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Automatic Landmarking of Magnetic Resonance brain Images

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ABSTRACT

Landmarking MR images is crucial in registering brain structures from different images. It consists in locating the voxel in the image that corresponds to a well-defined point in the anatomy, called the landmark. Example of landmarks are the apex of the head (HoH) of Hippocampus, the tail and the tip of the splenium of the corpus colosum (SCC). Hand landmarking is tedious and time-consuming. It requires an adequate training. Experimental studies show that the results are dependent on the landmarker and drifting with time.

We propose a generic algorithm performing automated detection of landmarks. The first part consists in learning from a training set of landmarked images the parameters of a probabilistic model, using the EM algorithm. The second part inputs the estimated parameters and a new image, and outputs a voxel as a predicted location for the landmark. The algorithm is demonstrated on the HoH and the SCC. In contrast with competing approaches, the algorithm is generic: it can be used to detect any landmark, given a hand-labeled training set of images.

Keywords: brain MRI, anatomical landmarks, automatic landmarking, EM-algorithm, probabilistic model, feature selection.

1. INTRODUCTION

An anatomical landmark is a location (pixel or voxel) in an image corresponding to a specific point of the anatomy. Landmark data are useful on their own, since they can be processed and statistically analyzed to perform morphometrics.¹ In addition, landmarks provide a unique tool for coarse registration of anatomical shapes, preceding some finer registration techniques.² Medical images and more specifically functional neuroimages offer many motivating applications.

Location, size and shape of the brain structures vary considerably from one person to another. Techniques for whole-brain alignment exist, but sacrifice accuracy of regional alignment for global accuracy. Furthermore, typical whole brain alignment techniques, such as the Talairach transformation or the related Montreal Neurological Institute (MNI) transformation, are not designed to respect neuroanatomical boundaries or landmarks and are therefore often quite poor in their alignment (here, we note variability of 10mm following the Talairach alignment). The outcoming spatial blur results in reduced precision in localization of functional results and reduced statistical power in cross-participant analyzes.³

Identifying landmarks, or landmarking images, will facilitate the process of aligning multiple participant's scans, while respecting neuroanatomical structures. Landmarking brain images consists in selecting the voxels whose location is characterized by the surrounding anatomy and which are distinguishable in all participants. Examples of such landmarks are the anterior commissure (AC) and the posterior commissure (PC), identified by Tournoux and Talairach⁴ to define a common coordinate system, the head of the hippocampus, the tail of the hippocampus and other outstanding points on structures. Although it is tough, time-consuming and error-prone, neuroscientists have been landmarking manually brain images. Studies show that the accuracy depends on the landmarker and that the landmarking precision drifts with time. Using automatic methods would improve the current situation and allow large scale quantitative studies.

More generally point landmarks are defined as prominent locations in the anatomy. 3D operators are used to

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detect them automatically.^{5,6} However the points selected by this technique do not necessarily correspond to manually defined landmarks, as used by neuroscientists. Some efforts have been done on several peculiar landmarks, like AC and PC, using scene analysis⁷ or template matching⁸ methods. More recently techniques have been developed to detect tip-like, saddle-like or sphere-like structure landmarks, thanks to deformable templates⁹ or 3D parametric intensity models.¹⁰ All these approaches require a prior knowledge about the landmark sought. The method we propose is generic, so that it could be applied to any point landmark, given a training set of hand-labeled images. It is based only on the gray levels of the image and needs no additional information about the landmark, since it is designed to find automatically the informative structures. We test the algorithm on a tip-like landmark, the splenium of the corpus colosum (SCC) and the apex of the head of hippocampus (HoH). The latter is anatomically speaking the tip of the hippocampus, but its detection is more challenging than SCC, even for trained experts, due to indistinctive structure, see Figure 1.

We define a probabilistic model of the image intensities conditionally on the landmark location. The model parameters are estimated using a training set of images whose landmark location is known. The intensity distribution is learned on each image using the Expectation-Maximization (EM) algorithm, whereas the geometric parameters are estimated transversally, using all images simultaneously. Finally the learning procedure ends by selecting the informative features in the image. It produces a probability map for the different matters of the brain conditionally on the location sought, as well as a set of informative voxels. Then, they are used on new images to predict the landmarks location.

We detail the probabilistic model in section 2, the estimation of the model parameters in section 3 and the selection of the informative voxels in section 4. Finally the algorithm is demonstrated on HoH and SCC in section 5.

2. METHOD OUTLINE

2.1. Dataset

We use 23 MR brain images acquired on a Philips-Intera 3-Tesla scanner, with resolution 1mm³, encoded in gray-level intensity from 0 to 1462. Brains were first transformed into standardized Talairach space using Analysis of Functional Neuroimages (AFNI) to provide a canonical orientation (anterior and posterior commissures (AC and PC) made co-linear) and approximate alignment. All the images have the same size after the transformation: 161 × 191 × 151 voxels or mm. Brains were viewed in continuously synchronized sagittal, axial, and coronal planes about a common point in space. One of us, referred in the rest of the paper as "the expert" landmarked the image set. For both the head of the hippocampus and the splenium of the corpus colosum, visualization was best in the sagittal and coronal planes. For the splenium of the corpus colosum (SCC), the mid-sagittal plane was first identified. The splenium was then marked as the most posterior extent of the corpus colosum. In several instances, the corpus colosum's most posterior extent did not lie along the mid-sagittal slice, but 1mm to either the left or the right of the midline. In these cases, the splenium was identified as the most posterior extent in this slice, as shown in Figure 1. For the head of the hippocampus (HoH), an imaginary line following the principal axis of the hippocampus was drawn diagonally in the sagittal plane. The head was identified as the furthest extent of this line in three dimensional space (in the anterior and inferior directions). Some examples are pictured in Figure 1

Once landmarked the dataset is split in a training set composed of 14 images and a 9-image testing set. The a priori location of the landmarks in the Talairach space is evaluated thanks to the instances of the training set.

