Automatic brain segmentation into substructures using quantitative MRI

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Master of Science Thesis in Electrical Engineering

**Automatic brain segmentation into substructures using quantitative MRI**

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Abstract

Segmentation of the brain into sub-volumes has many clinical applications. Many neurological diseases are connected with brain atrophy (tissue loss). By dividing the brain into smaller compartments, volume comparison between the compartments can be made, as well as monitoring local volume changes over time. The former is especially interesting for the left and right cerebral hemispheres, due to their symmetric appearance. By using automatic segmentation, the time consuming step of manually labelling the brain is removed, allowing for larger scale research.

In this thesis, three automatic methods for segmenting the brain from magnetic resonance (MR) images are implemented and evaluated. Since neither of the evaluated methods resulted in sufficiently good segmentations to be clinically relevant, a novel segmentation method, called SB-GC (shape bottleneck detection incorporated in graph cuts), is also presented. SB-GC utilizes quantitative MRI data as input data, together with shape bottleneck detection and graph cuts to segment the brain into the left and right cerebral hemispheres, the cerebellum and the brain stem. SB-GC shows promises of highly accurate and repeatable results for both healthy, adult brains and more challenging cases such as children and brains containing pathologies.
Acknowledgments

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Linköping, June 2016
Karin Stacke
## Contents

Notation  

<table>
<thead>
<tr>
<th>1 Introduction</th>
</tr>
</thead>
</table>
| 1.1 Aim | 2  
| 1.2 Approach | 2  
| 1.3 Limitations | 3  

| 2 Theory | 5  
|----------------|
| 2.1 Magnetic Resonance Imaging | 5  
| 2.1.1 Spin physics | 5  
| 2.1.2 RF-pulse and relaxation times | 7  
| 2.1.3 Pulse sequences | 8  
| 2.1.4 Quantitative magnetic resonance imaging | 10  
| 2.2 The Human Brain | 12  
| 2.3 Segmentation Methods | 13  
| 2.3.1 Shape bottleneck detection | 14  
| 2.3.2 Graph cuts | 16  
| 2.3.3 FreeSurfer | 18  

| 3 Method | 21  
|----------------|
| 3.1 Adaptive Disconnection Algorithm | 21  
| 3.2 Graph Cuts | 22  
| 3.3 FreeSurfer | 24  
| 3.4 Volume Calculations | 25  
| 3.5 Proposed Improved Method | 26  

| 4 Results | 33  
|----------------|
| 4.1 Healthy Subjects | 33  
| 4.1.1 Adaptive disconnection algorithm | 33  
| 4.1.2 Graph cuts method | 34  
| 4.1.3 FreeSurfer | 34  
| 4.1.4 SB-GC | 35  
| 4.2 Challenges | 39  

ix
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.3 Volume Calculations</td>
<td>43</td>
</tr>
<tr>
<td>5 Discussion</td>
<td>47</td>
</tr>
<tr>
<td>5.1 Method Evaluation</td>
<td>47</td>
</tr>
<tr>
<td>5.2 Further Developments</td>
<td>51</td>
</tr>
<tr>
<td>6 Conclusions</td>
<td>53</td>
</tr>
<tr>
<td>A Detailed Descriptions</td>
<td>57</td>
</tr>
<tr>
<td>A.1 Shape Bottleneck Detection</td>
<td>57</td>
</tr>
<tr>
<td>A.2 Region Growing Details in Adaptive Disconnection Algorithm</td>
<td>58</td>
</tr>
<tr>
<td>A.3 FreeSurfer Compartment Labels</td>
<td>59</td>
</tr>
<tr>
<td>B Additional Resulting Images</td>
<td>63</td>
</tr>
<tr>
<td>Bibliography</td>
<td>65</td>
</tr>
</tbody>
</table>
# Notation

## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPV</td>
<td>Brain Parenchymal Volume</td>
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<tr>
<td>BS</td>
<td>Brain Stem</td>
</tr>
<tr>
<td>CB</td>
<td>Cerebellum</td>
</tr>
<tr>
<td>CBB</td>
<td>Cerebellum + Brain Stem</td>
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<tr>
<td>CH</td>
<td>Cerebral Hemispheres</td>
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<td>CMD</td>
<td>Compartment Mean Difference</td>
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<td>CSF</td>
<td>Cerebrospinal Fluid</td>
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<td>GM</td>
<td>Gray Matter</td>
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<td>ICV</td>
<td>Intracranial Volume</td>
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<tr>
<td>IPV</td>
<td>Information Potential Value</td>
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<tr>
<td>IPM</td>
<td>Information Potential Map</td>
</tr>
<tr>
<td>LCB</td>
<td>Left Cerebellar Hemisphere</td>
</tr>
<tr>
<td>LCH</td>
<td>Left Cerebral Hemisphere</td>
</tr>
<tr>
<td>MR</td>
<td>Magnetic Resonance</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PD</td>
<td>Proton Density</td>
</tr>
<tr>
<td>PDE</td>
<td>Partial Differential Equations</td>
</tr>
<tr>
<td>PVE</td>
<td>Partial Volume Estimation</td>
</tr>
<tr>
<td>qMRI</td>
<td>quantitative Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>RCB</td>
<td>Right Cerebellar Hemisphere</td>
</tr>
<tr>
<td>RCH</td>
<td>Right Cerebral Hemisphere</td>
</tr>
<tr>
<td>TMD</td>
<td>Total Mean Difference</td>
</tr>
<tr>
<td>WM</td>
<td>White Matter</td>
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</tbody>
</table>
Magnetic resonance imaging (MRI) is used for in vivo imaging of soft tissue in the body. By using magnetic fields together with physical properties of atoms in the body, different tissue types can be distinguished and visualized. MRI is especially suited for imaging the brain, since the magnetic fields not are hindered by the dense skull surrounding the brain, which may cause problems in other medical imaging modalities. After acquiring images of the brain, a wide range of analytical operations can be performed in order to reveal important physical and physiological characteristics. One such analytical operation is segmentation, which aims to partition the brain into segments (like tissue types or by anatomical function) using image information (like intensity value or spatial location). Segmentation of the brain into large compartments, such as the left and right hemispheres, the cerebellum and the brain stem are of interest both in order to study the regions separately but also to help locate inner brain structures, to monitor development and to aid surgical planning [1]. Using the result from the segmentation, volume calculation are possible for the compartments. Monitoring volume change over time is of interest since some neurological diseases are associated with a higher rate of brain atrophy (tissue loss) than normal [2, 3].

During this project, quantitative MRI (qMRI) [4] will be used, generated by an imaging sequence developed by SyntheticMR AB, based in Linköping, Sweden. In conventional MRI, the desired contrast in the image (i.e. weighting) between tissues is decided prior to image acquisition. Due to a number of intrinsic characteristics of the acquisition procedure, the intensity values of the images will not have any direct meaning; only the contrast between tissues has any physiological significance. It can therefore be hard to compare images acquired from different scanners. In qMRI however, the vendor- and machine-specific elements are removed since the acquired data are quantitative maps, where values directly correspond to tissue characteristics. These characteristics are the T1-relaxation value,
the T2-relaxation value and the proton density (PD); the maps contain T1, T2 and PD-values respectively for each sampled point in the imaged region. It is from these maps possible to reconstruct any type of image, for example T1-weighted, T2-weighted or proton density weighted images that are the conventional output from an MR imaging sequence. The contrast in conventional MR images is dependent on all tissue properties (in contrast to quantitative maps that reflect only a single tissue characteristic); the weighting simply allows one of them to affect more, resulting in varying tissue contrast between differently weighted images.

SyntheticMR has also developed a method for extracting the intracranial volume (ICV) and a method for segmentation of brain into tissue types (white matter, gray matter and cerebrospinal fluid) [5]. Thus, the data available for this project consists of a number of data sets, i.e. volumes of the brain, which include quantitative maps, ICV and tissue segmentations.

1.1 Aim

The aim of this master’s thesis is to present an automatic method for segmentation of the brain into left and right cerebral hemispheres, cerebellum and brain stem from quantitative magnetic resonance images. In order to do this, three automatic segmentation methods developed for conventional MRI will be tested and evaluated. The methods will be evaluated on perceived accuracy, repeatability and how qMRI can be used to improve the results. Repeatability is here evaluated though the mean and standard deviation of the volume difference between two data sets of the same subject acquired with the same MR scanner close in time (i.e. any volume difference should originate from the image acquisition or segmentation method). The methods will be applied to both healthy, adult brains, as well as more challenging cases such as children and subjects with pathologies. Using the results from this evaluation process, an improved method, specifically designed for qMRI, will be proposed and evaluated.

The master’s thesis will answer the following questions:

• Which of the investigated methods is the most repeatable method for correctly segmenting the left and right cerebral hemispheres, cerebellum and brain stem from MR images?

• Can any of these methods be improved when applied to qMRI, and if so, how?

1.2 Approach

This project consisted of two main parts: evaluation and comparison of segmentation pipelines, and investigation on how to improve them.

The comparative study included the following three different methods: the Adaptive disconnection algorithm [6], a graph cuts based method [7] and the segmentation method implemented in the software FreeSurfer [8]. The methods
were evaluated on healthy subjects, as well as for subjects that for various reasons have abnormal brain anatomy. Since the methods have been developed for T1-weighted MR images, the evaluation was done on similar types of images.

An investigation was then conducted to see if any of the methods could be improved upon when applied to quantitative MR images, and if so, in what way. Selected suggested improvements were then implemented.

1.3 Limitations

The choice of methods to investigate was constrained to include only fully automatic methods that had previously been applied to conventional MR images. The methods to be investigated were to the highest degree feasible implemented in their originally published form. Modification, where needed, is clearly described and motivated. All methods were evaluated using synthetic MR images, which may differ slightly from conventional ones.

If a pre-existing implementation was used, then this is also clearly stated.
The first two parts of this chapter aim to give an overview of magnetic resonance imaging (section 2.1) and the relevant anatomical structures in the brain (section 2.2). The third part provides a theoretical background to the segmentation methods evaluated (section 2.3).

