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Immune System Inspired Model and its Applications

[1]Hongwei, D., [1]T. Zheng, [1]T. Hiroki and [2]Y. Yu
[1]Faculty of Engineering, Toyama University, Gofuku 3190, Toyama Shi, 930-8555, Japan
[2]Tele Electric Supply Service Co. Ltd. 9-2 Office Park, Takaoka shi,Toyama 939-1119, Japan

Abstract: Immune system is a network of cells, tissues, and organs that work together to defend the body against attacks by foreign invaders. Self/nonself discrimination ability based on the pattern recognition of molecular is a key feature in the defense of the host organism. T and B lymphocytes (we also call them T cells and B cells respectively) are two main types of immune cells which play principal roles in immune response. They express receptors on their surfaces to determine a given antigen. In this paper, we use metaphors extracted from natural immune systems and propose an artificial immune system model by considering both T cells dependent antigen recognition and T cells independent antigen recognition. We illustrate the ability of the proposed model in clustering analog patterns and recognizing noisy binary patterns. Simulation results are presented in support of the model and compared the results with that of other artificial immune models.

Key words: Artificial immune system, immune response, pattern recognition, self/nonself discrimination

INTRODUCTION

Recently, there has been a growing interest in the use of immune metaphors as a source of inspiration for solving computational problems. The immune system is one of the most intricate bodily systems and its complexity is sometimes compared with that of brain. With the advances in the biology and molecular genetics, the comprehension of how the immune system behaves is increasing very rapidly[1]. The immune system contains many useful information-processing abilities, including pattern recognition, learning, memory and inherent distributed parallel processing. For these and other reasons, the immune system has received significant amount of interest to use as a metaphor within computing. This emerging field of research is known as Artificial Immune Systems (AIS)[2]. The applications of artificial immune system are vast, ranging from data analysis to robotic autonomous navigation. In[3-5] the authors proposed different approaches to computer network security. In[6], the authors used a binary Hamming shape-space, to describe each of the reactants and products for spectra recognition in chemical analysis. We can also find other applications of artificial immune system in[7-9].

In our previous works, we also have proposed some immune models based on the biological immune response[10-13]. In this study we propose an artificial immune network model by considering not only the T cells dependent antigen recognition process, but also the activation of T cells independent antigen recognition. That is to say, B cell activation proceeds by different routes, one dependent upon Th cell, the other not[14].

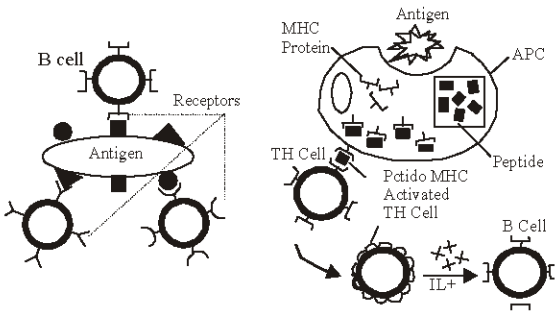
NATURAL IMMUNE SYSTEMS

B cells and T cells: Immune system, consists of a great variety of molecules, cells, and organs, is known to protect living body from attack by foreign invaders (such as viruses and bacteria). The tissue and organs that compose the immune system are distributed throughout the body. They are known as lymphoid organs, once they are related to the production, growing and development of lymphocytes, the leukocytes that compose the main operative part of the immune system. Lymphocytes are small leukocytes that play an important role in the immune system. There are two main types of lymphocytes: B lymphocyte and T lymphocyte, we also call them B cell and T cell respectively. The B and T lymphocytes express, on their surface, receptors highly specific for a given antigenic determinant. These two types cells are rather similar, but differ with relation to how they recognize antigens.

The main functions of B cells include the production and secretion of antibodies (Ab) as a response to exogenous proteins such as bacteria, viruses and tumor cells. Every element which can elicit an immune response is called an antigen (Ag). Each B cell is programmed to produce a specific antibody. The antibody is specific protein that recognize and bind to another particular protein. The production and binding of antibodies is usually a way of signaling other cells to kill, ingest or remove the bound substance.