2.2. Model description

We denote S the set of voxels of an image, x_s is the gray-level at the voxel s , y the location of the landmark sought. We adopt a probabilistic modeling approach. Y , a random variable, is the unknown location of the landmark in the image, $(X_s)_{s \in S}$ is a collection of random variables modeling the voxel values. $A \subset S$ is a subset of selected voxels, we write $x_A = \{x_s, s \in A\}$ the collection of voxel values in the set A . The selection method will be detailed in section 4. What should be the cost of landmarking y when the true landmark is at y' ? The answer might depend on the application. In what follows we use the squared Euclidian distance. The bayesian prediction is then the expectation of the landmark location, given the observations at the selected voxels, x_A . The formula

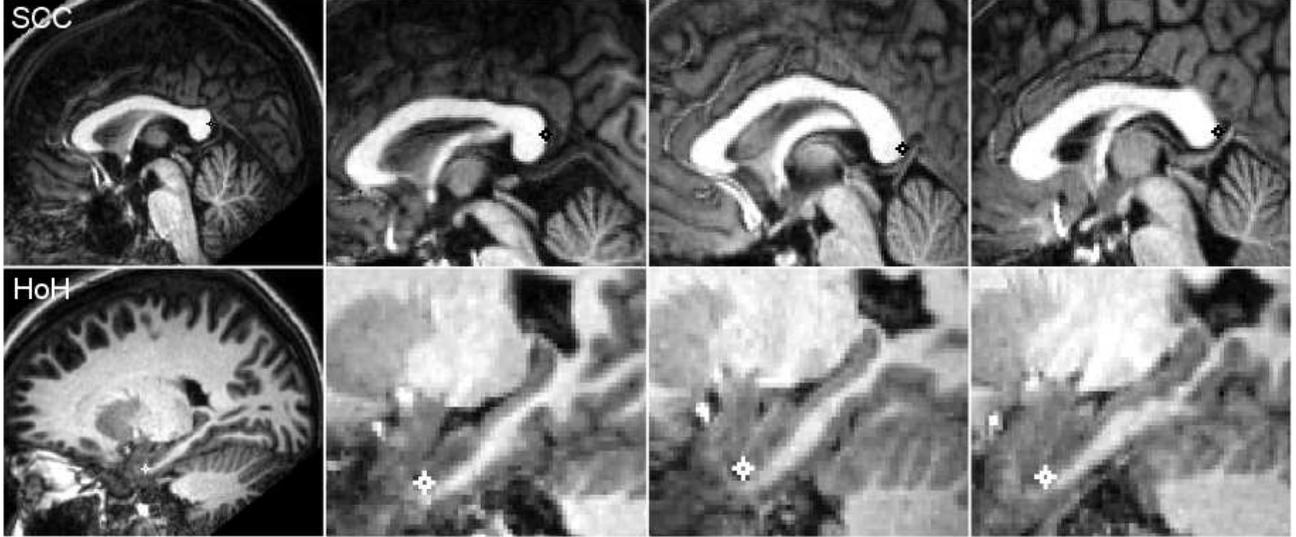


Figure 1. Location of landmarks in different brain images. The central voxel of the cross represents the exact location of the landmark, as defined by the expert. The leftmost images represent a general view of the brain. The other zoom on the landmark for different patients. On the first line, SCC: the posterior extremity of the splenium of the corpus callosum. The shape of the structure varies a lot and even the geometry of the splenium itself varies. On the second line, HoH: the apex of the head of the hippocampus. The angle of the hippocampus, the geometry and the size of the head are patient-dependent.

is given below and the rest of this section will be devoted to the exploration of the different components.

$$E[Y|X_A = x_A] = \sum_{y \in \mathcal{Y}} y P(Y = y | X_A = x_A) \quad (1)$$

$$= \sum_{y \in \mathcal{Y}} y \frac{P(X_A = x_A | Y = y) P(y)}{\sum_{y' \in \mathcal{Y}} P(X_A = x_A | Y = y') P(y')} \quad (2)$$

(2) is obtained using Bayes' formula. $P(y)$ is the prior distribution of the landmark. We choose it to be the Uniform distribution over a box $\mathcal{Y} \subset S$, that is guaranteed to contain the landmark. We choose a $6 \times 9 \times 10$ -voxel box for the SCC and a $12 \times 12 \times 12$ -voxel box for the HoH. Next, we model the probability to observe x_A given the location of Y , that is $P(X_A = x_A | Y = y)$.

First, we assume that the intensities are independent given the landmark location y . This is a standard simplifying assumption. A more precise model would involve modeling Markov dependencies. The conditional probability $P(X_A = x_A | Y = y)$ is then written as a product:

$$P(X_A = x_A | Y = y) = \prod_{s \in A} P(X_s = x_s | Y = y)$$

Hence, we need to define $P(X_s = x_s | Y = y)$.

