3D Reconstruction of Mouse Brain from Allen Brain Atlas

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Abstract: *The paper describes a method for fully automatic 3D-reconstruction of mouse brain from a sequence of histological coronal 2D slices. The model is constructed via non-linear transformations between neighboring slices and further morphing for interpolation. We also use rigid-body transforms in pre- and post-processing stages for smoothing transitions. The obtained 3D-model is then used for getting 2D-images of brain in arbitrary section-plane. We use this approach for automatic annotation of brain structures with the aid of Allen Brain Atlas which is available in electronic form.*

Keywords: *3D-Reconstruction, neuroimaging, image transformations, morphing.*

1. INTRODUCTION

The problem of automatic annotating of brain structures using only images of histological brain slices is very important in modern brain research [1]. Biologists are now able to monitor the activity of various genes. This is usually done in vitro, i.e. on dead species. The extracted brain is frozen and then cut into slices. Each slice is double-stained by Nissl method to highlight histology and by special stain which reveals the neurons with expression of corresponding genes. The main problem is to determine brain structures where active genes are located. This problem is difficult even for experts especially in cases when slices are obtained using non-standard section-plane. However there are several atlases for various animals which contain both histological images and the corresponding images where all brain structures are marked by expert [2]. The intriguing problem is to use such atlases for constructing annotated 2D-image in arbitrary section-plane.

In the paper we suggest an algorithm which is fully automatic and allows one to get such 2D-images in various sections. To do this we use histological images from atlas to construct brain 3D-model. First we perform rigid-body transforms to align the neighboring slices and eliminate contour fluctuations. Second we find non-linear transforms which map each slice to the previous ones in the best way. The family of B-splines is used as a set of basis deformations. We use morphing approach to compute virtual intermediate sections between real slices. Our 3D-model is not voxel-based. Instead we keep the initial slices and a set of B-spline coefficients. This allows us to save memory and at the same time supply high spatial resolution which is important for obtaining virtual slices in different planes. When 3D-model is constructed we use it to synthesize 2D virtual slice by setting arbitrary section-plane. Then we use the same transforms to calculate the anatomic structure for this virtual slice.

The rest of paper is organized as follows. In section 2 we briefly characterize particular brain atlas we use - Allen Brain Atlas [4]. Section 3 gives a list of steps for 3D-modelling. We describe preprocessing of brain images in section 4 and non-linear interpolation of slices in section 5. Section 6 contains some experimental results. Some conclusions are given in the last section.

2. ALLEN BRAIN ATLAS

The Allen Brain Atlas [3, 4] is a set of full-color, high-resolution coronal digital images (132 images) of mouse brain accompanied by a systematic, hierarchically organized taxonomy of mouse brain structures. The Allen Brain Atlas is obtained from 8-week old C57Bl/6J male mouse brain prepared as unfixed, fresh-frozen tissue.

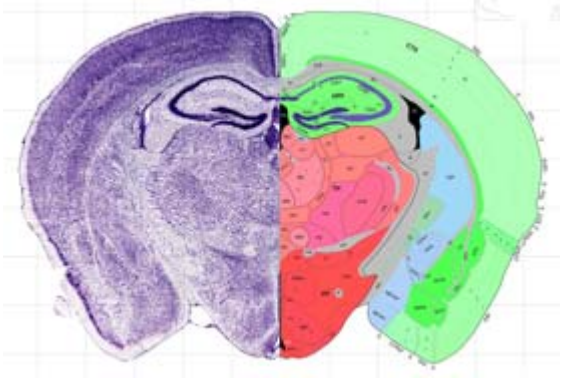

Fig.1 – Allen Brain Atlas image.

On Fig.1 the left half is a histological image of one slice of mouse brain, the right half is a structural color segmentation of mouse brain.

3. STAGES OF MOUSE BRAIN 3D MODELLING

Here we consider the problem of 3D mouse brain model reconstruction using a set of coronal 2D slice images obtained from Allen Brain Atlas. In the paper we propose to solve this problem using 3 main steps:

1) *Illumination correction.* For different brain images illumination level is different and even within one separate image there are areas with different illumination levels.

2) *Proportional alignment.* Due to technological aspects of brain cutting procedure some brain slices may change a little in their actual size and shape. This deformation can be significant for automatic 3D model reconstruction.

