Tools for Automatically Finding and Visualizing Interest Areas in MRI Data to Support Decision Making by Medical Researchers

V. P. Fralenko*, M. V. Khachumov**, and M. V. Shustova***

*Ailamazyan Program Systems Institute, Russian Academy of Sciences, Yaroslavl Region, Pereslavl-Zalessky District, Veskovo Village, 152021 Russia
**Institute for Systems Analysis, Computer Science and Control Federal Research Center, Russian Academy of Sciences, Moscow, 119333 Russia
***e-mail: m.v.shustova@gmail.com

Abstract—This article gives a detailed description of the techniques developed by the authors for primary and deep processing of magnetic-resonance imaging that are aimed at detecting areas of ischemic lesion in the rat brain. The tools include the techniques for bringing MRI images of different samples to the normalized form (size, shape, and brightness). Another set of tools is associated with the detection of anomalies based on T2 and MDC images using artificial neural networks and specific metrics. It is assumed that the created algorithms and programs will be part of the developed research software system that is oriented to support decision making by medical researchers.

Keywords: magnetic resonance tomography, brain, ischemic lesion, image recognition, visualization, metric, convolutional neural network

INTRODUCTION

This paper develops tools for the automated processing of MRI data. It is assumed that these methods and algorithms, as well as the available software, will be used in complex to support decision making by medical researchers that are engaged in the lifelong observation of the brain of animals (rats). The developed algorithms and programs provide calculations that are related to unifying the representation of the brain for various individuals to subsequently evaluate damaged areas; deep processing and cognitive visualization that is associated with scientific highlighting of the areas that are of interest for a researcher.

The need to automate the processing of MRI images occurs due to a number of reasons: an intensive flow of incoming data (each MRI scan of the brain of an individual rat yields dozens of images that require further processing); the limited number of experts; and the lack of software and necessary high-quality devices for scientific visualization of information. Automation involves two aspects of research: preliminary and deep processing of data flows. The obtained MRI images are characterized by unstable brightness and contrast indices, which requires their normalization. The segmentation of interest areas is associated with significant difficulties, which are due to the heterogeneity of information on MRI sections and the presence of only one characteristic feature: the signal level. This requires the artificial expansion of the feature space and the introduction of powerful tools for segmenting interest areas from other areas of the brain (segmentation). The currently known means of automatic brain segmentation almost do not provide the quality required by experts [1–3]. In this connection, the present work is devoted to the elimination of existing gaps on the basis of artificial intelligence tools: artificial neural networks, methods for distinguishing informative textural features, special metrics, and thematic visualization.

The experimental part of the work was performed based on the data of layered MRI studies of rat brain. A ClinScan (Bruker BioSpin) high-field tomograph for small animals with 7T magnetic field induction under inhalation anesthesia was used. To search for ischemic lesion zones, T2-weighted images were used at the late stages, and diffusion-weighted images were used at the acute phase of ischemia.

1. TOOLS FOR PRETREATMENT OF MRI DATA

1.1. Image Brightness Leveling Using the Method of Blending with a Gradient

An important place in brain research is taken by the pre-processing tools that improve the quality of data
and images as a whole or their individual fragments. They include the algorithms for controlling brightness, image sharpness and contrast, enhancing borders, etc. The ClinScan tomograph has some design features due to which images are obtained with uneven illumination, which leads to a deterioration in the quality of post-processing. Hence, there is a need for normalization of the brightness gradient. This problem is solved by the authors using the pixel-by-pixel overlay of a gray–white gradient image (Fig. 1a) on the original image (Fig. 1b). The overlap is performed using the following formula:

$$\begin{align*}
    f(a, b) &= \begin{cases} 
        \frac{a b}{127.5}, & \text{if } a < 127.5 \\
        2a + 2b - \frac{a b}{127.5} - 255, & \text{otherwise}
    \end{cases}
\end{align*}$$

where $a$ is the brightness value of the pixel of the original image and $b$ is the brightness value of the corresponding pixel of the gradient image; the brightness values of the pixels of both images change from 0 (black) to 255 (white).

The gradient image is chosen empirically based on the available images that are typical for the tomograph. The result of brightness leveling is shown in Fig. 1c.

The method was applied for the subsequent study of T2-images and improved the segmentation quality.

1.2. Bringing the MRI Image of the Rat Brain to the Reference

When processing MRI images of the brains of various rats that have individual structural features, the problem arises of comparing (recording) target images with a certain standard. The urgency of this problem for segmenting the brain into anatomical areas was emphasized in [4, 5]. The method developed within the framework of this study is focused on preliminarily prepared images, where the animal’s brain is separated from the background. For this purpose, ready-made software exists [1–3]. Figure 2 shows an example of a reference image; the test sample should be brought to its form.

