

An Artificial Immune Network with Multi-layered B Cells Architecture

Wei-Dong Sun* Non-member
 Zheng Tang* Non-member
 Hiroki Tamura* Member
 Masahiro Ishii* Non-member

This paper describes an artificial immune network with multi-layered B cells architecture. It is not our concern to reproduce with confidence any immune phenomenon, but to show that immune concepts can be used to develop powerful computational tools for engineering applications. As an important result of our model based on multi-layered B cells architecture, the network is capable of creating better immune response and describing pattern category for arbitrary sequences of analog (gray-scale, continuous valued) input patterns, as well as binary input patterns.

Keywords: Immune Network, Immune Response, Multi-layered B cells, Pattern Classification

1. Introduction

In recent years, the immune network discipline has attracted biologists who are interested in modeling biological immune networks and physicists who envisage analogies between immune network models and the non-linear dynamical systems. The theoretical development of immune networks was initiated by Jerne⁽¹⁾, who constructed a differential equation to describe the dynamics of a set of identical lymphocytes. After that, most efforts have been made to put the network proposal into mathematical terms^{(2)~(7)}. Immune network concept has also been incorporated into neural networks in machines learning problems⁽⁸⁾, in genetic algorithm^{(9)~(11)}, in learning stimulus-response behavior⁽¹²⁾ and some other applications^{(13)~(14)}. However, in these research the details how an immune response was concretely applied on an engineering system were not seen.

In our previous work, an immune network based on biological immune response network was proposed⁽¹⁵⁾. A class of immune networks has since been characterized as a system of recognition to arbitrary sequences of binary input patterns, either 0 or 1^{(16)~(19)}. However, the models of those immune networks have the problem that they cannot be applied to the large-scale analog pattern classification. Since real life systems, such as image, voice, often have higher radix data upon which processing has to be made, it is an area of engineering significance.

Furthermore, the immune system is a complex of cells, molecules and organs that has been proven to be capable of performing several tasks, like pattern recognition, learning, memory acquisition, generation of diversity, noise tolerance, generalization, distributed detec-

tion and optimization⁽²⁰⁾. The powerful computation capability may come from the immune system's intrinsically multi-layered architecture^{(21)~(25)}. Based on the immunological principles, new computational techniques are being developed, aiming not only at a better understanding of the system but also at solving engineering problems. In this paper, we focus our attention on the immune system's intrinsically multi-layered architecture and propose a new artificial immune network with multi-layered B cells architecture. This network is applied to pattern classification problems and is shown to be capable of clustering arbitrary sequences of analog input patterns, as well as binary input patterns into stable categories. Computer simulations are used to illustrate the system dynamics and its effectiveness.

2. Immune System

2.1 Immune Cells The immune system is a complex of cells that are originated in the bone marrow, molecules and organs with the primary role of limiting damage to the host organism by pathogens (called antigens, Ag), which elicit an immune response. Lymphocytes are small leukocytes that possess a major responsibility in the immune system. There are two main types of lymphocytes: B lymphocyte (or B cell), which, upon activation, differentiates into plasmocyte (or plasma cells) capable of secreting antibodies; and T lymphocyte (or T cell).

The B lymphocytes expresses, on its surface, receptors highly specific for a given antigenic determinant. The B cell receptors are a form of the antibody molecule bound to the membrane, and which will be secreted after the cell is appropriately activated. The another main functions of the B cells include the production and secretion of antibodies (Ab) as a response to exogenous proteins like bacteria, viruses and tumor cells. Each B cell is programmed to produce a specific antibody. The anti-

* Faculty of Engineering, Toyama University
 Gofuku 3190, Toyama city, 930-8555, JAPAN.

bodies are specific proteins 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.

The T lymphocytes can be subdivided into three major subclasses: T helper cells (T_H), cytotoxic (killer) T cells and suppressor T cells (T_s). T cells mature within the thymus. Their functions include the regulation of other cells' actions and directly attacking the host-infected cells. The T helper cells, or simply T_H cells, are essential to the activation of the B cells, other T cells, macrophages and natural killer (NK) cells. They are also known as CD4 or T4 cells. The killer T cells, or cytotoxic T cells, are capable of eliminating microbial invaders, viruses or cancerous cells. Once activated and bound to their ligands, they inject noxious chemicals into the other cells, perforating their surface membrane and causing their destruction. Without their activity, immunity would certainly lose control resulting in allergic reactions and autoimmune diseases. The T cells work, primarily, by secreting substances, known as interleukin (IL), lymphokines and their relatives, the monokines produced by monocytes and macrophages. These substances constitute powerful chemical messengers. The lymphokines promote cellular growth, activation and regulation. In addition, lymphokines can also kill target cells and stimulate macrophages.

2.2 Immune Response Specialized antigen presenting cells (APCs), 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 compatibility complex (MHC) molecules and are displayed on the surface of the cell. Other white blood cells, called T cells or T lymphocytes, have receptor molecules that enable each of them to recognize a different peptide-MHC combination. T cells activated by that recognition divide and secrete lymphokines, interleukin or chemical signals, which mobilize other components of the immune system. The B lymphocytes, which also have receptor molecules of a single specificity on their surface, respond to those signals. When activated, the 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. This represents the immune response process, an outline of which is shown in Fig.1⁽²⁰⁾.

2.3 Multi-layered immune architecture Furthermore, the immune system's architecture is intrinsically multi-layered, with defenses spread about several levels (see Fig.2)⁽²⁰⁾. For example, living body's skin works as a shield to the body's protection against invaders, either malefic or not. It is now recognized as our body's largest immunologic organ and immunological mechanisms that are essential in protecting us from sunlight, bacteria, fungi, viruses and all the things that do not belong to our bodies. The skin has a complex, multi-layered structure. The complex, intricate structure allows the skin to have many complex functions.

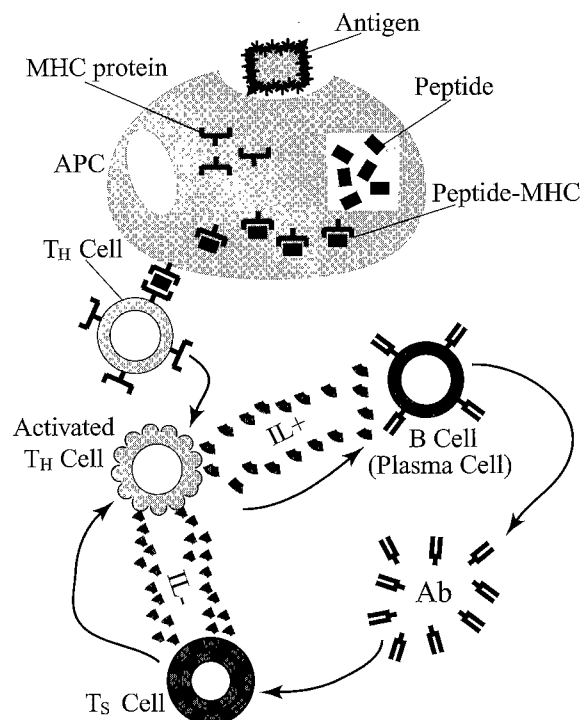


Fig. 1. How does the immune system protect the living body?.

