Medical Image Segmentation and Applications
Lab 2 Solution: Construction of Brain Atlas

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1 Introduction and problem definition

One of the most important important tasks in the analysis of medical images is segmentation. Generally speaking, it is defined as the process of separating an image into a series of different components, which implies that each of the original image pixels will be classified as belonging to one of those components. Segmentation plays a key role in the computer aided diagnosis systems, since it can provide regions of anatomical interest and that allows Machine and Deep Learning models to further improve their performance by actually being trained to detect key features in relevant areas for any specific medical application.

Even though segmentation is an essential part of every CAD system, it still remains to be an active field of research due to its difficulty. There are so many variables that can affect the accuracy of segmentation e.g, poor image resolution, low contrast, noise, image irregularities, etc. One of the most well-known techniques to improve the results of segmentation is by using prior information from an atlas. As its name suggests, and analogous to its geographical pair, an anatomical atlas is a collection of medical images from several individuals mapped into a common space (fixed frame), which aims to describe any given anatomical structure in a very robust way, since it takes into account the variability of the size and shape of organs from person to person. The main objective of this lab session was to build a probabilistic atlas from brain volumes and labels (with three classes: CSF, WM and GM) of 15 different patients. To achieve this, all the volumes were registered taking one volume as fixed using elastix tool (an algorithm was designed for finding which volume should be used as fixed in order to maximize the value of similarity metrics). In the end, an intensity volume and a probabilistic volume for each of the tissues are provided as well as the tissue models.

2 Design and implementation of the proposed solution

The design and implementation of the solution for the lab consisted of several steps, which are listed and explained in details in the following subsections.

2.1 Image Registration

For this task, 15 brain images and their corresponding 3D segmentation with three tissue levels (CSF, GM, WM) labels were given. The images were of different sizes and orientations, as shown in Figure 1. The first step for atlas creation is registering all the images with respect to one fixed image. A toolbox named ***Elastix*** was used for the registration of images. It is open-source software, based on the well-known Insight Segmentation and Registration Toolkit (ITK). The software consists of a collection of algorithms that are commonly used to solve (medical) image registration problems for which it was also chosen in this lab. Elastix offers many parameter files which can be applied for different types of registration. Out of all, **inter-patient** Brain 3D MRI Parameter file 0009

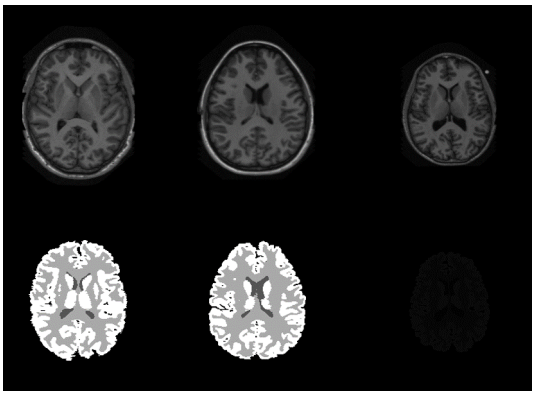

Fig. 1. Sample training image slices and their corresponding Ground Truth.

was chosen as it offers affine and B-Spline information using mutual information as a similarity metric. Many other parameter files like Par0010 and Par0033 were also explored but the best results were obtained using par0009. To do image registration with Elastix, The modular design of elastix allows the user to quickly configure, test, and compare different registration methods for a specific application. A command-line interface enables the automated processing of large numbers of data sets, by means of scripting. To do so, first, the executable file for windows was downloaded and then added to the directory of the desired drive. Then using command-line commands the images were registered with respect to one fixed image. The following command was used to register images using Elastix [1].

```
elastix -f fixedImage.ext -m movingImage.ext -out outputDirectory
-p parameterFile.txt
```

Through the command, fixed and moving images directory should be given also with the parameter files downloaded from Par0009. The question now arises is which image should be chosen as fixed image.