Let us consider the algorithm. Let $C = c_1, c_2, \ldots, c_n$ and $Q = q_1, q_2, \ldots, q_q$ be the contour of the reference and processed images, respectively, where $c_i, q_i$ are the contour points and $n$ is the number of points. We will transform the processed image so that its contour with the reference shape of the brain will coincide with the new contour of the processed image.

At the first stage, the rigid affine transformation of the input image takes place; the main steps are shown in Fig. 3. The contour of the processed image is shown in gray and the contour of the reference object is black.
The algorithm of rigid affine transformation is as follows:

— the points of the contour of the displayed image are re-indexed so that \( \sum_{i=1}^{N} d(c_i, q_i) \rightarrow \min \), where \( d(c_i, q_i) \) is the Euclidean distance between \( c_i \) and \( q_i \);

— let \( \bar{c} = \frac{1}{N} \sum_{i=1}^{N} c_i \), \( \bar{q} = \frac{1}{N} \sum_{i=1}^{N} q_i \) be the centers of the contours; the processed image is shifted in such a way that the centers of the contours coincide (Fig. 3b);

— the rotation angle \( \alpha = \frac{1}{N} \sum_{i=1}^{N} \alpha_i \) is calculated, where \( \alpha_i \) is the angle between the corresponding points \( c_i \) and \( q_i \) relative to the center; in order to accelerate the operation, the integral rotation of the reference image by the angle \( \alpha \) is performed (Fig. 3c) [6]. The new coordinates \( (X', Y') \) of the point \( (X, Y) \) are determined as follows: \( X' = (M/L)X + (N/L)Y \), \( Y' = -(N/L)X + (M/L)Y \). During the rotation, the angle is in the general case given as a triplet \( (M, N, L) \) of integers, and \( L^2 = M^2 + N^2 \), \( M/L = \cos(\alpha) \), \( N/L = \sin(\alpha) \). The table of sines and cosines in the form of integer ratios is computed in advance and stored in the memory of the rotation control system.

At the next stage, the input image is deformed so that the contours of the brain will coincide. The deformation algorithm is as follows:

— the points of the contour of the displayed image are re-indexed so that \( \sum_{i=1}^{N} d(c_i, q_i) \rightarrow \min \), where \( d(c_i, q_i) \) is the Euclidean distance between \( c_i \) and \( q_i \);

— let \( \bar{c} = \frac{1}{N} \sum_{i=1}^{N} c_i \), \( \bar{q} = \frac{1}{N} \sum_{i=1}^{N} q_i \) be the centers of the contours; the processed image is shifted in such a way that the centers of the contours coincide (Fig. 3b);

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At the next stage, the input image is deformed so that the contours of the brain will coincide. The deformation algorithm is as follows:

— for each ray, the coefficient of extension (compression) \( k_i \) is determined, where \( i \) is the ray number; let \( c_i \) and \( q_i \) be the points of the contours that belong to the same ray, then \( k_i = d(q_i, \bar{q})/d(c_i, \bar{c}) \), and \( \bar{q} = \bar{c} \);

— for each ray, the extension (compression) of the points of the reference image that belong to this ray is performed using the coefficient \( k_i \); it is known that a point with integer coordinates \( (X, Y) \) belongs to the straight line that goes from the origin or coordinates with a slope coefficient \( k = (\Delta Y/\Delta X) \), if the following condition is satisfied: \( |Y - (\Delta Y/\Delta X \cdot X)| \leq \varepsilon \), where \( \varepsilon \leq 0.5 \) [7].

The result of the deformation of the reference contour is shown in Fig. 4b; the resulting image is shown in Fig. 4c. As an example, let us consider the problem of reducing the image making allowance for a simplified rat brain atlas with segmentation into three interest areas. Figure 5 shows the original image and the result of the desired transformation.

After the contours coincide, it is possible to segment the target image for a possible prospective solution of the problem of training the classifier while taking the atlas into account. Here, we give an example of the segmentation of a brain with an ischemic lesion: Fig. 6a shows the original image and Figs. 6b–6d show its segmentation into interest areas.
The developed segmentation algorithm as a tool for preliminary processing enables a more qualitative recognition of ischemic lesions that are characteristic for individual anatomical areas, which is confirmed by the preliminary studies performed up to the present moment.

2. TOOLS FOR SEGMENTATION OF ISCHEMIC LESION AREAS

The central part of the developed tools is made up by algorithms for identifying characteristic features and segmentation methods. The most important part of the system for classification and scientific visualization is the spectrographic analysis of medical images, which allows the segmentation of special areas.