Helper T cells (Th) and suppressor T cells (Ts) are two main types T lymphocytes. Their functions include the regulation of other cells' actions and directly attack

Corresponding Author: Hiroki, T., Faculty of Engineering, Toyama University, Gofuku 3190, Toyama shi, 930-8555, Japan



(a) (b)

Fig. 1: Immune response to Ag of B cells (a) and Th cells (b)

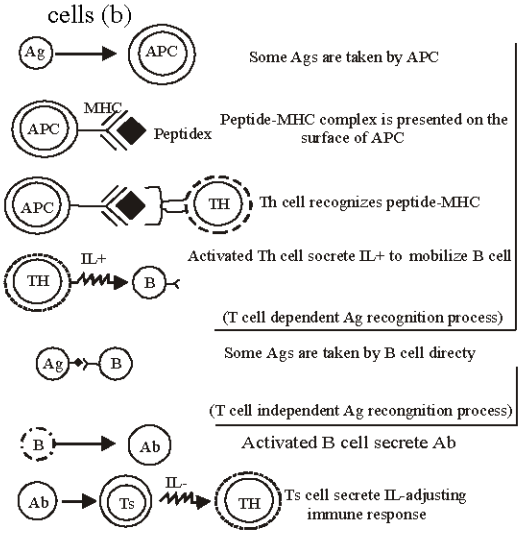


Fig. 2: Immune response process

the host infected cells. The T helper cells, or simply Th cells, are essential to the activation of B cells, other T cells and macrophages. They are also known as CD4 or T4 cells. The suppressor T lymphocytes are vital for the maintenance of the immune response. They are sometimes called CD8 cells and inhibit the action of other immune cells. Without their activity, immunity would certainly loose control resulting in allergic reactions and autoimmune diseases[1,12,15].

Principles of the immune system: Immune system is a complex of cells, molecules and organs with the primary role of limiting damage to the host organism by pathogens. Antigen, which elicits an immune response, is the ultimate target of all immune system. As previously mentioned, B cells and Th cells are rather similar, but differ with relation to how they recognize antigens and by their functional roles.

Figure 1 (a) illustrates antigen is covered with molecules, named epitopes. These allow it be recognized by the receptors on the surface of B cells. Each B cell is genetically programmed to produce a single specific antibody with a particular molecular shape. The specific shape receptors recognize and bind with antigen free in solution through a complementary without T cells. We call this process as T cells independent antigen recognition. Fig. 1 (b) shows how an antigen is recognized by Th cell. The antigen has to be processed by other accessory cells, such as antigen present cell (APC). Activated Th cells secrete IL+ signal and mobilize B cells.

This process is known as T cells dependent antigen recognition[8,14].

Figure 2 illustrates a simple flowchart of the immune response. When an antigen invades the host, specialized antigen present cell, such as macrophages, roam the body, ingesting and digesting the antigens they find and fragmenting them into antigenic peptides. Pieces of these peptides are joined to major histocompatibility complex (MHC) molecules and are displayed on the surface of the cell. Other white blood cells Th cells have receptor molecules that enable each of them to recognize a different peptide-MHC combination. Th cells activated by that recognition divide and secrete interleukin (IL+), or chemical signals, which mobilize other components of the immune system. The B cells, which also have receptor molecules of a single specificity on their surface, respond to those signals. Unlike the receptors of T cells, however, those of B cells can recognize parts of antigens free in solution, without MHC molecules[15]. B cells activation by antigen protein require binding of the antigen to the B cell surface receptors and also require costimulation by T cells and the secretion of cytokines, such as interleukin[17]. Activated B cells divide and differentiate into plasma cells that secrete antibody proteins, which are soluble forms of their receptors. By binding to the antigens they find, antibodies can neutralize them or precipitate their destruction by complement enzymes or by scavenging cells. Once the antigens are destroyed by the antibody, Ts cells are stimulated, the activated Ts cells secrete suppressing signal interleukin (IL-) to Th cells to modulate the immune response.

ARTIFICIAL IMMUNE SYSTEM

Natural system, either an intricate nervous system, or an ant population, has amazing capability to deal with the external stimuli and to maintain the inner satiability.

