Atlas-assisted Segmentation of Cerebral Structures of Mice

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Abstract—The segmentation of different cerebral structures of mice is becoming more and more important due to the growing interest in finding small animal models of human diseases. In this work, variational atlases are constructed by manual segmentation of various MRI brain images of reference and trisomy 21 mice. These atlases are then registered to assist the segmentation of fine cerebral structures such as the cerebellum and the hippocampus. A modified Chan-Vese segmentation method is used for the detection of these structures. Global as well as local comparison of the reconstructed surfaces and volumes are hence conducted to better understand the gene involved in the morphological malformations associated to trisomy.

Keywords- Atlas registration; Chan-Vese segmentation; MRI cerebral images; Trisomy 21.

I. INTRODUCTION

The motivation of the work presented in this paper is to understand better the morphological malformations of the brain associated to Trisomy 21 or Down syndrome. Characterization of morphological malformations associated to trisomic mouse models for particular chromosome segments will help to link genes from these segments to specific dysmorphologies. It would also help to look after the consequences of this disease, and to improve the quality of life of the patients.

Biologists are interested in the reconstruction of cerebellum surfaces to better understand the morphological malformations of the brain associated to Down syndrome.

In order to extract different cerebral structures, MRI images should be segmented. Since manual segmentation is difficult and computationally expensive, automatic methods have been proposed [1]. This problem can be solved using a variety of techniques. The Chan-Vese method is one of the most used techniques [2]. However, since the contrast between different objects in the brain is low, a semi automatic technique that considers information given by the user could be more efficient and less complicated to develop. A good review of current medical image segmentation methods can be found in [3].

Most automatic segmentation methods are initialized by a contour that best describes the target object, i.e., circle or ellipse. However, the cerebellums and the hippocampus are difficult to segment due to their complicated shape. In addition, limits of these objects included in the brain are unclear Atlas data could be a good solution to initialize segmentation since it approaches better these internal cerebral structures. But due to different acquisition positions, the Atlas should commonly be registered to targeted object before it can be used. Variants of the Iterative Closest Point (ICP) algorithm have widely been used for the estimation of rigid transformation parameters of 3D closed surfaces. For instance, the Comprehensive ICP (CICP) algorithm has been proven to be robustness to Gaussian noise and efficiency in terms of precise estimation of registration parameters.

In this work, we present a complete procedure for the segmentation of cerebellum that includes an initialization step using a registered brain Atlas and a segmentation step using a modified Chan-Vese method. The reconstructed surfaces make it easier to study the characterization of morphological malformations associated to trisomic mouse models. As a first step, measured volumes are compared.

The next section gives a brief description of used Atlas. Section 3 presents the used registration technique, required prior to the use available Atlas. The use of a new variant of the well-known Chan-Vese method is then demonstrated in section 4. The results are then presented and discussed. Finally, conclusions are given.

II. ATLAS PRODUCTION

Three lines of mice carrying the trisomy of chromosome 21 as well as a normal line are provided by the IEM laboratory of the National Centre of Scientific Research in France (CNRS) as shown in Fig. 1.

High resolution three-dimensional (3D) Magnetic Resonance Imaging (MRI) images of mouse models are realized at the CBM laboratory of CNRS, France. Several experiments were conducted to obtain images

with high spatial resolution (118.2×88.5×118.2 µm3/voxel) with many details of the neuro-architecture, thanks to the power of the magnetic field and imaging gradient available on the used imaging system, first of its kind in France. Fig. 2 shows a 3D image (110×341×110 voxels) as a result of one of these experiments.

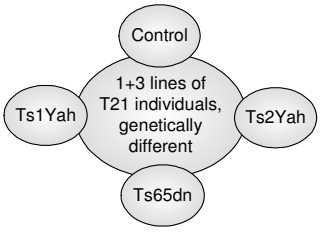
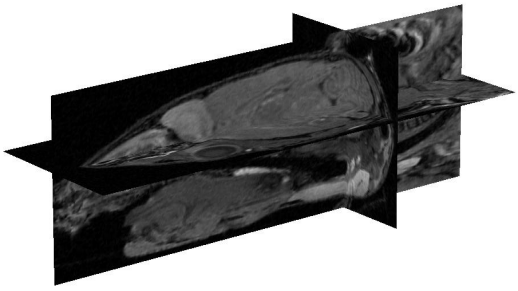
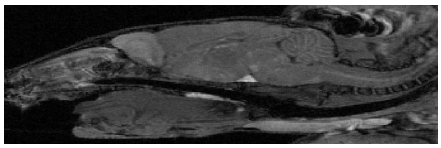


Figure 1. Considered mouse brain models

a) 3D view



b) Sagital slice c) Axial slice



d) Coronal slice

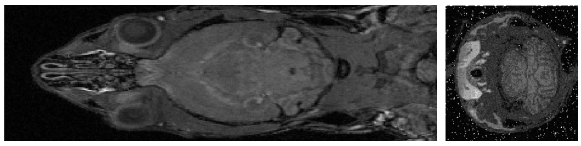


Figure 2. Example of a 3D image and its related slices

An atlas for each of the brain, cerebellum and hippocampus structures is obtained by manually tracing their contours on a sequence of corresponding coronal slices. This has been done by IEM experts. The pixels of the selected contours represent the 3D atlas data as presented in Fig. 3 for a normal cerebellum. One 3D MRI image from each line is selected as a reference.