2.1. The Method for Segmenting Ischemic Lesion Areas in T2-Images

The points of the resulting image are shown in some color, depending on the degree of proximity to the interest area. A set of interest areas is set by the expert doctor as a training sample. The size of the scanning window (width and height) is set to process data from the tomograph. Instead of the brightness values in the area under the scanning window, this study used the features that were proposed in [8], including Haralick’s textural features [9]. In total, there are seven features: three general-purpose features and four basic ones.

The general-purpose features are as follows [8]:

—expected value \( \mu \)

\[
\frac{1}{MN} \sum_{i=1}^{M} \sum_{j=1}^{N} p_{ij},
\]

—standard deviation

\[
\left[ \frac{1}{MN} \sum_{i=1}^{M} \sum_{j=1}^{N} (p_{ij} - \mu)^2 \right]^{\frac{1}{2}},
\]

—asymmetry of the gray level

\[
\left[ \frac{1}{MN} \sum_{i=1}^{M} \sum_{j=1}^{N} (p_{ij} - \mu)^3 \right]^{\frac{1}{3}},
\]

where \( M \) and \( N \) are the linear dimensions of the scanning window, \( p_{ij} \) is the brightness value of the pixel in the \( i \)th row and \( j \)th column of the scanning window.

The main Haralick textural features are as follows [9]:

—entropy \( \sum_{i} \sum_{j} \frac{c_{i}(i, j) \log (c_{i}(i, j))}{\sum_{i} \sum_{j} c_{i}(i, j)} \)

—energy \( \sum_{i} \sum_{j} c_{i}^{2}(i, j) \)

—contrast \( \sum_{i} \sum_{j} (i - j)^2 c_{i}(i, j) \)
Table 1. The results of processing tomographic MDC images using the CNN

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<thead>
<tr>
<th>Initial image with a supposition in the ischemic lesion area</th>
<th>The result of processing the original image</th>
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To work with the listed features, a classifier is applied that uses the Euclid-Mahalanobis distance [10]. The distance between the class $Y$ (for example, the “ischemic lesion” class) and the point $p$ (the point is the vector of features that were extracted from some position of the scanning window) is calculated by the formula:

$$R_G(p, Y) = \sqrt{(p - \overline{y})^T A^{-1} (p - \overline{y})},$$

where the matrix is $A = C_Y + E$.

The covariance matrix $C_Y$ for the class $Y$ is calculated by the formula:

$$C_Y(i, j) = \frac{1}{|Y| - 1} \sum_{k=1}^{|Y|} (s_i^k - \overline{y_i})(s_j^k - \overline{y_j}),$$

where $s_i^k$ is the $i$th component of the $k$th point in class $Y$.

—homogeneity $\sum_i \sum_j \frac{Co(i, j)}{1 + |i - j|}$, where $Co(i, j)$ is the element of the Gray-Level Co-occurrence Matrix in the $i$th row of the $j$th column.
where $s_i^k$ is the $i$th feature of the $k$th point from the class $Y$ and $\overline{y}_i$ is the mathematical expectation of the value of this feature in the class $Y$.

To perform image processing, it is required to define two classes: in our case, this is the area of the healthy brain ("norm," class $Y_1$) and the area of ischemic lesion ("lesion," class $Y_2$). Each area is represented by a set of small reference images of one of the brain sections (the basic section). The features that are necessary to adjust the classifier are taken out from these images. Image processing is performed as follows:

— the scanning window moves over the image with a step of one pixel;
— the brightness of the pixels that got into the scanning window is used to calculate all the features;
— the Euclid-Mahalanobis distance from the window to both classes is calculated and the class with the minimum distance wins;
— only the fragments that were assigned to the "lesion" class are fixed on the resulting image.

As an example, Fig. 7a shows the image that is used simultaneously as a basic section and as a processed image and Fig. 7b shows the result of the processing. The image in Fig. 7c is used as a processed one (not previously considered by the classifier), while the image in Fig. 7a remains the basic section. False responses of the classifier are possible, as shown in Fig. 7d.

Additional post-processing by filtering small areas makes it possible to avoid such artifacts. The experimentally selected size of the scanning window that suits the data received from this tomograph best is $49 \times 49$ pixels. Ten non-intersecting reference windows were selected at the basic section in the conducted experiments for each of the classes. The total time of classifier training is less than one millisecond. Each brain section, with a size of $870 \times 610$ pixels, is processed for approximately $95$ s. The current implementation is carried out using general-purpose processors (in particular, the experiment was carried out on a dual-core Intel Core 2 Duo E6750 @ 2.66 GHz processor); it is planned to adapt the implementation for the work with Nvidia graphic accelerators, which will significantly reduce the processing time.