The model is based on the gray-level values of the image. Since the gray-level intensity histogram is different from one image to another, the same component in the brain appears at different intensities in two different images. To deal with this difficulty, we introduce for each voxel s , the hidden discrete variable Z_s , corresponding to the matter of the brain at the voxel s . The brain is composed of 3 matters: the CerebroSpinal Fluid (CSF), the Gray Matter (GM) and the White Matter (WM), characterized by distinct intensities, respectively the lowest, the intermediate and the highest ones. Some mixed voxels have intensities that do not correspond to one matter but to a mixture of two matters. Because of the brain configuration only 2 mixtures are observable: CSF-GM and GM-WM. It is important to model them too, since they are present at the boundaries of structures, locations that will turn out to be informative, see section 4. Hence, the gray-level intensities are modeled by a 5-component

mixture. Using Bayes' formula,

$$P(X_s = x_s | Y = y) = \sum_{j=1}^5 P(Z_s = j | Y = y) P(X_s = x_s | Z_s = j, Y = y)$$

Second, we assume that the gray-level intensity at a given voxel s , given the matter j , is independent of the landmark location y . This is a mild simplification. Consequently, the second term of the product becomes $P(X_s = x_s | Z_s = j)$ and contains only the information about the gray level intensities whereas the first term $P(Z_s = j | Y = y)$ characterizes the geometry. Modeling the quantity $P(X_s = x_s | Z_s = j)$ is a fairly common and standardized problem in photometric modeling of MR images. We use a 5-component mixture of Gaussian densities.¹¹

Finally, we model the geometry, using a translation model: the probability to observe the matter j at the voxel s depends only on the translation between s and the landmark y . Hence,

$$P(Z_s = j | Y = y) = \pi_{s-y}(j)$$

This is clearly an over-simplification for the specification of the anatomy of the brain. However it leads to a tractable model which is worth investigating. The conditional probability is then:

$$P(X_A = x_A | Y = y) = \prod_{s \in A} \sum_{j=1}^5 \pi_{s-y}(j) P(X_s = x_s | Z_s = j) \quad (3)$$

We need to learn offline the parameters of this model to apply it online to new images.

2.3. Algorithm

We describe now the general procedure of the algorithm.

The learning procedure, also called the off-line algorithm, consists in 3 successive tasks:

1. For each image of the training set, estimate the 5×2 parameters of the gray-level Gaussian densities,
2. Compute the probability map $\pi_{s-y}(j)$: the proportions of the matter j at the voxel s , given that the landmark is at y , which makes a total of 4 parameters per voxel,
3. Select the informative voxels in the probability map.

The on-line procedure predicts the location of the landmark in a new image. It is made of 2 parts:

1. Estimate the 5×2 parameters of the gray-level Gaussian densities in the new image,
2. Compute the landmark location, using eq.(2) and eq.(3).

3. PARAMETER ESTIMATION BY EM-ALGORITHM

3.1. Learning the gray-level distribution

Modeling the inter-scan intensity inhomogeneities with a mixture of Gaussian densities is a common procedure in MRI segmentation and is usually combined with the EM algorithm to estimate the density parameters.¹² The 2-step EM-algorithm¹³ iteratively alternates between estimation of intensity model parameters and voxel classification. We choose to model the intensities as a 5-component mixture of Gaussian densities, each of them corresponding to one matter (CSF, CSF-GM, GM, GM-WM, WM). We made the assumption that the intensity parameters are constant on the images, i.e. we neglect the bias field produced by the scanner and the patient interactions.¹⁴ Therefore, it is possible to learn the parameters of the mixture in a cube $S_\Omega \subset S$. The cube is chosen centered on AC, since this point has already been detected for the Talairach transformation, independently of the landmark. The size of S_Ω is $41 \times 41 \times 41$ voxels.

The EM algorithm consists in maximizing the likelihood over the parameters of the model, considering the

matter z_s as missing data. The E-step computes the posterior probabilities, given the estimated parameters of the previous step $(\alpha_j^{(n)}, \mu_j^{(n)}, \sigma_j^2^{(n)})$:

$$P^{(n+1)}(Z_s = j | X_s = x_s) = \frac{\alpha_j^{(n)} N_j^{(n)}(x_s)}{\sum_{j'=1}^5 \alpha_{j'}^{(n)} N_{j'}^{(n)}(x_s)} \text{ with } N_j^{(n)}(x_s) = \frac{1}{\sqrt{2\pi\sigma_j^2^{(n)}}} \exp\left(-\frac{|x_s - \mu_j^{(n)}|^2}{2\sigma_j^2^{(n)}}\right)$$

The M-step maximizes over $(\alpha_j^{(n+1)}, \mu_j^{(n+1)}, \sigma_j^2^{(n+1)})$, $j \in \{1, \dots, 5\}$ the log-likelihood:

$$\sum_{s \in S_\Omega} \log \sum_{j=1}^5 \alpha_j N_j(x_s) \quad (4)$$

leading to:

$$\begin{aligned} \alpha_j^{(n+1)} &= \frac{\sum_{s \in S_\Omega} P^{(n)}(Z_s = j | X_s = x_s)}{|S_\Omega|} \\ \mu_j^{(n+1)} &= \frac{\sum_{s \in S_\Omega} P^{(n)}(Z_s = j | X_s = x_s) x_s}{\sum_{s' \in S_\Omega} P^{(n)}(Z_{s'} = j | X_{s'} = x_{s'})} \\ \sigma_j^2^{(n+1)} &= \frac{\sum_{s \in S_\Omega} |x_s - \mu_j^{(n)}|^2 P^{(n)}(Z_s = j | X_s = x_s)}{\sum_{s' \in S_\Omega} P^{(n)}(Z_{s'} = j | X_{s'} = x_{s'})} \end{aligned}$$