Similarly to the way the nervous system inspired the development of the notable Artificial Neural Networks (ANNs), Ant Colony Optimization (ACO) algorithm based on the natural ant population has been designed for combinational optimization problems[18].

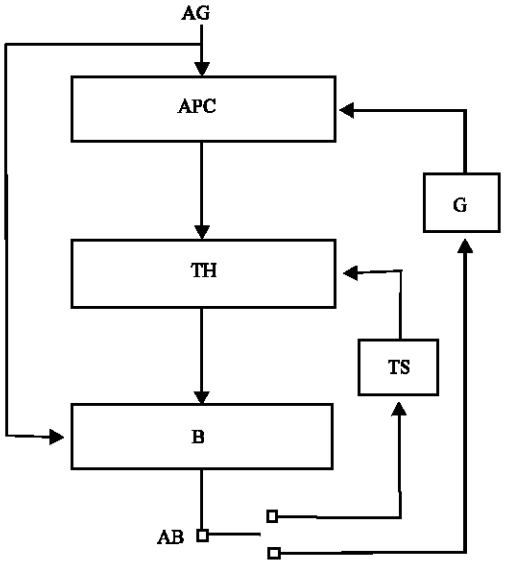


Fig. 3: Artificial immune system model

The immune system, as a complicated and precise system, has received significant amount of interest to use as a metaphor within computing. It can be said that the most appealing aspect of research on immune system is applying artificial immune model to engineering problems.

Artificial immune model: An appropriate artificial model should preciously capture many of the natural system's essential characteristics. At the same time, it should not be too complicated. According to the natural immune system, we proposed an artificial immune system model illustrated in Fig. 3. We will describe the proposed model in the following.

First, we present a general description of this model. We map the immune system as a three layers network. That is, input layer APC layer, hidden layer TH cell layer and output layer B cell layer. Antigen AG is the input of network and antibody AB is the output of the network.

The route AG → APC → TH → B → and AG → B → correspond with T cells dependent antigen recognition and T cells independent antigen recognition respectively. According to the costimulation magnitude of B cell by the antigen-receptor binding and Th cells, the system decides to re-recognize the input antigen or to lunch an immune response under the control of suppressor T cells TS.

Before introducing the operation of the artificial immune system, it is necessary to introduce basic concept of shape-space model. In natural immune system, the interactions between antigen and antibody are measured by regions of complementarity. If the epitopes (antigen) and the paratopes (antibody) shapes are not quite complementary, they may still bind, but with lower

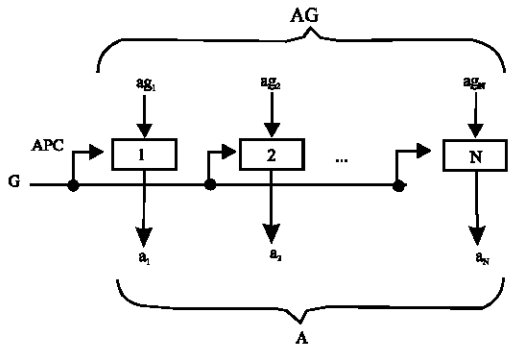


Fig.4: Antigen presentation

affinity. In order to quantitatively describe the interactions between antigen and antibody, the authors in[16] introduced an abstract model based on shape-space. In this model, antigens and antibodies are treated as points in a shape-space. Antibody can recognize all antigens within a certain volume surrounding it. Furthermore, according to the concept of generalized shape, antigen and antibody can be expressed as a set of real valued coordinates $(\alpha_1, \alpha_2, ..., \alpha_N)$ .Thus, we can easily quantify the interactions between antigen and antibody via two points' relationship in an N-dimensional real valued space.

Operation of the artificial immune model: As introduced previously, antigen and antibody can be considered as points in a real valued space. If we assume that antigen and antibody have the same length, we can describe them as AG = $(ag_1, ag_2, ..., ag_N)$ AB = $(ab_1, ab_2, ..., ab_{N0})$, respectively. Interactions among natural immune cells are presented by weights between the different layers.

According to the description in Section 3.1, the operation of this model consists of four phrases: antigen presentation, Th cells activation, B cells activation and immune regulation.