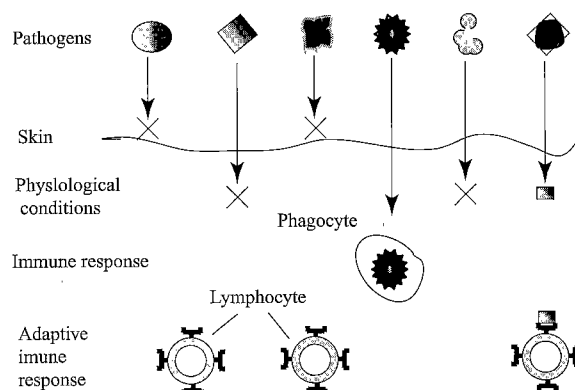


Fig. 2. Multi-layer structure of the immune system.

Multiple functions would not be possible without complex structure. Each layer of the skin expresses its own unique reaction when disturbed. The three basic layers of skin are epidermis (outermost layer), dermis (middle layer) and subcutaneous tissue (deep layer).

3. Artificial Immune Network Model

Recent papers^{(15)~(19)} have explored the ability of a system of interaction between B cells and T cells to have useful pattern category classification properties. These models have been based on single layer B cells that are not only different from real immune systems but also confine the classification to binary patterns.

In this paper, we propose a new artificial immune network with multi-layered B cells architecture. First we suppose that each B cell involves three levels: B1, B2 and B3 depending upon essential multi-layered immune system. This makes the proposed model to include sev-

eral processing levels and the gain control system in B cell layer. In the different position of B cell layer, B cell can accept and transform the patterns from bottom and signals from top and feed the processed results back to the bottom or top of B cell layer. This can strengthen the remarkable recognition characteristic and the noise elimination in the positive feedback circulation of B cell layer.

In the meantime, we restrict our discussion on the interaction between B cells and T cells only, although various cells participate in the immunity mechanism (immune response). Fig.3 shows the principal elements of the artificial immune network.

In the following simple scheme, the interactions about one cell within immune system are considered.

(1) $Ag(input) \rightarrow B \text{ cell} (\rightarrow B1 \rightarrow B2 \rightarrow B3) \rightarrow Output$

When antigen (Ag) invades living bodies, it can be regarded as an input to the immune network and taken in by B cell, i.e., antigen insults living body and presents on the surface of skin.

First in level B1, not only the stimulation to living bodies from the specific antigen can get a buffering but also all the information about it will be gathered and normalized, then new rearranged information can be given to level B2 as an output of level B1. For example, epidermis sends a signal to each underlying skin layer which type of inflammation is needed for protection against "insult".

Second in level B2, variety of information from level B1 and level B3 about Ag will be transformed, compared and saved. Just as the dermis is the major part of the skin, level B2 plays an important role, too. Here, the information about antigen can be normalized once again before it arrives at level B3.

Finally in level B3, which is connected to level B2, encodes the high level abstraction of the information, and transfers it to T_H cell.

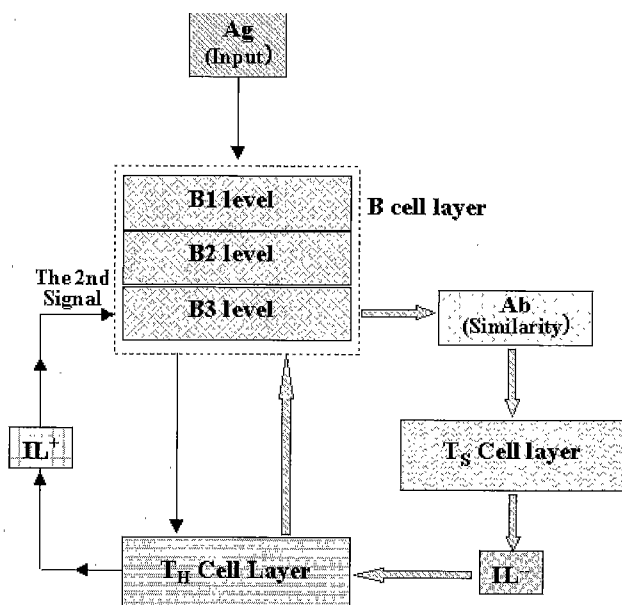


Fig. 3. The artificial immune network model.

(2) $Output \rightarrow T_H \text{ cell} \rightarrow IL+$

T_H cell can recognizes the antigen information from B cell and secretes the interleukin ($IL+$) that activates the immune response.

(3) $IL+ \rightarrow B \text{ cell} \rightarrow Antibody (Ab)$

The interleukin ($IL+$) becomes the second signal to the B cell. Once B cell recognizes this signal, it divides into antigen synthetic cells (plasma cells), and then synthesizes and secretes the antibody finally. Here, B represents both B cell and plasma cell.

(4) $Antibody \rightarrow Ts \rightarrow IL-$

If the antibody excludes the antigen, we can say that the immune of living body is effective. At this time, the suppressor T_s cell will be stimulated to secrete suppressing interleukin ($IL-$) to suppress the immune response. The immune response is finished as long as the generation of the antibody stops.

According to the immune response process mentioned above we can obtain three important features about our network:

- If we consider antigen as an input and antibody as an output, the output is determined not only by B cells but also by the interaction between B cells and T_H cells.
- B cells including B1, B2 and B3 levels plays an important role in normalizing antigen information and presenting the feature of the antigen input.
- T_s cells can adjust the sub-system constructed by B cell layer and T_H cell layer.

4. Algorithms

This section describes the algorithms in details, and the formulation of the following is derived from the conceptual model mentioned above.

