmented scalp in an adjacent image if the adjacent image has been segmented already and every point in the curve segment is no more than three pixel units from the previously segmented scalp. Determining if the pair of curve segments border on air is as described before – they border on air if, for all pairs of curve segments having the other features, they are at the lowest intensity threshold. The essential change in this set of features is the replacement of a “size” feature with a “proximity” feature. Since the width of the scalp is no longer a reliably distinctive feature, it is replaced by the predictable proximity of the scalp to its last known position. The method for estimating the center of the head is changed slightly. The center of the head is taken to be the average position of two computed points. The first computed point is equidistant from both endpoints of the first curve segment and one endpoint of the second curve segment. The second computed point is equidistant from one endpoint of the first curve segment and both endpoints of the second curve segment.

2.7 SEGMENTATION OF THE SKULL’S SURFACE

The surface of the skull is found because it is closer to the brain than the surface of the scalp and is therefore a better reference point for precisely locating the brain. The general procedure for locating the surface of the skull is as before – generate contours at each intensity threshold and test each contour for a set of features. Each contour is tested to determine if it has a curved segment that
1) is an approximate arc of a circle about the center of the head,
2) is wide,
3) is smooth,
4) is symmetric about the vertical,
5) and has a local intensity gradient such that the outer convex side of the arc is brighter than the inner concave side.

The method of measuring the features wide and smooth is the same as described previously for segmenting the head. The method of measuring the other features is described below.

A curve segment is an approximate arc of a circle about the center of the head if each short section of the curve is perpendicular to a line that radiates from the head’s center through the short section. The length of each short section is arbitrarily set at ten units, and a line drawn between the two endpoints of each short section must be perpendicular to the radial line that bisects it, within plus or minus thirty degrees. An additional restriction is placed on the slope of each short section, in that the slope must have a value between minus forty-five degrees and plus forty-five degrees. The purpose of doing this is to restrict the curve segment to the top of the skull. Note that the center of the head is determined from the scalp’s curve segment, as previously described.

The curved segment is symmetric if each of its endpoints is the same distance horizontally from the center of the head, within a margin of ten percent.

The tissues on either side of the curved segment determine the local intensity gradient. Bone lacks free hydrogen nuclei, so the skull on the inner concave side of the curve appears darker than the scalp tissue on the outer convex side. Therefore, the sign of the local intensity
gradient is positive in any direction away from the center of the head. This feature distinguishes
the surface of the skull from the similarly shaped and nearby surface of the scalp.

The curve segment with all of the above features at the lowest intensity threshold is
chosen to be the surface of the skull because bone has one of the lowest signal intensities for
tissues in the body.

2.8 SEGMENTATION OF THE WHOLE BRAIN

The general procedure for segmenting the whole brain is the same as before – generate
contours at each intensity threshold and test each contour for a set of features that only the
brain’s true contour will possess. Each contour is tested to determine if it is

1) large,

2) hyper-intense in appearance,

3) located in the upper portion of the head,

4) “blob”-shaped,

5) and if it has the characteristic “v” shape at the entrance to the longitudinal fissure.

The method of measuring these features follows.

A contour is large if its area is greater than 100 square pixel units. This size threshold is
significantly less than the typical size of a single cerebral hemisphere of the brain. No
corresponding upper size limit is explicitly set because other features implicitly exclude contours
that are too large.

The method of measuring the hyper-intense feature is as described previously in the
description of contour properties. The brain appears hyper-intense because its tissues – gray and
white matter – are brighter than the tissues immediately surrounding it, namely CSF, bone, and
air. Specifying that the brain is hyper-intense is intended to exclude large CSF filled cavities trapped between the skull and brain.

The method of determining if the brain contour is inside the head contour is as described previously in the description of contour properties. In addition to being inside the head, the brain is in the upper portion of the head and not in the neck region, so that at least a portion of the brain contour must be above the previously found center of the head. Another feature to be measured is the minimum distance of the brain contour from the outer surface of the head, which must not be less than 2 pixel units. This short distance is a conservative minimum estimate of the thickness of the scalp, and acts as a buffer zone to exclude the large contours related to the head’s outline.

Before measuring this minimum distance, a suitable representation of the outer surface of the head needs to be found. The head’s outline from the head segmentation step is usually adequate for this purpose except in the few images where the ear cavity is continuous with the outside air. In these images, the outline enters the ear cavity and passes very closely to the underside of the brain, so that a legitimate brain contour would be incorrectly rejected. A simple solution to avoid this problem is to modify the outline slightly. The modification consists of rolling a circle with a non-critical radius of 10 pixel units around the outline, and then generating the representation of the outer surface of the head from the points of contact. Since the diameter of the circle is greater than the entrance to the ear canal, the circle never enters the ear and neither does the resulting surface representation. This procedure is a generalization of the well-known convex hull algorithm. In this procedure, the convex hull would result from the special case of using a circle with infinite radius.
The word “blob” is borrowed from [Marr 1976]. Marr creates a set of primitives to describe intensity changes in an image. These primitives include “edge”, “line”, “blob” and a few others. The dictionary defines “blob” as “an indistinct shapeless form”. In this dissertation, a contour is considered “blob”-shaped if it is more rounded than elongated. The first step in measuring the roundness of the contour is to obtain the hull of the contour, as described previously. The ratio of the hull’s area to the square of its perimeter is used as a measure of its roundness. If this ratio is greater than that of an ellipse having a major axis five times its minor axis, then the contour is considered to be blob-shaped, that is

\[
\frac{A}{P^2} > 0.0306. 
\]