Antigen presentation: In immune system, Antigen Present Cell (APC) has the ability to present antigens to immune cells, such as Th cells. They play an important role in the beginning of the immune response. In artificial model, as shown in Fig. 4, APC layer receives the input information of antigen AG = $(ag_1, ag_2, ..., ag_N)$ and translate them to Th layer. Output of APC is A = $(a_1, a_2, ..., a_N)$.

Each element in APC layer receives two input signal: antigenic information from antigen and control signal from gain G. Initially, because no stimulus is detected by the immune system, no antibody is generated. Gain G is excited and enables the antigen present cells present antigen to Th cells.

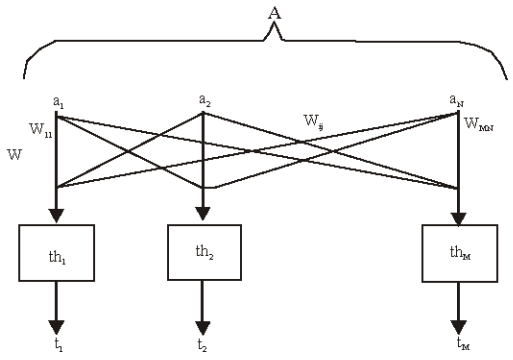


Fig. 5: Th cells response to the presented antigen

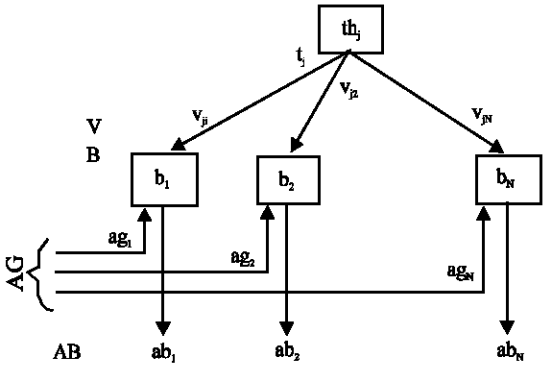


Fig. 6: Activation of B cells

Th cells activation: Th cells recognize antigens by engaging the Th Cell Receptor (TCR) with the complex peptide-MHC displayed on the surface of antigen present cells. Th cells with different TCRs have different response to input antigen.

As illustrated in Fig. 5, pattern A = (a_1, a_2,..., a_N) is translated to each Th cell through different weights 'route' W_j (j = 1,2,..., M). The value of each set of weights differ from others, Th cells receive different stimuli magnitude from the same antigen. Mathematically, each Th cell computes a dot product between its associated weight vector W_j = (w_{j1}, w_{j2},..., w_{jN}) and input antigen AG = (ag_1, ag_2,..., ag_N). Obviously, the Th cell that has associated weight most like the input antigen will have the largest output.

As discussed previously, Ts cells play an important role in modulating the immune response, such as antibody secretion. However, the immune system just considers the antigen as a stimulus at present. There is no antibody is secreted. As a result, Ts cells keep silent and have no effect on Th cells.

Th cells response to antigen can be expressed as follows:

$$th_j = AG.\ W_j \qquad (1)$$

B cells activation: In immune system, Th cells with different receptors have various responses to the input antigen. In the proposed model, we select the Th cell which has associated weights most like the input antigen. That is, only the Th cell with the highest activation level is activated, all others are inhibited.

T cells are essential to the activation of the B cells. The activated Th cell secretes interleukin (IL+) to mobilize the B cells. In operation, t_j, the output of Th cell, is presented to B cells through the weights^V. In addition, according to the T cells independent antigen recognition, the B cells can recognize antigen directly. Fig. 6, each B cell receives two inputs: an input from antigen and another stimulus input from Th cell. In operation, the antibody secreted by B cells is considered as the difference between the input antigen and the memory weights^V. In symbols:

$$AB = (ab_1, ab_2,..., ab_N) = (ag_1 - {}^{V}_{j1}, ag_2 - {}^{V}_{j2},..., ag_{jN}) \qquad (2)$$

Immune regulation: As we know, self/nonself discrimination ability based on the pattern recognition of molecular is a key feature in the defense of host organism. The phenomenon that immune system has no responding against a self cell is call self-tolerance, or simply tolerance[15]. It is the tolerance ability of immune system protects host against autoimmune diseases. In contrast, a silence to the external antigen is malfeasance of the immune system.

