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Research Article

Application of Artificial Immune System Approach in MRI Classification

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Numerous scholars have submitted the theory and research of artificial immune systems (AISs) in recent years. Although AIS has been used in various fields, applying the AIS to medical images is very rare. The purpose of this study is using the clonal selection algorithm (CSA) of artificial immune systems for classifying the brain MRI, and displaying a single organism image which can finally offer faster organism reference information to a doctor; hence reducing the time to ascertain large number of images, so that the doctor can diagnose the nidus more efficiently and accurately. In order to verify the feasibility and efficiency of this method, we adopt statistical theory for manifold assessment and compare with the perceptron network of double layers, FCM method. The result proves that the method of this study is both feasible and useful.

1. INTRODUCTION

The treatment of diseases is on the basis of diagnosis. Only according to a lot of pathologies and the doctor's erudition which accumulated over a long time to determine the focus could diseases be treated. But many pathological changes are unobservable by the human eye. X-ray is a very important noninvasive medical instrument for diagnosis. From X-rays, the doctor can learn the status of internal organs without operating. But X-rays carry the dangers of radiation, so it is unsuitable to be used in observing patients for extended periods. Magnetic resonance imaging (MRI) was later developed and has made great progress in medical imaging. Given its high resolution, noninvasive nature, and having no need to use the developer under the normal situation, MRI has become the new favorite of the modern image modality. With better and better MRI instrument technology, it is becoming more and more popular in the medical field. From the detection of cardiovascular disease to tumors, MRI is being implemented. The medical circle even thinks MRI has the potential to gradually replace the present invasive examination method.

MRI has the characteristic of a great amount of image information and high sensitivity which may cause noise and artifacts. Therefore, at present, the most common way of tissue classifying is transferring it to professional medical personnel to judge, or judge by algorithm, such as artificial neural *networks* [1–3], Fuzzy C-Means, K-Means [4–6]. Many relevant methods have been proposed in recent years. Artificial immune systems (AISs) [7] have been researched and discussed by many scholars in recent years. We can see AIS applied in different fields, for instance: data analysis [8], and TSP problems [9]. Because AIS has these characteristics: uniqueness, self/nonself discrimination, learning, and memory, it is very appropriate for the pattern recognition field. In this paper, we propose a suitable method of MRI brain image classification and use statistical theory to assess its accuracy of classification.

The following article is divided into six sections: Section 2 will introduce the concept of the natural immune system and related terms. Section 3 is the present research situation of artificial immune systems and the clonal selection algorithm (CSA). Section 4 illustrates our experiment of

using CSA to classify the brain MRI tissue. Section 5 shows experimental results. The final section is the conclusion.

2. THE NATURAL IMMUNE SYSTEM

The immune system has guaranteed the health of the human body. Through identifying self and nonself mechanisms, the immune system can get rid of foreign matter (antigens) to perform this basic defense.

Generally speaking, the immune system can be divided into the adaptive immune system and innate immune system, the greatest difference being the adaptive immune system has a function of memory, whereas the innate immune system does not. The memory function of the adaptive immune system is identifying specific invaders. If the system cannot find the pathogen immediately or take precautions, the pathogen may propagate and result in the host's death.

The immune system has two main functions: (a) identifying invaders and (b) effectively dispelling outside pathogens or materials harmful to the host organism or cell. The structure and function of the immune system are very complicated, with many phenomena still left unexplained explicitly. So we will make some simple exposition about the terminology and concepts that are often involved in immunology in the following few paragraphs.

2.1. The concepts of the immune system

2.1.1. Antigens (Ag)

In the immune system, all foreign bodies are called antigens—molecules which will cause an immune response. When the antigen is found, antibodies will be produced by the immune system, and cell proliferation causes the immune response to resist the invaders. In organ transplants or blood transfusions, repulsion is a frequent problem because also human's cell membrane contains the antigen molecule. Because people's antigen molecules differ, when another person's organs or blood are transplanted to another human body, it often causes an immune response.

2.1.2. Immune responses

Generally, the immune response can be divided into primary and secondary immune responses. The first immune response means the immune system first finds the antigen. The second immune response means the immune system acts against the antigen that has already been identified (see Figure 1).

When the unknown antigen invades the body and is perceived by the immune system, through a series of mutation and clone selection, it will produce an antibody that has a close affinity to the antigen, so that it can eliminate the antigen rapidly. In other words, the immune systems can "remember" every kind of pathogen and if the same infection takes place again, the immune system will be able to deal with and react to it more efficiently.