This shape threshold is nominal, and could just as easily be described in terms of a rectangle instead of an ellipse. The blob-shaped feature of a brain contour excludes the narrow crescent-shaped contour of the occasional large skull fragment.

Using the above four features alone usually results in a conservative outline that does not follow the surface of the brain closely, everywhere. The outline tends not to dip into the sulci, i.e. grooves, of the brain’s convoluted surface and it also tends to include small pieces of non-brain tissue that are near the surface. Therefore, the fifth feature is included – the potential brain contour must contain a characteristic “v” shape at the surface opening of the longitudinal fissure. To test for this property, the longitudinal fissure must be found first.

The longitudinal fissure is a deep groove that separates the left and right cerebral hemispheres that dominate the brain. Since the large cerebral hemispheres are present in essentially all image slices, the longitudinal fissure between them makes a good landmark. The longitudinal fissure is usually the deepest groove on the brain’s highly convoluted surface and it
is located along the head’s line of symmetry in a normal brain image. Note that the patient’s entire head might be tilted, so one cannot expect the longitudinal fissure to be perfectly vertical.

The first step in locating the longitudinal fissure is to strip away the gray matter cortex that comprises the brain’s surface, leaving behind the inner white matter. The surface of the brain is removed because it folds over and touches itself in many places, closing the grooves in the brain. Removing this surface effectively opens the grooves, and makes them easier to identify. Although, the intensity threshold that separates gray from white matter is unknown, the approximate proportion of the two tissue types is known from previous manual segmentations, so the intensity threshold is increased until one-third of the initial brain’s area is removed. The actual proportion of gray matter is non-critical, hence a rough estimate of one-third is adequate.

After removing the gray matter surface, the next step is to identify the longitudinal fissure. This method might be compared to dragging one’s finger across a surface to find a hole in the surface. Specifically, a circle (the “finger”) of radius five pixel units is rolled around the outside of the segmented white matter. At any time, the circle will touch the white matter contour at two points. These points are close together on a relatively smooth section of contour, or they span a groove in the surface. The points span a groove if the deepest point within the section of contour between them is at least five units below the level of the two points (measured in a direction toward the center of the head). In this case, the two points mark the surface opening of the groove. The longitudinal fissure is the deepest of those grooves whose surface opening lies within 45 degrees on either side of a vertical line that originates from the center of the head.

Finally, after locating the position of the opening to the longitudinal fissure, we can now test each potential brain contour for the characteristic “v” shape. The contour must satisfy two
conditions – it must enter the opening of the longitudinal fissure, and the “v” shape at the opening must be sufficiently wide. The contour enters the opening of the longitudinal fissure if it crosses the imaginary line between the two points that mark the surface opening. The “v” shape of the contour at the opening of the longitudinal fissure is sufficiently wide if a circle of radius 5 units can fit into the “v” such that the center of the circle is within 5 pixel units of the center of another equally sized circle that touches the two points that mark the opening of the longitudinal fissure.

The contour with all of the above features at the lowest intensity threshold is taken to be the brain contour. Selecting the contour with the lowest intensity threshold promotes the inclusion of the thin gray matter cortex that covers the brain’s surface. In most images, this chosen brain contour accurately represents the brain’s surface. However, in a few images the contour sometimes includes a piece of the skull. This problem occurs whenever the skull touches the brain in images with unusually bright bone tissue – approximately the same brightness as the gray matter tissue that constitutes the brain’s surface cortex. In general, the occurrence of this problem can be detected because the contour includes a portion of the skull and invariably passes near to the scalp.

Since the surface of the brain and the skull tissue are roughly the same intensity in these problem cases, a global intensity threshold cannot separate the two and simultaneously produce an accurate delineation of the brain. Instead, the problem is corrected locally where it occurs by automatically cutting the contour where the brain touches the skull, and then closing the open ends with a short arc. To find where the brain touches the skull, the distinctive inner surface of the skull is first located. The main features of the inner surface of the skull are

1) it is an approximate arc,
2) it is not more than 15 pixel units from the outer surface of the skull, and

3) its intensity gradient is positive in any direction away from the center of the head.

2.9 SEGMENTATION OF THE LATERAL VENTRICLES

The lateral ventricles are a pair of large CSF filled cavities. Each lateral ventricle follows a C-shaped course within a cerebral hemisphere. The method used to segment the lateral ventricles does not require the whole brain to be segmented first. There are two stages in segmenting the lateral ventricles. The first stage is to search all the image slices for a specific distinctive shape of the lateral ventricles. The second stage is to use the position of this distinctive shape to segment the lateral ventricles in neighboring slices.