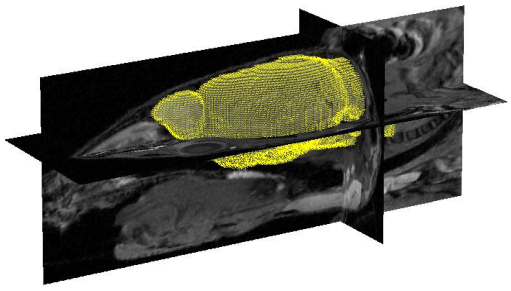


Figure 3. Considered mouse brain models

III. CICP REGISTRATION ALGORITHM

The CICP algorithm is recently developed in our institution as a method of surface registration. Although More details on this variant of the well-known ICP algorithm can be found in [4], we recall its general functionality. Let us assume that the given two surfaces to be registered can be described as point sets; the scene data points, **P**, with Np points, $\{p_i,\ i=1, \ldots, N_p\}$, and the reference data points, **M**, with Nm points, $\{m_j,\ j=1, \ldots, N_m\}$. Depending upon the sampling of the surfaces, N_p is not necessarily equal to Nm. Furthermore, the point p_i of the scene surface does not necessarily represent exact 3D correspondence to the point mi of the reference surface. However, the search space is determined by the size of the scene data set; i.e., N_p. The CICP algorithm can be summarized as follows:

A. *Initialization*

- Let the initial scene surface P_0, be equal to P.
- Define the maximum number of iterations k_{max}.
- Initialize the translation vector and the rotation matrix as follows:

$$\mathbf{T}=\begin{bmatrix} t_1 \\ t_2 \\ t_3 \end{bmatrix} \quad \alpha\nu\delta \quad \mathbf{R}=\begin{bmatrix} r_{11} & r_{12} & r_{13} \\ r_{21} & r_{22} & r_{23} \\ r_{31} & r_{32} & r_{33} \end{bmatrix}. \qquad (1)$$

with the initial coefficient of the translation vector and rotation matrix set as follows: t_u=0, $r_{u,v}$= 0 if $u \neq v$, and $r_{u,u}$= 1, u =1,2,3, v= 1,2,3. This corresponds to zero translation and no rotation.

B. *Iterations*

- For each point $p_i \in \mathbf{P}$, (i = 1, ..., N_p), the algorithm computes the Euclidian distance $d_{i,j}$ to each point $m_j \in \mathbf{M}$, (j = 1, ..., N_m). Then, for N_p times, the algorithm:
  - looks for the location (i,j) that corresponds to the minimum distance $d_{i,j}$ in the current look up matrix,
  - assigns p_i to m_j as a correspondence pair $_j$,
  - removes this correspondence pair from future consideration.
- Using the selected correspondence pairs, compute the transformation, rotation (**R**) and translation (**T**), that minimizes the mean square error (MSE) of the estimated correspondence pairs:

$$\text{MSE}=\frac{1}{\mathbf{N_p}}\sum_{\mathbf{i}=1}^{\mathbf{N_p}}\left\|\hat{\mathrm{m}}_{\mathbf{i}}-\mathbf{R}(\mathrm{p}_{\mathbf{i}})-\mathbf{T}\right\|^2 . \qquad (2)$$

Different close-form solution techniques of the original ICP algorithm can be used, i.e., quaternion [5, 6] or single value decomposition [7]. The resulting transformation from the minimization of the above equation at step k will be denoted $\mathbf{R}_k$ and $\mathbf{T}_k$. This step also provides the minimum distances which correspond to the matched pairs.

- Compute $\mathbf{P} = \mathbf{R}_k \times \mathbf{P}_0 + \mathbf{T}_k$ and restart a new iteration if the change in the MSE is above a predefined threshold ζ, and if the maximum number of iterations k_{max} is not reached. If not, stop the iterations and exit.

The high quality results of segmentation of the brain that we obtained using a Chan-Vese based method could be used to perform such a task. A possible strategy is described in the following for the segmentation of the cerebellum (it would be identical for the hippocampus).

We start from a reference brain and a reference cerebellum of a given mouse which are manually segmented. On the mouse under consideration, we first could use a rigid registration process (only translations, rotations and homothetic deformations are allowed).