Initially, the weights of the system are in a state of untrained. Perhaps no immune cells have answer to the antigen. Hence, we define a tolerance parameterç. If the response of the immune system to the antigen is above the level of tolerance, that is ||AB|| <ç, we think this antigen has been previously encountered and related information about this antigen also have been stored in the weights associated with the Th cell $^{th}_{j}$. Furthermore, weights update is performed to move the weights closer to antigen. On the other hand, if all stored antigens information have been tried, found to mismatch the presented antigen, a previously unallocated Th cell $^{th}_{j}$. is selected and adjust associated weights to match the presented antigen.

Once antibody is secreted, immune response is mounted immediately. As a result, the suppressor T cells TS is activated. TS cell is vital for the maintenance of immune response. Without its activation, immune response will certainly loose control and result in allergic

reactions and autoimmune diseases. If we assume T as the period of immune response to one certain antigen, the TS cell should perform its adjusting function during period T.

In immune system, the effectiveness of the immune response to secondary encounters is considered by storing some high affinity antibody producing cells from the first infection. Thus, we must continuously improve the model's capability to effectively response to the future input antigen. In operation, we adjust the weights related with the activated Th cell to match the presented antigen. In symbols:

$$W_j(t+1) = W_j(t) + \eta (A - W_j(t)) \quad (3)$$

where

η is learning rate of the weights.

The weights update equation between Th cells and B cells can be expressed as:

$$v_{ji}(t+i) = v_{ji}(t) + \Delta(t)_i T_s(t) \quad (4)$$

$$\Delta(t)_i = (ag_i - v_{ji}(t)) \quad (5)$$

$$T_s(t) = e^{-t/T} \quad (6)$$

where

$v_{ji}(t)$ is the value of weight before adjustment

$v_{ji}(t+1)$ is the value of weight after adjustment

$\Delta(t)_i$ is the correction value of weight

$T_s(t)$ is the state of TS cell in time t.

This way, the system can remember the encountered input patterns and rapidly respond to the future infections with the same or related input patterns. This phenomenon, in natural immune system, is called secondary response.

SIMULATIONS

In order to test the ability of the proposed artificial model, simulations on the model are described in this section. Analog and binary input patterns, similar to the antigen in immune system, are presented respectively to test the classification ability and noise immunity of the model.

Analog Input pattern classification: Response to analog pattern: A set of input vectors including 10 arbitrary sequences is presented to the model. 10 elements in each vector are taken from the interval [0.0 1.0] randomly.

All of weights must be initialized before learning starts. The weights from APC layer to TH layer are all initialized to the same value $w_{ij} = \sqrt{M}$. The weights from TH layer to B layer are all initialized to 1, namely $v_{ij} = 1$. The system tolerance parameter ς is set as 0.1.

Initially, pattern 1 is presented to the untrained system. Because there is no memory category that