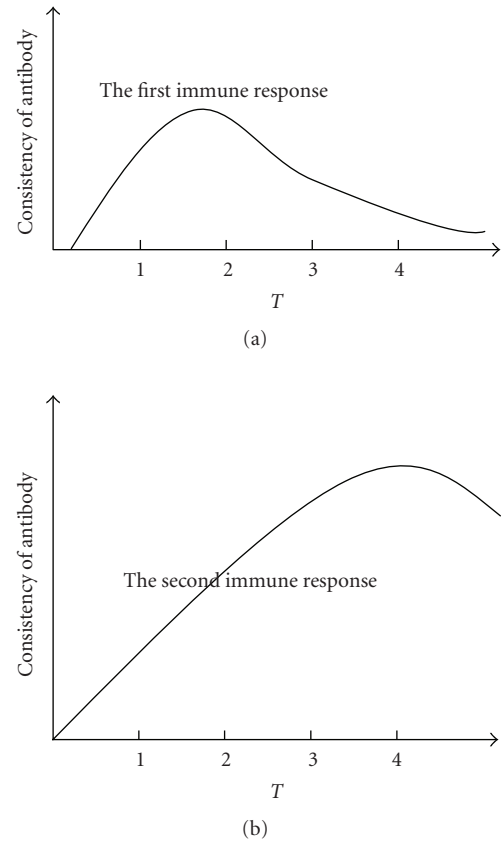


Figure 1: Immune response curve.

2.1.3. Antibodies (Ab)

The antibody is a kind of protein complex produced from plasma cells when the immune system is under the stimulus of the antigen material. The antibody is made up of four polypeptides. It contains two *light* chains and two *heavy* chains. This protein complex has the characteristics of identifying and restraining the invading substance. The immune system can create special antibodies matched to specific antigens. The binding site of the antibody and antigen is the notch between the *light* chain and the *heavy* chain, called the *antigenic* determinate.

2.1.4. Affinity

Through the combination of the immune cell and antibody, it can make the lymphocyte recognize the antigen. The coordination of the immune cell's receptor and antigen is the way to defend against the antigen. The intensity of this combination is called *affinity*.

2.1.5. B Cells

The B cell is the essence of the immune system. They usually mature in the bone marrow. The function of B cells is producing antibodies. Stimulation by T cells is one condition for producing antibodies. When it exceeds certain quantity, the B cells will begin to proliferate. If stimulation by T cells

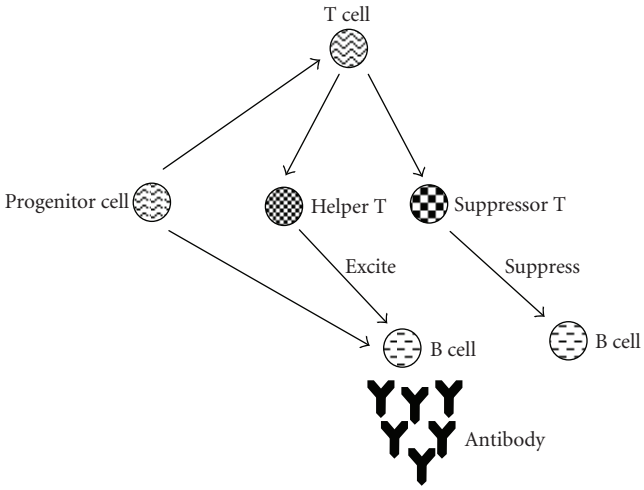


Figure 2: Relation of immune cell.

were less than a certain level, the B cells will no longer proliferate or differentiate.

2.1.6. T Cells

The T cell plays an important role in the immune response. It is differentiated in the thymus. The major function is ensuring that other cells operate normally and attack the pathogen directly. After a T cell is ripe, it will move to the lymphoid tissue. As regards to the regulating function, T cells can be divided into a Helper T cells and suppressor T cells. The function of the former is to excite B cells, achieving the purpose of a warning transmission. The latter is used to suppress B cells from proliferating because an over-abundance of B-cell duplication may cause overimmunity. Figure 2 illustrates the relationships between the cells and the behavior of how they help and suppress the activation of B cells.

3. ARTIFICIAL IMMUNE SYSTEM

Originally, the Immune network theory was developed by Jerne in 1973. In 1986, Farmer brought up the artificial immune system model [10] that sparked a lot of theoretical research about the artificial immune network system and its relevant applications. In the theoretical research, most emphasis is put on the immunity algorithms, network model, and so forth. The applications are wide enough to involve data mining, trouble diagnostics, network security, pattern recognition, and adaptive control. A lot of papers about its application had been issued at the beginning of 1990. This study focuses on the use of the CSA of the immune system in MRI Classification.