2.2 Fixed Image Selection

To make the image registration process automatic, a simple python script is used with a loop so that all the registered images with different combinations of fixed images can be used for comparison. To compare the registered image with the original one, the normalized root-mean-square error metric was used. At each iteration, the registered images were generated picking one as a fixed image, and the average rmse value was measured for that case. After all the iterations, the rmse values obtained can be seen in Table 1. From the table, it can be seen that registration with Image **1008.nii** obtained the best result whereas with **1036.nii** the result was poor. So it can be deduced that image 1008.nii has the most similarity with all the other images and can be selected as a fixed image for further processing.

2.3 Label Propagation

To be able to build probabilistic atlas, the labels are needed to be registered also with respect to the label of the fixed image. After the registration process of all the images with respect to the

Table 1. RMSE Comparison for Fixed Image Selection.

Fixed Image	RMSE
1000.nii	0.350595
1001.nii	0.461044
1002.nii	0.499629
1006.nii	0.346033
1007.nii	0.38417
1008.nii	**0.329731**
1009.nii	0.37723
1010.nii	0.380148
1011.nii	0.355938
1012.nii	0.488612
1013.nii	0.354709
1014.nii	0.46018
1015.nii	0.430695
1017.nii	0.439301
1036.nii	**0.627759**

fixed image 1008.nii, the resulting image after registration as well as the transformation matrix that was used to transform the original image were generated. As there were two transforms (affine and elastic) that were used sequentially, the last transformation matrix hold the both transformation and can be used to transform the labels in the same way as the intensity images. For that, the following command with Transformix was used.

```
transformix -in inputImage.ext -out outputDirectory -tp
TransformParameters.txt
```

Here, the input image is each of the ground truths of the registered images and the Transformation parameter is the transformation matrix generated in the Elastix/Registration step. After that, the labels of all the registered images with respect to the best fixed image 1008.nii were also transformed and the results were stored.

2.4 Atlas Creation

Intensity Atlas : Intensity from the fixed image and all the registered images were summed together. And then the result was divided by the total number of the images. Thus, intensity atlas can be obtained.

Probabilistic Atlas : For probabilistic atlas, the registered labels as well as the label of the fixed image were used. Three probabilistic atlas for each of the 3 tissue label (CSF, WM, GM) were generated. Here, the labels used for CSF, WM and GM are 1,2 and 3 respectively. To create the atlas for each tissue label, the labels not the same as that are converted to zero. The resulting image will be a binary image with only the parts of each specific tissue. And then all the images of same tissue labels are summed and divided by total number of the images, Thus, three probabilistic atlas for each three tissue labels (CSF, WM, GM) were generated.

2.5 Histogram Model

For building the tissue models, the following procedure was followed:

- For each of the 15 patients, collecting the intensity values of the voxels that belong to every class: CSF, WM and GM. These voxels were saved in separate vectors
- In every run of the loop, the new group of voxels (for a new patient) would be concatenated with the previous one.
- After having all the three vectors, namely intensities csf, wm and gm, the histogram for each of those is generated, using as number of bins the maximum intensity value along all three tissues.
- Afterwards, a new variable known as sum of histograms is generated, containing the sum of each of the tissue histograms.
- Finally, the histograms are normalized by dividing its values over the sum of all the histograms, and then they are plotted in the same graph with a range from 0 to the maximum intensity value among all three tissues.
  Figure 3 in the appendix presents a flowchart of the algorithm built for generating the histogram and tissue models.