### 2.1 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a non-invasive imaging technique that is used for visualization of soft tissues in the body. The exact physical principles and technical details about MRI are too extensive to be covered here, thus only the very basics will be presented, using [9].

#### 2.1.1 Spin physics

Magnetic resonance is based on the physical phenomenon that spinning charged particles create a magnetic field. In MRI the charged particles of interest are hydrogen nuclei (i.e. protons), due to their abundance in the body (the body consists of approximately 60% water). The protons spin around their own axis, generating a small magnetic field. The strength of the field generated by only one proton is too small to detect, but the net magnetization (denoted $M_0$), i.e. the total magnetization from sufficiently many nuclei, is detectable. When the nuclei are unaffected, the net magnetization is zero since the axes are not aligned. However, when subjected to a strong external magnetic field (denoted $B_0$), the spins will align either parallel or anti-parallel to the field and start to precess around the axis of the external field (see figure 2.1). Unpaired protons (belonging to atoms with odd numbers of protons) will cause a slight surplus of protons aligned in
one orientation, causing the net magnetization (which otherwise would have been canceled out) to point in one direction, specifically the $B_0$-direction. The strength of this net magnetization depends on the number of protons and whether their environment allows them to align with the external field. The frequency which the spins precess around the $B_0$-axis is called the Larmor frequency. It depends on intrinsic parameters of the atom as well as the $B_0$-field strength, and is given by the equation

$$w = \gamma B_0,$$

(2.1)

where $\gamma$ is the gyromagnetic ratio specific to the precessing nucleus and the $B_0$ is the external magnetic field strength. The angular frequency $w$ can be expressed in either Hz/T or radians per second, depending on the units used for $\gamma$.

![Diagram of a single spin precession around the $B_0$-axis with the Larmor frequency $w$. (Image source: [10])](image)

The strength of the $B_0$-field is measured in Tesla (T); today the most common strengths used for imaging are 1.5 T and 3 T (the earth’s magnetic field is 30 000 times weaker than 1.5 T). The direction of the $B_0$-field will henceforth be denoted as the $z$-direction. The field strength of the $B_0$-field greatly affect the resulting image, as higher field strengths generate stronger tissue signals and different tissue contrasts, and the image may include effects from previously invisible phenomena (such as varying ion content between regions) [11].
2.1 Magnetic Resonance Imaging

2.1.2 RF-pulse and relaxation times

The signal measured in MRI is an oscillating magnetic field, that originates from the hydrogen nuclei and is detected by a receiver coil. The receiver coil converts magnetic fluctuations along a certain axis into electric signals. The $B_0$-field along the $z$-axis is static, and can therefore not be detected by the coils, and due to the placement of the receivers neither will any signal along this axis.

$\textbf{Figure 2.2: Net magnetization flipped to the xy-plane as a result of the RF-pulse.}$

A radio frequency (RF) pulse, with the same frequency as the Larmor frequency, can be used to excite the spins that then are "flipped" to the $xy$-plane (see figure 2.2, net magnetization in this plane is denoted $M_{xy}$). Due to the $B_0$-field, the spins will want to return to their lower energy state and their alignment along the $z$-axis. This relaxation process will cause an emission of energy that is detectable by the receiver coil. The time it takes for the spins to return to the $z$-axis is called the T1-relaxation time, and depends on the tissue type (i.e. the spins’ neighborhoods) and the strength of the external magnet. The recovery of the net magnetization along the $z$-axis (denoted $M_z$) is described as

$$M_z = M_0(1 - e^{-t/T_1}),$$

(2.2)

where $M_0$ is the total magnetization and $t$ is the time. The net magnetization in the $xy$-plane will also decay due to dephasing of the spins. Right after the RF-pulse, the spins are precessing in phase in the $xy$-plane, giving rise to a strong net magnetization in this direction. However, due to interaction between spins and due to external field inhomogeneities, they will soon be out of phase, and the signal will decay. The time for the net magnetization to disappear from the $xy$-plane is called the T2-relaxation time, and is typically 5 to 10 times shorter
than the T1-relaxation time. The decay of $M_{xy}$ is described as

$$M_{xy} = M_0 e^{-t/T^2},$$

where $M_0$ is the total magnetization and $t$ is the time.

Both of these relaxation properties are dependent on the environment of the spins, and will therefore be different for different tissue types. Disregarding effects caused by for example field inhomogeneities, the non-ideality of the RF-pulse (i.e. deviations from the desired theoretical appearance) and the receiving coil, the measured image can be seen as a combination of three components: the proton density (PD), the T1-relaxation time and the T2-relaxation time.

### 2.1.3 Pulse sequences

Sending an RF-pulse only once is not sufficient to generate an image. There must also be some spatial encoding, so the signal’s spatial origin can be determined. To do this, gradient coils are used to apply gradient fields along different axes, and thus small, spatial changes are made to the total magnetic field. A slice-selection gradient field along the z-direction is applied before the RF-pulse. Since the external magnetic field now varies along the z-axis, so will the Larmor frequency for hydrogen atoms at different locations. Since only the spins with the Larmor frequency corresponding to the frequency of the RF-pulse will be affected, spatial encoding in the z-direction is achieved. See figure 2.3 for a schematic drawing of the change in the external magnetic field. A phase-encoding gradient field in the y-direction is applied for a short period of time after the RF-pulse to slightly change the phase for spins inside the slice. When the gradient field is applied, the spins will experience different magnetic field strengths in the y-direction, and thus precess at different frequencies. By deactivating the gradient coil, they return to precess coherently with their original frequency, but now with a position dependent phase-shift. This makes their position distinguishable in the y-direction. Finally, the x-positions are encoded using a frequency-encoding gradient field, along the x-direction. This gradient field is applied during the readout (i.e. the detection of the signal), and the detected signal will contain frequencies above and below the Larmor frequency. The variation in frequency is directly correlated to position in x-direction. The measured signal will in this way be spatially encoded in all three dimensions.

Pulse sequences (example shown in figure 2.4) define the order and timing for when to send radio frequency pulses, apply the gradient fields and to make the readout. Two important parameters are the repetition time (TR) and echo time (TE). The TR is the time between consecutive RF-pulses and the TE is the time after the RF-pulse before the readout. Both these parameters are determined by the operator and by changing them, different tissues can be saturated or highlighted. For example by using a longer TE, the spins will have time to dephase, and tissues with short T2-relaxation time will generate a weaker signal than tissues with longer T2 during the readout. This way, the generated images have different weightings (for example T1-weighted, T2-weighted or PD-weighted), depending of what characteristic is allowed to affect the images most. It is however
2.1 Magnetic Resonance Imaging

Figure 2.3: The slice-selection gradient field (denoted $G_{\text{slice}}$ in the image) is applied which changes the total magnetic field experienced by the protons in the body in the $z$-direction. Only protons experiencing the $B_0$-field strength will be affected by the RF-pulse. This is marked as the slice center.

Figure 2.4: Example of a pulse sequence for acquisition of one line along the $y$-axis. $G_{\text{slice}}$, $G_{\text{phase}}$ and $G_{\text{freq}}$ denote the gradient coil signals. Then during the readout, data samples are collected by a receiving coil. For further details, see [9].

important to remember that all tissue properties (T1, T2 and PD) affect the image, the weighting is just a way to highlight the affect of one of them.
2.1.4 Quantitative magnetic resonance imaging

In conventional MRI, the output image will have a specific contrast between tissues, but the specific image intensities will not have any direct meaning. Not only sequence specific parameters such as TE and TR influence pixel intensity, but also machine specific parameters such as the $B_0$- and gradient field inhomogeneities, RF-pulse and receiver coil sensitivity. Quantitative MRI [10, 4] however, aims to measure tissue properties such as T1, T2 or PD directly. This would allow direct measurement in the image on a pixel basis, with comparable values between images, independent of machine or vendor. Quantitative MRI have been possible for some time, but the clinical use has been limited due to long acquisition times and radiologists’ uncertainty in how to interpret the resulting values. In recent years, these issues have been addressed. New acquisition sequences have been developed that allow for scanning times around 5 minutes for the whole brain and techniques to synthetically construct conventional brain MR images from the quantitative data, making the method clinically relevant.

Quantitative T1, T2 and PD maps are calculated from data acquired using specific pulse sequences. These maps however do not look like conventional MR images, and a method to create more familiar looking images is critical. The answer to this problem is to synthetically combining these maps, and thus reconstruct weighted MR images. These synthetic images will look familiar, but are however not identical to conventional ones, since they are based on models of tissue parameters.

Tissue segmentation

Segmentation of the different tissues in the brain, specifically white matter, gray matter and cerebrospinal fluid (see section 2.2 for further information about brain tissues) is widely reported in the literature, but then using conventional MR images as input data. Segmentation challenges when using these types of images are for example that the intensity values lack anatomical meaning, and that normalization, filtering or other types of processing of the images often is required in order to obtain sufficiently good results. Tissue segmentation using qMRI [10] circumvent some of the issues, since specific tissue properties are obtained (T1, T2 and PD), but how these values correlate to the tissues in the brain is not trivial, since the qMRI properties vary across the brain. Cerebrospinal fluid is typically easier to distinguish than gray and white matter, since it has more consistent qMRI properties. Figure 2.5 shows the theoretical visualization of a R1-R2-PD feature space of qMRI tissue properties in relation to tissue types. The relaxation rates R1 and R2 are related to the relaxation times such that $R1 = 1/T1$ and $R2 = 1/T2$.

A deviation of the theoretically calculated tissue values is expected due to acquisition noise and anatomical differences of the measured values, resulting in clusters of tissue values with a mean and finite distribution. Using this 3D
feature space, tissue segmentation is possible by clustering the values. Figure 2.6 shows an example of a tissue segmentation using qMRI. Voxel values denote the percentage of the specific tissue type, which is visualized as gray scale image intensities in the figure.