Fig.4 shows the proposed immune network with multi-layer B cells architecture. The model consists of three cell layers, a B cell layer, a T_H cell layer, and a T_s cell layer. B cell layer involves B1 level, B2 level and B3

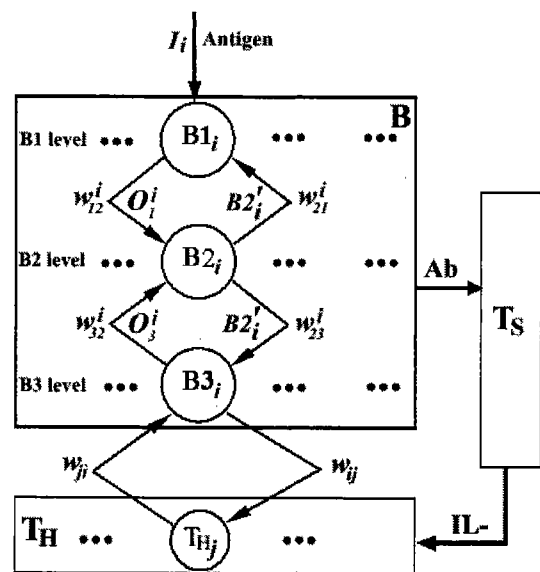


Fig. 4. An artificial immune network with multi-layered B cells architecture.

level. The antigen corresponds to input and antibody to output. In the meantime, we assume the number of cell as N in B cell layer and as M in T_H cell layer.

We assume input Ag as a vector I in this immune system. It is a N dimensional vector, and its N 's component vector corresponding to N 's processing units in B cell layer are I_1, I_2, \dots, I_N . Each unit corresponds a B cell column and each B cell column involves three levels, B1 level, B2 level and B3 level.

In each B cell column, for example the i th B cell column as shown in Fig.4, $B1_i$ cell and $B2_i$ cell, $B2_i$ cell and $B3_i$ cell are connected with the weights: w_{12}^i ($B1_i \rightarrow B2_i$) and w_{21}^i ($B2_i \rightarrow B1_i$), w_{23}^i ($B2_i \rightarrow B3_i$) and w_{32}^i ($B3_i \rightarrow B2_i$), respectively. They form two feedback circuits. Note that each B cell here has two important functions: producing the sum of the weighted inputs and applying it to a nonlinear activation function. Of course, it is highly desirable (but not mandatory) to normalize all input vectors before applying them to the network. This is finished through dividing each component of an input vector by that vector's length. This length is found by taking the square root of the sum of the squares of all of the vector's components defined by $\|X\|$. In symbols

$$x'_i = \frac{x_i}{\|X\|} = \frac{x_i}{(x_1^2 + x_2^2 + \dots + x_N^2)^{1/2}} \dots \dots (1)$$

This converts an input vector (x_1, x_2, \dots, x_N) into a unit vector pointing in the same direction; that is, a vector of unit length in N -dimensional space.

Consider the i th B cell column. The $B1_i$ cell receives the input signal I_i and the signal of $B2_i$ with the weight w_{21}^i , computes the summation of the weighted inputs simply as

$$B1_i = I_i + w_{21}^i B2'_i \dots \dots \dots (2)$$

where $B2'_i$ is the normalized summation of the B2 cells:

$$B2'_i = \frac{B2_i}{\|B2\|} = \frac{B2_i}{(B2_1^2 + B2_2^2 + \dots + B2_N^2)^{1/2}} \dots (3)$$

Then, the $B1_i$ signal is normalized to be

$$B1'_i = \frac{B1_i}{\|B1\|} = \frac{B1_i}{(B1_1^2 + B1_2^2 + \dots + B1_N^2)^{1/2}} \dots (4)$$

and usually further processed by an activation function F to produce the cell's output signal, O_1^i .

$$O_1^i = F(B1'_i) \dots \dots \dots (5)$$

where the function F may be a simple piecewise linear function,

$$F(x) = \begin{cases} x & \text{if } x \geq \theta \\ 0 & \text{if } 0 < x < \theta \end{cases} \dots \dots \dots (6)$$

where θ is a threshold vigilance. The output O_1^i is then applied to $B2_i$ cell with the weight w_{12}^i .

Similarly, $B2_i$ cell computes the summation of the weighted inputs from $B1_i$ cell and $B3_i$ cell.

$$B2_i = w_{12}^i O_1^i + w_{32}^i O_3^i \dots \dots \dots (7)$$

and its normalization form $B2'_i$ (equation(3)) is fed to $B1_i$ cell and $B3_i$ cell.

$B3_i$ cell receives the normalized signal $B2'_i$ from $B2_i$ cell with the weight w_{23}^i and feedback signal from T_H cell, computes the summation

$$B3_i = B2'_i + d w_{ji} \dots \dots \dots (8)$$

where $d(0 < d < 1)$ is feedback parameter from T_H cell layer and w_{ji} is the weight from the j th T_H cell to i th $B3_i$ cell. $B3_i$ cell then normalized to be

$$B3'_i = \frac{B3_i}{\|B3\|} = \frac{B3_i}{(B3_1^2 + B3_2^2 + \dots + B3_N^2)^{1/2}} \dots (9)$$

then processed by the piecewise linear function F

$$O_3^i = F(B3'_i) \dots \dots \dots (10)$$

and fed to $B2_i$ cell.

Meanwhile, $B3_i$ cell whose activity is sufficiently large generates excitatory signals along pathways to target cells at the next processing stage T_H cell layer. T_H cell layer is the category representation field, its key properties are contrast enhancement of the filtered antigen pattern, and reset, or enduring inhibition, of active T_H cell layer cells.

Contrast enhancement is carried out by competition within T_H cell layer according to winner-take-all rule. Choice is the extreme case of contrast enhancement. T_H cell layer makes a choice when the cell receiving the largest total input quenches activity than all other cells. In other words, let T_j be the summed filtered antigen input to the j th T_H cell in T_H cell layer:

$$T_j = \sum_i B3_i w_{ij}, (j = M + 1 \dots N) \dots \dots \dots (11)$$

T_H cell layer is said to make a choice if the j^* th cell in T_H cell layer becomes maximally active, while all other cells are inhibited, then

$$T_{j^*} = \max\{T_j : j = M + 1 \dots N\} \dots \dots \dots (12)$$

At this time T_H cell which has the value of T_{j^*} can secrete interleukin (IL+). The interleukin (IL+) is then weighted and sent back to B cells once again by the pathway of w_{ji} . We call it memory pattern.

The interleukin (IL+) becomes the second signal to B cells. Once B cell recognizes this signal, it divides into antigen synthetic cells (plasma cells), and then synthesizes and secretes the antibody finally. Here, antibody is regarded as the similarity between the input vector and memory vector and we compute the similarity as follow.

$$r_i = (B2'_i + c B3_i) / (e + \|B2\| + c \|B3\|) \dots \dots (13)$$

where, c is constant, $0 < c < 1$, e is a positive real number, $e \ll 1$. The T_H cell layer can be reset whenever an input pattern is active and

$$\frac{\rho}{e + \|r\|} > 1 \dots \dots \dots (14)$$

where the vigilance parameter ρ is set between 0 and 1.