Figure 2-3: Distinctive shape of lateral ventricles and the surrounding anatomical structures

In a few image slices near a particular cross-section of the brain, the lateral ventricular cavities have a distinctive appearance due to the anatomical structures that form their walls (Figure 2-3). These structures include a thin vertical membrane, called the septum pellucidum,
that separates the lateral ventricles in the middle; a band of fibers called the corpus callosum, that forms a concave roof at the top; and the caudate nuclei that form the concave sides of the lateral ventricles. Since the appearance of the lateral ventricles is so distinctive in these image slices, the first stage is to search all the images for these distinctive features. In the first stage, the general procedure for segmenting the lateral ventricles is to generate contours at each intensity threshold, and test pairs of contours for a specific set of features. Each pair of contours is tested to determine if

1) both contours are “blob”-shaped,

2) both contours are at the center of the head,

3) there is a narrow vertical separation between the contours,

4) and the roof of the contours is concave.

The methods for measuring these features are described below.

As described before, a contour is considered “blob”-shaped if it is more rounded than elongated. Specifically, the ratio of the contour’s area to the square of its perimeter is such that

$$\frac{A}{P^2} > 0.0306.$$  

The contours are at the center of the head if they are entirely within $\frac{R}{2}$ pixel units from the center of the head, and are at least partially within $\frac{R}{4}$ pixel units from the center of the head, where $R$ is the distance between the center of the head and the scalp. The scalp, the center of the head, and the distance from the center to the scalp, are determined during the prior segmentation of the head from the background.
There is a narrow vertical separation between the contours if the contours are close together for at least 7 pixel units. The contours are close together if they are no more than 3 pixel units apart when measured along a horizontal line.

The method to determine if the roof of the contours is concave starts with computing the convex hull around both contours. Assuming that the convex hull has clockwise orientation, two consecutive points on the convex hull are found such that the first point belongs to the contour on the left and the second belongs to the contour on the right. These points define the width of the concave roof, and must be separated by a distance of at least 10 pixel units. In addition, the distance from each of these points to the top of the narrow vertical separation between the contours must be at least 5 pixel units.

The pair of contours with all of the above features at the lowest intensity threshold is considered to be the lateral ventricles. These features are absent in most image slices. When the above features are found in an image slice, the second stage of segmenting the lateral ventricles begins.

In many image slices, the lateral ventricles are similar in appearance to other anatomical structures. To differentiate the lateral ventricles, the image being segmented is compared to a previously segmented image slice since the appearance of the lateral ventricles changes only gradually between consecutive images. Beginning with the segmented image from the first stage, the second stage of segmenting the lateral ventricles uses previously segmented images to segment neighboring images in turn. In the second stage, the general procedure for segmenting the lateral ventricles is to generate contours at each intensity threshold, and test each contour for a specific set of features. Each contour is tested to determine if it is

1) hypo-intense,
2) approximately the same size as a previously segmented lateral ventricle contour in a neighboring image slice,

3) overlaps a single lateral ventricle contour in the neighboring image, and

4) does not overlap the third ventricle’s contour in the neighboring image.

The method for measuring the hypo-intense feature is as described previously in the description of contour properties. The methods for measuring the other features are described below.

A contour is approximately the same size as a lateral ventricle contour in the previously segmented image if its area is between half and twice the area of the previously segmented contour.

A contour overlaps a lateral ventricle contour in the previously segmented image if the area of intersection between the contour and the lateral ventricle is at least half the area of the smaller. The contour must overlap only one and not both lateral ventricles in the previously segmented image.

Each lateral ventricle is connected to the third ventricle through a narrow channel called the interventricular foramen or foramen of Monro. In the few image slices of any data set where one or both foramina are present, the third ventricle will appear attached to one or both lateral ventricles. To avoid including the third ventricle, a potential lateral ventricle contour must not overlap the region of the third ventricle found in the previously segmented image. A contour overlaps the third ventricle’s contour in the previously segmented image if the area of intersection between the contour and the third ventricle contains at least one pixel. The method of segmenting the third ventricle will be described later.

A contour with all of the above features that overlaps the right lateral ventricle in the previously segmented image, with the greatest average gradient, is taken to be the right lateral
ventricle. The contour with all of the above features that overlaps the left lateral ventricle, with the greatest average gradient, is taken to be the left lateral ventricle. It should be noted that the orientation of the MR image is consistent with the patient facing the observer, so that the right lateral ventricle is to the observer’s left, and the left lateral ventricle is to the observer’s right.