![R1-R2-PD feature space](image)

**Figure 2.5:** Schematic drawing of the R1-R2-PD feature space with projections on the R1-PD plane. (Image source: [10]).

(a) White matter segmentation. (b) Gray matter segmentation. (c) Cerebrospinal fluid segmentation.

**Figure 2.6:** Horizontal view of brain tissue segmentation generated from qMRI data.

**Intracranial volume**

The *intracranial volume* (ICV) [12] can be calculated by classifying voxels as belonging to either the brain or the skull. This is done by including all voxels found in the tissue segmentation that form the largest contiguous volume, with the border voxel criterion of having a proton density of 50%. This threshold is motivated by the fact that bone has 0% PD, and CSF has 100% PD. Due to partial volume effects, voxels containing 50% PD are thus assumed to be the border between the brain and the skull. The output of the ICV calculations is the total volume in
milliliters, as well as an ICV mask. This mask separates the skull from the brain, and is therefore used for skull-stripping of brain volumes. An example is shown in figure 2.7. The brain parenchymal volume (BPV) [13] is the ICV minus the CSF volume.

![Figure 2.7: Horizontal view of a brain, where the intracranial mask is shown in white, used for skull-stripping.](image)

### 2.2 The Human Brain

Below follows a short description of the anatomical structures and compartments of the brain that are relevant for this project, using [14]. Understandably, this section does not aim to give a full description of the topic, merely to the degree that is needed in order to understand the subsequent sections.

The biggest anatomical compartments of the brain are the cerebrum, cerebellum (CB) and the brain stem (BS). The cerebrum is divided into two: the left and right cerebral hemispheres (CH), which are connected by the bridge like structure corpus callosum, as well as a few minor commissural tracts. Below the cerebrum is the cerebellum, and between them the tentorium cerebelli, a septum functioning as a floor for the cerebrum and roof for the cerebellum. This keeps them separated, as they are only connected indirectly though the brain stem. The brain stem is a bundle of white matter fibers forming a pathway from the spinal cord to the cerebrum, with excursions to the cerebellum. Both the cerebellum and the cerebrum have a highly folded structure that allows for large surface areas. At the surface, called the cortex, is gray matter (GM). Gray matter consists of billions of neurons that are connected by the deeper lying white matter (WM). It is at the cortex thoughts originates, whereas the white matter functions as a linking network between neurons and different parts of the brain.

A third tissue type found in the brain is the cerebrospinal fluid (CSF). It is a
colorless fluid that consists mainly of water. It circulates in cavities (called ventricles) in the brain as well as around it, functioning primarily as a shock absorber.

Figure 2.8 shows T1-weighted images of the brain relative different anatomical planes, highlighting the relevant structures. The horizontal plane is the plane that divides the brain into superior (upper) and anterior (lower) portions, the sagittal plane divides it into left and right portions and the frontal plane divides it into anterior (front) and posterior (back) portions.

Figure 2.8: Different planes of a T1-weighted brain with the relevant structures highlighted.

2.3 Segmentation Methods

A wide range of methods for medical image segmentation has been reported in the literature. The most common aim is either tissue segmentation or target smaller regions such as inner brain structures like the hypothalamus. Since the
task at hand is different, with focus on larger structures, a lot of the approaches were not directly applicable. Three methods were however found suitable. The first is based on shape bottleneck detection (described in section 2.3.1), the second is a graph based method (described in section 2.3.2) and the third is an atlas-based segmentation tool implemented in the software FreeSurfer (described in section 2.3.3).

2.3.1 Shape bottleneck detection

Shape bottlenecks refer to bridge-like connections between complex objects, which is highly relevant in medical image analysis, since many anatomical structures do not have clear borders but are separated by narrow pathways. Perhaps the clearest example of this is the left and right cerebral hemispheres and how they are connected only by a few white matter commissural tracts. Mangin et. al. [15] presented a method for shape bottleneck detection using partial differential equations (PDE). First, two disjoint areas are selected, initialized to have high and low information potential respectively. By simulating information flow between the regions, shape bottlenecks lying in-between can be detected as areas where the information flow is high. This assumes that the information flows from sources outside the region and that it is conserved inside, which is a highly simplified model of the gray and white matter in the brain. An example of a region where the information flow will be high is the fiber bundle connecting the left and right hemispheres, thus enabling a boundary detection between the compartments.

Mangin et. al. [15] denotes \( i(x, y, z) \) as the information potential value (IPV) in the voxel \( z \) located at point \( (x, y, z) \). The local neighborhood is simplified to a six voxel neighborhood as shown in figure 2.9. Since there is no information sources in the WM region (only outside), the flow in this region is conservative. This gives

\[
\int_{\Omega} \text{div}(\text{grad } i) dx dy dz = 0, \tag{2.4}
\]

where \( \Omega \) denotes an arbitrary WM region. Since (2.4) is true for all white matter regions, the information potential for WM can be described as

\[
\Delta i = 0, \tag{2.5}
\]

which is the Laplace equation (describing the state of equilibrium). With proper boundary conditions, the solution of (2.5) can be used to find shape bottlenecks (such as the ones connecting the left and right hemispheres). For a description of how the information potential is calculated, see appendix A.1. The shape bottleneck detection method results in an information potential map (IPM), containing the information potential values in each voxel.
2.3 Segmentation Methods

Figure 2.9: Illustration of the voxel $z = \{x, y, z\}$ and its 6-neighborhood environment.

Figure 2.10: Pipeline of Adaptive disconnection algorithm, visualized with a 512x512x30 dimensional volume. The images have been up-sampled in the $z$-direction for visualization purposes. A: Initialization of high potential area (white) and low potential area (dark gray) for CH/CBB segmentation, found in the WM∪(GM/WM) region (sagittal view). B: Information potential map. Red denotes higher potential and blue denotes lower. Bottlenecks are clearly visible in yellow (sagittal view). C: Resulting segmentation of IPM by $k$-means clustering (sagittal view) of both the IPM shown in B as well as the subsequently calculated IPM of the CB/BS. D: After region growing (sagittal view). E: Initialization of high potential area (white) and low potential area (dark gray) for hemisphere segmentation (horizontal view). F: Information potential map. Red denotes higher potential and blue denotes lower. Bottlenecks are clearly visible in yellow (horizontal view). G: Segmentation of IPM by $k$-means clustering (horizontal view). H: Resulting segmentation of five compartments (frontal view).

Adaptive disconnection algorithm

The Adaptive disconnection method presented by Zhao et. al. [6] incorporates the PDE based shape bottleneck detection method presented in [15], together

\[1\] Information flow as it is defined in the context of partial differential equations.
with partial volume estimation (PVE). Partial volume refers to the problem that due to resolution inadequacy, voxels in a MRI volume may contain more than one type of tissue. In order to get satisfactory segmentation results, this must be taken into account. Due to the anatomical composition of the tissue types in the brain, the partial volumes can be approximated with maximum two types of tissues in one voxel. Zhao et. al. [6] limited the possible mixture types to GM/WM, CSF/GM and CSF/background.

The pipeline described in [6] can be split into two parts; first the separation of the cerebral hemispheres (CH), cerebellum (CB) and brain stem (BS), and then the segmentation of the left and right hemispheres of the cerebrum and the cerebellum. The algorithm outline is shown in figure 2.10.

For the segmentation of CH, CB and BS, a WM \(\cup\) (GM/WM) region found from the PVE is used as compartment seed for the bottleneck detection. The WM \(\cup\) (GM/WM) region is used to attain a clear distinction between the cerebrum and the cerebellum. Even though there is no direct connection between them (only an indirect connection through the brain stem), spurious connections may occur in the gray matter region due to PVE effects. This is however assumed by Zhao et. al. [6] not to occur in the white matter region. The shape bottleneck detection method is in the first step applied twice. First, the bottleneck that separates CH and the CB \(\cup\) BS (abbreviated as CBB) is found. This is done in a top-to-bottom direction, and figure 2.10 A shows the initialization of the high and low potential regions. Figure 2.10 B shows the resulting IPM. Secondly, the bottleneck separating the BS and CB is found by calculating an IPM in a front-to-back direction. A k-means clustering algorithm is applied and the three resulting compartment segmentations are shown in figure 2.10 C. After the CH, CB and BS are found in the WM \(\cup\) (GM/WM) region, a region growing method is used to reconstruct the original areas. Details of the region growing step are described in appendix A.2, and the result is shown in figure 2.10 D.

In the second step, shown in figure 2.10 E-G, the shape bottleneck method is applied on the reconstructed volume (WM and GM), with low and high potential regions to the far left and right of the volume respectively. Voxels containing more than the threshold value of 30% of CSF are discarded in this step, in order to make the bottleneck areas more visible. Once again, a k-means clustering algorithm is applied to the resulting information potential map in order to segment the compartments. The final step is assemblage of the five segmented compartments: the left and right hemispheres of the cerebrum and cerebellum, and the brain stem, as shown in figure 2.10 H.

