Introduction: focus of the project

In human, vision is a complicated process which requires numerous components of the human eye and brain to work together. The sense of vision has been one of the most vital senses for human survival and evolution. In digital era, an emerging field is the one that regards image processing, which focuses on automating the process of acquiring and processing visual information.

Those techniques and technologies have many applications, such as biometrics (face recognition, fingerprint identification, iris scanning), satellite imaging for remote sensing and environmental monitoring, automated optical inspection (AOI) in manufacturing for quality control, object recognition in autonomous vehicles, medical imaging for tumor detection, security and surveillance through video analytics.

The focus of this project is on medical applications of image processing traditional techniques. In particular, the goal is to successfully segment the brain tumor which is one of the leading causes of death in the today world. Brain cancer is also called glioma and meningioma, and it manifests itself as an uncontrolled growth of cancer cells in the brain. In this project, the detection is done taking functional 4-dimensional MRI as input.

State of the art of image processing techniques in medical imaging field

A brain tumor is characterized by the uncontrolled growth of a section of brain tissues. These additional tissues present a significant danger as their presence adversely affects surrounding brain tissues, impeding their proper functioning.

Among the over 100 types of brain tumors have been identified and named based on the specific tissue and region of the brain where they originate, Glioma stands out as the most life-threatening among these brain tumors.

It occurs in the glial cells of the brain, that are non-neuronal cells in the central nervous system. Grade I and II, are known as Low-Grade Glioma (LGG), which are benign tumors. Grades III and IV are known as High-Grade Glioma (HGG), which are malignant tumors. When symptoms are nausea, vomiting, fatigue, loss of sensation or movement and difficulty in balancing persist for a long duration, the patient takes a medical consultation and medical images are one of the best way to build an accurate diagnose.

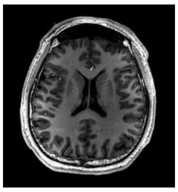
Types of Medical Images

Medical imaging plays an important role in modern healthcare, enabling doctors to visualize and diagnose a wide range of medical conditions. Here's an overview of the main medical image modalities.

- Plain X-rays is a type of radiation called electromagnetic waves, that penetrate the body to create a 2- D showing the parts of the body in different shades of black and white.
  This happens because different tissues absorb different amounts of radiation: Calcium in bones absorbs x-rays the most, so bones look white while fat and other soft tissues absorb less radiation, so they look grey. Air absorbs very few light, so if there are parts of the body filled by air, they look black.

- Computed Tomography is commonly known as CT or CAT scan (in Italian TAC – Tomografia Assiale Computerizzata). CT uses X-rays to create detailed cross-sectional images of the inside of our body. A CT scan is typically used for: bone fractures, Tumors, cancer monitoring, finding internal, bleeding. La foto è della cervicale.

- Magnetic Resonance Imaging (MRI) is a sophisticated radiology test that uses magnetic fields and radio waves to produce 3-D images. MRI scanners and a computer produce images of the internal body structures, including the brain and spinal cord, bones and joints, the heart and blood vessels, breast tissue and other internal organs. Comparing with CT, the MRI is slower and more expensive, but it has a better accuracy and acquires better fine tissue details.



- Ultrasound
- Positron Emission Tomography

MRI modalities

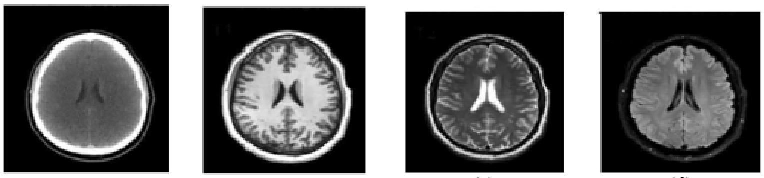
This project is focused on the crucial task of brain tumor detection, task for which Magnetic Resonance Imaging (MRI) emerges as the optimal medical image acquisition technique to reach the objective.