Clonal selection algorithm (CSA)

De Castro and Von zuben developed the clonal selection algorithm [11] on the basis of the clonal selection theory.

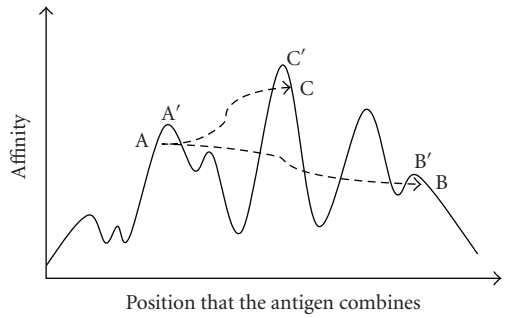


Figure 3: Schematic representation of receptor editing.

The basic concept follows biological evolution theory, with "survival of the fittest" as its foundation. The immune system has the phenomenon of evolution. Burnet proposed the clonal selection theory in 1959: as the system is excited by an antigen, it will cause antibodies to increase to certain levels and combine with the antigen. Briefly, after the pathogen has invaded the body, it will start to proliferate, and destroy the internal cells. In order to maintain the balance of physiological function, one of the ways the immune system fights against the pathogen is to proliferate the immune cells, then recognize and eliminate the pathogen.

The diversity of clonal selection algorithm is one of the topics often discussed by researchers. George and Gray et al. presented a clear answer in discussion of 1999, and proposed that CSA has the ability to prevent the local convergent. Figure 3 illustrates this idea by considering all possible antigen-binding sites depicted in the x-axis, with the most similar ones adjacent to each other. The Ag-Ab affinity is shown on the y-axis. In CSA mathematical calculation processes, the antibody (A) is selected during a primary response; the mutations allow the immune system to explore the antibodies with higher affinity in the local areas around the antigen and keep the antibody with higher affinity. This phenomenon may cause local convergence (A′). However the explored antibody was calculated by its affinity and sifted again and again—this will stop it from changing to lower affinity. The result of sifting will only be better and better, and the global optimum solution will finally be found. This famous characteristic is named receptor editing.

The CSA can be described as follows.

(i) Available P repertoire that can be decomposed into several different subsets. Let M represent the set of memory cells and let P_r represent the set of remaining, $P = P_r + \mathrm{M}$.

(ii) According to the affinity, select n of the highest affinity elements P_n.

(iii) Clone the n-selected elements, generating new clone set C and higher antigenic affinity, the higher the number of clones generated for each of the n selected.

(iv) Do hypermutation to C, hypermutation is dependent on the affinity between antibody and antigen. After hypermutation, we got new antibody set (C*).

(v) Select these mutated individuals from new antibody set C^* and add them to the population M. The mutated individuals in set C^* will instead be some individuals in P.

(vi) Use the new antibody to replace the older antibody of D to fit with various. Antibodies with low affinity can easily be replaced.

4. CSA IN CLASSIFICATION OF BRAIN TISSUE

This experiment classifies the background and tissue such as gray matter (GM), white matter (WM), and cerebral spinal fluid (CSF) in an MRI. This chapter will introduce our CSA experiment procedure and method in MRI. This experiment procedure is shown in Figure 6. The experiment procedure can be described as follows.

4.1. Determine AIS configuration

This experiment is based on described clonal selection algorithm (CSA) to do the MRI classification.

4.2. Determine the initial antibody population

This experiment adopts 9 initial antibody populations—the number of initial antibody population should not be too large or small. If the quantity of antibodies is too small, it will cause the comparative sample to find the optimum solution with greater difficulty.

If the quantity of antibodies is too great, it will consume calculation time. This experiment adopts a method that can get adaptive numbers as Figure 4 shows.

While selecting the antibody, we can expand the two-dimensional tissue in the X and Y directions by two pixel units. This will form a $5*5$ neighborhood data matrix. We can consider this $5*5$ matrix as the source of the 9 antibody population sets.

After all antibodies of the spectrum tissue are selected, it must save the antibodies in a memory buffer for follow-up processing.