If the two patterns differ by more than the vigilance parameter, a reset signal is sent to disable the firing unit in the T_H cell layer. The effect of the reset is to force the output of the T_H cell layer back to zero, disabling it for the duration of the current classification in order to search for a better match. Namely, in this case inhibitory interleukin (IL-) is secreted from Ts cells. The inhibitory interleukin (IL-) tends to suppress T_H cells that secrete the excitatory interleukin. Thus, a new competition in T_H cell layer occurs.

If the two patterns differ by less than the vigilance parameter, the memory pattern must be searched, seeking one that matches the input vector more closely, or failing that, terminating on an uncommitted cell that will then be trained. That is to say, the winner j^* th T_H cell is accepted and it represents the category of this kind of antigen, i.e., the recognition for this kind of antigen is successful. And then the network enters a training cycle that modifies the weight w_{ij} and w_{ji} .

Training is the process in which a set of input vectors are presented sequentially to the input of the network, and the network weights are so adjusted that similar vectors activate the same T_H cell. If the same antigens invade once again, the immune response can be activated by the network recognition rapidly; a large quantity of antibodies is generated in a very short period (the secondary immune response). The adjusting weight equations can be given

$$w_{j^*i} = d(B3_i w_{j^*i}) \dots \dots \dots (15)$$

$$w_{ij^*} = d(B3_i w_{ij^*}) \dots \dots \dots (16)$$

with $0 < d < 1$, for all $j \neq j^*$.

The following procedure describes the proposed algorithm.

- Step 1:** For all i and j , set initial weights: w_{ij} and w_{ji} , w_{21}^i and w_{32}^i , w_{12}^i and w_{23}^i .
- Step 2:** Using equations (1)-(10), compute output of the B cell layer.
- Step 3:** As B cells reach stable state, they send signals to the T_H cell layer. The inputs to the T_H cell layer are computed by equation (11).
- Step 4:** Use equation (12) to find the maximally active j^* th T_H cell.
- Step 5:** Compute the similarity (Ab) between the input vector and the memory vector by equation (13) and check if to reset or not by equation (14). If reset, return to step 4 until reset does not occur. Otherwise, go to next step.
- Step 6:** Update weights by equations (15)(16).
- Step 7:** Go to step 2 for next input pattern.

5. Simulations

The simulations on the proposed artificial immune network are described in this section to test its effectiveness and the system dynamics. Our computer is Intel(R) Pentium(R) 4, CPU 3.06GHz, memory 512MB; OS: Windows 2000(Japanese), and the program was compiled by Microsoft Visual C++ 6.0. Antigen is regarded as an input in our simulations. In order to express the

Table 1. The parameters of our simulations.

N	M	θ	c	d	e
10	20	0.3	0.225	0.9	0.000001

complexity and diversity of antigen, a pattern set consisting of 20 arbitrary sequences continuous valued different patterns is presented in different random orders. Pattern values are taken from the interval $[0.1, 1.0]$. The parameters of Table 1 are used in the simulations.

Our supposition starts when the network has not memorized any pattern yet, but B cell and T_H cell all are in the static condition. In order to avoid activating a cell that has never been memorized, it is necessary to initialize the weight to be small values for B cell and T_H cell. Thus, for all i and j we let the weights be

$$w_{ij}(0) = \frac{1}{(1-d)\sqrt{N}} = \frac{1}{0.1\sqrt{10}} = 3.1623$$

Reset must be inhibited while a new category is being established. This can be accomplished by making all w_{ji} small before any learning occurs; in particular, we let the initial values of w_{ji} satisfy:

$$w_{ji}(0) = 0$$

In addition, in order to express the inputs better, we set the weights:

$$w_{12}^i = w_{23}^i = 1.$$

Consider that setting w_{21}^i and w_{32}^i smaller has the effect of weakening the importance of the expectation feedback relative to the inputs, we set the feedback weight a large value:

$$w_{21}^i = w_{32}^i = 10.00$$

5.1 The process of system response Fig.5 illustrates a typical process of system response with $\rho = 0.980$. In Fig.5, each row shows that the proposed system response to a sequence of 4 input patterns (A, B, C and D) presented in the order ABCAD on learning trial 1-5 (left) and on recognition trial 6-10 (right). Two graphs are depicted for each trial: the top graph shows the input pattern (A, B, C and D) and the bottom graph shows the memory pattern at the end of the trial. The category number, the value of T_{j^*} (by equation (12)) and the value of similarity (by equation (13)) are shown beside the memory pattern graph respectively.

On trial 1, input A establishes category 0. It is necessary to note that pattern A is enhanced contrastively between B cell layer and T_H cell layer, due to the fact that the pattern troughs are below the noise level defined by the signal threshold (equations (6)). In fact, θ is set equal to $1/\sqrt{N} = 0.3$ in our simulation. This is the level at which uniform patterns are treated as pure noise but any nonuniform pattern can be enhanced contrastively and stored in the memory of B cell layer and T_H cell layer. On trial 2, pattern B, which shares all its features with A, first searches category 0. The high vigilance level leads to the T_H cell layer reset, and pattern B establishes the new category 1. On trial 3, pattern

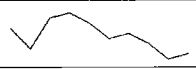
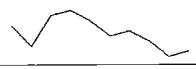
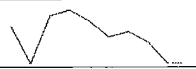
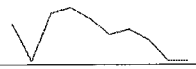
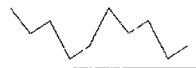
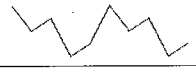
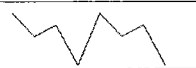
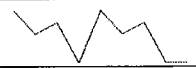
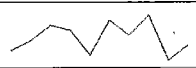
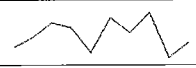


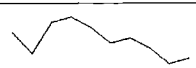

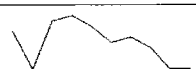
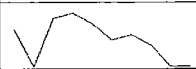
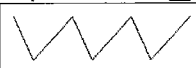

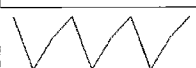
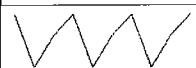
Learning Trial			Recognition Trial		
1		Input Pattern A	6		Input Pattern A
		Category (e+ r =1.00) 0 (T ₀ =3.4816)			Category (e+ r =1.00) 0 (T ₀ =24.1569)
2		Input Pattern B	7		Input Pattern B
		Category (e+ r =1.00) 1 (T ₁ =3.1379)			Category (e+ r =1.00) 1 (T ₁ =19.1926)
3		Input Pattern C	8		Input Pattern C
		Category (e+ r =1.00) 2 (T ₂ =3.4816)			Category (e+ r =1.00) 2 (T ₂ =19.1926)
4		Input Pattern A	9		Input Pattern A
		Category (e+ r =1.00) 0 (T ₀ =19.1926)			Category (e+ r =1.00) 0 (T ₀ =24.8833)
5		Input Pattern D	10		Input Pattern D
		Category (e+ r =1.00) 3 (T ₃ =3.1623)			Category (e+ r =1.00) 3 (T ₃ =19.1926)

Fig. 5. System matching processes with input pattern A, B, C and D.