3) *Non-linear transformation between neighboring slices.* Such transformation allows to find the correspondence not only between brain shapes but also between internal structures of mouse brains.

In the paper we provide methods for solving all three mentioned problems.

Although atlas images are given as positives we decided to work with negatives due to some

implementation aspects. Hence all further illustrations are given as negatives.

Atlas images resolution is very high. In our implementation image resolution was reduced because of computational costs. Resolution decreasing gives an additional image smoothing as well.

4. ILLUMINATION CORRECTION

For illumination correction we apply a gauss filter with large radius. Then initial image is divided by obtained filtered image. Fig. 2 and fig. 3 illustrate this procedure.

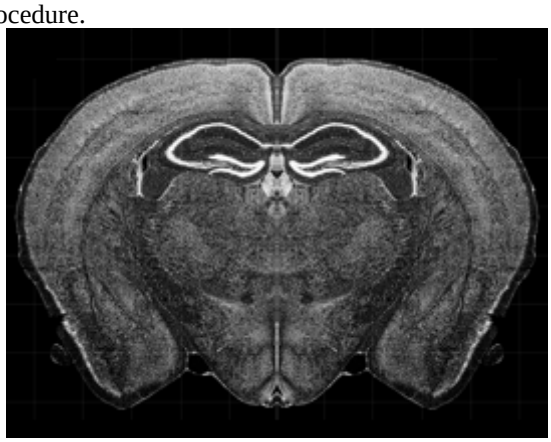

Fig.2 – Atlas image without illumination correction.

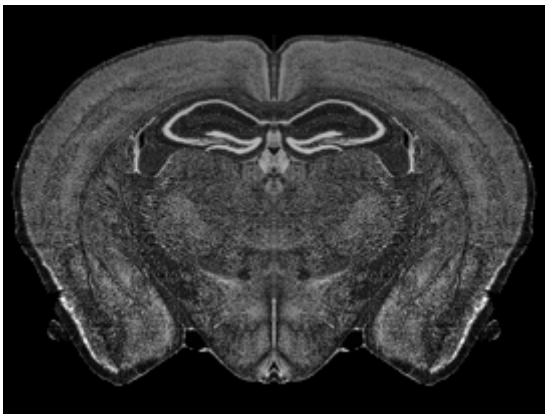

Fig.3 – Atlas image after illumination correction.

5. ALLIGNMENT OF ATLAS IMAGES

For alignment of atlas images we find the smallest surrounding rectangle for each slice. Afterwards we consider rectangle border as a function of slice number. Fig. 4 shows top and bottom borders of brain rectangles without alignment. These functions are not smooth enough for building 3-dimensional model. Here we apply Savitzky-Golay filter to smooth these functions.

Savitzky-Golay filters can be thought of as a generalized moving average. For each point we fit a polynomial to the points in the moving window using least squares (we used window width 15), and then set the new value to be the value of that polynomial at the same position. Such choice of coefficients preserves higher moments in the data, thus reducing the distortion of essential features of the data like peak heights and line widths in a spectrum, while the efficiency of the suppression of random noise is effectively unchanged.

Fig. 5 shows top and bottom borders of brain rectangles after alignment.

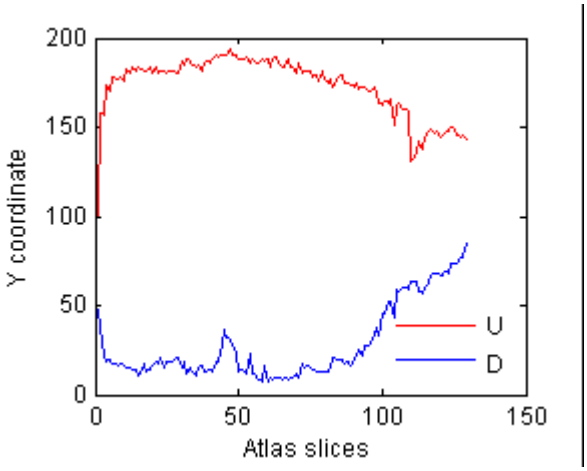

Fig.4 – Not aligned top (U) and bottom (D) borders of mouse brain.