There are two types of MRIs

1. Functional MRI (fMRI): it measures the brain activities from the change in the blood flow
2. Structural MRI (sMRI): it captures the anatomy and pathology of the brain.
   Various modalities of sMRI are
   a. Diffusion Weighted Image(DWI): MR imaging technique measuring the diffusion of water molecules within tissue voxels (voxels are 3D pixels)
   b. FLAIR: an MRI pulse sequence which suppresses the fluid and enhances an edema.
   c. T1w: MRI pulse sequence that captures longitudinal relaxation time differences of tissues.
   d. T1Gd: a contrast enhancing agent, Gadolinium is injected into the body and after that a T1 sequence is acquired. This contrast enhancing agent shortens the T1 time which results in bright appearance of blood vessels and pathologies like tumors.
   e. T2w: basic MRI pulse sequence that captures transverse relation time differences of tissues.

Examples of medical images:

- fig. a CT
- fig. b T1 MRI
- fig c T2 MRI
- fig. d DWI MRI

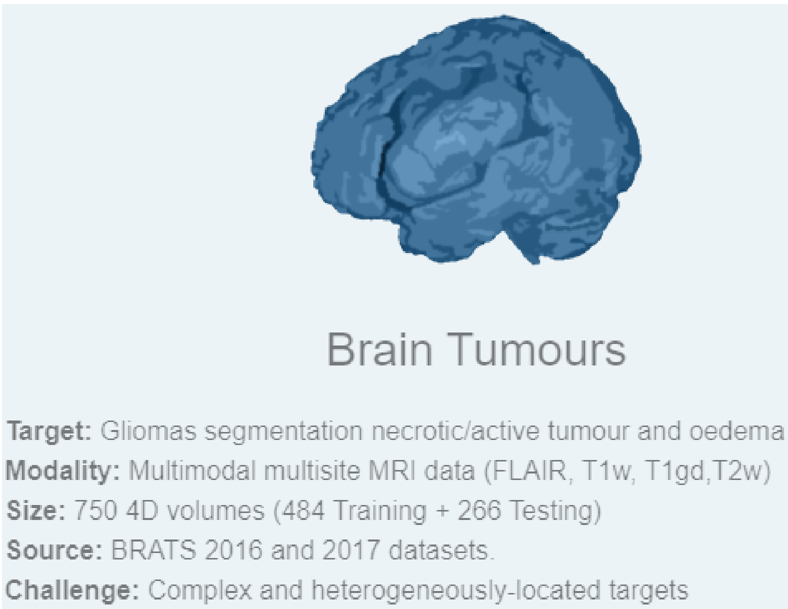


(a) (b) (c) (d)

Brain Tumor Segmentation (BraTS) challenge dataset

The images used in this project belong to the BraTS dataset are provided for the BraTS challenge. This dataset contains multi-parametric MRI pre- and post-operative scans in T1, T1Gd, T2, and T2-FLAIR volumes.

The page on which the challenge is published is: Medical Segmentation Decathlon (medicaldecathlon.com), while the dataset used for this project is available at the following link: Task01_BrainTumour.tar - Google Drive. Here's the description on the provided website about the task of our interest:



State of the art of Image Segmentation Techniques

Region-based Segmentation

- Threshold Segmentation: simplest and most common method of image segmentation which directly divides the image grey scale information processing based on the grey value of different targets. The advantage of the threshold method is that the calculation is simple, and the operation speed is faster; the disadvantage is that it is difficult to obtain accurate results for image segmentation problems where there is no significant grey scale difference which makes this method sensitive to noise. It is often combined with other methods.
  Threshold segmentation can be divided into local threshold method and global threshold method.
    - The global threshold method divides the image into two regions of the target and the background by a single threshold.
    - The local threshold method needs to select multiple segmentation thresholds and divides the image into multiple target regions and backgrounds by multiple thresholds.

  The most commonly used threshold segmentation algorithm is the Otsu method, also known as “largest interclass variance method”, which selects a globally optimal threshold by maximizing the variance between classes. In addition to this, there are entropy-based threshold segmentation method, minimum error method, co-occurrence matrix method.