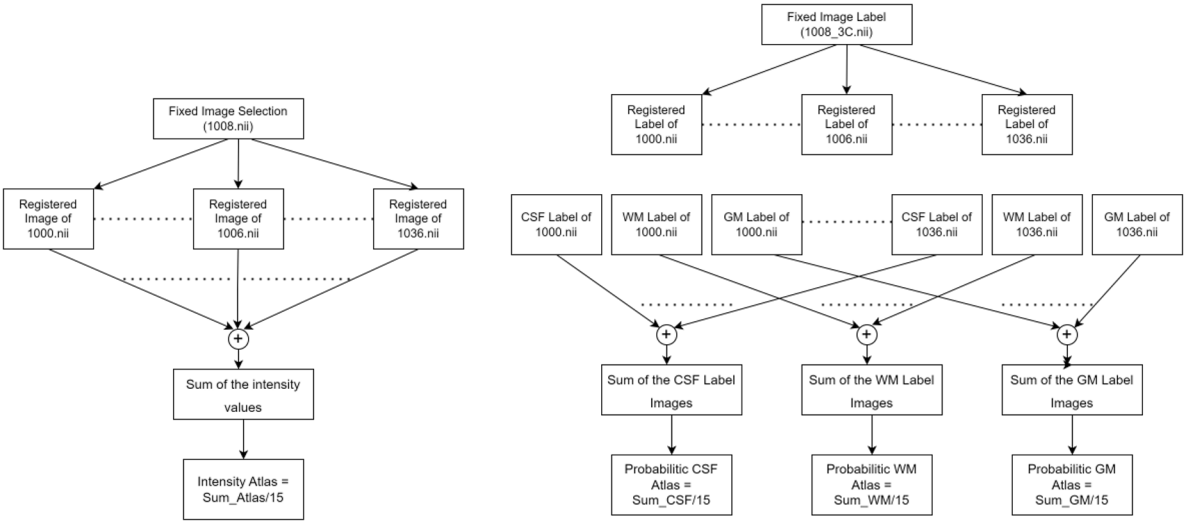

Fig. 2. Block Diagram for Atlas Generation.

3 Algorithm Analysis

3.1 Atlas creation

The whole atlas creation process was divided into three tasks.

- Fixed Image Selection
- Label Propagation
- Atlas Computation

Fixed image selection is an important step for the atlas computation as it will ensure the best registration which is an essential part for atlas. For the fixed image selection, RMSE (root-mean-squared error) was chosen as the similarity metric. The process can be described by the following pseudocode.

```
data_list: List contatining image ID's
for image in data_list:
        choose image as fixed_img;
        for image in data_list:
            if image != fixed_image:
                perform registration;
                compute rmse;
                sum all rmse;
            compute average rmse;
Find fixed_image with lowest rmse;
```

After finding the Best fixed image, label propagation of the registered images were also done using the label of the fixed image.

```
label_list: List contatining label ID's
get fixed image label;
for image in data_list:
    if image != fixed_image:
        perform label transformation of the current image;
        save the results;
```

Finally, for atlas creation fixed image as well as the registered images were used. The steps are:

- First the intensities from all the registered images were summed
- The intensity values from the fixed image was also added
- the accumulated result was divided by 15 (total number of the images)
- thus intensity atlas was obtained, can be shown in Figue 2(a)

For probabilistic atlas

- First from the registered labeled images CSF, WM and GM labels were extracted separately
- each CSF, WM and GM labeled images from all the images were summed together
- CSF, WM and GM labeled images from fixed image were also summed
- the accumulated results for each of the tissues were divided by 15 (total number of the images)
- thus three probabilistic atlas were obtained for CSF, WM and GM which can be shown in Figure 2(b)

3.2 Histogram model

The whole process for creating the tissue model was divided in three tasks:

- Generating three vectors to store all the intensity values of the voxels that belong to each of the classes.
- Generating the histogram models of the vectors
- Normalizing the histogram so that for a given intensity, the graph will tell what is the probability of the voxel to belong to each of the tissues.

The process can be described by the following pseudocode:

```
data_list: List containing image ID's
for image in data_list:
    if image == fixed_image:
        load original image
        load original label
        get mask_csf, mask_wm and mask_gm
        mask_csf=1 where original label=1,
        mask_wm=1 where original label=2,
        mask_gm=1 where original label=3.
        save in intensities_csf original_image[mask_csf==1]
        save in intensities_wm original_image[mask_wm==1]
        save in intensities_gm original_image[mask_gm==1]
    else:
        load registered image
        load registered label
        get mask_csf, mask_wm and mask_gm
        mask_csf=1 where registered label=1,
        mask_wm=1 where registered label=2,
        mask_gm=1 where registered label=3.
        save in intensities_csf registered_image[mask_csf==1]
        save in intensities_wm registered_image[mask_wm==1]
        save in intensities_gm registered_image[mask_gm==1]

    compute histograms
    normalize histograms dividing over the sum of tissue histograms
    plot tissue models
```