C also searches category 0; having nothing in common with pattern B, it then goes directly to an uncommitted cell and establishes category 2. When pattern A is again presented on trial 4, it directly accesses its original category 0. On trial 5, pattern D searches category 2, then category 1 and 0, then establishes the new category 3. Learning is stabilized on the first trial. Thus, on the second set of trials, when A, B, C and D are again presented on trial 6-10, they directly access their original categories 0, 1, 2 and 3. The categorization is stable, or consistent, in the sense that each pattern recognizes its unique category immediately every time it appears.

5.2 Immune Memory Fig.6 illustrates matching process of pattern R in detail(primary response). The first row on matching 1 shows the response of the memory pattern A (category 0) to the input pattern R (stimulus). The input pattern and memory pattern are matched and the similarity value of $e + ||r||$ between them is computed to be 0.974. Because the system vigilance is 0.980, the similarity (0.974) is less than vigilance (0.980). It suggests that the input pattern R is not belong to category 0. Therefore, category 0 is suppressed, namely IL- is secreted. The second row on matching 2 shows the response of memory pattern B (category 1) to the input pattern R. In the same way as the first row, two patterns are matched and similarity between them is computed to be 0.963. It is also less than system vigilance. Therefore, the category 1 is suppressed, too. It is repeated in the third row on matching 3 for the response of the memory pattern C. In the fourth row on matching 4, category 3 responses to the stimulus. The similarity is computed to be 0.998 that is bigger than the system vigilance (0.980). Thus, the input pattern R

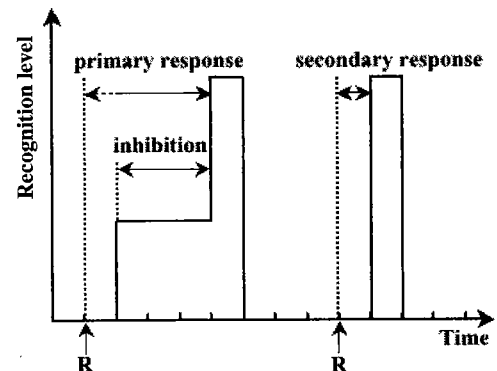


Fig. 8. The simulated primary response and secondary response.

is classified into this category 3. The fifth row shows the adjusted memory pattern in category 3. When the input pattern R is presented again, as shown in Fig.7, there is no matching process. Input pattern R accesses its category 3 directly. This illustrates the immune network's performance on immune memory function. The immune memory is a function that once a person caught a sickness like measles, will not become sick even the same virus infects him (her) once again because immune system has powerful exclusion capabilities. Namely, If the same antigen invades once again, the immune memory cells can divide into plasma cells rapidly, and a large quantity of antibodies are generated in a very short period. It is called secondary immune response. A sample of pattern R for this function is illustrated in Fig.8.

5.3 Influence of the Classification of the System by Parameter ρ One simulation to illustrate system dynamics is summarized in Fig.9, which shows how the architecture has quickly learned to group 20 in-

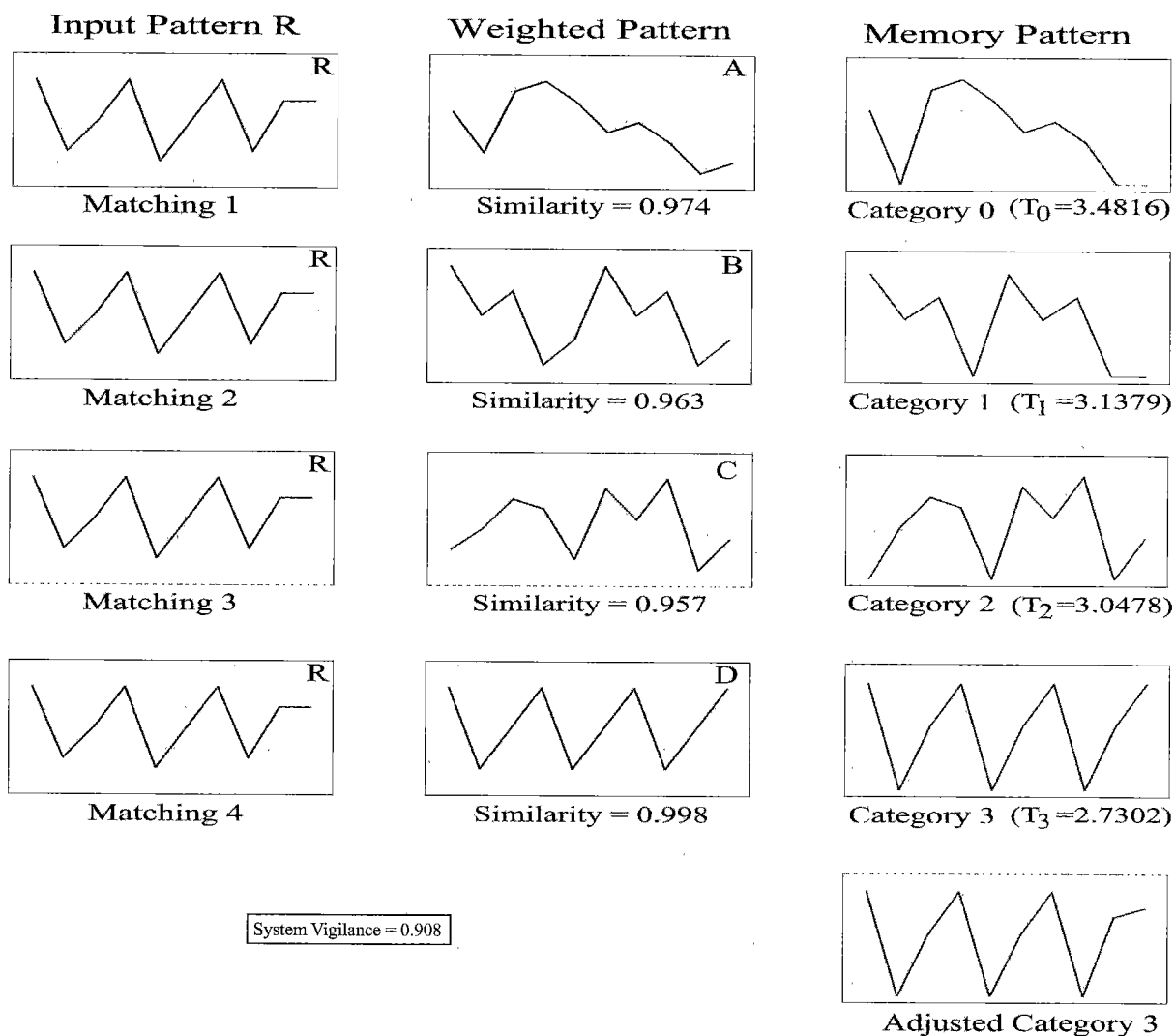


Fig. 6. The match process of pattern R in detail(primary response).