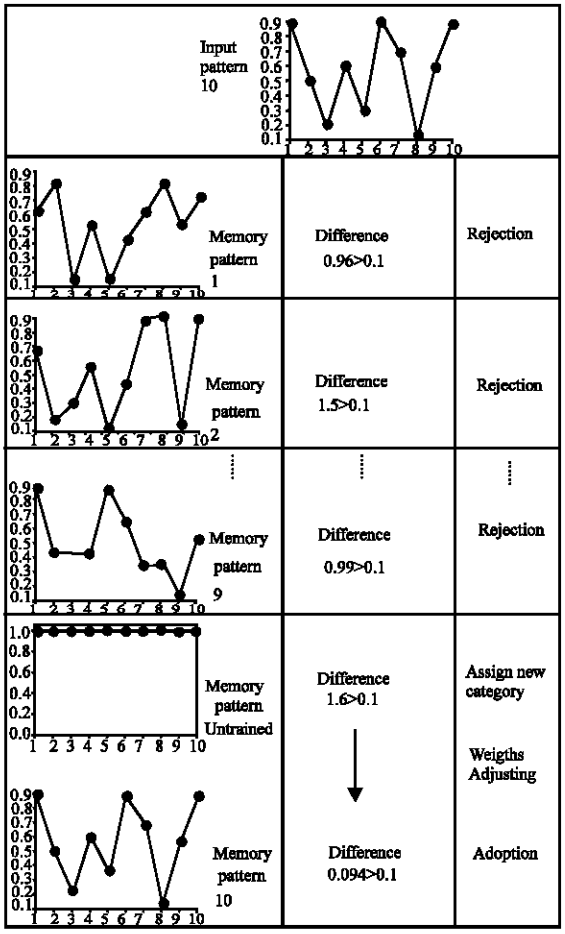


Fig. 7: Response to the 10th input pattern

matches the first presented pattern within the tolerance parameter, the system will assign a category for saving input pattern 1, namely category 1. The weights associated with category 1 are also adjusted according to the former operation.

Secondly, pattern 2 is input to the trained system. This also fails in the classification because of the tolerance parameter. Then another new category is assigned. This process is repeated for the last input vector 10.

We select the 10th input pattern as an example to explain the response process of the trained system. When the input pattern 10 is input to the system, the matching degrees with memory categories are calculated. Because of the difference are too large to class successfully. A new category is assigned to the input vector 10. Figure 7 indicates the classification process in detail. Difference between the 10th input pattern and the entire trained categories are too large to adopt. A new category is assigned to the input pattern 10, the related weights are also adjusted to match the input pattern. The learning

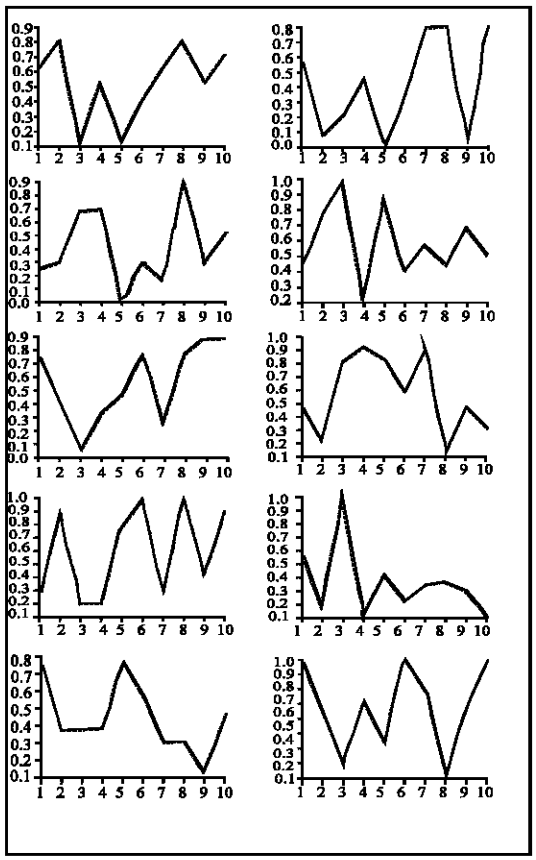


Fig. 8: Presented patterns and memory results of the system

Figure 8 illustrates the learning results of the immune system. The broken line with little square indicate process is over until all the input vectors being presented to the system the input patterns and the real line with little circle indicate the memory patterns.

Influences of tolerance parameterς on pattern classification: How to set the tolerance parameter ς, depending upon the degree of mismatch that is to be accepted between the input vector and memory vector. At a high level of ς ,the immune system makes fine distinctions. On the other hand, a low value causes the grouping of input patterns that may be only slightly similar. In this section, we will give the classification results to demonstrate the influence ogf ς on the immune response.

Figure 9 shows that the proposed system classifies 10 input patterns to 7 categories when parameter ς = 0.3. When the parameter ς gets a larger value, we get classification results of classifying 10 input patterns to 5 categories illustrated in Fig. 10.

According to the classification results in this section, we can found that a larger tolerance parameter will classify the input patterns into fewer categories. It means that, in natural immune, the host considers the similar antigens as identical. In order to avoid the incorrect activation of the immune system, we set the tolerance parameter ς at a lower level.