- Regional Growth Segmentation**:** typical serial region segmentation algorithm, and its basic idea is to have similar properties of the pixels together to form a region. The criterion used here is that if the absolute value of the grey value difference between the pixel and the seed pixel is considered to be less than a certain threshold T, the pixel is included in the region where the seed pixel is located. This method usually provides good boundary information and segmentation results, but the computational cost is large. Also, the noise and grayscale unevenness can lead to voids and over-division.
- The Watershed method: segmentation technique that draws an analogy between the image and a topographic landscape. In this approach, the grayscale intensity of each pixel in the image is treated as the elevation of a landscape. The fundamental concept is to simulate a flooding process, where the lower intensity regions act as basins that fill with water, and the watersheds are defined by the boundaries between these basins.

Edge Detection Segmentation

The edge of the object is defined as a discontinuity of local features of the image; we expect there is an edge if a region has a high spatial frequency, so when two close pixels present high intensity change.

This discontinuity can be often detected using derivative operation: the widely first-order differential operators are Prewitt operator, Robert’s operator and Sobel operator while the second-order differential operator has nonlinear operators such as Laplacian, Kirsch operator and Walli’s operator.

- Sobel Operator: The Sobel operator is mainly used for edge detection, and it is technically a discrete differential operator used to calculate the approximation of the gradient of the image luminance function. The influence of the Sobel operator on the position of the pixel is weighted, which is better than the Prewitt operator and the Roberts operator. The Sobel operator consists of two sets of 3x3 matrices, which are transverse and longitudinal templates, and are plotted with the image plane, respectively, to obtain the difference between the horizontal and the longitudinal difference.

$$Gx = \begin{bmatrix} -1 & 0 & 1 \\ -2 & 0 & 2 \\ -1 & 0 & 1 \end{bmatrix} \qquad Gy = \begin{bmatrix} 1 & 2 & 1 \\ 0 & 0 & 0 \\ -1 & -2 & -1 \end{bmatrix}$$

The horizontal and vertical gradient approximations of each pixel of the image can be combined to calculate the size of the gradient using the following formula:

$$G = \sqrt[2]{G_x^2 + G_y^2}$$

Finally, the gradient can then be calculated using the following formula:

$$\Theta = \arctan(\frac{G_y}{G_x})$$

- Laplacian Operator**:** Laplace operator is an isotropic operator (doesn't depend on direction), second order differential operator. The Laplace operator's response to isolated pixels is stronger than the edge or line, and therefore applies only to noise-free images. In the presence of noise, the Laplacian operator needs to perform low pass filtering before detecting the edge. Laplace operator can also be expressed in the form of a template

$$\begin{bmatrix} 0 & 1 & 0 \\ 1 & -4 & 1 \\ 0 & 1 & 0 \end{bmatrix}$$

Segmentation based on neural networks

Many segmentation techniques have observed significant advancements with the advent of neural networks, able to handle complex and diverse image structures, making it well-suited for medical image analysis, autonomous vehicles, and other fields where accuracy and adaptability are paramount.

- K-means: clustering is one of the Unsupervised Learning tasks and K-means is one of the most commonly used algorithm to solve this task. Its basic idea is to gather the samples into different clusters according to the adopted distance metric. This method is fast and simple, but k is difficult to estimate.
- Segmentation based on weakly-supervised learning in CNN**:** Convolutional Neural Networks (CNNs) have proven particularly effective in image segmentation tasks, as they can learn hierarchical features at various levels, capturing both global and local information. U-Net, a popular architecture for semantic segmentation, incorporates a contracting path to capture context and a symmetric expansive path for precise localization.

Model based algorithms

It is another important category of techniques which, in contrast to the data-driven approaches discussed earlier, relies on predefined mathematical models or structures to interpret and process images. These algorithms often leverage prior knowledge about the characteristics and patterns inherent in the data, offering a more structured and deterministic approach to image analysis. Main algorithms of this type are:

- Markov Random field models**: i**t is a simple stochastic process in which future states' distribution relies only on the current state and not how it arrived in the current state
- Atlas-based approach**:** Atlas consists of images, including anatomical subtleties to join earlier data for partitioning and outcome changes depending on the Atlas' particulars. The informational indexes of clinically debilitated subjects and ordinary subjects are used to advance an atlas.
- Graph cut approach**:** the graph cut algorithm's fundamental idea is to borrow tools from the graph theory to partition the image into foreground and background. In graph theory, every pixel will be a node, and the edges are the links that connect those nodes.
- Lattice Boltzmann method (LBM): Powerful techniques with a high degree of accuracy. They simulate various systems by taking the behaviour of a group of particles suppose to behave similarly, rather than a single particle behaviour. Each such collection of particles is given as a distributive function.