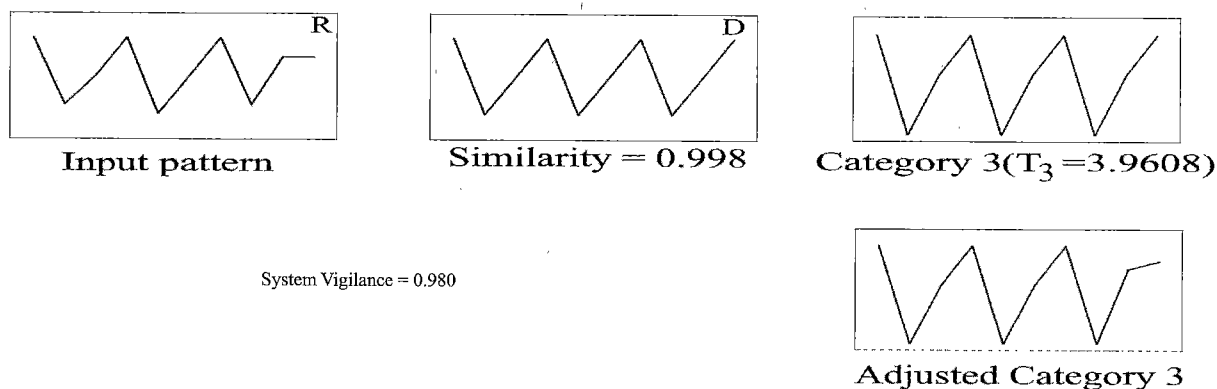


Fig. 7. The match process of pattern R in detail(secondary response).

puts into 14 stable recognition categories within 0.016 seconds while we let the vigilance parameter $\rho = 0.980$ and the other parameters are the same with Table 1.

On the first trial, we input pattern A. Pattern A is presented in the B cell layer first, i.e., antigen is taken in by B cell and is presented in the B cell layer.

Among the B cell layer, the input data is presented at B1 level first, and B1 level is iterated 10 times un-

til all the values stabilize. B2 level is then iterated for 10 iterations until its values reach equilibrium. Finally, another 10 iterations are performed simultaneously with the B cell layer and the T_H cell layer until equilibrium is achieved, testing for reset. In all these loops, test runs confirmed that 10 iterations were plenty for equilibrium to occur. Because the network has not remembered any other pattern, pattern A is very easy to learn

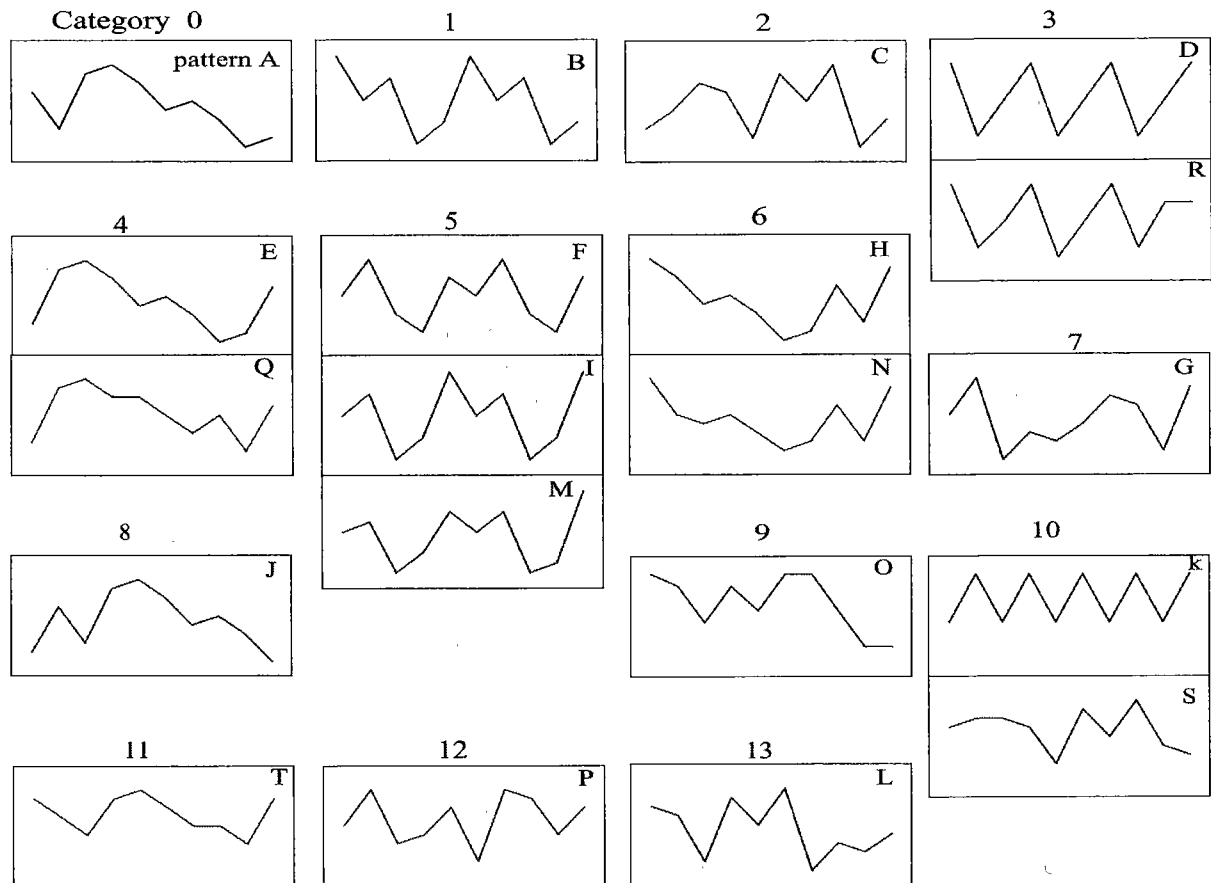


Fig. 9. Category grouping of 20 input patterns into 14 recognition categories with $\rho = 0.980$.