Since the EM algorithm is sensitive to the initialization, the estimation is performed 3 times with random initialization. We keep the parameters which give the best approximation, measuring the χ^2 -distance between the estimated histogram and the observations. The user may have to validate visually the fitted Gaussian

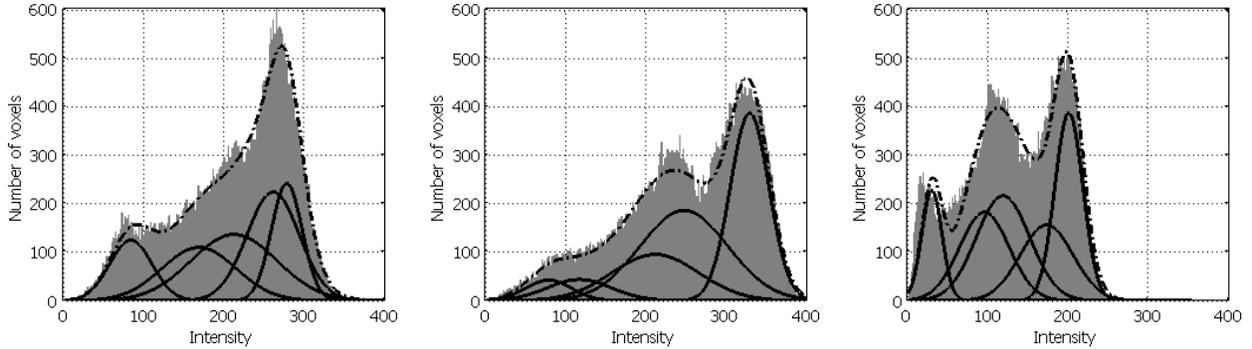


Figure 2. Examples of Gaussian mixture parameters estimation on the 41-by-41-by-41 voxel box around AC. The plain lines are the 5 estimated Gaussian densities and the dot line represents the estimated histogram.

densities. Figure 2 presents some examples of intensity histograms and fitted Gaussian densities. Some images are more difficult to model with a Gaussian mixture, because of the intensity peaks in the histogram and because there are no negative intensities. However, since we just need a probabilistic classification of the voxels, we are satisfied even if the model is imperfect.

3.2. Learning the geometry

Learning the geometry consists in estimating the probability $\pi_{s-y}(j)$ to observe at the location $s - y$ the matter j . We firstly superimpose the images i , applying a translation such that the landmark sits at the same voxel all the images. Then we use the EM-algorithm transversally to estimate the proportions of each matter j in the mixture observed at a given voxel s . The resulting image is called the probability map.

Here the location of s is fixed and the gray-levels are observed in the different images, using the estimated

parameters of the Gaussian densities from the section 3.1. The E-step computes the posterior probability, given the estimated parameters $\pi_{s-y}^{(n)}(j)$ estimated at the previous step.

$$P_i^{(n+1)}(Z_s = j | X_s = x_s^{(i)}) = \frac{\pi_{s-y}^{(n)}(j) N_{ij}(x_s^{(i)})}{\sum_{j'=1}^5 \pi_{s-y}^{(n)}(j') N_{ij'}(x_s^{(i)})} \text{ with } N_{ij}(x_s^{(i)}) = \frac{1}{\sqrt{2\pi\sigma_{ij}^2}} \exp\left(-\frac{|x_s^{(i)} - \mu_{ij}|^2}{2\sigma_{ij}^2}\right)$$

The M-step maximizes the Log-likelihood over the proportions of the mixture of matters at the fixed voxel s , $\pi_{s-y}(j), j \in \{1, \dots, 5\}$:

$$\sum_i \log \sum_{j=1}^5 \frac{\pi_{s-y}(j)}{\sqrt{2\pi\sigma_{ij}^2}} \exp\left(-\frac{|x_s^{(i)} - \mu_{ij}|^2}{2\sigma_{ij}^2}\right) \quad (5)$$

leading to:

$$\pi_{s-y}(j)^{(n+1)} = \frac{\sum_{i=1}^{14} P_i^{(n+1)}(Z_s = j | X_s = x_s^{(i)})}{14}$$

The whole probability map is obtained, by running one EM-algorithm per voxel. Figure 3 shows slices of the