4.3. Calculate the initial affinity

The affinity of antibodies and antigens is a calculation of similarity. It can be represented by spatial distance. For the calculation of distance, we adopt the Euclidean distance formula. The affinity of the antibody can be expressed as

$$R = \sum_{p=1}^{z} \min \{D_{1p}, D_{2p}, D_{3p}, \ldots, D_{cp}\}. \quad (1)$$

D is the distances between the antigens (input data) and each population's center (antibody). Using the Euclidean equation to calculate, where Z is the total number of pixels in the image, P is the reading sequence number of the input data (pixel), and C is the quantity of antibodies in the antibody set.

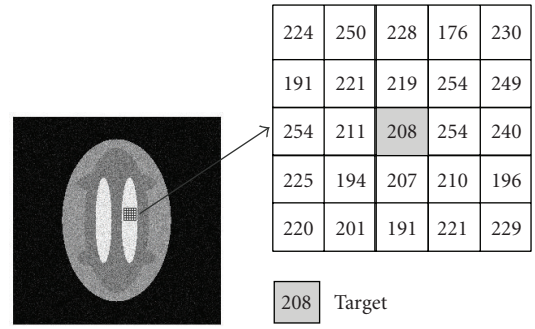


Figure 4: Sketch of antibody population selected.

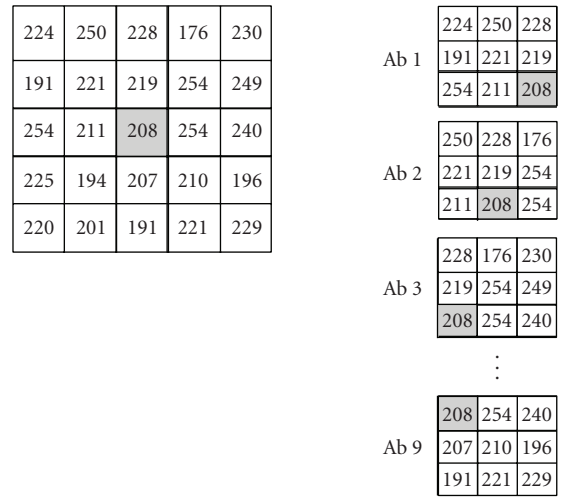


Figure 5: Initializing of the antibody population.

4.4. Selection and differentiation

After initially calculating the affinity, then according to the affinity to screen. The screening samples of this experiment are 5, meaning that only the highest five antibody sets will be kept. The other 4 sets of antibodies will be knocked out and wait for the next selection and screening. After the screening is finished. It will assign the clone's number according to the affinity as shown in

$$N_c = \sum_{k=1}^{n} \text{round}\left\{\frac{\beta \bullet N}{k}\right\}. \quad (2)$$

where N_c is the total amount of clones generated for each of the antigens, β is a multiplying factor, N is the total number of antibodies, and k is the sequence number (rank) of n highest affinity antibody. *Suppose* $N = 9$ and $\beta = 1$, the highest affinity antibody ($i = 1$) will produce 9 clones, while the secondhighest affinity antibody produces 5 clones, the thirdhighest affinity antibody produces 3 clones, and so on.The meaning of this operation is as follows: when an antibody with higher affinity is congenital, it has relatively higher probability to keep its gene; if that with lower affinity

is congenital, it is relatively easy to be eliminated or hard to survive.

4.5. Muturate

Muturate is equivalent to the mutation in genetic algorithms. It is a very important step in the artificial immune system. This step will promote some individuals' affinity. It is an important procedure in solving for the local optimum solution. The principle of muturate is: the higher affinity, the lower muturate rate. The muturate method of this experiment is using randomize normal distribution for maturation. The principle of randomized normal distribution is as follows.

In order to present normal distribution, two parameters must be obeyed. These two parameters determine the range and position of distribution: expected value μ and standard deviation σ^2. Expected value μ determines the center position of distribution, and standard deviation σ^2 determines the range of distribution. Generally, it is presented in the shape of a bell, so we often call this figure the bell curve. The expected value μ of the normal distribution is always 0, and the standard deviation σ^2 is always 1. The distribution can be written as (3). The probability density function (PDF) can be written as (4).

$$X \sim N(\mu, \sigma^2), \tag{3}$$

$$f(X) = \frac{1}{\sigma\sqrt{2\pi}} e^{-(X-\mu)^2/2\sigma^2}. \tag{4}$$

The reason we consider using randomized normal distribution is because the distribution of images' gray level intensity is continuous. If using general random, it is unable to find the optimum solution that correlates with images' characteristics. If we add a set of randomized normal distribution in individual muturate, it can gradually get rid of the optimum situation.