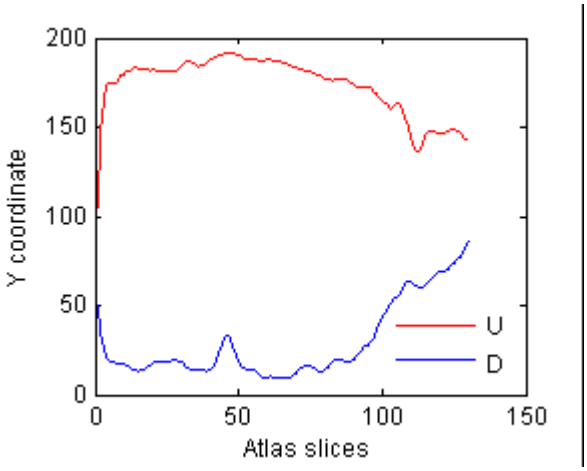

Fig.5 – Aligned top (U) and bottom (D) borders of mouse brain.

If we are interested in any specific section of mouse brain we can make additional alignment in appropriate plane. Such alignment makes specific section smother but the whole model becomes less smooth. So in general we don't use specific plane alignment for 3D-model reconstruction.

6. NON LINEAR DEFORMATIONS

A 3D model of mouse brain is a function:

$$F : \square^{3} \rightarrow [0,1]. \qquad (1)$$

From atlas slices we know F values only at some discrete points. In slice plains expansion of discrete function to its continuous version is a weighted sum of surrounding discrete point color. Expansion in other plains can be done in the same way (weighted sum of neighboring slices). However, this simple solution makes a 3D model not smooth enough. A better solution can be obtained using nonlinear image deformations.

The input images are given as two 2-dimensional discrete functions:

$$f_1, f_2 : I \subset Z^2 \rightarrow [0,1]. \qquad (2)$$

Here I is a 2-dimensional discrete interval covering the set of all pixels in the image. Functions values stand for intensities of corresponding pixels.

Denote continuous expansions of two images as

f_1^c, f_2^c.

Our goal is to find a deformation of the first image to the second one in the following way:

$$f_1^c(g(x,y)) \approx f_2(x,y). \quad (3)$$

Here $g(x,y): \mathbb{R}^2 \to \mathbb{R}^2$ is a deformation (correspondence) function between pixels.

We measure the difference between images by SSD (sum of squared deviations) criterion:

$$E = \sum_{(i,j)\in I} (f_1^s(g(i,j)) - f_2(i,j))^2. \quad (4)$$

So the problem is to minimize E with respect to deformation function *g*.

We consider deformation function as a linear combination of some basis functions:

$$g(x,y) = \sum_{k\in K} \vec{c}_k b_k(x,y). \quad (5)$$

Here *K* is a set of the basis function indexes.

Family of deformation functions (5) transforms optimization problem in functional space into finite-dimensional optimization problem.

We use uniformly spaced cubic B-splines as basis functions.

A B-spline β_r of degree r is recursively defined as

$$\beta_r = \beta_{r-1} * \beta_0, r > 0. \quad (6)$$

β_0 is a characteristic function of $[-0.5, 0.5]$, * is convolution operator.

Specifically cubic B-spline is the following function:

$$\beta_3(x) = \begin{cases} 2/3 - (1 - |x|/2)x^2, 0 < |x| \le 1, \\ (2-|x|)^3/6, 1 < |x| < 2, \\ 0, |x| \ge 2. \end{cases} \quad (7)$$

So we are looking for deformation function in the family:

$$g(x,y) = \sum_{(k_x,k_y)\in K} \vec{c}_{k_x,k_y} \beta_3(x/h_x - k_x)\beta_3(y/h_y - k_y) \cdot \quad (8)$$

Centers of B-spline functions are placed on the regular grid $(k_x h_x, k_y h_y)$. Working with uniform splines is significantly faster with respect to nonuniform splines. In order to get complete control over *g*, we put some spline knots outside the image.

Finally the problem is to optimize SSD criteria E w.r.t. set of parameters c. Here we use gradient descent algorithm with feedback step size adjustment. In this algorithm parameter update rule is $\Delta c = -\mu \nabla_c E(c)$. After a successful step μ is multiplied by some value μ_f, otherwise it is divided by some other value μ_f^*.

An example of deformation field obtained from B-spline basis functions for a pair from Allen Atlas is shown in Fig, 6.