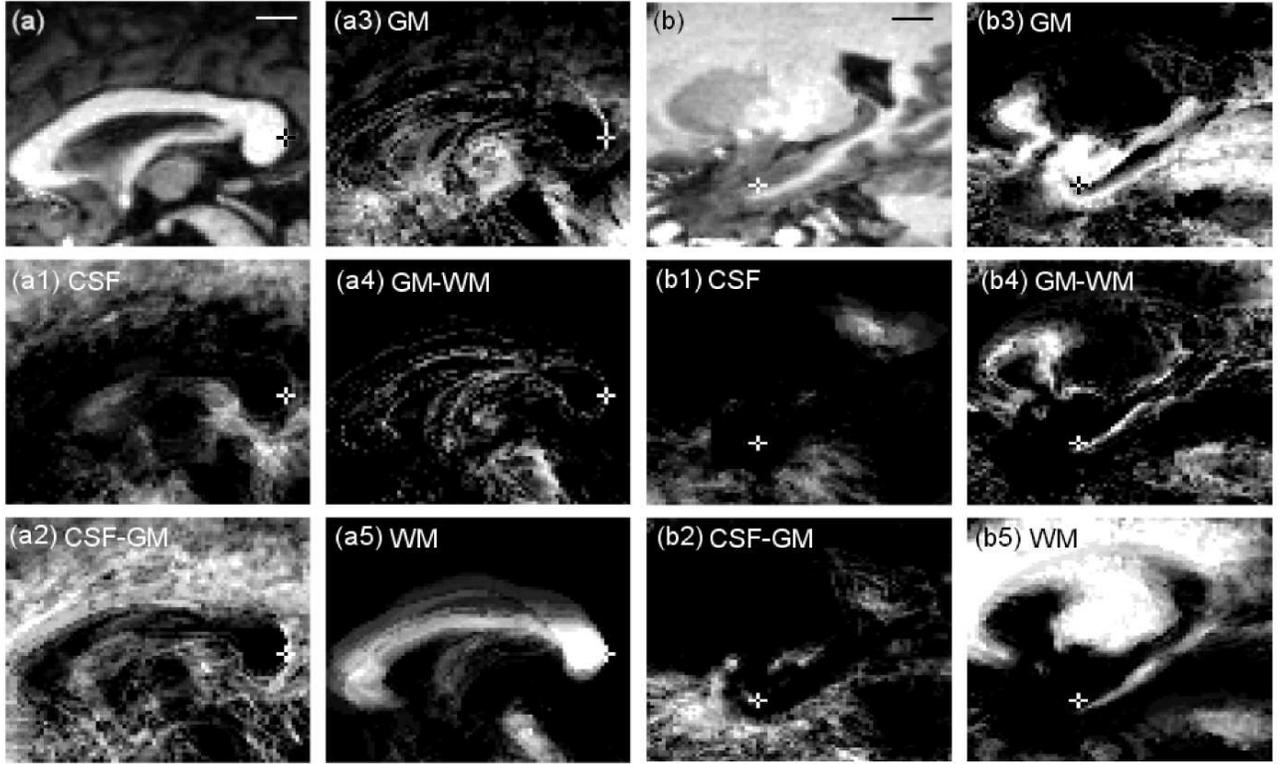


Figure 3. Slices of the probability maps obtained when the images are superimposed on the landmark SCC (a) or on the landmark HoH (b). The cross represents the location of the landmark. The images (a) and (b) are examples of the brain structures corresponding to the part of the probability map shown in the images a1-a5 and b1-b5. The images from 1 to 5 represent both for (a) and (b) the probability $\pi_{s-y}(j)$ given the location of the landmark y of respectively the CSF, the CSF-GM, the GM, the GM-WM, the WM. The white and black lines are 10mm long.

probability maps obtained when the training images are superimposed on the SCC (a) or on the HoH (b). The images 1 to 5 show the different matters: respectively CSF, CSF-GM, GM, GM-WM, WM.

For example, in (a5), one visualizes the probability that a voxel from a random image, registered at the SCC, would correspond to white matter (WM). Notice that some structures appear with sharp boundaries, often close

to the landmark. In the case of the SCC probability map, the corpus collosum is identifiable. Along the shape the contour evaluates to be sharper near the landmark. One expects it, since the images are registered at this point.

We refer the reader to the Figure 4 to understand the details of the anatomy around the HoH, which are observ-

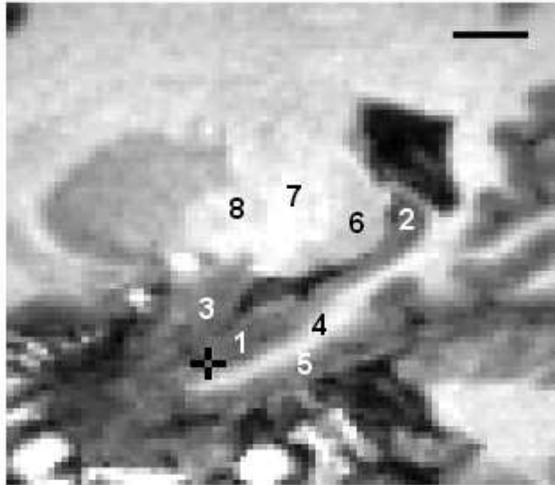


Figure 4. Details of the anatomy around the head of the hippocampus. The black bar gives the scale: 10mm. The cross represents the HoH. 1, head of the hippocampus; 2, tail of the hippocampus; 3, amygdala; 4, white matter of the parahippocampal gyrus; 5, gray matter of the parahippocampal gyrus; 6, pulvinar; 7, posterior limb; 8, globus pallidus.

able in the probability map, Figure 3. In the HoH probability map, the hippocampus appears in gray matter with a high probability, surrounded by an elongated structure of gray matter below it. This is the gray matter of the parahippocampal gyrus. The white matter of this structure appear clearly in the image b5 of Figure 3. In addition, on this same image, one notices the large white structure composed of the posterior limb, the pulvinar and partially the globus pallidus.¹⁵

4. SELECTING THE INFORMATIVE VOXELS

The probability map obtained as explained in section 3.1, is almost as large as the initial images: $161 \times 191 \times 151$ voxels. Computing the conditional expectation with all the points of the probability map is untractable and inefficient. Most of the voxels contain indeed no information about the landmark location. For example, the points belonging to large structures with constant color are useless to locate the landmark. In contrast, contours of brain structures should intuitively be informative.