System Response to Binary Input Pattern: Binary patterns are presented to the system to evaluate noise

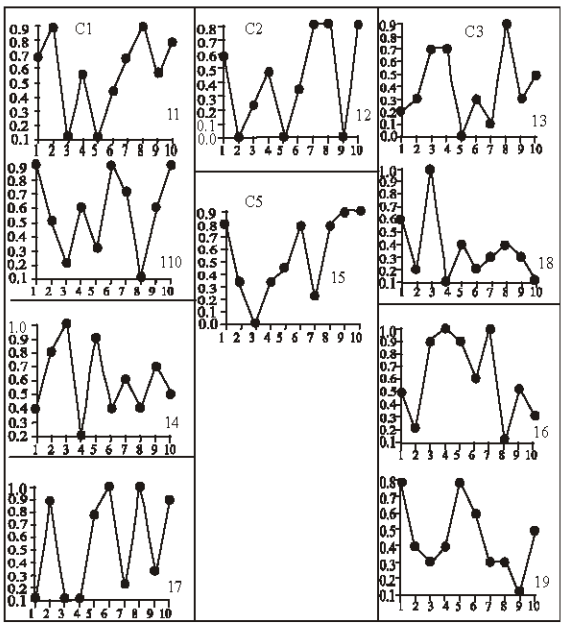


Fig. 9: Classification results of the system with parameter ς = 0.3

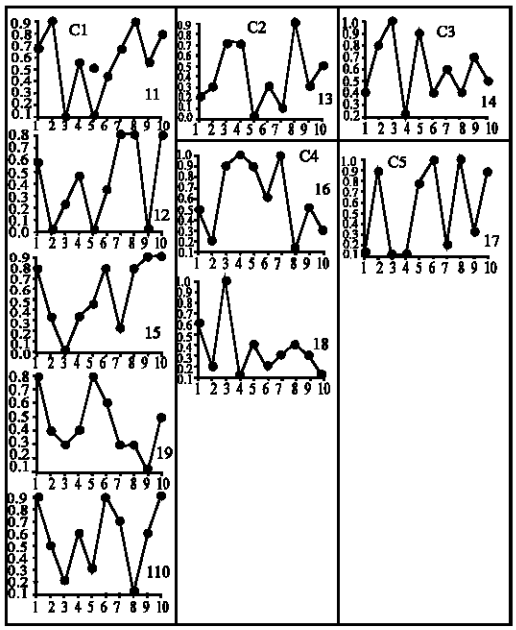


Fig. 10: Classification results of the system with parameter ς = 0.7

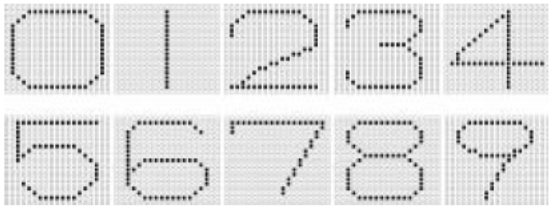


Fig. 11: Binary patterns

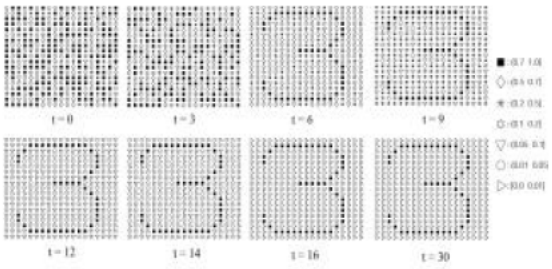


Fig. 12: Adjusting process of category 3

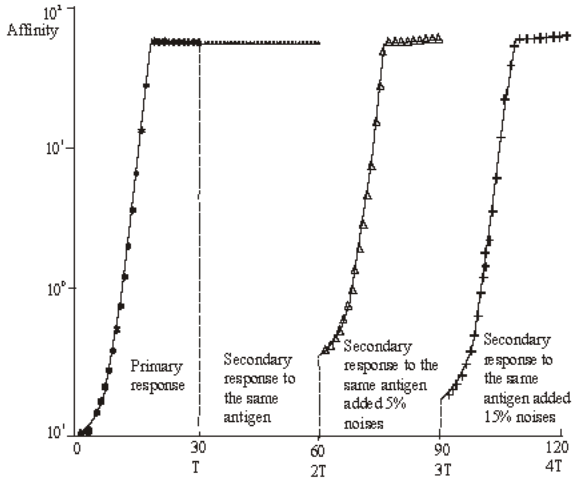


Fig. 13: Primary response and secondary response

sensitivity and recognition ability of the proposed artificial immune system model with different system parameters.