2.10 Segmentation of the Third Ventricle

The third ventricle is a narrow slit-shaped CSF filled cavity situated at the midline of the brain. It is connected to the lateral ventricles via the interventricular foramina and is situated just below the pair of lateral ventricles (Figure 2-4). The segmentation method described here over-segments and finds a little more than the actual third ventricle in some images. This extra portion is an extension of the third ventricle’s cavity but is not considered a part of it. Since the sole purpose of segmenting the third ventricle is to ensure that the segmentation of each lateral ventricle does not include other portions of the ventricular cavity, this over-segmentation of the third ventricle is acceptable and is also desirable. A more accurate representation of the true extent of the third ventricle requires a more detailed description of its features, but this is not done since the third ventricle is not the important segmentation objective.
The image containing the previously mentioned distinctive shape of the lateral ventricles usually contains the third ventricle, since the lateral ventricles are close together when the third ventricle is present. The general procedure for segmenting the third ventricle in this initial image is to generate contours at each intensity threshold, and test each contour if it is

1) hypo-intense,

2) small,

3) just below the lateral ventricles,

4) and narrow.

The method of measuring the hypo-intense feature is as described previously in the description of contour properties. The methods for measuring the other features are described below.

A contour is considered small if its perimeter is less than 200 pixel units.

A contour is just below the lateral ventricles if the topmost point of the contour is less than 15 pixel units from bottommost point of both the right and left lateral ventricles. Also, the
topmost point of the contour must be to the right of the bottommost point of the right lateral ventricle and to the left of the bottommost point of the left lateral ventricle. (Note that the right lateral ventricle is actually on the observer’s left.)

A contour is narrow if it is never more than 5 pixel units wide when measured along a horizontal line. Additionally, the perimeter of the contour must be greater than 10 pixel units.

Beginning with this initial image, the position of the third ventricle in a segmented image is used to segment neighboring images in turn.

2.11 SEGMENTATION OF THE CAUDATE NUCLEI

The caudate nucleus is the gray matter body that forms the sidewall of the lateral ventricle. It is involved in voluntary motor control and its impairment is related to Parkinson disease and Huntington disease. The method of segmenting the caudate nucleus requires the prior segmentation of the lateral ventricles. Since a section of the lateral ventricle’s outline forms one side of the caudate, the emphasis of the segmentation method is to find the remaining section of the caudate nucleus’ outline, which is the boundary interface between the gray matter caudate and the surrounding white matter tissue of the brain (Figure 2-5). The general segmentation method is to generate contours at every intensity threshold and find a section of contour that

1) is next to the lateral ventricle,

2) has a positive intensity gradient in a direction away from the lateral ventricle,

3) has one end terminating near the top of the lateral ventricle,

4) and has a locally maximum average intensity gradient.
Each caudate nucleus adjoins a lateral ventricle on the side away from the brain’s midline. That is, the left caudate nucleus is on the patient’s left side of the left lateral ventricle, and the right caudate nucleus is on the patient’s right side of the right lateral ventricle. As noted before, MR images are oriented as if the patient is facing the observer, so that the patient’s left is the image observer’s right, and vice-versa. To avoid possible confusion of the meaning of “left” and “right” in the description that follows, the word “outer” or “outward” will be used preferentially instead to refer to the direction away from the head’s midline.

A section of contour is considered to be next to the lateral ventricle if it has a point $P$ that is within thirty pixel units in the outer direction from a specified point on the lateral ventricle. The lateral ventricle is divided into a left side and a right side by its topmost and bottommost points, and the above-mentioned specified point is one-third the vertical distance from the topmost point to the bottommost point on the side that is away from the midline. The
point $P$ on the section of contour must be the nearest such point of all contours at the current intensity threshold, meaning, the section of contour must be the nearest one to the lateral ventricle. Since a caudate nucleus is entirely on one side of a lateral ventricle, the topmost and bottommost points of the lateral ventricle limit the possible extent of the boundary with the caudate nucleus.

The section of contour has a positive intensity gradient in a direction away from the lateral ventricle if the sign of the gradient at the above-mentioned point $P$ is positive when measured in the outward direction. When moving along a path away from the midline, there is a transition from the darker gray matter caudate to the brighter white matter of the brain, so that the sign of the intensity gradient is positive.

The contour has a section that terminates near the top of the lateral ventricle if there is a point on the contour above the topmost point of the lateral ventricle. White matter tissue forms the top of the lateral ventricle, so the contour that separates the caudate nucleus from the surrounding white matter will also pass immediately above the adjoining lateral ventricle. Since the caudate does not extend above the lateral ventricle, the topmost point of the lateral ventricle is taken as a limit on the possible range of the caudate.

Depending on the particular cross-section of the brain, gray matter tissue may or may not be present near the bottom of the lateral ventricle. Consequently, the contour that separates the caudate nucleus from the surrounding white matter will curve away from the bottom of the lateral ventricle if gray matter tissue is present, or curve towards it if not. If the contour curves towards the lateral ventricle, the point immediately below the bottommost point of the lateral ventricle is taken as a limit on the possible range of the caudate. If instead the contour curves away, the first point with the same $y$-coordinate as the bottommost point of the lateral ventricle,
or the first local minimum in the curve, is taken as the limit on the range of the caudate, depending on whichever is encountered first. This endpoint and the one near the top of the lateral ventricle mark the section of contour along which the average gradient is computed.