We choose to measure the amount of information contained in a voxel by the expected variance reduction of the landmark location, Y , when the gray-level is observed at the voxel s :

$$E_{Y, X_s} \|Y - E_Y(Y|X_s = x_s)\|_2^2 \tag{6}$$

This quantity ranks the voxels and allows us to select only the most informative ones. However, because of the gray-level variations from one image to another one cannot easily compute (6). Consequently we choose to consider the expected reduction of variance when the matter at the voxel s is given, that is:

$$E_{Y, Z_s} \|Y - E_Y(Y|Z_s = j)\|_2^2 \tag{7}$$

One can prove that (6) and (7) would be equivalent, leading to the selection of the same voxels, if the 5 densities $P(Z_s = j|X_s = x_s)$ had disjoint supports.

The information at a voxel s , defined by (7) depends only on the prior distribution and the probability map.

Using the definition of the variance and the model of the matters in the image, the information at the voxel s can be expanded as follows:

$$\begin{aligned}
E_{Y,Z_s} \|Y - E_Y(Y|Z_s = j)\|_2^2 &= \sum_{k=1}^3 \sum_{j=1}^5 [E_{Y_k}(Y_k^2|Z_s = j) - E_{Y_k}(Y_k|Z_s = j)^2] \\
&= \sum_{k=1}^3 \sum_{j=1}^5 \left[\sum_{y_k \in \mathcal{Y}_k} y_k^2 \frac{\pi_{s-y_k}(j)}{\sum_{y''_k \in \mathcal{Y}_k} \pi_{s-y''_k}(j)} - \left(\sum_{y_k \in \mathcal{Y}_k} y_k \frac{\pi_{s-y_k}(j)}{\sum_{y''_k \in \mathcal{Y}_k} \pi_{s-y''_k}(j)} \right)^2 \right]
\end{aligned}$$

where $Y = (Y_1 \ Y_2 \ Y_3)^T$ and $y = (y_1 \ y_2 \ y_3)^T$, and $\mathcal{Y} = \mathcal{Y}_1 \otimes \mathcal{Y}_2 \otimes \mathcal{Y}_3$. The lower the expected variance is, the more informative are the corresponding voxels. We called the resulting image the information map.

To understand the connection between the informative points and the landmark we use synthetic images on which we compute the probability map and then the information map. In order to simplify we consider only three matters corresponding to the three major matters of the brain (CSF, GM, WM). A set of synthetic data is created using the gray-level parameters estimated on the images of the training set. The synthetic images are composed of a sphere A rigidly related to the landmark location, and of a sphere B whose center location is fixed, independently of the landmark location. The radii of both the small sphere and the large sphere are constant. We compute the probability map of the superimposed images and the information map. Figure 5 shows the result of the experiment. The probability map, Figure 5 (CSF, GM, WM), presents a sharp boundary

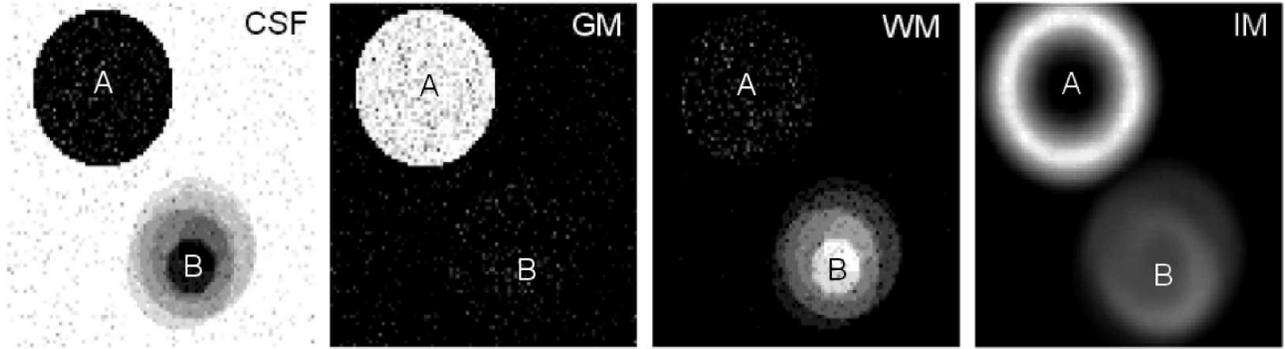


Figure 5. Probability map and information map obtained on synthetic images. The images are composed of three matters, the sphere A in GM, the sphere B in WM and the background in CSF. The sphere A is rigidly related to the landmark sought. The center of B is independent of the landmark. CSF, GM, WM are the three components of the probability map which are visualized in the three leftmost images. The white voxels in the information map (IM), in the rightmost image, are the most informative to locate the landmark, the black ones are the least informative.

for the sphere A whose center is fixed with respect to the landmark location, whereas the sphere B has a blurred boundary. The information map, Figure 5 rightmost image, shows that the boundary of the sphere A is the location of the informative voxels, in white, as intuition suggests.