### 2.3.2 Graph cuts

Graph cuts is a technique for separation of two regions by defining terminal nodes (denoted source and sink nodes) in the respective regions, and then using a cost function to classify intersecting nodes as members of either one of the regions. When graphs are used for image segmentation, as presented by Boykov et. al. [16], each voxel in the volume is treated as a node, and the connection between them as edges.
Figure 2.11 shows a simple example of a 2D graph with an 8-neighborhood edge connectivity, however the concept of graphs can be generalized to any dimension and connectivity. The leftmost node in figure 2.11 is the source node (denoted with S), and the rightmost node is the sink node (denoted with T). The circles represent pixels (generalized to voxels in the 3D case), and the lines between the nodes represent edges, where each edge is assigned a directed cost. In [16], the problem was formulated as a minimum-intensity surface problem, where the goal is to find the minimum cost surface that cuts the graph in two (no convergence proof exists for multi-label segmentation using graph cuts). The cost \( w(p, q) \) between two adjacent nodes \( p \) and \( q \) is defined as

\[
w(p, q) = \exp(I(p)/s) + \exp(I(q)/s),
\]

where \( I(p) \) and \( I(q) \) are the intensity values at each voxel \( p \) and \( q \), and \( s \) is a constant. By using an exponential function the cut is less likely to cut in high intensity areas. The task is thus to find the cut where \( \sum w(p, q) \) of the border voxels \( p \) and \( q \) is minimized. There are multiple ways of efficiently solving this problem.

\[\text{Figure 2.11: 2D example of a graph with 8-connectivity. The leftmost and rightmost nodes are source (S) and sink (T) nodes respectively.}\]

Liang et. al. [7] proposed a method for segmentation of left and right cerebral hemispheres and cerebellum using the graph cuts algorithm by Boykov et. al [16]. Since the cost function described in (2.6) is more likely to cut at low intensity areas, a problem could arise at the center of the volume, at the division of the ventricles, since the ventricles contain CSF that in T1-weighted images appear dark. The membrane \textit{septum pellucidum} that divides them is however not CSF, and will appear bright. To force the cut to be made along the membrane, [7] uses pre-defined tissue segmentation to find the CSF and then “fills” the ventricles with “light CSF” (i.e. substituting corresponding voxels with higher intensity ones). The problem and solution are visualized in figure 2.12.

In order to find the right voxels to define as source and sink nodes, [7] uses an affine registration of a template volume (in which the interesting compartments are labelled) to the target volume. This will not ensure correct segmentation, but
Figure 2.12: Horizontal view of a T1-weighted brain before and after ventricle filling. In (a) the septum pellucidum membrane is marked.

serves to approximate the locations of the compartments. These approximations are used to automatically find source and sink regions.

Both tissue segmentation and registration are done using third-party software, not developed by the authors.

2.3.3 FreeSurfer

FreeSurfer [8] is a suite of tools for image analysis of MRI data, and the segmentation tool for separation of anatomical compartments in the brain is based on atlas registration. An atlas [17] is a set of two image volumes, one target volume containing the image intensity values, and one labelled volume, containing the segmented areas. Since segmentation of the brain is challenging due to a number of reasons, incorporating a priori knowledge about brain structures is often necessary in order to obtain a good result. Atlas-based methods use atlases as a priori information, which are registered with the target brain in order to match the labelled areas of the atlas to the corresponding areas of the target brain. There are of course other ways of incorporating prior knowledge, but atlas-based methods are popular since they enable distinction between small structures that have little difference in intensity or texture. However, the quality of the result depends heavily on the quality of the atlas. Registration may also introduce errors and computational times are often long.

Using only one manually labelled brain as atlas is not robust, since the appearance of the brain is quite different for different individuals. More commonly a set of labelled brains is used, and the final label is then chosen by for example majority-vote or using statistical methods (for example probability).

FreeSurfer provides an automated pipeline for analysis of the brain volume, which can be divided into two sub-streams: the cortical stream and the sub-cortical stream. The cortical stream computes normalization and skull-stripping of the
brain, as well as brain matter segmentation. White and gray matter are segmented in order to create a surface model of the brain, and are used for skull-stripping. For this segmentation, seed point are used that are found by registering the volume to a Talairach [18] coordinate system, which is a standardized 3D-space. The cortical stream pre-processes the brain volume which then is used in the sub-cortical stream.

The sub-cortical stream uses a probabilistic atlas (i.e. coordinates in the atlas may belong to different labels with different probability) with a more sophisticated registration and segmentation procedure than in the previous stream (including an affine registration to maximize a joint probability), making it more robust to pathologies. It aims to label multiple regions in the sub-cortex region, such as the putamen, hippocampus and the ventricles. To get the best segmentation result possible, the assigning of labels is done with regard to both the probabilistic atlas and the segmentation estimate. These set of operations result in a labelled volume. For a description of the cortical stream, see [19] and [20], and for a description of the sub-cortical stream, see [21] and [22].
This chapter includes a description of how the evaluated segmentation methods were implemented. It ends with a description of the set of modifications that were made to improve the result.

For all methods, synthetic T1-weighted volumes were generated from the qMRI data using SyMRI StandAlone 7.2.

3.1 Adaptive Disconnection Algorithm

A MATLAB implementation [23] was used for the Adaptive disconnection algorithm. Input data to the algorithm are segmented tissue volumes, and since the authors of [6] used a PVE method [23] to generate these volumes, this approach was investigated, as well as using tissue segmentation generated by SyMRI. A schematic overview of the algorithm pipeline with two different inputs is shown in figure 3.1. The first step after acquisition of tissue segmentations was to define threshold values for brain matter (i.e. not including pure CSF voxels), WM and GM regions as well as the CSF/GM region. These values was for the PVE input volumes chosen as in [6]. Since the tissue types were slightly differently defined by SyMRI, the thresholds using those volumes were adapted to give a visually similar result.

The Adaptive disconnection algorithm was then applied, where in all instances the shape bottleneck detection was applied according to the settings used in [6]. The potential values were set to

\[
i(z) = \begin{cases} 
5000 & \forall z \in H \\
1000 & \forall z \in L,
\end{cases}
\]

for all instances of IPM calculations. The regions \(H\) and \(L\) were set differently depending on the compartments to segment, in the same way as in [6]. The number
Figure 3.1: Schematic overview of the Adaptive disconnection algorithm pipeline. Two different input data result in two tracts; one using tissue segmentation from a PVE algorithm and the other using tissue segmentation generated by SyMRI. The variable step is the threshold determination.

of iterations was 1000 and the constant $w$ was fixed to $w = 1.5$ throughout the whole algorithm, as recommended by [15].

3.2 Graph Cuts

A C++ implementation of the graph cuts algorithm [24] was used together with a MATLAB wrapper [25], since all supplementary steps were implemented in MATLAB. The algorithm was implemented as in [7]. First a pre-processing step with ventricle filling, then initialization of source and sink nodes followed by graph cuts separation of CH and CBB. The CBB was then removed and new source and sink nodes were defined, followed by the graph cuts separation of the cerebrum hemispheres. Finally all parts were assembled, resulting in a brain labelled with three compartments. A schematic overview of the pipeline is shown in figure 3.2.

Liang et. al. [7] used external software for tissue segmentation in order to find CSF voxels. Since tissue segmentation from SyMRI was available, this was used instead. The template volume used for registration to find source and sink nodes was not available, so an alternative approach, described below, was used.

The initial nodes of the graph cuts were found by incorporation prior knowledge of the brain’s position and the relative locations of the compartments of interest. In the first step (separation of CH and CBB), the center point of the volume was found, secondly the source and sink nodes were defined with the center point as reference. Source nodes were located inferior and posterior in the
3.2 Graph Cuts

**Figure 3.2:** Schematic overview of the graph cuts algorithm pipeline. After the necessary pre-processing of ventricle filling and source and sink definition, the graph cut algorithm is defined to divide first the CH and then the CBB. Finally all compartments are assembled, resulting in a labelled volume. The variables are the edge connectivity used, as well as the pre-processing steps of node initialization and ventricle filling.

brain. Inferior was defined as the lower 25% of the slices. The largest group of connected voxels were assumed to be the CB, with a maximal volume corresponding to 1% of the total volume per slice, and with the most anterior voxel in the posterior 60% space of the volume. These restrictions served to ensure that sufficiently many voxels were set as source nodes, and to avoid misclassifying voxels belonging to CH occurring at the anterior of the volume. Figure 3.3 shows an example of voxels set as source nodes. The sink nodes were chosen as all voxels in the top (superior) third of the slices.

In the second step (hemisphere separation of CH), the initial nodes were found by taking the 25% leftmost voxels as source nodes and the corresponding 25% rightmost voxels as sink nodes. The weight function and constants were set as in [7].

The ventricle filling step also needed a different approach, since no template volume was available. The ventricle filling was instead implemented in a similar way to the definition of source and sink nodes. The center point of the volume was found, and instead of finding the exact borders of the ventricles, a rectangular region surrounding the center was defined. Using the CSF segmentation provided by SyMRI, containing intensities between 0 and 1 (corresponding to the amount of CSF in the voxel), the CSF values in the specified region was added to
24

3 Method

Figure 3.3: Horizontal view of the lower parts of a brain, where source nodes are shown in white that were used for CH/CBB segmentation. The upper areas are not included as source nodes, since they belong to the cerebrum.

the brain volume.

The edge connectivity used was 26, i.e. each voxel was connected to all surrounding voxels.

3.3 FreeSurfer

FreeSurfer [26] consists of a number of functions running from the terminal, as well as a few GUI based function for inspection of results. The recon-all commando is an automatic reconstruction and segmentation process. The input is a volume of the brain, and all necessary pre-processing such as normalization, skull stripping and registration is performed in the first part of the function. The second part includes segmentation and surface rendering. For a full list of the processing steps, see the FreeSurfer documentation [27]. Below is example of code that performs the necessary pre-processing steps as well as tissue segmentation (step 1-18 out of 31). The last flag, -openmp 4 allows the usage of four processing cores, considerably speeding up the computational time.

recon-all -i <pathToFiles> -subjid <subjectID> -autorecon1 -openmp 4
recon-all -subjid <subjectID> -autorecon2-inflate1 -openmp 4

Figure 3.4 shows the pipeline of the FreeSurfer usage. Some post-processing of the resulting labelled volumes had to be made. Included in the automatic pre-processing step is a resampling of the input volume to voxel size of 1x1x1 mm, and consequently the labelled output volume from the segmentation step will have this voxel dimension. A FreeSurfer function for returning to native voxel size was used, which however resulted in somewhat distorted labels. This was
3.4 Volume Calculations

For each compartment, the volume was calculated. This was done by counting the number of voxels belonging to each compartment and then multiplying with the voxel dimension. The dimensions of the voxels was extracted from the DICOM-headers of the data sets.