4.6. Calculate affinity again

After the muturate is finished, we should calculate affinity again immediately. Observing each group for any individual's affinity being superior to the best individual in the previous generation, if the affinity is superior to the previous generation's, sift this individual and place it in the memory cell zone. If this group has not produced a better individual, it means that during the muturate there is no better distribution location in the individual, no action to do.

4.7. Keep diversity

During recalculation of affinity, we can find the superior individual. We just need to replace the original individual with the new one that can achieve the goal of keeping the better individual. The individual with lower affinity during initial affinity calculation is not knocked out forever, but some mechanisms are used to investigate individuals again, such as produce at random, until the second time calculation of affinity. If up to high-standard affinity, it has an opportunity to participate in the competition which guarantees the diversity of the antibodies.

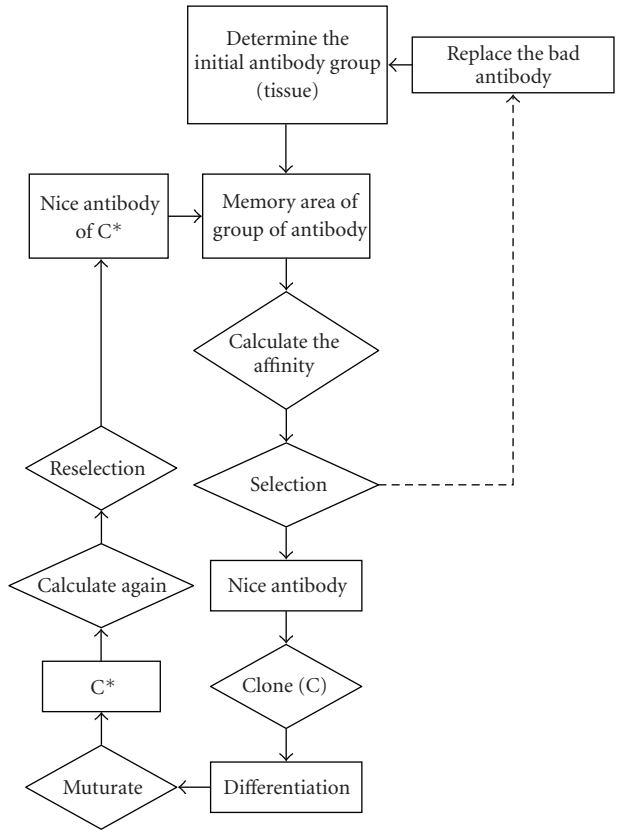


Figure 6: Experiment flow chart.

5. EXPERIM ENTAL RESULTS

5.1. Brain simulation images

In order to understand the efficiency of classification before the experiment assessment and dealing with the real brain MRIs, we use the simulated brain MRIs for the preliminary experiment. The computer-generated phantom images shown in Figure 7 have five bands, each of which have the same size of and were made up of six overlapped ellipses. The total number of image pixels is 65536. These ellipses represent structure areas of three interesting cerebral tissues corresponding to gray matter (GM), white matter (WM), and cerebral spinal fluid (CSF). From the periphery to the center are background (BKG), GM, WM, and CSF. The gray level values of these areas in each band were simulated in such a fashion that these values reflect the average values of their respective tissues in real MR images shown in Figure 10. In addition, in order to approach the characteristic appearing in brain MRIs, we add Gaussian noise in the simulated brain MRIs and the gray level of each tissue is unique without added noise. The purpose of adding various levels of noise is to assess the noise resistance of the algorithm. So, it is