The section of contour has a locally maximum average intensity gradient if it has the greatest average intensity gradient of all contour sections with the other features described above. The average intensity gradient $G$ of a section of contour $ab$ is computed as

$$G = \frac{\int_a^b f(s) \, ds}{\int_a^b ds}$$

where $f(s) = \| \nabla I(x(s), y(s)) \|$ if the point $(x, y)$ is more than three pixel units from the lateral ventricle, otherwise $f(s) = 0$. Points close to the lateral ventricle are not included in the integral because the contour around the lateral ventricle, being a boundary between tissue types, has a relatively large average gradient.

The section of contour with all of the above features separates the gray matter caudate nucleus from the white matter tissue. This is then connected to another section of contour taken from the topmost to the bottommost points of the adjoining lateral ventricle, to create a complete outline of the caudate nucleus. Before connecting the two sections, the point of the widest separation between them is located, which should be somewhere in the middle of the caudate nucleus. From this point, the caudate nucleus is considered to extend upwards and downwards to the ends of the two contour sections, or to the point at which they are separated by less than three pixel units.
2.12 **Overlap Metric**

An overlap metric is used to quantify the similarity of the automatic segmentations to the “gold standard” manual segmentations of an expert radiologist. For a given category, if \( A \) is the set of pixels assigned to the category by the automatic segmentation, and \( M \) is the set of pixels assigned to the category by the manual segmentation, then the overlap metric is defined to be

\[
\frac{n(A \cap M)}{n(A \cup M)}.
\]

This overlap metric is the same as the Tanimoto coefficient as described by [Duda 1973]. It approaches a value of 1.0 for segmentations that are very similar and is near 0.0 when there are few similarly classified pixels.

In the IBSR V2.0 data files, the reference manual segmentation of each anatomic structure is given as a sequence of coordinates that specify its boundary pixels. These coordinates are taken from an enlarged 512 x 512 image and not from the original 256 x 256 image. Consequently, the coordinates of the contours from the automatic segmentation in this research were doubled to match the enlarged size of the reference manual segmentation. In addition, the reference manual segmentation was translated slightly by subtracting half of a pixel unit from its coordinates since a visual inspection of both segmentations showed evidence of a systematic error without the translation. After so aligning the two coordinate systems, the number of pixels that were inside both segmentations’ boundaries \( n(A \cap M) \) and the number of pixels that were inside either segmentations’ boundaries \( n(A \cup M) \) were counted in order to compute the overlap metric. It should be noted that the pixels on the boundary of a segmented region were included as being inside the region.
3 RESULTS AND DISCUSSION

3.1 THE LATERAL VENTRICLES

The lateral ventricles in eighteen subjects were automatically segmented using the algorithm described previously in this dissertation and the results compared to the corresponding reference manual segmentations performed by expert radiologists. The image data sets used were IBSR_01 through IBSR_18, which comprised the entire IBSR V2.0 dataset. As part of the agreement for using these images, the following statement is included here:

“The MR brain data sets and their manual segmentations were provided by the Center for Morphometric Analysis at Massachusetts General Hospital and are available at http://www.cma.mgh.harvard.edu/ibsr/.”

Each of the eighteen data sets contains approximately 120 images, and the detailed breakdown of the raw results for each of the more than two thousand images is given in the appendix. The tables in the appendix list, for each image, the number of pixels belonging to the left lateral ventricle as determined (a) by the automatic segmentation algorithm, (b) by the manual segmentation, and (c) by both segmentation methods jointly. The tables also list the results for the right lateral ventricle.

The overlap metric \( \frac{n(A \cap M)}{n(A \cup M)} \) was calculated separately for the left and right lateral ventricles in each of the eighteen data sets, where \( A \) is the set of left (or right) lateral ventricle pixels as determined by the automatic segmentation algorithm, and \( M \) is the set of left (or right) lateral ventricle pixels as determined by the expert manual segmentation. The numerator \( n(A \cap M) \) was calculated from each table in the appendix as the sum of the column tallying the number of pixels common to both the automatic and manual segmentations. The denominator
\( n(A \cup M) \) was calculated using the identity \( n(A \cup M) = n(A) + n(M) - n(A \cap M) \), where \( n(A) \) was calculated as the sum of the column tallying the number of pixels determined by the automatic segmentation, and \( n(M) \) was calculated as the sum of the column tallying the number of pixels determined by the reference manual segmentation.