4 Experimental section and result analysis

Figure 4 located in the annex presents the results obtained from the intensity atlas for 4 different slices. In the top row of the figure it is possible to see the corresponding slice for the fixed image, and in the bottom row the atlas for that slice can be seen. From left to right, the slices represented are 90, 110, 120 and 130, respectively. From this figure it can be seen that, at least visually, the atlas does a very good job to explain the general anatomic structure of the fixed image, and it can also be seen that the thickness of the structures are bigger since it is also including information from all other 15 subjects.

On the other hand, figures 5 and 6 present the results obtained, from left to right, of the probabilistic atlas for the tissues CSF, WM and GM, respectively. Top and bottom rows of figure 5 correspond to slices 90 and 110, respectively, whereas top and bottom rows of figure 6 correspond to slices 120 and 130, respectively. After doing a visual analysis of these probabilistic atlas, it can be seen that they correctly describe their respective anatomic structures, as the resulting figure have the typical look of CSF, WM and GM tissues.

Figure 7 shows the results for the tissue models for CSF, WM and GM. This models compute the probability of a given voxel intensity to belong to a certain tissue. In order to better appreciate the graph, a digital filter was used to denoise the signal. This filter has to parameters, a and b, which correspond to the numerator and denominator coefficient vectors, respectively. For this case,

$a = 1$, b is a vector of length n, with all its components equal to $\frac{1}{n}$. Here, the larger the n, the more smoothing is applied. Figure 8 represents the smoothed version of the tissue models. From these two graphs, it can be seeing that the voxels with intensities between 100 and 500 are most likely to be CSF voxels, whereas voxels with intensities between 500 and 1100 (approximately). There is one point (approximately 500) where there is equal probability of the voxel to belong to grey matter or csf. There is also one point (between 1100 and 1200 intensity) where there is equal probability for the voxel to belong to either white matter and grey matter. After this value, the voxel is most likely to be white matter.

5 Project Management and Details

For this lab, one problem arised due to selection of fixed image for registration and then it was solved by making the whole process automatic and choose the image with lowest rmse value. Later, there were some doubts regarding histogram models of the tissues which were also solved. Other than that, no problems were faced and the workload has been divided equally between the partners both for coding and writing part.

6 Conclusions

The main objective of this lab is to compute intensity and probabilistic atlas which can be later used to improve the results of segmentation. Some findings led us to conclude the following:

- Good Image Registration is important for creating better atlas. Choosing which image to be selected as fixed is an important step. Therefore, it is essential to design algorithms that can automatically determine the best image to be selected as fixed.
- The atlases obtained do a good job in terms of describing the anatomical structure of the brain since the resulting image is similar to the fixed one (the template) but it also has ticker edges as it incorporates information for all the other 15 volumes available. Also, in terms of the probabilistic atlases, they all correctly describe the typical anatomical shapes of the corresponding tissues. The actual impact of the use of atlas for segmentation will be quantified during the next lab session.
- From the tissue models it can be concluded the lower intensities are most likely related to CSF voxels, whereas the highest intensities are most likely related to white matter voxels. On the other hand, middle intensity values are most likely related to grey matter voxels.

References

1. K. M. M. V. J. P. S. Klein, M. Staring, "elastix: a toolbox for intensity-based medical image registration," *IEEE Transactions on Medical Imaging*, vol. 29, no. 1, pp. 196–205, 2010.