We now compute the information map for the HoH and SCC. Figure 6 shows one slice of the result. The algorithm selects automatically the informative locations. For the SCC, the most informative voxels are located on the boundary of the splenium itself. In this case, the algorithm selects automatically the voxel located at the "corner". The current best method¹⁰ to detect tip-like landmark uses an intensity model for corner, fitted on the shape.

The results are more difficult to interpret for the HoH. The informative voxels are located on a boundary between gray matter and white matter. This boundary was already visible in the probability map, Figure 3. On the other hand, one notices that the voxels corresponding to the parahippocampal gyrus are not selected even if

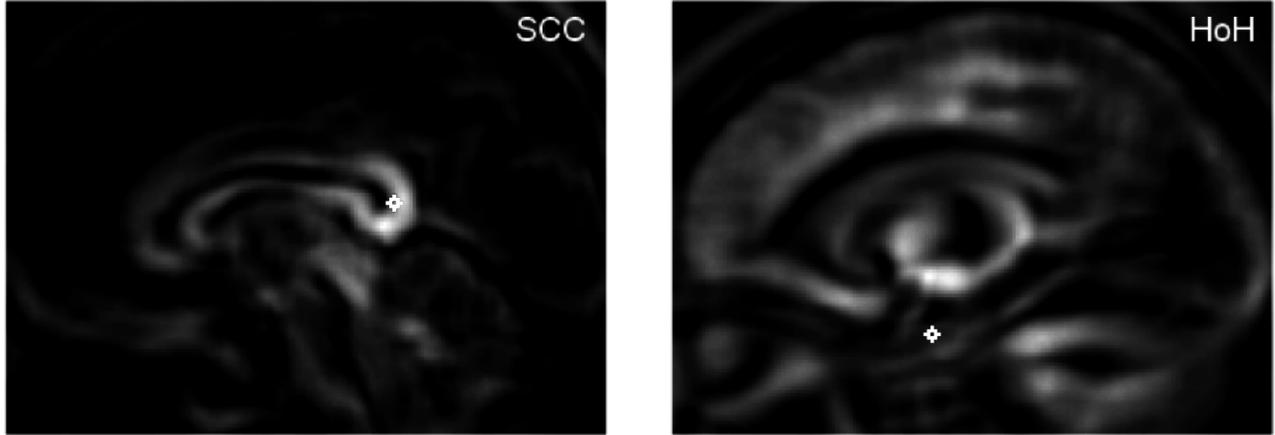


Figure 6. Sagittal slices of information map obtained from the probability map of SCC on the left and HoH on the right. The mean landmark location is represented in white.

sharp white and gray structures appeared in the probability map, Figure 3. We believe that this is due to the thinness of the structure. The computation of the information is indeed a spatial average on a box as large as the prior box \mathcal{Y} . Because of the surrounding constant matter, the expected information of the voxels on the hippocampal gyrus is erased. The following experiment confirms this intuition: the information map is computed with decreasing prior box size, so that the spatial average is more localized. While the box size decreases, the information contained in the voxels of the parahippocampal gyrus increases.

The selection step reduces drastically the computation, but there is a risk to lose some informative voxels too. Once ranked, we picked only the 100, 500, 2000 and 4500 first points, corresponding to less than one per thousand voxels. In Figure 3 only the white voxels are selected.

Once the parameters estimated and the informative voxels selected, we can use the model on new images. The first part of the online algorithm is identical to the gray-level estimation detailed in section 3.1. Then it consists in computing the conditional expectation of Y , as detailed in the equations (2) and (3).

5. EXPERIMENTAL RESULTS

In this section we firstly evaluate the human performance in landmarking brain images. Then we detailed the experimental results obtained on the two landmarks SCC and HoH, with our method.

5.1. Manual performance in detecting landmarks

Landmarking manually MR brain images is a tough task. Results vary depending on the landmarker and the experiment. To evaluate his consistency, the expert landmarked a first time SCC and HoH on all the images. Then several weeks later, he landmarked a second time in similar conditions 15 among a total of 23 images. For SCC, the mean Euclidian distance between the landmarks is 0.71mm with standard deviation of 0.61mm. For HoH, the mean distance is 1.22mm and the standard deviation 0.92mm. We consider these results as gold standard for the considered scans.

A second experiment has been performed on the HoH. The expert taught a graduate student to landmark this point. As the expert did, the student landmarked a first time the images, and after several weeks relandmarked them. The mean Euclidian distance between his two landmarking is 3.58mm with standard variation of 0.98mm. In addition we measure the Euclidian distance between student's and expert's landmarks. The mean distance is 3.26mm with standard deviation of 0.98mm. Even if we think that the student would eventually achieve the expert performance with additional training, this experiment shows how difficult it is to landmark consistently the images and to teach another person to do the same.

5.2. Algorithm results

We demonstrate the algorithm for the detection of SCC and of HoH, using 14 images in the training set, and 9 images for the test.

The estimation of the gray-level densities is common to the two experiments. We performed it only once and used the same estimated parameters. The algorithm is implemented in Matlab and runned with a Xeon 2.2GHz processor. The first EM-algorithm takes 10 seconds per images, when the box size is $41 \times 41 \times 41$. However, because of its sensitivity to the initialization, the EM-algorithm has to be runned several times on each image, in order to define the best parameters.