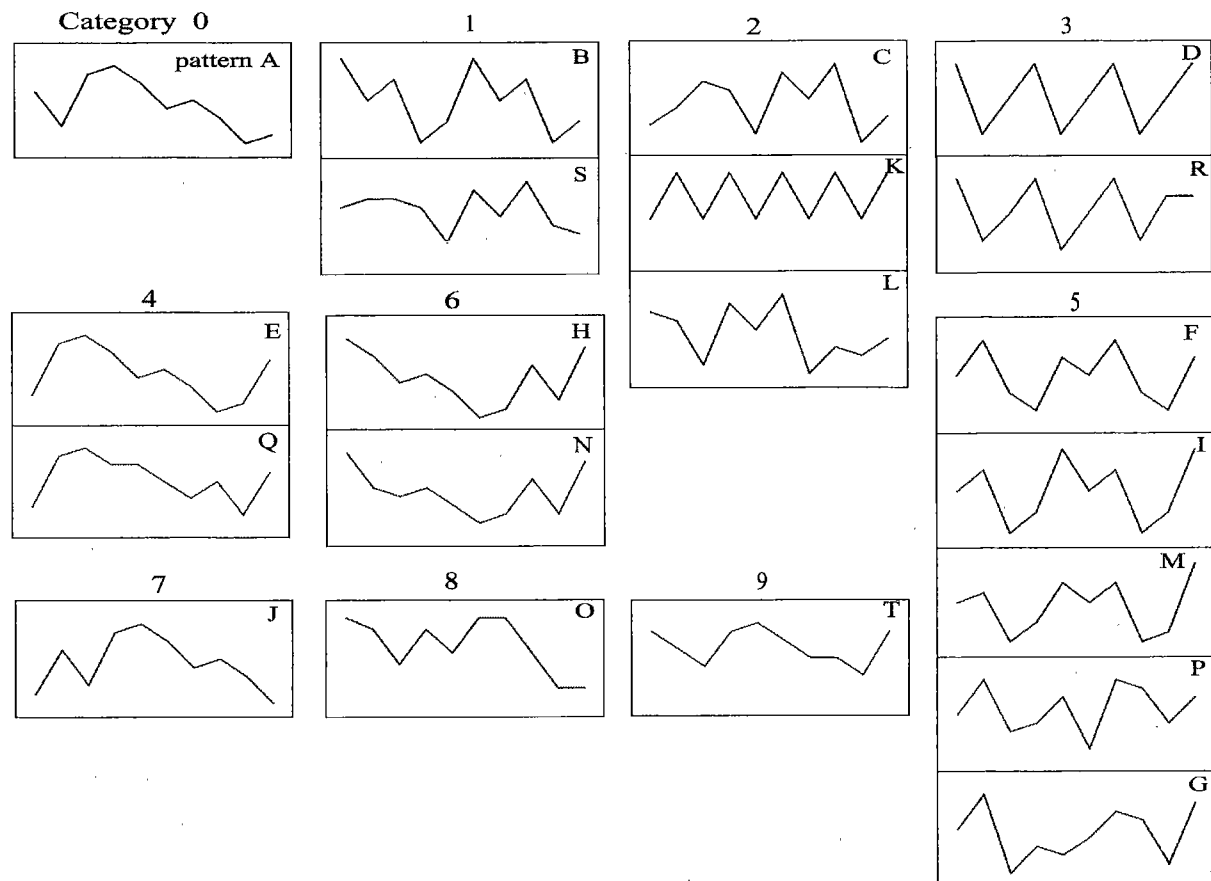


Fig. 10. Category grouping of 20 input patterns into 10 recognition categories with $\rho = 0.850$.

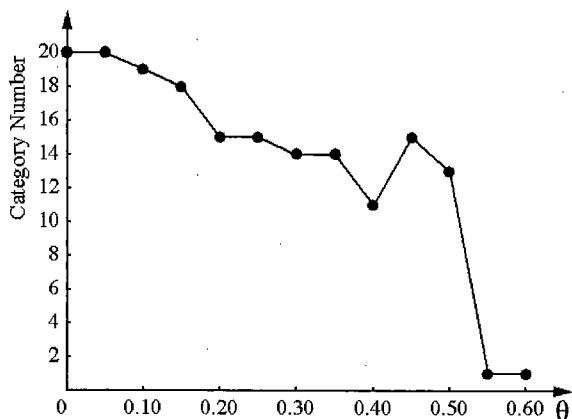


Fig. 11. The change situation of category number with parameter θ .

successfully. At this time, the value of $e + \|r\| (=1.00)$ is bigger than $\rho (=0.980)$, pattern A establishes category 0. Learning of the stabilized pattern follows by updating the weights of w_{ij} and (w_{ji}) , and B cell layer is re-computed with the new values. This procedure is repeated for 1000 iterations, which was sufficient for equilibrium to occur. The algorithm is now ready for next input pattern until the last input pattern T establishes its own category.

In another simulation we let the vigilance parameter $\rho = 0.850$, the same system as used in Fig.9 has grouped the same 20 inputs into 10 recognition categories within 0.015 seconds (Fig.10). For example, that categories 7 and 12 of Fig.9 are here joined in category 5.

All other things being equal, higher vigilance imposes a stricter matching criterion, which in turn partitions the input set into finer categories. Lower vigilance tolerates greater top-down/bottom-up mismatches at B cell layer, leading in turn to coarser categories. In addition, at every vigilance level, the matching criterion is self-scaling: a small mismatch may be tolerated if the input pattern is complex, while the same featural mismatch would trigger reset if the input represented only a few features.

5.4 Influence of the Classification of the System by Parameter θ (noise) Now, we change parameter θ to observe the classification situation of all input patterns. All parameters except θ are as in Fig.9. The classification result is shown in Fig.11. It shows that 20 input patterns are grouped into 20 categories when $\theta = 0.0$. But, as we have known, the same 20 input patterns are grouped into 14 categories when $\theta = 0.3$ in Fig.9.

Here, the threshold parameter θ is set to 0.0 so that the signal function F in equation (5)(10) is linear. The B cell layer therefore loses the properties of contrast enhancement and noise suppression. Even though the feedback weights w_{21}^i , w_{32}^i and parameter d are all large, mismatched features in input patterns are never eliminated.

6. Conclusions

In this paper, we have proposed a new artificial im-

mune network with multi-layered B cells architecture and tested its system dynamics by computer simulations. According to our simulations, the proposed network is able to solve the problem of restricted input that exists in our previous work⁽¹⁵⁾ and has several useful properties:

a) It is able to learn a stable recognition code in response to an arbitrary sequence of analog input patterns as well as binary input patterns.

b) It carries out a parallel search in order to regulate the selection of appropriate recognition codes during the learning process, yet automatically disengages the search process as an input pattern becomes familiar. Thereafter the familiar input pattern directly accesses its recognition code no matter how complex the total learned recognition structure may have become.

c) A given class of analog signals may be embedded in variable levels of background noise. A combination of normalization and nonlinear feedback processes within the B cell layer determines a noise criterion and enables the system to separate signal from noise.