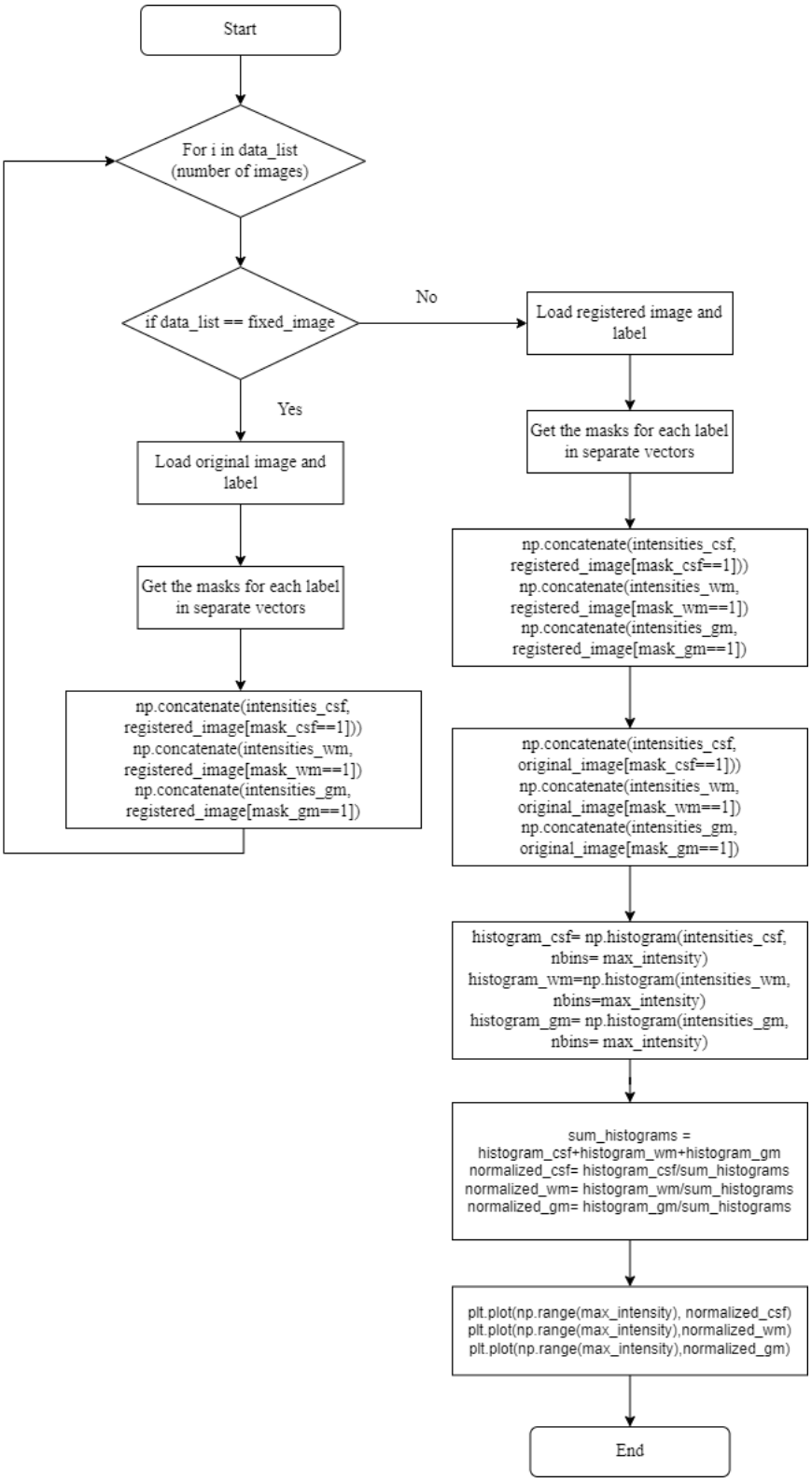

Fig. 3. Flowchart for creating histogram of intensities and tissue models

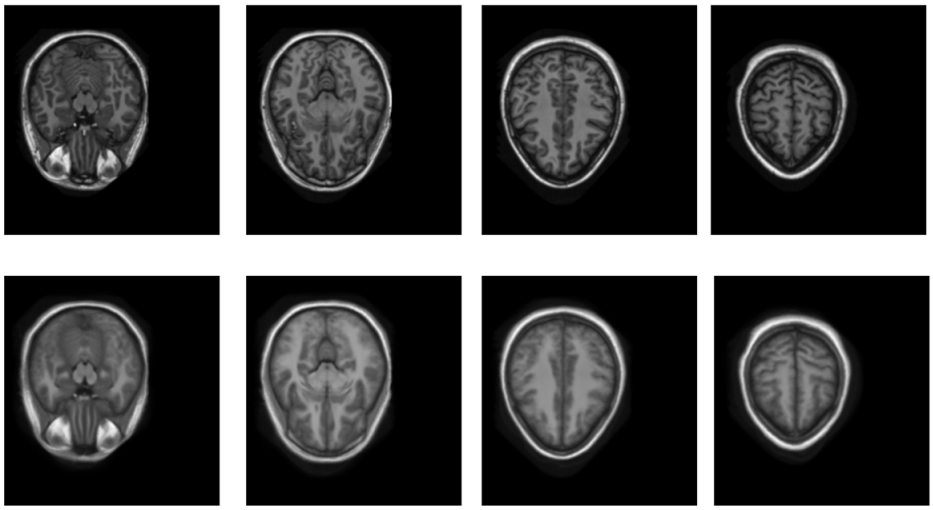

Fig. 4. Comparison between the fixed image and the intensity atlas for 4 different slices. Top row: fixed image. Bottom