2.2. The Method for Segmenting the Ischemic Lesion Area in MDC images

Diffusion-weighted magnetic resonance imaging [11] reflects the diffusion capacity of the molecules of the object under study. In the presence of pathological processes in the brain of an examined animal, the degree of permeability of cell membranes changes, which directly affects the overall diffusion of water molecules. MRI makes it possible to calculate the corresponding measured diffusion coefficient (MDC) that characterizes the mean square of the distance that molecules pass per unit of time. The size of a rat-brain section is within the image range of $40 \times 30$ pixels,
which covers approximately 1200 points, each of
which is characterized by only one number: the inten-
sity of the signal (or brightness of the image). An isch-
emic brain lesion is characterized by the presence of
darkened areas in MDC maps. Figure 8 shows the
examples of MDC maps for animals with an ischemic
lesion of the brain, where an expert marked the con-
tour of the damaged area on the right. An expert is able
to confidently find areas with abnormal tissues.
However, our task is to fully automate this process.
An artificial neural network device is used as the
instrument for processing MDC images. This device
has been effectively used by the authors in various
medical studies [12–14]. In this article, a convolu-
tional neural network (CNN) is used as a classifier
[15]. It is believed that its architecture contains the
most effective methods for generalizing and classifying
information. Let us provide some explanation. For the
tasks of segmenting areas by the method of thematic
filling, the size of an input CNN window is equal to
the number of pixels in the mask that moves over the
original image, the optimal size of which is selected
based on a specific task and initial data. The CNN
consists of alternating layers of convolution and subsa-
mpling, which are supplemented with specialized lay-
ers, for example, [16, 17]. At the output, the CNN can
contain one or more fully connected layers. The last
layer of the neural network contains the number of
neurons that corresponds to the number of classes in
the problem.
A neural network based on the nnForge library
[18], which previously successfully proved itself in var-
ious applied problems, was used as a prototype in the
experiments [19–21]. As a result, the following neural
network configuration was obtained (Fig. 9):
— an entrance window of $4 \times 4$ elements (in total,
16 intensity coefficients);
— a convolution layer with $3 \times 3$ feature maps;
— a maxout-layer with neurons with a learning
activation function;
— a subsampling layer that selects a maximum
(max-pooling) [22];
— a dropout-layer with adjustable probability $p$ of
disconnection between neurons (it was experimentally
established that $p = 0.05$);
— a convolution layer with $1 \times 1$ feature maps;
— a layer of neurons with the activation function of
the hyperbolic tangent type.
Different feature maps serve to highlight various
peculiarities in the images of the training sample. In
order for the neural network to remember several mil-
lion different input windows, it was necessary to sig-
ificantly increase the number of the feature maps. In
particular, the first convolution layer contains 2000
such maps, and the second one contains 1000 maps.
The total training time using a Nvidia GeForce GTX
980 video display card is no more than 1 h.
Table 1 shows the results of processing tomo-
graphic MDC images using the CNN. In a series of
images, the original image with a lesion area outlined
by an expert and the result of processing by the neural
network are shown in pairs.
These studies showed that the CNN of the chosen
configuration is fairly successfully trained based on
reference images, but works with a certain error when
analyzing unknown samples. The authors intend to
eliminate this shortcoming in their future research.
The trained neural network is capable of processing
tens of thousands of images per second, which pro-
gresses good support for a medical researcher.
3. THE INTEGRATED HARDWARE AND SOFTWARE COMPLEX

The general scheme of the developed integrated software and hardware complex is presented in Fig. 10.

The client part includes a graphical user interface that provides the formation of schemes for solving application problems in the paradigm of visual-block programming and display of the results from processing biomedical data, which were obtained using research equipment. The server part of the software and hardware complex provides the storage and multi-user access of the data of the conducted research and possibility of their highly effective pipeline-parallel processing in accordance with user-generated tasks using the core of the software system that provides the computing environment and processing modules that perform the required algorithms.

CONCLUSIONS

A complex of studies was conducted, in which various instruments for processing MRI data were tested. As a result of the experiments, the following points were established:

— the results on brightness equalization and reduction of some images to others allow the correct comparison of MRI images of different samples;

— the best results on the segmentation of ischemic lesion areas in T2-images are achieved using a method based on analyzing Haralick’s textural characteristics with the use of the classifier based on the Euclid-Mahalanobis distance;

— the best results on the segmentation of ischemic lesion areas in the MDC images are achieved using the convolutional neural network.

Currently, studies are continuing to search for effective tools for analyzing MRI data that minimize possible errors in the segmentation of affected areas.

As an improvement, it is proposed to make allowance for the rat-brain atlas with the segmentation of main segments. It is assumed that this approach will allow a more accurate adjustment of the classifier to an ischemic lesion. It is also necessary to make allowance for the characteristics of individual sections of the animal brain. The wide use of graphic and other accelerators is proposed to achieve the real-time processing mode. It is expected that the development of models, methods, and algorithms aimed at supporting the scientific research on ischemic lesion of the brain tissue will be a common scientific result.

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