The available data sets included three healthy subjects, with four data sets each: two were acquired from a 1.5 T MR-scanner and two from a 3 T MR-scanner. Using the result from these 12 data sets, a small statistical study was conducted in order to evaluate the repeatability of the segmentation methods. Looking at each field strength separately, the mean value of the total volume and the mean value of the separate compartment volumes was calculated as

---

**Figure 3.4:** Schematic overview of the FreeSurfer pipeline. A T1-volume is sent to the recon-all steps (cortical and sub-cortical processing), which result in a labelled volume. Post-processing is performed, including resampling and morphological operations, resulting in a three-label segmentation. The FreeSurfer pipeline is highly automated, and the only variable is the morphological operation.
Mean volume = \( \frac{\sum_{n=1}^{N} (V_{n1} + V_{n2})}{2N} \),

(3.2)

where \( N \) is the number of subjects, \( V_{n1} \) is the first acquisition for subject \( n \), and \( V_{n2} \) is the second, acquired with the same field strength. When calculating the total mean volume, \( V \) is the sum of the compartment volumes, otherwise it denotes the specific compartment volume of interest.

The mean value was also calculated for the volume difference between the first and second data sets from one subject (\( V_{n1} \) and \( V_{n2} \)), acquired using the same field strength, according to

\[
\text{Mean diff.} = \frac{\sum_{n=1}^{N} \text{abs}(V_{n1} - V_{n2})}{N}.
\]

(3.3)

The standard deviation (\( \sigma \)) was calculated according to

\[
\sigma = \sqrt{\frac{\sum (x - \bar{x})^2}{N - 1}},
\]

(3.4)

where \( x \) is the sample value, \( \bar{x} \) is the mean value of the included samples and \( N \) is the sample size. When used to calculate the standard deviation for the total mean value, \( x \) was simply the total volume for each data set, and for the compartment mean volume, \( x \) was the specific compartment volume for each data set. When used to calculated the standard deviation for the mean difference, \( x \) was the volume difference of interest.

Since the two different input data for the Adaptive disconnection method gave different output results, the results are presented separately. In order to compare the methods with each other, only three compartments were used, since this was the lowest common denominator. The compartments were the left cerebral hemisphere, the right cerebral hemisphere and the cerebellum with the brain stem included. The compartments volumes generated by FreeSurfer were calculated before resampling to original voxel sizes.

### 3.5 Proposed Improved Method

Below follows a description of the proposed improved method, denoted SB-GC, as it is a combination of the shape bottleneck detection introduced by Mangin et al. [15] and graph cuts. The input data is tissue segmentations available from SyMRI together with a T1-weighted volume. The resulting labelled volume consists of the left and right cerebral hemispheres (CH), the cerebellum (CB) and the brain stem (BS). The pipeline of the algorithm is shown in figure 3.5.

The method can be divided into three parts: separation of CH and CB including BS (CBB), separation of CB and BS and finally separation of the left and the right
3.5 Proposed Improved Method

Figure 3.5: Schematic overview of the SB-GC pipeline. Three different weight functions are used for graph cuts segmentation. The first step is separation of CH and CBB, then CH is divided into left and right and CBB is divided into CB and BS. Finally all compartments are assembled, resulting in a labelled volume.

CH. The shape bottleneck detection serves as a spatial encoding for the weight function, which is used in graph cuts for determining the minimum cut.

In the first step, separation of CH and CBB, the IPM was calculated from the WM $\cup$ (WM/GM) region, to ensure the detection of bottlenecks (see figure 2.10 B for an example of the IPM). The weight functions used is defined as

$$w_{CH/CBB} = w_0 + d(max(w_1) - w_1), \quad (3.5)$$

where $w_0$ denotes the original weight function used by Liang et. al. [7] (given by (2.6)), and $d$ is a constant. The mapping of the IPM is denoted $w_1$ and is calculated according to

$$w_1 = jI(z)^3 + kI(z)^2 + lI(z) + m, \quad (3.6)$$

where $I(z)$ denote the information potential value in the voxel $z$, normalized to a value between 0 and 1 and $j, k, l$ and $m$ are constants. The desired appearance of this function is to be close to 0 for IPV:s close to the mean IPV of the high and low potential regions, and 1 for IPV:s close to 0 and 1. Using the IPV:s as in (3.1) (5000 and 1000), normalized to a value between 0 and 1, gives a mean value of 0.6. Thus, the mapping function should have a global minimum at 0.6.

The resulting mapping function is shown in figure 3.6, using constant values of $j = 2.56, k = 0.83, l = -3.54$ and $m = 1.27$. An heuristic approach gave $d = 5$ for the constant in (3.5). By construction the weighting function like this, voxels
in the WM ∪ (GM/WM) region, especially the ones close to the bottleneck, will get higher values. This might be counter-intuitive, since the desired cut should be made at the bottlenecks, which then should have low values. However, (3.5) pushes the cut to be made around the cerebellum, and decreases the risk of it taking short cuts. Figure 3.7 shows the resulting weights for CH/CBB separation from a horizontal and a sagittal view, as well as the resulting segmentation.

![Mapping Function](image)

**Figure 3.6:** Plot of mapping function described in (3.6) used for mapping the IPM to values close to 0 at the bottleneck, with higher values for remaining values.

In the remaining two steps, the information potential maps were calculated from the two compartments separated in the first step. The weight functions for these steps are defined as

\[ w_{CH} = (w_0(w_1 + c)^a)^b, \]
\[ w_{CB/BS} = w_1, \]

where the constants \(a, b\) and \(c\) were found heuristically to be \(a = b = 0.9\) and \(c = 0.23\). Figure 3.8 shows the resulting weights for CH separation from a horizontal view.

The graph cuts method described in section 3.2 utilizes a ventricle filling, which in this method is substituted by the incorporation of IPM in the weight functions. The previous method did not separate the brain stem from the cerebellum. This is with this novel approach possible by using the mapped IPM as weight function. The terminal nodes for CBB separation are found in the front-to-back (anterior-posterior) direction, with source nodes at the brain stem and sink nodes at the anterior part of the cerebellum. In this direction, the number of voxel rows in each slice is determined, and the voxels in the frontmost 1% of the rows are set as source nodes, and the voxels in the backmost 1% rows are set as sink nodes. This allows for a gradual increase in terminal nodes as the size of
the cerebellum increases along the z-axis. The terminal nodes for separation of CH/CBB and CH are found as described in section 3.2.

The three segmentation steps results in four segregated compartments, that together form a segmented volume of left and right cerebral hemispheres, cerebellum and brain stem. The edge connectivity used was 10, i.e. each voxel is connected to all 8 voxels in the same slice, as well as the voxels in the slices directly below and directly above.
(a) Horizontal view of left: $w_0$, right: $d(\max(w_1) - w_1)$.

(b) Sagittal view of left: $w_0$, right: $d(\max(w_1) - w_1)$.

(c) Horizontal view of $w_{CH/CBB}$.

(d) Sagittal view of $w_{CH/CBB}$.

(e) Horizontal view of $w_{CH/CBB}$ with resulting CBB in yellow.

(f) Sagittal view of $w_{CH/CBB}$ with resulting CBB in yellow.

Figure 3.7: Showing resulting weights for separation of CH and CBB. (a) and (b) show the two parts of (3.5) that together make up $w_{CH/CBB}$, which is shown in (c) and (d). The resulting segmentation is shown in the bottom row.
Figure 3.8: Resulting weights for cerebral hemisphere separation.
In this chapter the visual results are presented from the three evaluated segmentation methods, as well as the resulting volumes for the labelled compartments. The resolution of the input data varied slightly, but the resolution in z-direction (i.e. number of slices) was always poor. Due to this, the results of the segmentations will only be shown in the horizontal plane. The labelled compartments are shown in different colors, overlaying the T1-weighted brain volume for illustration purposes. For more images of results, see appendix B.

4.1 Healthy Subjects

All segmentation methods were tested on data sets from healthy, adult subjects. These data sets all had the resolution 512x512x30, voxel size of 0.47x0.47x5 mm and were acquired with either 1.5 T or 3 T field strength. The results shown in this section aim to give a representative picture of the segmentation results using the respective methods.

4.1.1 Adaptive disconnection algorithm

The method was tested using two different input data: tissue segmentation using a PVE method and tissue segmentation from SyMRI. The labelled compartments and their corresponding colors are listed in table 4.1.

Figure 4.1 shows two different slices from the same data set, using two different input data. The left column shows a lower horizontal plane, and the right column shows a plane higher up in the volume. The top row shows the result using the partial volume estimation method to generate the input tissue segmentation, and the lower row shows the result when using the tissue segmentation generated by SyMRI.
Table 4.1: Compartment label colors for the Adaptive disconnection algorithm.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Label color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right cerebral hemisphere</td>
<td>Light red</td>
</tr>
<tr>
<td>Left cerebral hemisphere</td>
<td>Dark red</td>
</tr>
<tr>
<td>Right cerebellum hemisphere</td>
<td>Yellow</td>
</tr>
<tr>
<td>Left cerebellum hemisphere</td>
<td>Orange</td>
</tr>
<tr>
<td>Brain stem</td>
<td>White</td>
</tr>
</tbody>
</table>

4.1.2 Graph cuts method

Below follows the result of the graph cuts segmentation method. The labelled compartments and their corresponding colors are listed in table 4.2.

Table 4.2: Compartment label colors for the graph cuts segmentation method.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Label color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right cerebral hemisphere</td>
<td>Light red</td>
</tr>
<tr>
<td>Left cerebral hemisphere</td>
<td>Dark red</td>
</tr>
<tr>
<td>Cerebellum hemisphere</td>
<td>Orange</td>
</tr>
</tbody>
</table>

Figure 4.2 shows the result for three different data sets, where the left column shows a lower slice in the respective data sets, and the right column shows a slice higher up.

As mentioned in section 3.2, the source and sink nodes for hemisphere segmentation were set to be the 25% leftmost and rightmost cerebrum voxels respectively. Figure 4.3 shows the segmentation result when using only the 10% leftmost and rightmost voxels respectively as source and sink nodes.