State of the art of Image Segmentation Algorithms

In this part, some image segmentation techniques to tumor detection from MRI are introduced; in the end, one of those algorithm is analysed in depth and implemented in MATLAB.

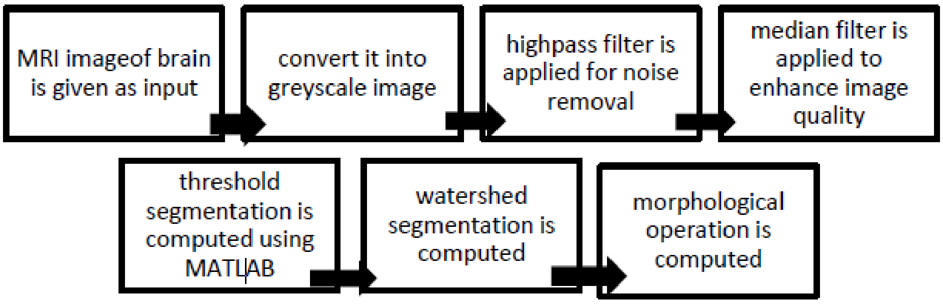
1. Noise Removal: "noise" means "unwanted signal", intended as a random variation of brightness or colour information in images that deteriorates the image; in [1] some strategies for noise removal are presented.
   The first approach is removing noise using filtering, modifying the image in some way which includes blurring, deblurring, locating certain features within the image. A filter is basically an algorithm for modifying a pixel value, over original value of the pixel and the values of the pixels surrounding it. There are literally hundreds of types of filters that are used in image processing. Among all the filtering techniques, common ones are:
   - Gaussian Filter or Gaussian smoothing
   - Mean Filter
   - Median Filter

   The second approach, that can be seen as a specialization of the first one rather than an alternative method, is the "Region filling method": Sometimes, infact, it is required to process a single sub region of an image, leaving other regions unchanged. This is commonly referred to as region-of-interest (ROI) processing. A process that fills a region of interest (ROI) by interposing the pixel values from the boundaries of the region is known as Region Filling.
2. In [2], a segmentation algorithm based on threshold segmentation is presented. In this algorithm, the threshold of a pixel in an image is estimated by calculating the mean of the grayscale values of its neighbor pixels, and the square variance of the grayscale values of the neighbor pixels are also calculated as an additional judge condition, so that the result of the proposed algorithm is the edge of the image. In fact, the proposed algorithm is equal to an edge detector.
   The first step of this algorithms sees the pre-processing of the image, with the goal of finding the best threshold useful for the second phase, which is the threshold step. The used filter is a square-shaped operator of different sizes, like 3x3, 5x5 or 7x7 depending on the situation.
   In this paper, the thresholds of the pixels in an image are estimated by looking at their probability density function (PDF), p(z).
   An image is segmented by classifying as background pixels with grayscale values greater than a threshold T, all other pixels are called object pixels. The main objective is to select the value T that minimizes the average error in making the decision that a given pixel belongs to an object or to the background. P1(z) and P2(z) are the PDF of the object and the background respectively.
   Here's a comparison between the Canny operator and the proposed algorithm:

(c) Result 2 by Canny operator

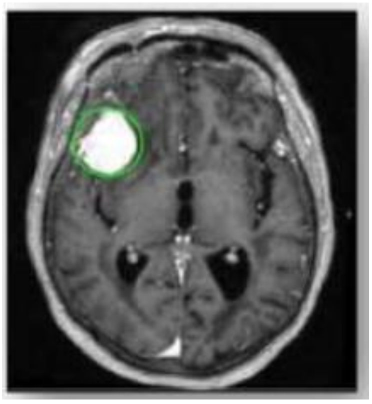
(d) Result by the proposed algorithm

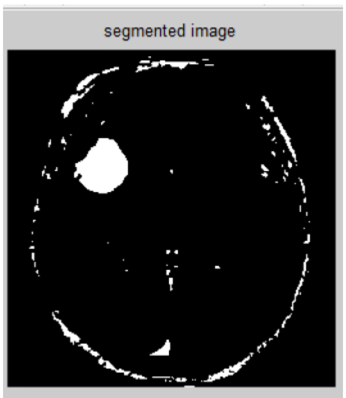
3. Paper [3] shows the full steps for brain tumor extraction from MRI using MATLAB. The algorithm is composed as described in the following scheme.