Learning the geometry, consists in learning $161 \times 191 \times 151 \times 4$ parameters, using 14 values at each location of the probability map. It takes around 30 minutes to compute it completely.

Finally the last step of the off-line algorithm selects the informative voxels. The computation takes around 20 minutes.

The online algorithm starts with the estimation of the gray-level densities and computes the conditional exp-

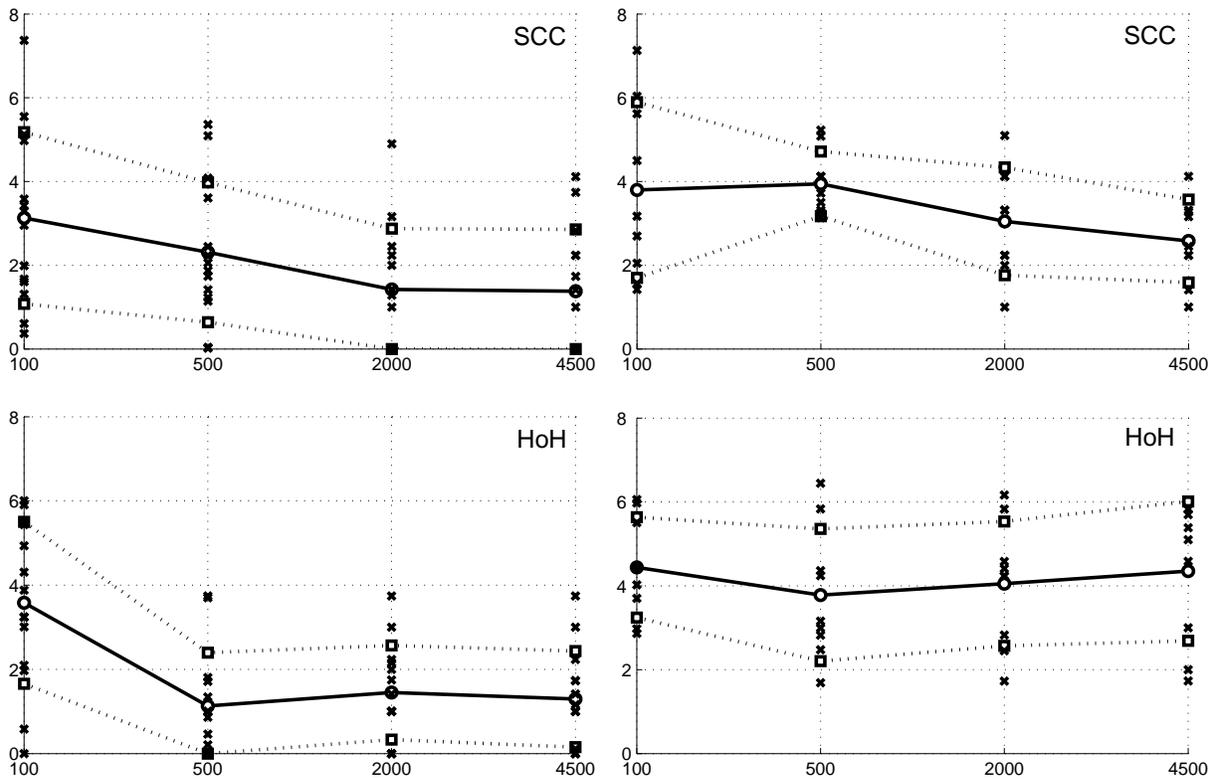


Figure 7. Prediction error when the number of selected informative voxels increases. X-axis: number of points used, Y-axis: Euclidian distance between the prediction and the ground-truth in mm. Each cross corresponds to one image, the line with circle marker to the mean error and the dot lines with square markers to the mean \pm one standard deviation. On the left: results on the training set, On the right: results on the testing set. First line: SCC, Second line: HoH.

tation $E[Y|X_A = x_A]$, A the set of selected voxels. Experimental results are obtained for increasing number of voxels in the set A : 100, 500, 2000 and 4500. The Euclidian distance between the prediction and the expert landmark measures the prediction error. Figure 7 presents the evolution of the mean error when the number of selected informative voxels increases.

The performances of the automatic landmarking algorithm on the test are comparable to the ones of the trained student, but still far from the expert's ones, see Table 1. The computing time is about 1 minute per image.

Table 1. Mean prediction error obtained with our algorithm for SCC and HoH using the training set (14 images) and the testing set (9 images).

Landmark	prior box (in voxels)	initial mean error	mean error (training set)	mean error (testing set)
SCC	$6 \times 9 \times 10$	6.01mm	1.38mm ($\sigma = 1.48\text{mm}$)	2.56mm ($\sigma = 0.99\text{mm}$)
HoH	$12 \times 12 \times 12$	8.48mm	1.13mm ($\sigma = 1.26\text{mm}$)	3.78mm ($\sigma = 1.58\text{mm}$)

6. CONCLUSION

The proposed method is a generic algorithm to detect a landmark in MR images. It is demonstrated on the HoH, the head of the hippocampus, and the SCC, the splenium of the corpus collosum. We were unable to find similar generic approach, since the competing approaches use geometrical properties of the landmark and hence need to be tailored for each type of landmark. Our algorithm is able to locate the informative points in the image and design automatically a probabilistic template used on new images. It gives a tentative location, comparable to the work of a non-expert landmarker. The expert could use it as an automatic way to provide an initial guess. The good performance on the training set are encouraging for further developments.

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