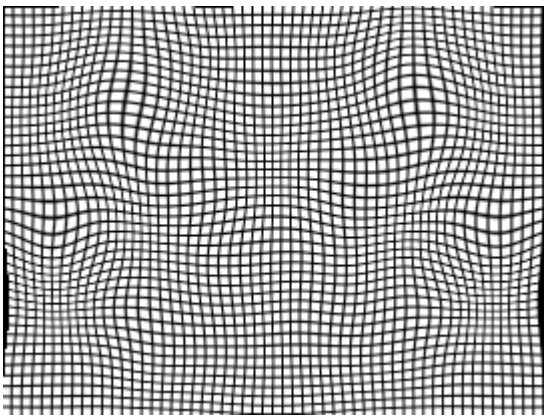

Fig.6 – Deformation field for B-spline method. This deformation field is obtained by applying deformation of neighbouring slices to regular grid.

After we have deformation of the first image to the second one and vice versa, we can fill gaps between atlas slices with weighted sum of deformated neighbouring slices:

$$F(x,y,z) = \alpha f_{1,k-1}^{\alpha}(x,y) + (1-\alpha) f_{2,k}^{1-\alpha}. \quad (9)$$

Here $\alpha = (z - z_{k-1})/(z_k - z_{k-1})$, $z_{k-1} \le z < z_k$, z_k is a z-coordinate of slice number k.

$$f_{1,k-1}^{\alpha} = f_{k-1}((x,y) + \alpha(g_{k-1}^k(x,y) - (x,y))). \quad (10)$$

$$f_{2,k}^{\alpha} = f_k((x,y) + \alpha(g_k^{k-1}(x,y) - (x,y))). \quad (11)$$

Here $g_i^j(x,y)$ is a deformation function of slice number *i* to slice number *j*.

6. EXPERIMENTAL RESULTS

Our 3D model allows to reconstruct brain image for arbitrary section plane. Fig. 7 shows sagittal brain view for 3D-model reconstructed from atlas without illumination correction, proportional alignment and nonlinear deformations between neighboring slices. Fig. 8 shows the same view for 3D-model built with illumination correction and atlas image alignment. Fig. 9 shows the result obtained with nonlinear deformations between neighboring slices.

It is easy to see that 3D model from Fig. 9 is much smoother than the previous ones. Besides, it provides better information about internal structures of mouse brain.

We can also reconstruct brain structure segmentation for each section plane using right parts of initial atlas images. Fig. 10 shows this result for the image from Fig. 9. This colored image can be compared to sagittal view taken from another atlas (Fig. 11). It is easy to see that this is a strong correspondence between two images with respect to brain structures.

Analogous results can be obtained for axial view (Fig. 12-16).

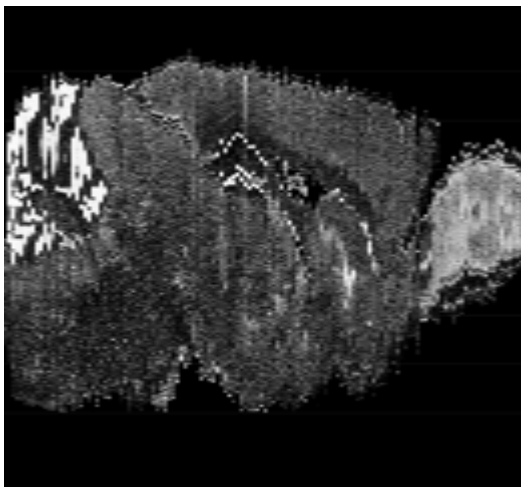

Fig.7 – Sagittal view of 3D model without illumination correction, alignment and nonlinear deformations.

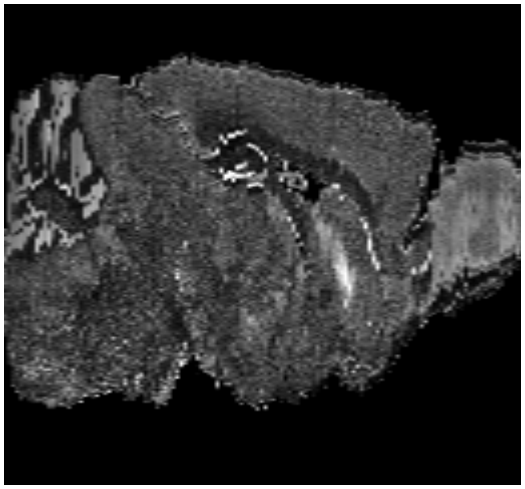

Fig.8 – Sagittal view of 3D model with illumination correction and alignment.