The first step, as shown, is to convert the MRI into a greyscale image. Subsequent steps of the preprocessing are noise removal through a high-pass filter, and application of a medial filter to improve the image. Then, a threshold segmentation is applied, followed by a watershed segmentation and in the end morphological operations are computed.

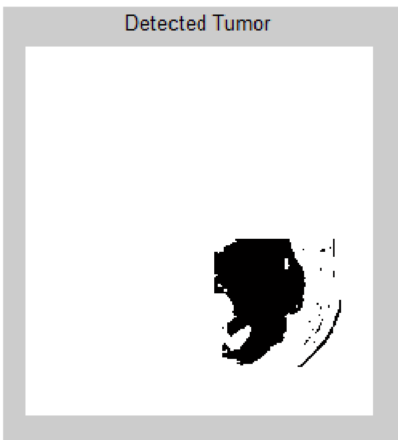
Here's a comparison between the initial image and the segmented image:



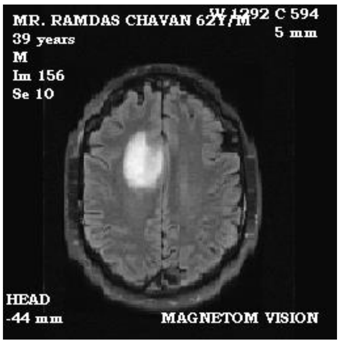


4. In [4] there is a proposal for an algorithm using morphological operation and extraction of features. Pre-processing stage removes the noise and high frequency artifact present in the image. It removes the patient's name, age and other marks present in the image. In the experimentation a Sobel filter is used for preprocessing and histogram equalization for image enhancement. After the pre-processing stage a binary mask is created using morphological operations. Then, the histogram equalization is used to enhance the quality of the image, followed by a thresholding operation. In the end, the segmentation algorithm composed by morphological operation (such as binary dilation and binary erosion) is applied.

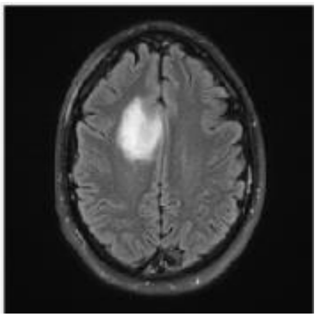
A comparison between the initial image and the segmented image:



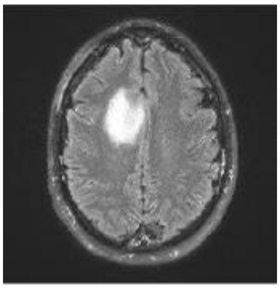
5. The last algorithm analysed in this project, proposed in [5], is the one that has been implemented in MATLAB. Main phases are preprocessing to prepare the image for the segmentation, which is followed by morphological operations. The algorithm steps are the following:
   a. Give MRI image of brain as input



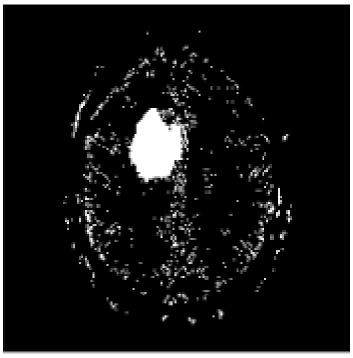
   b. Convert the image in a grey scale image: grayscale is a range of shades of gray without apparent color. Grayscale image is preferred format for image processing because gray scale images are much less complex, and one can talk in detail about contrast, brightness, and edges without considering colors. Colors are much more complex since they are composed of three channels. The lightness of the gray is directly proportional to the number representing the brightness levels of the primary colors. Black is represented by R=G=B=0 or R=G=B = 00000000 and white is represented by R=G=B = 255 or R=G=B = 11111111.