The resulting overlap metric for each of the data sets is presented in the following table:

**Table 3.1: Overlap metric for the right and the left lateral ventricles**

<table>
<thead>
<tr>
<th>Data Set</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBSR_01</td>
<td>0.851</td>
<td>0.857</td>
</tr>
<tr>
<td>IBSR_02</td>
<td>0.851</td>
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<tr>
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<tr>
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<tr>
<td>IBSR_05</td>
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<td>0.773</td>
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</table>
The above procedure for calculating the overlap metric included all the images in each data set. Since some images did not have both automatically and manually segmented pixels, the overlap metric was also calculated in a slightly different manner to better compare the automatic and manual segmentations within each image instead of over the entire volume. As before, 
\( n(A \cap M) \), \( n(A) \), and \( n(M) \) were calculated as the sum of their respective columns in each table, but this time, the only rows included (in the calculations) were those in which the number of pixels determined by the automatic segmentation and by the manual segmentation were both nonzero.
The resulting overlap metric for each of the data sets is presented in the following table:

Table 3.2: Overlap metric for the right and left lateral ventricles using only images in which both methods found lateral ventricle

<table>
<thead>
<tr>
<th>Image Data Set</th>
<th>RIGHT</th>
<th>LEFT</th>
</tr>
</thead>
<tbody>
<tr>
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<td>IBSR_17</td>
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<tr>
<td>IBSR_18</td>
<td>0.736</td>
<td>0.860</td>
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</table>

Figure 3-2: Overlap metric for right and left lateral ventricles using only images in which both methods found lateral ventricle
Figure 3-3: Illustrating range of values for the overlap metric. Automatic (red), manual (green), both (yellow). Overlap metric for left and right ventricles: (a) 0.953, 0.950; (b) 0.823, 0.776; (c) 0.646, 0.703; (d) 0.621, 0.584
One gets a sense of the meaning of the overlap metric by visually observing the results for the automatic and manual segmentation methods together. The selected segmented images shown in Figure 3-3 illustrate overlap metric values ranging from about 0.6 to above 0.9 in steps of approximately 0.1. These empirical results suggest that a value of 0.7 or more is indicative of very good agreement between the two segmentations. Segmentation differences for overlap metric values more than 0.7 are barely noticeable and can be dismissed as a judgment call after reviewing the original non-segmented image.

As can be seen from the histogram, the overlap metric for the IBSR_10 data set was extremely poor. The overlap metric for IBSR_03 was better but also poor. In both of these data sets, the thin membrane between the lateral ventricles – the septum pellucidum – was absent in a number of slices due to the low quality of the images. Because there was no explicit separation of the lateral ventricles, the algorithm erroneously identified the two lateral ventricles as one large ventricle. One could modify the algorithm to compare the potential contour with the segmented lateral ventricles in the previous slice, and if the potential contour overlaps both lateral ventricles the algorithm could insert an artificial septum pellucidum at the same location as in the previous slice.

Excluding the faulty data sets of IBSR_03 and IBSR_10, the average overlap metric for the right lateral ventricle is 0.81 and for the left lateral ventricle it is 0.81 also.

In a few of the data sets, the manual segmentation data shows that a small volume at the very end of the lateral ventricle’s posterior horn is disconnected from the rest of the lateral ventricle. For example, the table for IBSR_02 in the appendix shows a gap in the right lateral ventricle at images 27 through 31, which contain no manually segmented pixels. (Note that the posterior horn is located toward the back of the head, which consists of the low numbered
images.) The lateral ventricle becomes so narrow within these image slices that it is not visible. Because the automatic algorithm required the lateral ventricle be connected, it did not segment the disconnected volume at the posterior end. The algorithm’s strict connectivity requirement could be relaxed to allow such small and seemingly disconnected volumes to be segmented.

Sometimes the automatic segmentation algorithm determined that an image contained a few lateral ventricle pixels when in fact it did not. When this occurred, it was in the one or two images lying next to the last image containing actual lateral ventricle pixels. For example, in the table for IBSR_01, images 91 and 92 contain automatically segmented pixels but none manually segmented. Such spuriously detected pixels have an imperceptibly low contrast to their surroundings because they are really the same white matter tissue. To eliminate such spuriously detected pixels, a contrast feature could be added to the set of lateral ventricle features measured by the algorithm. The algorithm could require that the intensity gradient of the lateral ventricle contour be greater than some computed value. This threshold value could be established from a statistical analysis of the variation in intensity gradient values for previously segmented lateral ventricle contours in other images of the data set.

### 3.2 The Caudate Nuclei

The caudate nuclei in eighteen subjects were automatically segmented using the algorithm described previously in this dissertation and the results compared to the corresponding reference manual segmentations performed by expert radiologists. The image data sets used were IBSR_01 through IBSR_18. “The MR brain data sets and their manual segmentations were provided by the Center for Morphometric Analysis at Massachusetts General Hospital and are available at [http://www.cma.mgh.harvard.edu/ibsr/](http://www.cma.mgh.harvard.edu/ibsr/).”
The detailed breakdown of the raw results for each of the more than two thousand images is given in the appendix. The tables in the appendix list, for each image, the number of pixels belonging to the left caudate nucleus as determined by the automatic segmentation algorithm, by the manual segmentation, and by both segmentation methods jointly. The tables also list the results for the right caudate nucleus.