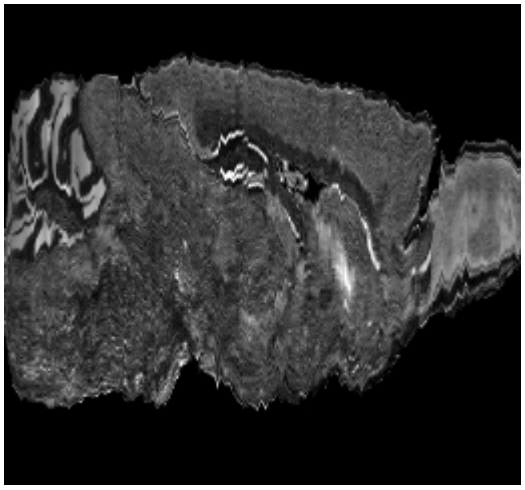

Fig.9 – Sagittal view of 3D model with illumination correction, alignment and nonlinear deformations.

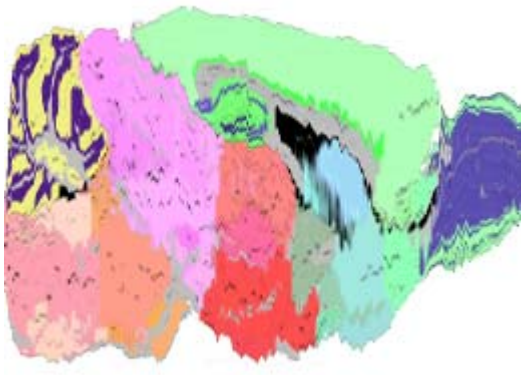

Fig.10 – Sagittal view of 3D model with structure color segmentation.

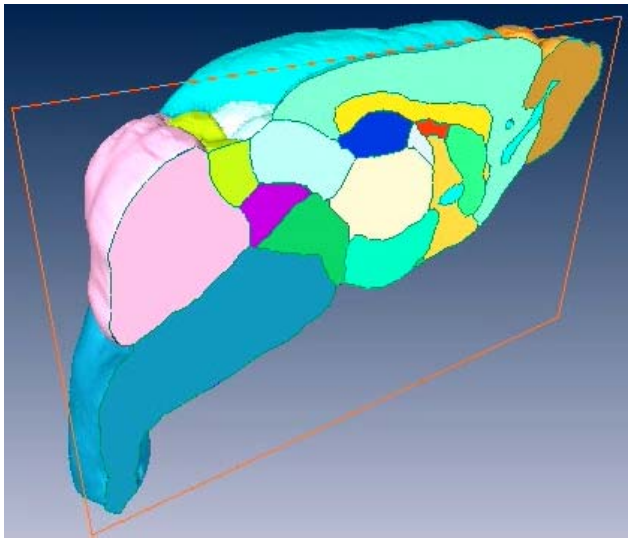

Fig.11 – Sagittal view from another atlas.

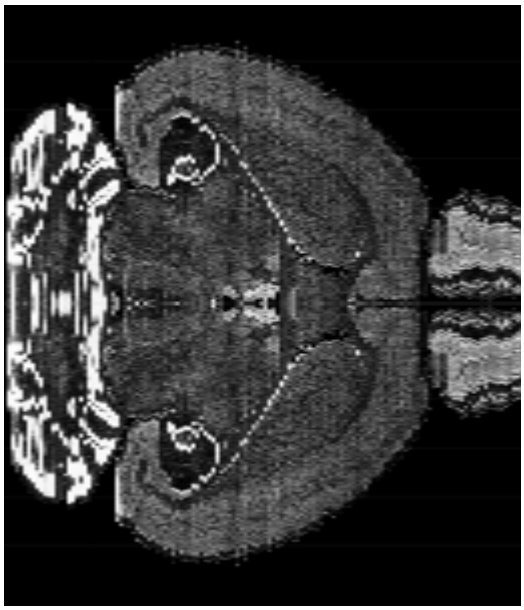

Fig.12 – Axial view of 3D model without illumination correction, alignment and nonlinear deformations