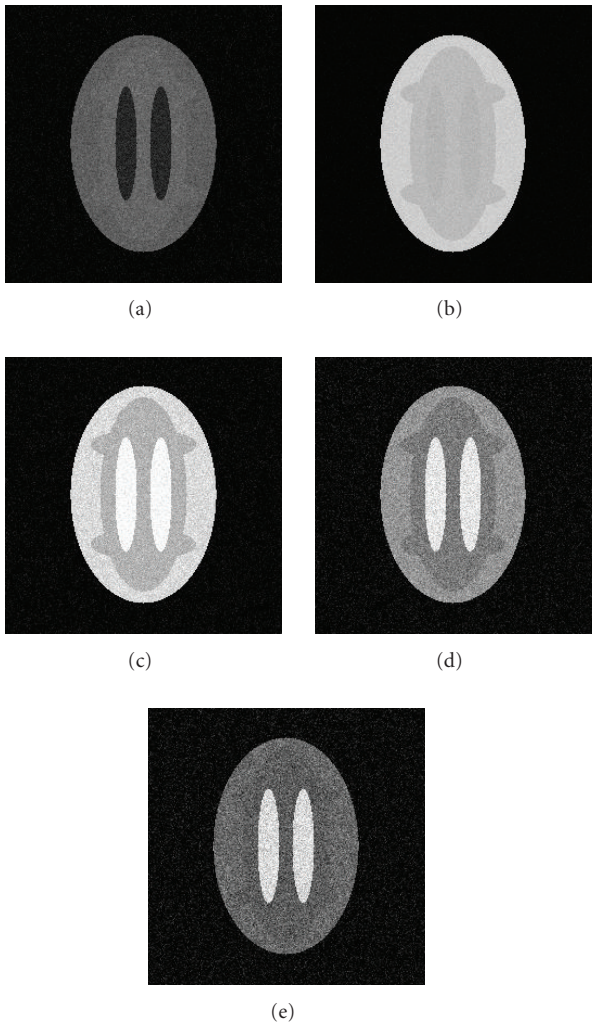


Figure 7: Simulated brain MRIs with 5 dB noise: (a) Sequence 1; (b) Sequence 2; (c) Sequence 3; (d) Sequence 4; and (e) Sequence 5.

necessary to add Gaussian noise in the simulated brain MRIs. Simulated brain MRIs with 5 dB Gaussian noise are shown in Figure 7.

5.2. Assessment method

This experiment assessment method uses statistical theory analytic to assess the classification results. First of all, we must get the classification result of the brain MRIs, and represent them in two-dimensional data form. Take this experiment for example; the tissue includes the background having four kinds of results (GM, WM, CSF, BKG). Then let $d = 4$. $R_D(d)$ and $R_F(d)$ are the detection rate and false alarm rate of classification, respectively.

Represented as in (5), N is the total number of single image; $N(d)$ is the total number of pixels specified by the object signature; $N_D(d)$ is the total number of pixels that are specified by the object signature and actually detected by the classifier; $N_F(d)$ is the total number of false alarm pixels that are not specified by the object signature:

$$R_D(d) = \frac{N_D(d)}{N(d)},$$
$$R_F(d) = \frac{N_F(d)}{N - N(d)}. \tag{5}$$

In addition, it has to have a set of perfect known results for assessing. This means that the result of the experiment with the condition $R_D(d)$ is 100% and $R_F(d)$ is 0, for the comparison and statistics. Though $R_D(d)$, $R_F(d)$ can already calculate the correct rates and false rates of each tissue, in order to get the total accuracy of algorithms, it must consider the proportion of each tissue in the image, so we can get the total correct rate and total false rate from (6) and (7). Among them, (8) calculates the proportion to all tissues (including background information):

$$R_D = \sum_{d=1}^{p} R_D(d)p(d), \tag{6}$$

$$R_F = \sum_{d=1}^{p} R_F(d)p(d), \tag{7}$$

$$p(d) = \frac{N(d)}{\sum_{d=1}^{p} N(d)}. \tag{8}$$

Table 1: Assessment results of AIS-CSA (10 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	44469	0	1	0	0.99910	0.000139
GM	9040	8988	7	0.99425	0.00012		
WM	8745	8738	52	0.9992	0.00091		
CSF	3282	3282	0	1	0		

5.3. Experimental results

The experimental results are divided into two parts for discussion. First, we examine use of the simulate brain MRIs for classifying statistical theory assessing. Second, we explore use of the real brain MRIs for classifying. Here we use some well-known algorithms for the experiment's purpose of comparison and assessment, such as FCM and perceptron network of double layers. Figure 8 is the classification results under the environment with 10 dB Gaussian noise. Figure 9 is the classification results under the environment with 5 dB Gaussian noise.

From the statistical data above, CSA is superior to two other methods in the classifying efficiency of the simulated brain MRIs. FCM method is relatively worthy of discussion since under the 10 dB noise environment, its nearly 0.04% accuracy is slightly superior to the CSA method. However, the CSA classifying efficiency is superior to FCM under the high-noise environment with 5 dB noise. The following will apply the CSA method to real brain MRIs: Figure 10 is an actual brain MRI. The parameters of this image are