4.1.3 FreeSurfer

Figure 4.4 shows the result of the FreeSurfer segmentation for two different data sets. The left column shows a lower slice in the respective data sets, and the right column shows a slice higher up. The labelled compartments and their corresponding colors are listed in table 4.3.

Table 4.3: Compartment label colors for the FreeSurfer segmentation method.

<table>
<thead>
<tr>
<th>Compartment</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Right cerebral hemisphere</td>
<td>Light red</td>
</tr>
<tr>
<td>Left cerebral hemisphere</td>
<td>Dark red</td>
</tr>
<tr>
<td>Cerebellum hemisphere</td>
<td>Orange</td>
</tr>
</tbody>
</table>
4.1 Healthy Subjects

Figure 4.1: Showing result of Adaptive disconnection algorithm from one subject. The left column shows a low horizontal slice, the right column a horizontal slice higher up in the brain. A: Input data for generated by PVE. B: Input data generated by SyMRI.

4.1.4 SB-GC

Results generated by the proposed improved method SB-GC is shown in figure 4.5. Each row shows a lower and an upper slice from three different subjects. The labelled compartments and their corresponding colors are listed in table 4.4.
Table 4.4: Compartment label colors for the SB-GC method.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Label color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right cerebral hemisphere</td>
<td>Light red</td>
</tr>
<tr>
<td>Left cerebral hemisphere</td>
<td>Dark red</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>Orange</td>
</tr>
<tr>
<td>Brain stem</td>
<td>White</td>
</tr>
</tbody>
</table>

Figure 4.2: Showing segmentation results using graph cuts. Each row is two slices from one data set from three different subjects; the left one at a lower position and the right one at a higher position.
4.1 Healthy Subjects

Figure 4.3: Segmentation result from graph cuts method using incorrectly initialized nodes.

Figure 4.4: Showing results using the FreeSurfer segmentation method. Each row shows a lower and a higher slice from two data sets of two different subjects.
Figure 4.5: Showing segmentation results using SB-GC. Each row is two slices from one data set from three different subjects; the left one at a lower position and the right one at a higher position.
4.2 Challenges

More challenging data sets were also used to test the methods. The resolution of these data sets varied. Figure 4.6 shows the segmentation results for each method when applied to a data set of a two-year-old child. Figure 4.7 shows the result when the methods were applied to a data set of a patient with a tumor. A gadolinium contrast agent was used when the images were acquired. The segmentation results for a data set of a child suffering from hydrocephalus (when CSF is abnormally accumulated in the brain) is shown in figure 4.8. FreeSurfer was unable to generate a result for this data set. The bottom row shows the ICV mask generated by SyMRI used for skull-stripping.
Figure 4.6: Result of each segmentation method when applied to data set of a two-year-old child. A: Adaptive disconnection method with input from PVE. B: Adaptive disconnection method with input from SyMRI. C: Graph cuts method. D: FreeSurfer. E: SB-GC.
4.2 Challenges

Figure 4.7: Result of each segmentation method when applied to data set containing a tumor. A: Adaptive disconnection method with input from PVE. B: Adaptive disconnection method with input from SyMRI. C: Graph cuts method. D: FreeSurfer. E: SB-GC.
Figure 4.8: Result from segmentation methods when applied to data set of a child with hydrocephalus. FreeSurfer failed to generate a result. A: Adaptive disconnection method with input data from PVE. B: Adaptive disconnection method with input from SyMRI. C: Graph cuts method. D: SB-GC. E: Intracranial mask.
4.3 Volume Calculations

Figure 4.9 shows the total volume for each of the 12 data sets used in the small repeatability study conducted (described in section 3.4). The reference line above the stacked columns represents the brain parenchymal volume (BPV) extracted from SyMRI (with mean difference value of 4.7 ± 1.2 ml for 1.5 T and 5.7 ± 4.2 ml for 3 T). The vertical axis shows the total volume in milliliters, and the horizontal axis shows each method for each data set.

Table 4.5 and table 4.6 show the mean values of compartment volume as well as the mean difference between acquisition 1 and 2 for three healthy subjects acquired with 1.5 T and 3 T field strength respectively. The mean difference values are also presented in figure 4.10 and figure 4.11.

![Figure 4.9](chart.png)

**Figure 4.9:** Chart showing the resulting compartment volumes for all 12 data sets from the different segmentation methods. On the horizontal axis the three different subjects are shown, first for 1.5 T field strength and then for 3 T field strength. The vertical axis shows the volume in milliliters.
**Table 4.5:** Mean value of compartment volume as well as the mean difference between acquisition 1 and 2 for three healthy subjects acquired with 1.5 T field strength. Method A: Adaptive disconnection with input data generated by PVE. Method B: Adaptive disconnection with input data generated by SyMRI. Method C: Graph cuts method. Method D: FreeSurfer. E: SB-GC.

<table>
<thead>
<tr>
<th></th>
<th>Method A</th>
<th>Method B</th>
<th>Method C</th>
<th>Method D</th>
<th>Method E</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Volume</strong></td>
<td>Total mean (ml) 1112.9 ± 75.7</td>
<td>1307.8 ± 90.7</td>
<td>1320.5 ± 90.4</td>
<td>1213.1 ± 72.8</td>
<td>1320.5 ± 90.4</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 2.1 ± 1.7</td>
<td>4.0 ± 1.9</td>
<td>3.4 ± 0.9</td>
<td>69.0 ± 85.0</td>
<td>3.4 ± 0.9</td>
</tr>
<tr>
<td><strong>RCH</strong></td>
<td>Total mean (ml) 489.7 ± 36.4</td>
<td>569.8 ± 40.5</td>
<td>592.1 ± 52.2</td>
<td>519.7 ± 38.7</td>
<td>566.4 ± 40.5</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 4.5 ± 1.5</td>
<td>1.1 ± 1.2</td>
<td>35.6 ± 22.4</td>
<td>40.0 ± 53.0</td>
<td>0.6 ± 0.3</td>
</tr>
<tr>
<td><strong>LCH</strong></td>
<td>Total mean (ml) 488.9 ± 35.2</td>
<td>563.9 ± 42.7</td>
<td>564.3 ± 41.0</td>
<td>528.9 ± 26.9</td>
<td>572.9 ± 40.6</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 4.6 ± 5.1</td>
<td>3.7 ± 1.5</td>
<td>24.0 ± 8.9</td>
<td>27.0 ± 27.9</td>
<td>3.7 ± 3.3</td>
</tr>
<tr>
<td><strong>CB + BS</strong></td>
<td>Total mean (ml) 134.3 ± 9.7</td>
<td>174.0 ± 14.1</td>
<td>164.1 ± 28.3</td>
<td>164.6 ± 12.5</td>
<td>181.2 ± 16.3</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 9.4 ± 4.3</td>
<td>4.3 ± 4.1</td>
<td>19.0 ± 13.6</td>
<td>3.2 ± 3.0</td>
<td>3.2 ± 0.7</td>
</tr>
</tbody>
</table>

**Table 4.6:** Mean value of compartment volume as well as the mean difference between acquisition 1 and 2 for three healthy subjects acquired with 3 T field strength. Method A: Adaptive disconnection with input data generated by PVE. Method B: Adaptive disconnection with input data generated by SyMRI. Method C: Graph cuts method. Method D: FreeSurfer. E: SB-GC.

<table>
<thead>
<tr>
<th></th>
<th>Method A</th>
<th>Method B</th>
<th>Method C</th>
<th>Method D</th>
<th>Method E</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Volume</strong></td>
<td>Total mean (ml) 1119.4 ± 74.1</td>
<td>1289.2 ± 86.3</td>
<td>1303.9 ± 86.8</td>
<td>1229.8 ± 68.4</td>
<td>1303.9 ± 86.8</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 9.9 ± 9.2</td>
<td>5.6 ± 5.7</td>
<td>5.5 ± 4.5</td>
<td>14.3 ± 14.1</td>
<td>5.5 ± 4.5</td>
</tr>
<tr>
<td><strong>RCH</strong></td>
<td>Total mean (ml) 491.3 ± 37.7</td>
<td>567.4 ± 44.9</td>
<td>570.1 ± 37.8</td>
<td>525.7 ± 30.0</td>
<td>561.9 ± 39.0</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 4.3 ± 0.9</td>
<td>3.5 ± 2.0</td>
<td>8.6 ± 11.8</td>
<td>4.5 ± 0.9</td>
<td>5.0 ± 1.6</td>
</tr>
<tr>
<td><strong>LCH</strong></td>
<td>Total mean (ml) 491.0 ± 33.7</td>
<td>562.0 ± 42.3</td>
<td>572.5 ± 39.4</td>
<td>535.7 ± 29.5</td>
<td>569.3 ± 42.7</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 5.0 ± 1.6</td>
<td>4.1 ± 2.0</td>
<td>8.1 ± 5.3</td>
<td>15.2 ± 17.8</td>
<td>4.8 ± 0.8</td>
</tr>
<tr>
<td><strong>CB + BS</strong></td>
<td>Total mean (ml) 137.1 ± 13.4</td>
<td>159.8 ± 18.2</td>
<td>161.2 ± 12.1</td>
<td>168.4 ± 14.1</td>
<td>172.6 ± 10.0</td>
</tr>
<tr>
<td></td>
<td>Mean diff. (ml) 10.3 ± 9.6</td>
<td>8.6 ± 7.9</td>
<td>6.4 ± 4.9</td>
<td>4.2 ± 3.6</td>
<td>4.3 ± 3.6</td>
</tr>
</tbody>
</table>
4.3 Volume Calculations

**Figure 4.10:** Chart showing the mean difference between two subjects for each segmentation method, acquired with 1.5 T field strength. The numerical values are presented in table 4.5. Method A: Adaptive disconnection with input data generated by PVE. Method B: Adaptive disconnection with input data generated by SyMRI. Method C: Graph cuts method. Method D: FreeSurfer. E: SB-GC.