The overlap metric \( \frac{n(A \cap M)}{n(A \cup M)} \) was calculated separately for the left and right caudate nuclei in each of the eighteen data sets, where \( A \) is the set of left (or right) caudate pixels as determined by the automatic segmentation algorithm, and \( M \) is the set of left (or right) caudate pixels as determined by the expert manual segmentation. The numerator \( n(A \cap M) \) was calculated from each table in the appendix as the sum of the column tallying the number of pixels common to both the automatic and manual segmentations. The denominator \( n(A \cup M) \) was calculated using the identity \( n(A \cup M) = n(A) + n(M) - n(A \cap M) \), where \( n(A) \) was calculated as the sum of the column tallying the number of pixels determined by the automatic segmentation, and \( n(M) \) was calculated as the sum of the column tallying the number of pixels determined by the reference manual segmentation.

The resulting overlap metric for each of the data sets is presented in the following table:
Table 3.3: Overlap metric for the right and the left caudate nuclei

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</table>

Figure 3-4: Overlap metric for the right and the left caudate nuclei

The above procedure for calculating the overlap metric included all the images in each data set.

Since some images did not have both automatically and manually segmented pixels, the overlap
metric was calculated in a slightly different manner to better compare the automatic and manual segmentations in each image instead of over the entire volume. As before, $n(A \cap M)$, $n(A)$, and $n(M)$ were calculated as the sum of their respective columns in each table, but this time, the only rows included in the calculations were those in which the number of pixels determined by the automatic segmentation and by the manual segmentation were both nonzero.

The resulting overlap metric for each of the data sets is presented in the following table:

Table 3.4: Overlap metric for the right and the left caudate nuclei using only images in which both methods found the caudate nucleus

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<td>IBSR_01</td>
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<td>IBSR_02</td>
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<td>IBSR_09</td>
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<td>IBSR_13</td>
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<td>IBSR_15</td>
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<td>0.597</td>
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</table>
The poor overlap metric values for IBSR_03 and IBSR_10 were caused by the incorrect prior segmentation of the lateral ventricles in these data sets, and are not a reflection on the efficacy of the segmentation algorithm for the caudate nucleus. The poor overlap metric values for IBSR_06 and IBSR_08 were due to the unusually low contrast between gray matter tissue and white matter tissue within the images. Upon visual inspection, IBSR_06 had the lowest contrast among all the data sets. IBSR_08 appeared to have the second lowest.

Excluding the faulty data sets of IBSR_03, IBSR_06, IBSR_08, and IBSR_10, the average overlap metric for the right caudate nucleus is 0.67 and for the left caudate it is 0.67 also.

Partial volume pixels that lie along a border between dark CSF and bright white matter tissue have intermediate gray intensity values. Such partial volume pixels are indistinguishable in appearance from a thin cross-section of gray caudate nucleus, since the caudate nucleus also lies between CSF and white matter. For images that contain a small cross-section, segmenting
the caudate nucleus is mostly guesswork and is not based on clear-cut evidence within the image. Because of this viewpoint, the algorithm was designed to stop segmentation when the thickness of the caudate nucleus approached the approximate width of partial volume pixels, which was considered to be about three pixel units. Therefore, the algorithm only segmented the head of the caudate nucleus and not its thin tail, which caused a large discrepancy between the automatic and manual segmentations with a correspondingly low overlap metric.

The automatic and the manual segmentation methods often gave different locations for the bottom of the caudate nucleus. In images where the bottom of the gray matter caudate nucleus joined the bottom of the gray matter putamen to form a “U” shape, the automatic segmentation algorithm tended to separate the caudate from the putamen at a higher point than the manual segmentation. In other images where the bottom end of the gray caudate transitioned into the similarly gray partial volume pixels, the algorithm terminated the caudate sometimes higher and sometimes lower than the manual segmentation. Instead of simply terminating the caudate with a horizontal line, the curvature at the middle of the caudate nucleus could be extrapolated to give a tapered bottom end, which should give an outline closer to the manual segmentation.

3.3 **THE WHOLE BRAIN**

The whole brain in twenty subjects was automatically segmented using the algorithm described previously in this dissertation and the results compared to the corresponding reference manual segmentations performed by expert radiologists. The image data sets comprised the entire “20 Normal Subjects” dataset. “The 20 normal MR brain data sets and their manual segmentations were provided by the Center for Morphometric Analysis at Massachusetts General Hospital and are available at [http://www.cma.mgh.harvard.edu/ibsr/](http://www.cma.mgh.harvard.edu/ibsr/).”
Unlike the IBSR V2.0 dataset, the manual segmentation for this dataset was in terms of tissue type (i.e. CSF, gray matter, and white matter). Neither the “IBSR V2.0” nor the “20 Normal Subjects” dataset included the whole brain as a segmented category. However, the extent of the whole brain was inferred for the “20 Normal Subjects” by combining the three segmented tissue types – CSF, gray matter, and white matter. No quantitative similarity measurements were made between the automatic and manual segmentations. Although it could have been used, the overlap metric was not appropriate because it does not measure the similarity between outlines. Instead, it measures the similarity between regions. When segmenting the whole brain, the important criterion is the similarity between the automatically and manually segmented surfaces of the brain.