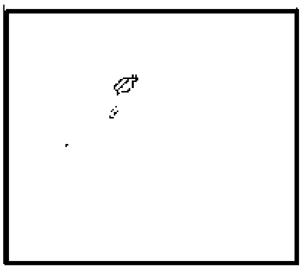
   c. Apply high pass filter to enhance the quality of the image: to work on images, especially to detect borders, it is preferrable that a sharpening operation is applied to enhance the contrast between adjacent areas. A high pass filter increases the brightness of the central pixel with respect to neighbour pixels. For this reason, a kernel that performs this operation usually contains a single positive value in its centre, surrounded by negative values.
   d. Apply median filter for noise removal: to perform a noise reduction which makes easier to apply subsequent transformations, we apply median filter which is a non-linear digital filtering technique. The choice of median filter is motivated by the fact it can do its job preserving the edges. The pattern of neighbors is called the "window", which slides, entry by entry, over the entire signal. Note that if the window has an odd number of entries, then the median is simple to define since it is just the middle value after all the entries in the window are sorted numerically. For an even number of entries, there is more than one possible median.



e. Compute threshold algorithm: image segmentation is the process of assigning a label to every pixel in an image such that pixels with the same label share certain visual characteristics. The result of image segmentation is a set of segments that collectively cover the entire image, or a set of contours extracted from the image. Each of the pixels in a region are similar with respect to some characteristic or computed property, such as color, intensity, or texture. Adjacent regions are significantly different with respect to the same characteristic. Sometimes in medical imaging, segmentation is applied to a stack of images, and the resulting contours can be used to create 3D reconstructions with the help of interpolation algorithms like Marching cubes. The thresholding method is the simplest method of image segmentation, and in this work it was adopted the Otsu method, which selects a globally optimal threshold by maximizing the variance between classes.



f. Compute watershed segmentation: after having performed a pixel-based segmentation, perform a region-based segmentation. A grayscale image can be thought of as a raised surface, where the shade of each pixel represents its height on the surface. Imagine a raindrop falling on this raised surface – it will follow a path until it reaches the lowest point. In simpler terms, the watershed of this raised surface corresponds to the boundaries of the nearby areas where raindrops gather.
In the early 90s, F. Meyer introduced a commonly used algorithm for identifying watersheds. This algorithm operates on a grayscale image. As the grayscale relief is gradually flooded, watersheds with neighbouring areas where raindrops gather are created. This flooding process is carried out on the gradient image.



g. Compute morphological segmentation: morphological image processing involves using certain operations that focus on the shape or structure of features in an image. These operations consider the order of pixel values rather than their actual numerical values, making them well-suited for handling binary images. In this approach, a small shape or template known as a structuring element is applied to different positions in the image. It is then compared to the surrounding pixels in the neighborhood. Some operations check if the element fits within the neighborhood, while others check for intersection or overlap with the neighborhood. The outcome of a morphological operation on a binary image results in a new binary image, where pixels have a non-zero value only if the test succeeds at that specific location in the original image.
h. Output the tumour region

Implementation in MATLAB of the algorithm and results discussion

Data acquisition

The dataset is provided for the BraTS challenge, in particular for its first task which is focused on brain tumor detection. Data are available at the following link: Task01_BrainTumour.tar - Google Drive.

The dataset is presented in TAR format, a widely used format to group files without compressing them. Once extracted, it presents .nii.gz files. The .nii extension represents NIfTI (Neuroimaging Informatics Technology Initiative) files, a common format for medical images; the .gz extension represents a kind of compression. It is possible to both upload the files in MATLAB, in a compressed or decompressed way, using the "*niftiread"* function. The dataset contains functional images, so 4-dimensional images where the fourth dimension represents time; so, each file contains MRIs of the same brain acquired in different moments.