The reference brain is first registered with the brain segmented using the semi automatic process presented in [8] (first line of Fig. 4). Using the CICP, the measured rigid transformation between the current brain and reference brain is then applied on the reference cerebellum (second line of Fig. 4). The resulting registered cerebellum is used for initializing the segmentation of the true cerebellum.

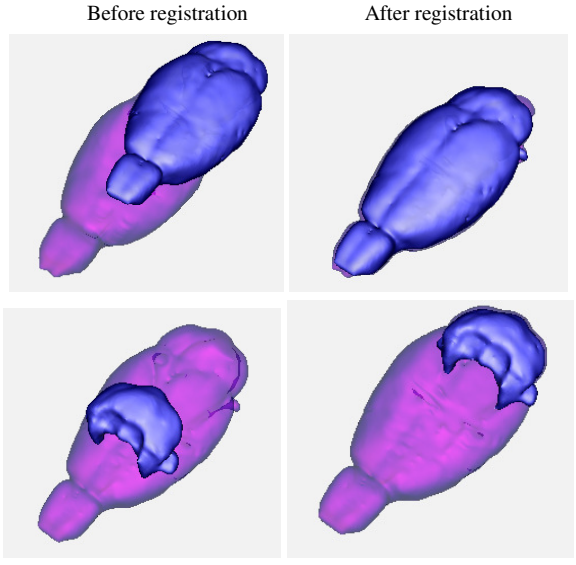


Figure 4. Reference data are presented in blue color, whereas segmented brain is in purple. Top of the figure, the reference brain is registered with the brain under consideration. Bottom of figure, the rigid registration is applied to the reference cerebellum. This will be the initialisation to the segmentation process

IV. RESULTS AND DISCUSSION

Once the atlas data is registered, our proposed Chan-Vese based segmentation method is applied. While preserving the advantages of level set methods, such as automatic handling of topological changes, the proposed method integrates region information to guide the evolution of the initial segmentation. By this way, the initial contour is very close to the objective structure, as show in Fig. 5b. In addition, using a level-set based active contour method will refine segmentation results while preserving object structure. In order to accelerate processing time, segmentation is limited to the pre-segmented brain region, since cerebellum is always found inside the brain.

Experimental results show that the proposed process works efficiently for most treated images, as seen in Fig 5c. However, it has occasionally some problems of detecting the barrier between brain and cerebellum, on which we are currently working by integrating 3D information to guide the segmentation process. More work has to be done on the choice of segmentation parameters that more suitable to our MRI images.

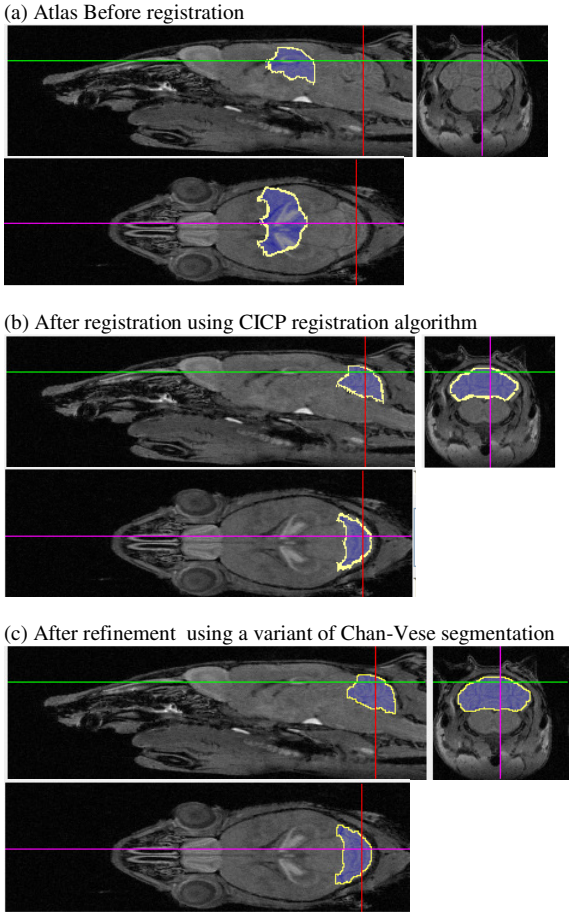


Figure 5. Atlas assisted segmentation: contour initialisation befor registration (a), after registration using the CICP algorithm (b), and after segmentation using Chan-Vese based method (c)

V. CONCLUSION

It is demonstrated in this paper that atlas data can help improving the segmentation precision of mouse cerebral structures and overcoming the common problem associated to the initialisation of the well-known Chan-Vese method. The quality of the registration-assisted segmentation process makes it possible for global and local comparison of internal cerebral structures that is of great interest to biologists to understand the characterisation of morphological malformations associated to trisomic mouse models.

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