row from left to right: intensity atlas for slices 90, 110, 120 and 130, respectively.

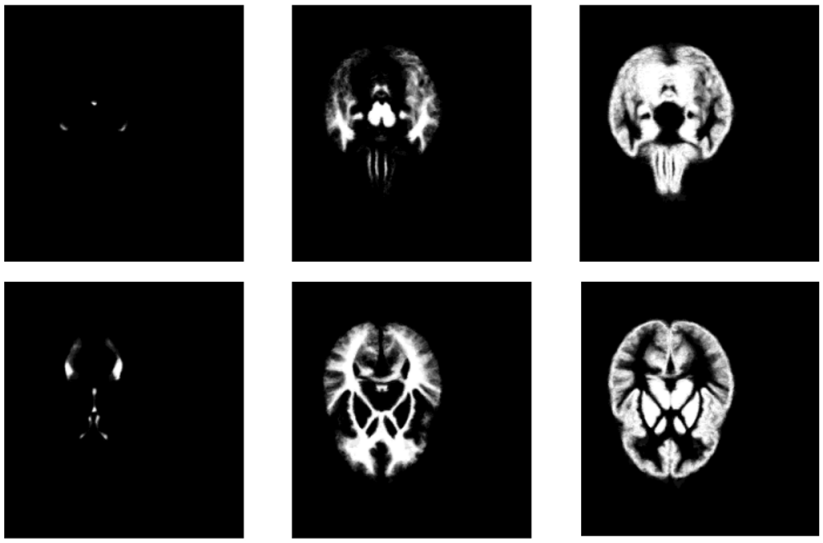

Fig. 5. Probabilistic atlas for each tissue (CSF, white matter and grey matter from left to right). Top row: slice 90, bottom row: slice 110.