Algorithm implementation

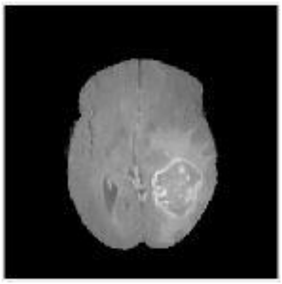
To manage the 3D shape, three two-dimensional slices are extracted (frontal, sagittal and horizontal), and the algorithm is applied on each of them. Here is shown the effect of the algorithm on the frontal view, but at the end it is shown the result for all the views. The steps of the algorithm are the followings

1. Upload the image

```
% Specify the path to the NIfTI file containing brain imaging data
path_func = "BRATS_008.nii";

% Read the NIfTI file and get its information
Vf = niftiread(path_func);
info = niftiinfo(path_func);
```

2. Turn the image in grey scale. This is done with a manual normalization, since the image is 4-dimensional and it is not possible to apply functions like rgb2grey, mat2grey or imbinarize on it.

```
% Normalize the voxel (volume pixel) values between 0 and 1 --> greyscale
% Not possible to normalize using rgb2grey, imbinarize or mat2grey because there are more that 3 channels
Vmax = max(Vfm,[],'all');
Vmin = min(Vfm,[],'all');
Vf_normalized = (Vfm-Vmin)./(Vmax-Vmin);
```

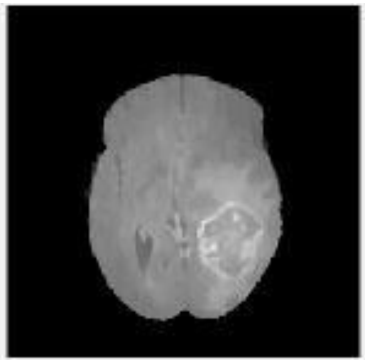


3. The third step consists in high passing the image to enhance its quality. This is done by using a Gaussian filter, chosen because of its smooth frequency response, few introduced artifacts, linear shift-invariance, and ability to control the filter's bandwidth through the standard deviation parameter.

```
% Apply a Gaussian high-pass filter to enhance the quality of the image
frontal_filtered = imgaussfilt(frontal, std(frontal(:)));
sagittal_filtered = imgaussfilt(sagittal, std(sagittal(:)));
horizontal_filtered = imgaussfilt(horizontal, std(horizontal(:)));
```

4. Then, a median filter is applied for noise removal. A median filter was chosen because of its effectiveness in preserving edges while effectively suppressing impulsive noise. It is a nonlinear filter, which makes the median filter particularly robust in scenarios where the image contains salt-and-pepper noise or other types of outliers.

```
% Define the size of the median filter for noise removal and apply it
median_filter_size = 3; % Sperimentally determined
frontal_median_filtered = medfilt2(frontal, [median_filter_size, median_filter_size]);
sagittal_median_filtered = medfilt2(sagittal, [median_filter_size, median_filter_size]);
horizontal_median_filtered = medfilt2(horizontal, [median_filter_size, median_filter_size]);
```



5. The fifth step consists in applying thresholding to segment the image. To determine an optimal threshold, Otsu's method is applied which works trying to minimize the intra-class variance of pixel intensities. It is done with the "multitresh" function because the spectrum was multimodal, and a binary thresholding wouldn't have worked well.

```
% Apply Otsu's multi-level thresholding
levels = 12; % Specify the number of desired regions. Sperimentally determined
thresholds_frontal = multithresh(frontal_filtered, levels);
thresholds_sagittal = multithresh(sagittal_filtered, levels);
thresholds_horizontal = multithresh(horizontal_filtered, levels);

frontal_otsu = imquantize(frontal_filtered, thresholds_frontal);
sagittal_otsu = imquantize(sagittal_filtered, thresholds_sagittal);
horizontal_otsu = imquantize(horizontal_filtered, thresholds_horizontal);
```

6. To improve the quality of the segmented area, a morphological operation is applied. In particular, dilatation was used to expand and strengthen the boundaries of structures, contributing to the refinement and modification of the original image, filling gaps, connecting regions, and highlighting the spatial relationships within the processed image.

```
% Morphological operation (Dilatation)
se = strel('disk', 3); % Structuring element (disk with radius 3)
dilatated_frontal = imdilate(binary_frontal, se);
dilatated_sagittal = imdilate(binary_sagittal, se);
dilatated_horizontal = imdilate(binary_horizontal, se);
```