In most of the images, the automatic segmentation produced by the algorithm fit the reference manual segmentation very well. The algorithm always segmented a significant portion of the brain (Figure 3-9). The algorithm had a tendency to include the eyeballs (Figure 3-8). Since the eyes are distinctly round, the algorithm could be modified to locate images containing the eyes, and remove the round eyeballs from any segmentation of the brain. The algorithm also had a tendency to include the spinal cord (Figure 3-7). Since the spinal cord has a distinct long and narrow appearance, the algorithm could be modified to automatically detect the spinal cord, and then truncate it just below the brain.
Figure 3-6: The automatic segmentation (red outline) fits the manual segmentation very well in most images
Figure 3-7: The algorithm includes the spinal cord

Figure 3-8: The algorithm includes the eyeballs
Figure 3-9: The automatically segmented brain-surface does not match the manual segmentation, but the algorithm still segments a significant portion of the brain.
4 SUMMARY AND CONCLUSIONS

This dissertation presents a novel approach to the automatic segmentation of the human brain in magnetic resonance images. The general approach involves searching each image for a contour with certain features that depend on the anatomical structure being segmented. Computational geometry is used to measure many features.

To test this segmentation approach, algorithms were developed to automatically segment a number of anatomical structures. These algorithms were applied to a standard collection of real clinical data sets obtained from thirty-eight different individuals. Reference manual segmentations of the lateral ventricles and the caudate nuclei were available for eighteen data sets. These were used to evaluate the performance of these new algorithms. The algorithm for segmenting the lateral ventricles performed very well with an overlap metric of approximately 0.8. The algorithm for segmenting the caudate nuclei performed well with an overlap metric of approximately 0.7. The algorithm for segmenting the whole brain performed well in many image slices, but in some images, the automatically segmented brain-surface did not closely match the manually segmented brain-surface.

Unlike other brain segmentation algorithms described in the literature, the algorithms described in this dissertation are truly automatic because they do not require a user to determine image-specific parameters, thresholds, or regions of interest. The algorithms are robust because they handle the range of anatomical variation between individuals, and they are insensitive to intensity variations between images.

More work can be done to improve the algorithms. The algorithms need to be tested on many more data sets to expose unexpected segmentation errors that might occur infrequently. The algorithms should also be tested with more recent images, since the IBSR data sets are old,
while MR technology has improved. It is expected that the algorithms will produce more accurate segmentations with newer MR images, but this needs to be confirmed.

The automatic segmentation of the lateral ventricles demonstrated in this dissertation is immediately useful for monitoring the progress of degenerative brain diseases, because any reduction in brain matter is indicated by a corresponding increase in the ventricular cavities. The automatic segmentation is also immediately useful for establishing an objective and repeatable standard free from any bias that may occur when different people view the same images. However, more anatomical structures need to be accurately segmented so that other pathologies can be detected and monitored. The algorithms should be modified to handle T2-weighted and PD-weighted images. The algorithms should also be expanded to handle images oriented in the sagittal and axial planes, although such MR image volumes can be re-sliced to produce images in the coronal plane.

The general segmentation approach and the implemented low-level routines can be applied to the automatic segmentation of other organs in the body and to other imaging modalities such as CT. Consequently, the automatic segmentation of other organs, such as the liver or the lungs, promises to be a fruitful direction for new research.
REFERENCES


[Sundsten 1994] Sundsten, J. W. Interactive Brain Atlas, 1994, University of Washington School of Medicine Seattle, WA.


APPENDIX 1: THE LATERAL VENTRICLES

The nine columns in the following tables list:

1) Image number

Number of pixels belonging to the left lateral ventricle as determined by

2) automatic segmentation

3) manual segmentation

4) both

(5) Overlap metric for left lateral ventricle

Number of pixels belonging to the right lateral ventricle as determined by

(6) automatic segmentation

(7) manual segmentation

(8) both

(9) Overlap metric for right lateral ventricle

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<th>Right Lateral Ventricle (pixels)</th>
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## APPENDIX 2: THE CAUDATE NUCLEI

The nine columns in the following tables list:

1. Image number

Number of pixels belonging to the left caudate nucleus as determined by

2. Automatic segmentation

3. Manual segmentation

4. Both

5. Overlap metric for left caudate nucleus

Number of pixels belonging to the right caudate nucleus as determined by

6. Automatic segmentation

7. Manual segmentation

8. Both

9. Overlap metric for right caudate nucleus

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**IBSR_04**
Kirk Spence is from Kingston, Jamaica. He received his Bachelor of Science degree with majors in Computer Science and in Applied Physics (Electronics) in 1989. In 1995, he received his Master of Philosophy degree in Computer Science.

Kirk Spence is currently employed at Intel.