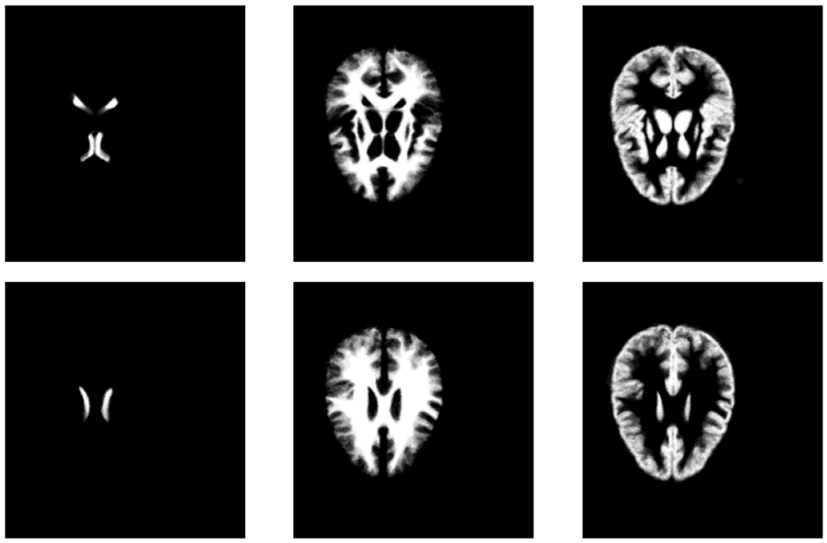

Fig. 6. Probabilistic atlas for each tissue (CSF, white matter and grey matter from left to right). Top row: slice 120, bottom row: slice 130.

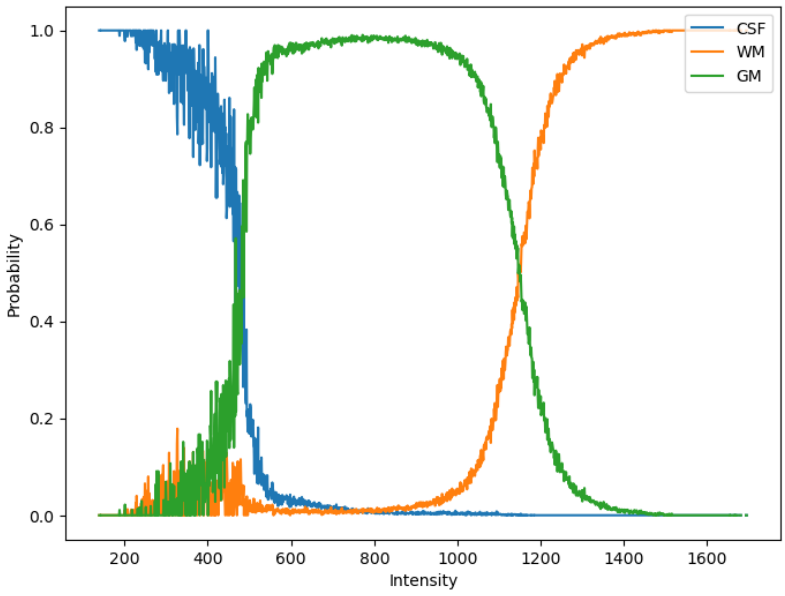

Fig. 7. Tissue models for CSF, WM and GM.

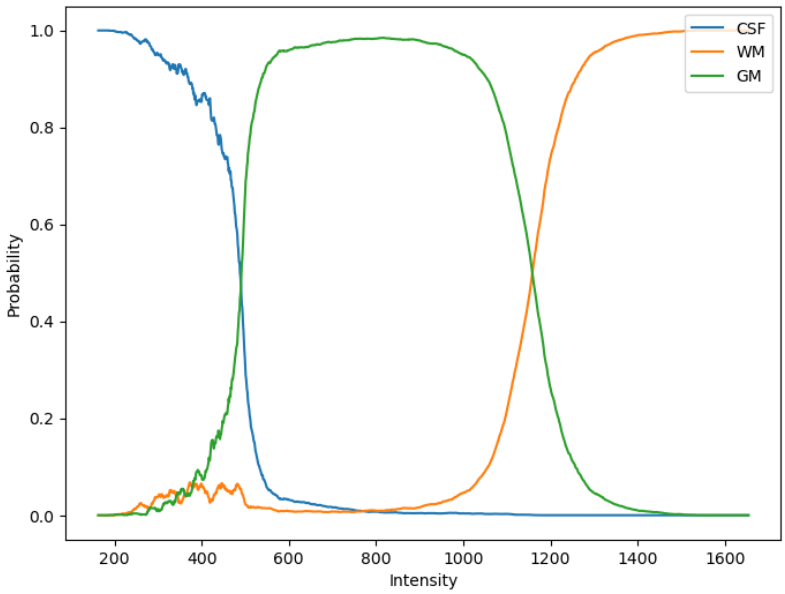

Fig. 8. Tissue models for CSF, WM and GM after filtering.