**Figure 4.11:** Chart showing the mean difference between two subjects for each segmentation method, acquired with 3 T field strength. The numerical values are presented in table 4.6. Method A: Adaptive disconnection with input data generated by PVE. Method B: Adaptive disconnection with input data generated by SyMRI. Method C: Graph cuts method. Method D: FreeSurfer. E: SB-GC.
In this chapter, the results of the segmentation methods are discussed, as well as possible future developments.

5.1 Method Evaluation

The methods were evaluated on perceived accuracy (based on visual inspection) and repeatability. Since no ground truth exists for the evaluated data, nor a gold standard method to compare against, the methods were compared against each other, and evaluated on any obviously noticeable classification error. Two error measures were used to evaluate the repeatability: the total mean difference (TMD), which denote the mean and standard deviation for differences in total volume, and the compartment mean difference (CMD), which denote the mean and standard deviation of volume differences for RCH, LCH and CB + BS. The values for TMD and CMD are found in table 4.5 and table 4.6.

The Adaptive disconnection method gave visually similar results for all evaluated data sets, proving that the shape bottleneck detection method works very well in finding compartment locations, even for subjects with pathologies. Figure 4.1 shows a representative result of the method’s performance. Since the aim of this project was to evaluate the segmentation performance for the cerebral hemispheres, brain stem and cerebellum, the cerebellum hemisphere segmentation performed by Adaptive disconnection will not be further discussed. As previously mentioned, the bottleneck detection algorithm worked well, the compartments’ locations were correctly identified in all evaluated data sets. However, the region growing method applied in order to reconstruct the volume after the bottleneck detection in the white matter region resulted in jagged and irregular borders between compartments, which corresponds poorly to the anatomical
construction of the brain. It also failed to classify many gray matter voxels due to restrictive stopping criteria. This is especially critical when using the PVE to generate the tissue segmentation. This phenomenon is clearly visible in figure 4.9, where the Adaptive disconnection method significantly underestimated the total volume in comparison to the other methods and the brain parenchymal volume generated from SyMRI. The TMD was however still quite low, as well as the CMD (see table 4.5, table 4.6, figure 4.10 and figure 4.11), indicating a high repeatability. The low CMD can most probably be explained by the accurate performance of the shape bottleneck detection, together with the voxel based region growing. Since every growing voxel is evaluated independently, any variance between adjacent compartments will be small. Using tissue segmentations generated by SyMRI generally gave a higher total volume, this due to slightly different threshold values, allowing for more voxels partially containing CSF to be considered brain matter. The CSF tissue segmentation of qMRI data is considered reliable, and thus validating the assumption that the results using these input tissue segmentations generated a more accurate result.

The perceived accuracy of the graph cuts method varied between the evaluated data sets to a higher extent than the previous method. This is apparent in the resulting images shown in figure 4.2, where especially the two lower rows show obvious classification errors. The TMD for the evaluated data sets was low (about the same size as for the BPV), as seen in table 4.5 and table 4.6. This is due to the fact that all voxels will inevitably be classified, unlike in the previous method. As seen in table 4.5, table 4.6, figure 4.10 and figure 4.11, the CMD was however greater than for the Adaptive disconnection method. There are a number of reasons for this. Contrary to the previous method, compartment separation is not a voxel by voxel operation, but a global cut throughout the whole volume. A change in voxel classification in the lower part of the volume may cause a change throughout the entire border, if this results in the lowest cost. Thus, the weighting function used (described in (2.6)) to generate the minimum cut did not result in a distinct global minimum, which sometimes resulted in the cut being made at clearly incorrect places. This also means that the voxels set as source and sink nodes greatly affect where the cut will be made. This is demonstrated in figure 4.3. Normally, a relatively large portion of the total voxels (50% for the hemisphere segmentation) in the volume were set as sink or source nodes, primarily to force the cut to be made somewhere in-between the regions. When too few nodes were set, the minimum cut was made just at the edge of the source or sink, i.e. all nodes (except the source and sink nodes) were set to belong to one region. The case shown in figure 4.3 only the leftmost 10% and the rightmost 10% of voxels were set as terminal nodes. Since the aim is to minimize the sum of the cost function, the number of edges that are needed to be cut is ideally low. This is most probably the reason why the cut is made at the edge of the source or sink region; the length of the cut is so short that despite higher costs per edge (i.e. higher intensity values of the voxels) the total cost was still the lowest. Using only the intensity to define the weight function makes the method incapable of separating the brain stem and the cerebellum, since there is no distinct intensity
difference between them.

For the results presented in [7], ventricles were found using external registration software. The ventricle fillings were made in order to force the cut for hemisphere segmentation to be made straight through the ventricles. For this implementation, an alternative approach was taken to locate the voxels belonging to the ventricles. As seen in the result shown in the two lower rows in figure 4.2, this sometimes seems to fail since the cuts were made too far to the left. The ventricle sizes and locations may vary significantly between different individuals, making it hard to implement a simple algorithm that will work for all cases. As discussed above, incorrectly including or excluding just a few voxels in this step may have significant consequences in the segmentation results.

The FreeSurfer segmentation pipeline is the most advanced and optimized method of the three evaluated. Quantitative comparison with the other two methods is hard due to the voxel resizing that is done by FreeSurfer. FreeSurfer also computes the skull-stripping, whereas the other methods use already skull-stripped volumes as input. The visually perceived accuracy of this method is good, but as seen in table 4.5, table 4.6, figure 4.10 and figure 4.11, the TMD and the CMD were high for this method. The repeatability for this methods was therefore the lowest of the evaluated methods. An atlas-based method is expected to be sensitive to pathologies, since the labelled volumes registered to the target are based on healthy subjects. With this in mind, FreeSurfer succeeds in labelling some of the more challenging volumes, but failed to output results for two data sets: one with a large brain tumor (using no contrast) and one child with hydrocephalus. Since the pipeline is automatic and highly optimized, the source of the errors is hard to back-track. The problems associated with atlas-based methods will however always remain, even though FreeSurfer utilizes strategies to make it more robust.

The SB-GC method was constructed as a combination between shape bottleneck detection and graph cuts, in order to combine the strengths of the Adaptive disconnection method and the graph cuts method. As discussed above, the Adaptive disconnection method gave repeatable results primarily due to the well performing shape bottleneck detection, but failed to generate very good results due to the region growing algorithm. The weight function used in graph cuts only depended on intensity values in the image, which proved not to be sufficient. SB-GC improved the weight function by incorporating the IPM generated by the shape bottleneck detection as spatial encoding. This way, the weight function contains more prior knowledge, allowing for a higher probability of a correct segmentation, without the need of a region growing algorithm. The ventricle filling used in the graph cuts method was thanks to this not necessary. Figure 4.5 shows examples of the segmentation result for SB-GC. The perceived visual accuracy is high, with only minor errors at the compartment borders between the cerebrum and the cerebellum. This is most likely due to poor resolution in the z-direction (which for the majority of the data sets was 5 mm, in comparison to the in-plane resolution of 0.47 mm). Table 4.5, table 4.6, figure 4.10 and figure 4.11 show a
generally very low TMD and CMD, showing a high repeatability for this method.

The segmentation results for the more challenging subjects varied greatly between the methods. Figure 4.6 shows the result for a two-year-old. The challenge with children is that the brain is not fully developed yet, so anatomical assumptions made for adults may not be valid. All methods handled the slight tilt in volume orientation and resulted in similar hemisphere segmentations, but with varying border definition between cerebrum and cerebellum. SB-GC failed to correctly separate the brain stem and the cerebellum. This due to different proportions of the cerebellum for a child than for an adult, thus the assumptions made when defining terminal nodes were invalid.

Segmentation of data sets containing tumors are difficult not only since the tumors cause anatomical shifts of the brain tissue, but also from a classification standpoint. Tumors are non-brain matter, and thus, no correct classification exists. All methods handled the tumor case differently, as seen in figure 4.7. The Adaptive disconnection method tended to classify the tumor as brain stem, or as part of the cerebellum. The graph cuts method classified parts of the tumor as cerebellum, parts of it as left cerebral hemisphere, and some parts not at all. FreeSurfer classified it as either left cerebral hemisphere or not at all. SB-GC classified the lower parts of the tumor as cerebellum, and upper parts not at all.

The case of hydrocephalus, shown in figure 4.8 is, despite the large anatomical deviation it causes, in some aspects an easier case than the tumor case, since the excessive fluids are CSF. Both Adaptive disconnection method, graph cuts method and SB-GC remove CSF before segmentation, so the question of whether or not to classify the fluids is removed. The bottom row shows the ICV mask used for skull-stripping, and since this mask contain visually noticeable errors (for example the blocky appearance shown in the middle column in figure 4.8), this is likely to have affected the segmentation results. The Adaptive disconnection method did classify all the compartments correctly, but with errors at the edges (partly due to the incorrect mask). The graph cuts method failed to separate the cerebral hemispheres. This is due to problem previously mentioned; the diagonal appearance of the right cerebral hemisphere resulted in the lowest cost cut at the very edge of the brain instead of in-between the hemispheres. SB-GC gave a similar result as the Adaptive disconnection method, but with more even compartment borders. FreeSurfer failed to generate a result.

As seen in Figure 4.10 and figure 4.11, the mean difference between the methods varied considerably for the different field strengths. Too few subjects were investigated to draw the conclusion that this variation solely depend on the field strength, this could just as well originate from one deviating data set. However, since this difference is more prominent for the graph cuts method and FreeSurfer, the conclusion that these two methods generate less repeatable results than the other methods can be drawn. SB-GC gave the most repeatable results with low mean and standard deviation for both 1.5 T and 3 T field strength.
5.2 Further Developments

Continued work in improving the weight function in SB-GC could potentially increase the accuracy at especially the border between the cerebrum and the cerebellum. Since the textures of CB and CH are different, this could potentially be incorporated in the weight function in order to discriminate these regions better. Expressing the weight function in a more uniform way for the different compartment segmentations, with just different constants, is also a further improvement. Since the balance between the intensity information and the spatial information (mapped IPM) was determined heuristically, a more structured optimization processes might result in a different weight function, that potentially could improve segmentation results. In order to use the segmentation method in clinical applications, it needs to be verified and tested more extensively, preferably against manually segmented ground truth data.
Clinical relevance is always at the very center of method development for brain image analysis. By creating a robust way of automatically segment out the cerebral hemispheres, the cerebellum and the brain stem, the door opens for brain compartment research at a larger scale, since the highly time consuming element of manual brain labelling is removed.