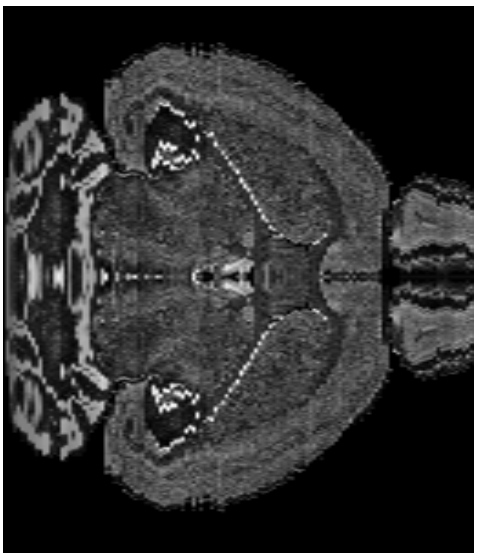

Fig.13 – Axial view of 3D model with illumination correction and alignment.

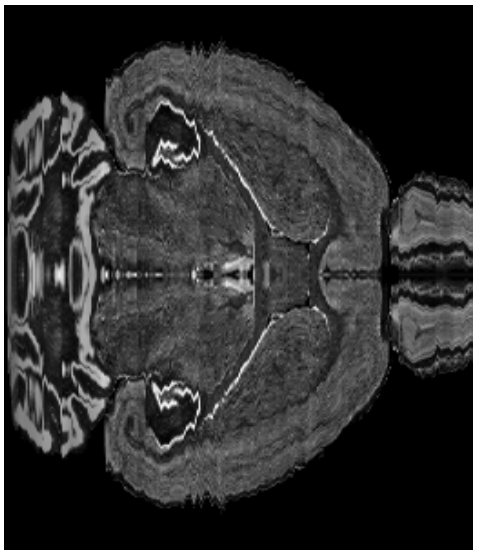

Fig.14 – Axial view of 3D model with illumination correction, alignment and nonlinear deformations.

7. CONCLUSION

We proposed an algorithm that constructs virtual slices of brain w.r.t. arbitrary section-plane. We have shown that this algorithm allows us to get synthetic images of relatively good quality both with histological and anatomical structure. The algorithm opens great perspectives for further brain research as it provides the opportunity of discovering anatomical structures in a single slice of real mouse brain. The procedure of slices' preparation is very time and labor consuming, that is why it is highly desirable to reduce the number of slices obtained from real mouse to minimum (in the limit to one which is of interest for biologists). The slice can be made in non-standard (coronal, sagittal, or axial) section-plane and it should be mapped into 3D-model of atlas brain. Our algorithm allows us to synthesize the image of an atlas brain w.r.t. any section-plane and hence is the key part of future method which will compute the best mapping. When it is computed the anatomical structures in real brain slice can be found easily by projecting anatomical structure of atlas brain onto the virtual slice with further performing inverse mapping to adapt it to real brain slice. The algorithm for automatic histological mapping of arbitrary slice to 3D model of atlas brain is our future work.

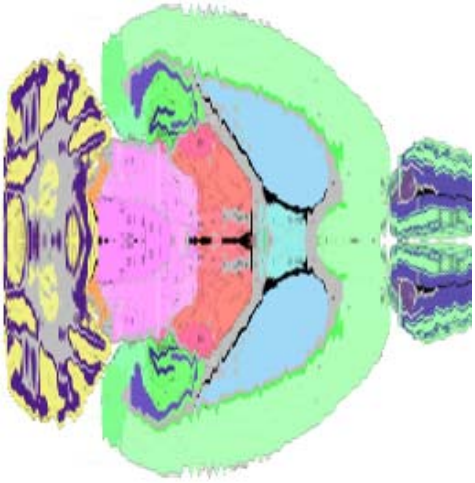

Fig.15 – Axial view of 3D model with structure color segmentation.

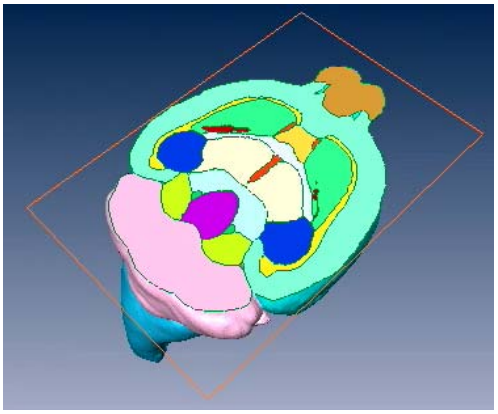

Fig.16 – Axial view from another atlas.

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