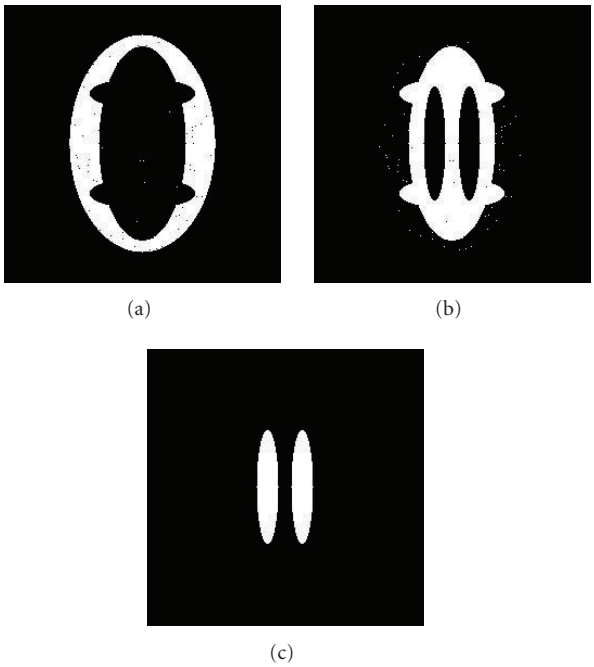


Figure 8: Classification results of AIS-CSA of simulated image with 10 dB noise: (a) GM; (b) WM; and (c) CSF.

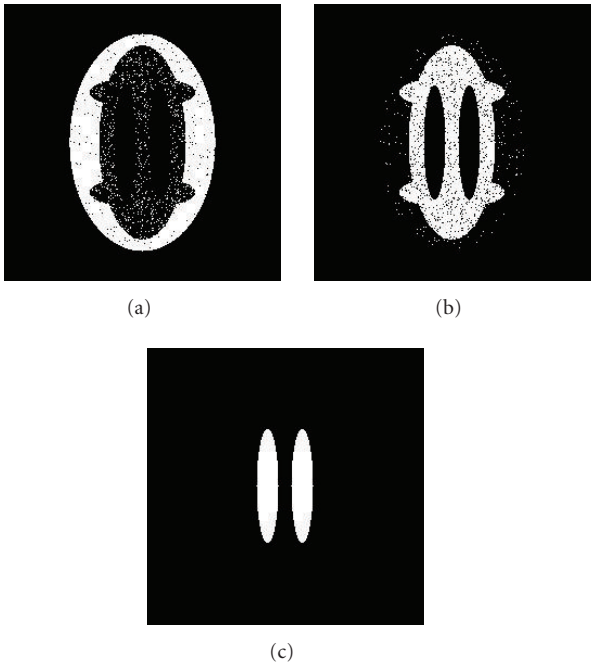


Figure 9: Classification results of AIS-CSA of simulated image with 5 dB noise: (a) GM; (b) WM; and (c) CSF.

R1/TE1 = 2500 milliseconds/20 milliseconds, TR2/TE2 = 1500 milliseconds/55 milliseconds, TR3/TE3 = 2500 milliseconds/75 milliseconds, TR4/TE4 = 2500 milliseconds/100 milliseconds, TR5/TE5 = 500 milliseconds/20 milliseconds. The data classification results by CSA are shown in Figure 11. Whether the classification result is good or not still needs to be judged by professional medical personnel. The following is an actual brain MRI and its classification results.