Three automatic brain segmentation methods have been implemented and evaluated. The Adaptive disconnection method had the lowest TMD and CMD, and managed to correctly identify the compartments in all data sets. It however resulted in a substantially lower total volume than the BPV, and the perceived visual accuracy was diminished by jagged and irregular compartment borders. The graph cuts method gave smoother compartment borders and a higher total volume, together with a low TMD. It however gave a high CMD, and resulted occasionally in severe label misclassifications. FreeSurfer is a well established and frequently used tool for MR image processing, and resulted in visually perceived accurate segmentations in most cases. However, the TMD and CMD was high, indicating a low repeatability. It also failed to generate results for two of the challenging data set containing pathologies. Therefore, the conclusion is that none of the methods gave sufficiently good results to be clinically relevant.

An alternative method, SB-GC, was proposed that addresses the shortcomings of the other methods. It utilizes qMRI which generates comparable results between different MR scanners, as well as reliable tissue segmentations. It combines shape bottleneck detection (as used in Adaptive disconnection method) with graph cuts, leading to both visually perceived accurate segmentations as well as low TMD and CMD. This confirms that this method has great potential value in clinical applications.
Appendix
A

Detailed Descriptions

In this chapter, more detailed descriptions of specific parts of the applied methods are presented.

A.1 Shape Bottleneck Detection

Below follow a description of how the information potential is calculated and iteratively updated in order to detect shape bottlenecks [15, 6]. The problem of separating cerebral hemispheres result in a Dirichlet-Neumann problem, since the region is divided into two disjoint subsets with different conditions imposed.

Let \( z \) denote a voxel, and \( \Omega \) denote all voxels at the boundary of a 3D object \( \Theta \). A boundary voxel is defined to have at least one of its six neighboring voxels outside of the object. Let \( H \subset \Omega \) be the information source, i.e. the region of high potential value, and let \( L \subset \Omega \) be the information terminal (region with low potential value). The information potential in these regions are then defined with the Dirichlet boundary condition as

\[
i(z) = \begin{cases} h, & \forall z \in H, \\ l, & \forall z \in L, \end{cases}
\]  

(A.1)

where \( z \) is a voxel in \( \Theta \), \( i(z) \) is the information potential value (IPV) at \( z \), \( l \) is a low value and \( h \) is a high value.

The IPV for all other boundary voxels not included in \( H \) or \( L \), i.e. \( z \in (\Omega \setminus (H \cup L)) \), is defined with the Neumann boundary condition as
\[ i(z) = \frac{1}{R} \sum_{\mathcal{N}} i(p) + \frac{1}{2R} \sum_{T} (i(q_1) + i(q_2)), \quad \forall z \in (\Omega \setminus (H \cup L)), \tag{A.2} \]

where \( \mathcal{N} \) is the set of directions \((x, y, \text{or} z)\) where one of the neighboring voxels (denoted as \( p \)) of \( z \) is in \( \Theta \) and \( T \) is the set of directions where two of the neighboring voxels (denoted as \( q_1 \) and \( q_2 \)) of \( z \) are in \( \Theta \). \( R \) is the number of grid directions \((\pm x, \pm y \text{or} \pm z)\) where at least one of the neighboring voxels of \( z \) belong to \( \Theta \).

For all voxels in \( \Theta \) that are not at the boundaries, the information flow is conservative, and fulfills the Laplace equation \((\Delta i = 0)\). For discrete applications, this can be approximated as finite differences as

\[
\begin{align*}
\frac{1}{h_x^2} (i(x-1, y, z) - 2i(x, y, z) + i(x+1, y, z)) + \\
\frac{1}{h_y^2} (i(x, y-1, z) - 2i(x, y, z) + i(x, y+1, z)) + \\
\frac{1}{h_z^2} (i(x, y, z-1) - 2i(x, y, z) + i(x, y, z+1)) = 0, \tag{A.3}
\end{align*}
\]

where \( h_x, h_y, h_z \) denotes the voxel size in the corresponding direction. Using a 6-neighborhood here will ensure convergence when solving (A.3).

The linear equations system in (A.1), (A.2) and (A.3) is solved iterative with the initial values

\[ i^0(z) = \frac{h + l}{2}, \quad \forall z \in (\Theta \setminus (H \cup L)), \tag{A.4} \]

i.e. all values inside \( \Theta \), except in \( H \) and \( L \), are set to the mean of \( l \) and \( h \). The IPV values for voxels in \( H \) and \( L \) are unchanged throughout the iterative scheme as stated in (A.1). The IPV for all other voxels (i.e. \( \forall z \in (\Theta \setminus (H \cup L)) \)) is updated as

\[ i^{k+1}(z) = (1 - w)i^k(z) + wI^k(z), \tag{A.5} \]

where \( k \) is the iteration number, \( 1 < w < 2 \) and \( I^k \) is the IPV calculated as (A.2) or (A.3) depending on if \( z \in (\Omega \setminus (H \cup L)) \) or \( z \in (\Theta \setminus \Omega) \).

After sufficiently many iterations the values will converge, and thus represent the steady state of the information potential flow in \( \Theta \). This results in an information potential map (IPM).

\section*{A.2 Region Growing Details in Adaptive Disconnection Algorithm}

The region growing used in [6] has the boundary condition of stopping when reached the CSF/GM region. The closing indicator, \( P_{\text{boundary}} \) is defined as

\[ P_{\text{boundary}}(z) = 2 - \frac{D(z)}{D_{\text{MAX}}} - \frac{J(z)}{J_{\text{MAX}}}, \tag{A.6} \]
A.3 FreeSurfer Compartment Labels

Figure A.1: Example of start, intermediate and final step of the region growing algorithm, where the volume is shown in a frontal view.

where $D$ is the Euclidean distance from each voxel $z$ to the background and $J$ is the Euclidean distance for each voxel $z$ to the CSF/GM region. Already labelled voxels from previous algorithm step (k-means clustering) are set as seed compartments. If $z_{seed}$ is a boundary voxel in one of the compartmental seeds, and $z_{neighbor}$ one of its 26 neighbors that is in the volume but not is labelled, then the growing criteria used by [6] states that it is to be included in the region where $z_{seed}$ is if

$$P_{boundary}(z_{neighbor}) > P_{boundary}(z_{seed}).$$

This iterative process will continue until no further growth is possible. Figure A.1 shows start, intermediate and final step of the region growing process.

A.3 FreeSurfer Compartment Labels

Table A.1 give a description of the value assigned by FreeSurfer to specific regions\(^1\), their description and the final label addressed to them. The descriptions

\(^1\)collected from the output text file “aseg.auto_noCCseg.label_intensities.txt”
only containing “-” lack description from FreeSurfer, and the label “Not included” means discarded values.

**Table A.1: Labels and descriptions of the resulting labelled volume. The rightmost column denote the resulting compartment affiliation.**

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
<th>Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Left Cerebral Exterior</td>
<td>Left Cerebral Hemisphere</td>
</tr>
<tr>
<td>2</td>
<td>Left Cerebral White Matter</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Left Cerebral Cortex</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Left Thalamus</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Left Thalamus Proper</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Left Caudate</td>
<td>Left Cerebral Hemisphere</td>
</tr>
<tr>
<td>12</td>
<td>Left Putamen</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Left Pallidum</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Left Hippocampus</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Left Amygdala</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>Left Accumbens area</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Left VentralDC</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>Right Cerebral Exterior</td>
<td>Right Cerebral Hemisphere</td>
</tr>
<tr>
<td>41</td>
<td>Right Cerebral White Matter</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>Right Cerebral Cortex</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>Right Thalamus</td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>Right Thalamus Proper</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>Right Caudate</td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>Right Putamen</td>
<td></td>
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<tr>
<td>52</td>
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<tr>
<td>53</td>
<td>Right Hippocampus</td>
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<tr>
<td>54</td>
<td>Right Amygdala</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>Right Accumbens area</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>Right VentralDC</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Left Cerebellum White Matter</td>
<td>Cerebellum and brain stem</td>
</tr>
<tr>
<td>8</td>
<td>Left Cerebellum Cortex</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>Right Cerebellum White Matter</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>Right Cerebellum Cortex</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Brain Stem</td>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>5</td>
<td>Left Inf Lat Vent</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Third Ventricle</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Fourth Ventricle</td>
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</tr>
<tr>
<td>24</td>
<td>CSF</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>Right Lateral Ventricle</td>
<td>Not included</td>
</tr>
<tr>
<td>44</td>
<td>Right Inf Lat Vent</td>
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</tr>
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In this chapter, additional results are presented. Figure B.1 and figure B.2 show one slice of the resulting segmentations from all methods applied to data sets from three healthy adults, acquired with 1.5 T and 3 T field strength respectively. Figure B.3 shows the results when the methods were applied to more challenging data sets.

(a) Adaptive disconnection, input data from PVE.  (b) Adaptive disconnection, input data from SyMRI.  (c) Graph cuts.  (d) FreeSurfer.  (e) SB-GC.

**Figure B.1:** Showing one slice from the resulting segmentation when applied to data sets of three healthy adults, acquired with 1.5 T field strength.
Figure B.2: Showing one slice from the resulting segmentation when applied to data sets of three healthy adults, acquired with 3 T field strength.

Figure B.3: Showing one slice of the resulting segmentation when applied to data sets of three more challenging data sets. Subject A: three-year-old child. Subject B: subject with mild multiple sclerosis. Subject C: subject with severe multiple sclerosis, acquired with contrast agent.
Bibliography