The binary input patterns[9] are numbers from 0 to 9 consist of 361 (19*19) pixels in a square area, shown in Fig.11.

The learning process of immune system for binary input pattern is similar to that of analog input patterns. So we explain it simply. Here we select number of 3 as an example to explain the learning process.

In case of binary model, we randomly set the initial values of the weights. As illustrated in Fig. 12 (t=0), the symbols with different shape indicate different random values.

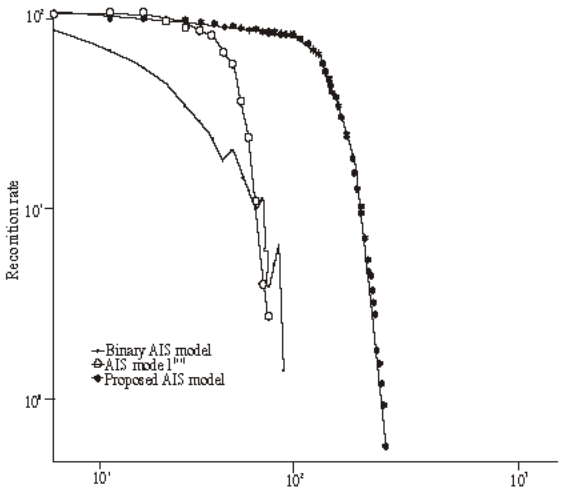


Fig. 14: Recognition results of different AIS models

Although the initial state of the category (t= 0) is disorganized, it seems that the proposed artificial immune system model can extract the features of input pattern step by step and rapidly reach the stable state (t=16). The respond period T is set as 30 in simulation.

As previously described, the effectiveness of the immune response to secondary encounters is considered by storing the high affinity antibody producing immune cells from the first infection. In artificial immune model, we treat the antibody as the difference between the input patterns and the memory weights. That is, the lower the difference, the better the input pattern recognized by the system.

We present the simulation results of the primary response and the secondary response of the system with different presented antigens in Fig. 13. During the first response period T, the immune system encounters the antigen for the first time and save related information of the antigen into immune system. If we present the same antigen, during T → 2T, to the immune system once more, we found that the immune system can recognize the input antigen immediately. Furthermore, we also present the same antigen with 5% and 15% noises to the immune system, based on the primary response, the system can effectively recognize the noisy antigen. It is necessary to point out that, the immune system needs more time to recognize a pattern with more noise points.

Finally, we test the recognition ability of the proposed AIS model with different noise number. Figure 14 depicts the recognition results of binary network[10], the fuzzy artificial immune mode[11] and the proposed artificial immune system model in this study. The results of simulation show that the proposed artificial immune

system model is less sensitive to noise than other artificial immune models. The proposed model can recognize noisy input patterns more effectively.

CONCLUSIONS

In this study, we have studied natural immune system and proposed an artificial immune system model by considering the natural immune principles. Based on the self/nonself discrimination mechanisms, we have built a three-layer network consists of T cells dependent and T cells independent antigen recognition processes. According to the state of the antibody, the proposed immune model selects an appropriate activation to deal with the presented antigen. Simulations on pattern classification and noisy pattern recognition also have been implemented, although it seems that the examples in simulation are too simple. According to the simulation results, we get the following conclusions: the proposed model, considering T cells dependent and T cells independent recognition capability to antigens of B cells, can remember the encountered patterns and classified the same or similar input pattern into proper category accurately. In addition, the proposed artificial immune system model has strong immune tolerance ability to noise. It can effectively recognize the noisy input patterns more than that of the models we proposed previously.

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