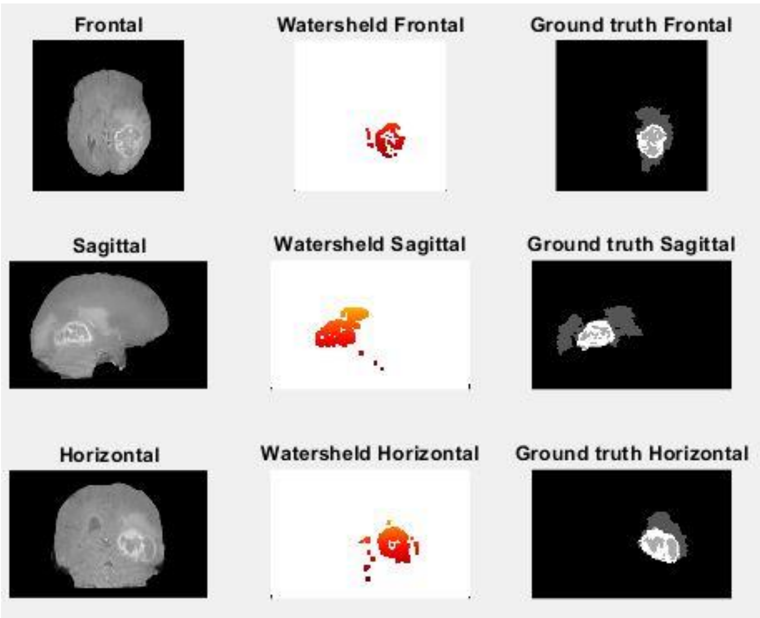
7. After having performed a pixel-based segmentation, a region-based segmentation is performed by using the watershed algorithm. This algorithm is particularly useful for delineating object boundaries and separating touching or overlapping objects in an image.

```
% Perform Watershed algorithm
watershed_frontal = performWatershed(dilatated_frontal);
watershed_sagittal = performWatershed(dilatated_sagittal);
watershed_horizontal = performWatershed(dilatated_horizontal);
```

The function performWatershed() has been written ad hoc because it incorporates additional preprocessing steps tailored for this specific context that were not available in the built-in function.

```
% Apply watershed segmentation to the binary images
function watershed_image = performWatershed(binary_image)
    % Calculate the negative distance transform
    C = -bwdist(binary_image);

    % Find markers for watershed segmentations
    C(binary_image) = -Inf;

    % Find markers for watershed segmentation using extended minima
    markers = imextendedmin(C, 1); % Connectivity 1

    % Perform watershed segmentation on the distance transform using the markers
    L = watershed(C, 1); % Connectivity 1

    % Set pixels outside the markers to 0 to create segmented regions
    L(~markers) = 0;

    % Generate a colored image using the watershed segmentation labels
    watershed_image = label2rgb(L, 'hot', 'w');
end
```

Comparison of obtained result with the ground truth



Comparing the initial image, the segmented region and the ground truth image (available in the directory "labelsTr" in the dataset) it is visible that the detected area has a high correspondence with the tumor.

While the algorithm's segmentation performance is promising, the presence of some extra unwanted pixels and a missed region indicate that further refinement may be necessary to improve its accuracy and reliability.

Proposals for future developments

- Design an automatic way to detect the best 2D slices on which perform the algorithm
- Perform a 3D reconstruction of the tumour
- Mathematically evaluate the comparison of the 3D segmented tumor with the ground truth file

References

[1] Daizy Deb1 ,Bahnishikha Dutta2, Sudipta Roy, “Noble Approach for Noise Removal from Brain Image using Region Filling”.

[2] Shiping Zhu, Xi Xia, Qingrong Zhang Kamel Belloulata, “An Image Segmentation Algorithm in Image Processing Based on Threshold Segmentation”.

[3] Rabia Ijaz, Mohsin Jamil, Syed Omer Gilani1, “Brain Tumor Extraction from MRI Images using MATLAB”

[4] Deepthi Murthy T.S., G.Sadashivappa, “Brain Tumor Segmentation Using Thresholding, Morphological Operations and Extraction Of Features Of Tumor”

[5] Rajesh C. Patil, Dr. A. S. Bhalchandra, “Brain Tumour Extraction from MRI Images Using MATLAB”