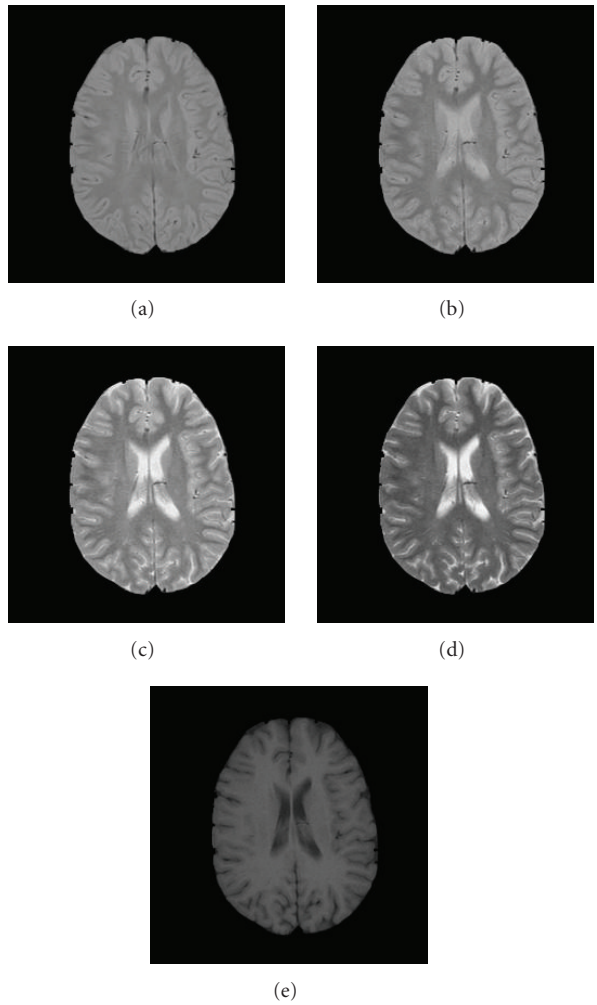


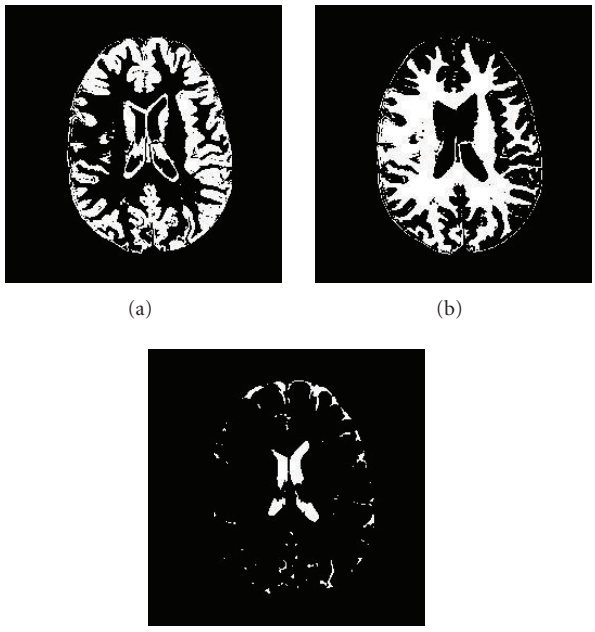
Figure 10: Actual brain MRIs: (a) TR1/TE1 = 2500 ms/20 ms; (b) TR2/TE2 = 1500 ms/55 ms; (c) TR3/TE3 = 2500 ms/75 ms; (d) TR4/TE4 = 2500 ms/100 ms; and (e) TR5/TE5 = 500 ms/20 ms.

Table 2: Assessment results of AIS-CSA (5 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	44469	0	1	0	0.98735	0.00197
GM	9040	8454	243	0.93517	0.0043		
WM	8745	8502	586	0.97221	0.01031		
CSF	3282	3282	0	1	0		

Table 3: Assessment results of perceptron network (10 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	44469	0	1	0	0.99487	0.00081
GM	9040	8950	246	0.99004	0.0043		
WM	8745	8499	90	0.97187	0.0016		
CSF	3282	3282	0	1	0		



(a) (b)

(c)

Figure 11: Classification results of CSA in actual brain MRIs: (a) GM; (b) WM; and (c) CSF.

Table 4: Assessment results of perceptron network (5 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	43088	509	0.96894	0.02416	0.96273	0.02092
GM	9040	8611	130	0.95254	0.0023		
WM	8745	8114	1785	0.92784	0.03143		
CSF	3282	3281	18	0.9997	0.00028		

Table 5: Assessment results of FCM (10 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	44469	0	1	0	0.99949	0.00008
GM	9040	9017	10	0.99746	0.00017		
WM	8745	8735	23	0.99886	0.0004		
CSF	3282	3282	0	1	0		

Table 6: Assessment results of FCM (5 dB)

	N	$N_D(d)$	$N_F(d)$	$R_D(d)$	$R_F(d)$	R_D	R_F
BKG	44469	44469	0	1	0	0.98167	0.00288
GM	9040	8420	581	0.93142	0.01028		
WM	8745	8166	620	0.93379	0.01092		
CSF	3282	3280	0	0.99939	0		

6. CONCLUSION

This study mainly researches the classification of spectral image of the brain with CSA of the artificial immune system. The main purpose is to propose a new method of classification and improve the classifying efficiency of the tradition algorithm at present. According to the experiment's procedures and results of the previous chapters, the conclusions are as shown below.

(i) The CSA of the artificial immune system can be applied to the spectral images of medical science. Even though the artificial immune system is used in various fields, spectral image classification of medical science is really rare. After verification by the experiment of the last chapter, CSA of the artificial immune system can really be applied in the image classifying field.

(ii) According to the experimental data, CSA is superior to clustering algorithms which are compared in this study.

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