Acknowledgement

This work was supported in part by the grant-in-aid for Science Research of the Ministry of Education, Science and Culture of Japan under Grant (C)(2)12680392. (Manuscript received Aug. 23, 2002,

revised June 24, 2003)

References

- (1) N.K. Jerne: "Towards a network theory of the immune system", *Ann. Immunol.*, Vol.125c, pp.373-389 (1974)
- (2) A.S. Perelson, ed.: "Theoretical Immunology, part I and II", Addison-Wesley, Redwood City, CA (1988)
- (3) H. Atlan and I.R. Cohen, eds.: "Theories of Immune Networks", *Springer-Verlag*, Berlin (1989)
- (4) N.K. Jerne: "The Immune System: A Web of V-Domains", *The Harvey Lectures*, series 70, pp.93-110, Academic Press (1976)
- (5) A.S. Perelson: "Immune Network Theory", *Immunology Review*, No.10, pp.5-36 (1989)
- (6) T. Ikegami: "Dynamical behavior of the immune network", *Progress of Theoretical Physics*, No.81, pp.309-320 (1989)
- (7) J.D. Farmer, N.H. Packard, and A.S. Perelson: "The immune system, adaptation, and machine learning", *Physical*, No.D22, pp.187-204 (1986)
- (8) J. Faro and S. Velasco: "Studies on a recent class of network models of the immune system", *J.Theor. Biol.*, No.164, pp.271-290 (1993)
- (9) J.D. Farmer: "A rosetta stone for connectionism", *Physic*, No.D42, pp.153-187 (1990)
- (10) H. Bersini and F.L. Varela: "The immune recruitment mechanism: A selective evolutionary strategy", *Proc. ICGA-91*, pp.520-526 (1991)
- (11) R. Hightower, S. Forrest, and A.S. Perelson: "The evolution of secondary organization in immune gene libraries", *Proc. Second European Conference on Artificial Life* (1993)
- (12) G.W. Hoffmann: "A neural network based on the analogy with immune system", *J. Theor. Biol.*, No.122, pp.33-67 (1986)
- (13) J.O. Kephart: "A biologically inspired immune system for computers", in *Artificial Life*, ed. C.G. Langton, Addison-Wesley, Redwood City, CA (1994)
- (14) S. Forrest, B. Jovornik, R.E. Smith, and A.S. Perelson: "Using genetic algorithms to explore pattern recognition in the immune system", *Evolutionary computation*, No.1, pp.191-211 (1993)
- (15) Z. Tang, H. Hebishima, K. Tashima, D. Ishizuka, and K.

Tanno: "An immune network based on biological immune response network and its immunity", *IEICE Trans. Fundamentals*, Vol.J80-A, No.11, pp.1940-1950 (1997)

- (16) K. Takenaka, Z. Tang, K. Tashima, D. Ishizuka, and K.Tanno: "An ImmuneNetwork for Pattern Recognition", *In Proc. NOLTA'97*, Vol.1, pp.189-192 (1997)
- (17) K. Tashima, Z. Tang, K. Takenaka, D. Ishizuka, and K. Tanno: "A self-organized Immune Network", *In Proc. NOLTA'97*, Vol.1, pp.193-196 (1997)
- (18) T. Yamaguchi, Z. Tang, O. Ishizuka, and K. Tanno: "Adaptive Multi-Valued Immune System", *I. IEE Japan*, Vol.121-C, No.11, pp.1747-1754 (2001)
- (19) Z. Tang, K. Tashima, and Q.P. Cao: "A Pattern Recognition System Using Clonal Selection-Based Immune Network", *IEICE Trans.*, Vol.J84-D, No.12, pp.2615-2622 (2001)
- (20) L.N. Castro and F.J.V. Zuben: "Artificial Immune Systems: Part I -Basic Theory and Applications", Technical Report, TR-DCA, 01/99, p.95 (1999)
- (21) Janeway Jr, C.A. and P. Travers: "Immunobiology The Immune System in Health and Disease", Artes Medicas (in Portuguese), 2nd Ed. (1997)
- (22) URL 1: "Immune System: An Internal Force Armed and Ready for Battle", Medical Essay, Mayo Clinic health Letter, URL: <http://www.mayohealth.org/mayo/9502/htm/immunesy.htm>, 1995.
- (23) B. Rensberger: "In Self-Defense", In *Life Itself*, B. Rensberger, Oxford University Press, pp.212-228 (1996)
- (24) S.A. Hofmeyr: "An Overview of the Immune System", *Tutorial about computational immunology*, <http://www.cs.unm.edu/~steveah/imm-html/immune-system.html> (1997)
- (25) S.A. Hofmeyr: "An Interpretative Introduction to the Immune System", In *Design Principles for the Immune System and Other Distributed Autonomous Systems*, (Eds.) I. Cohen and L.A. Segel, Oxford University Press (2000)
- (26) A.L. Hodgkin and A.F. Huxley: "A quantitative description of membrane current and its applications to conduction and excitation in nerve", *Journal of Physiology*, Vol.117, pp.500-544 (1952)

Wei-Dong Sun (Non-member) received the B.S. degree



from East China University of Science and Technology, Shanghai, China and the M.S. degree from Toyama University, Toyama, Japan in 1989 and 2001, respectively. Now, he is working toward the Ph.D degree at Toyama University, Japan. His main research interests are neural networks, immune networks and optimization problems.

Zheng Tang



(Non-member) received the B.S. degree from Zhejiang University, Zhejiang, China in 1982 and an M.S. degree and a D.E. degree from Tshinghua University, Beijing, China in 1984 and 1988, respectively. From 1988 to 1989, he was an Instructor in the Institute of Microelectronics at Tshinghua University. From 1990 to 1999, he was an Associate Professor in the Department of Electrical and Electronic Engineering, Miyazaki University, Miyazaki, Japan. In 2000, he joined Toyama University, Toyama, Japan, where he is currently a Professor in the Department of Intellectual Information Systems. His current research interests include intellectual information technology, neural networks, and optimizations.

Hiroki Tamura



(Member) received the B.E and M.E degree from Miyazaki University in 1998 and 2000, respectively. From 2000 to 2001, he was an Engineer in Asahi Kasei Corporation, Japan. In 2001, he joined Toyama University, Toyama, Japan, where he is currently a Technical Official in Department of Intellectual Information Systems. His main research interests are neural networks and optimization problems.

Masahiro Ishii



(Non-member) obtained a Diploma in Electronic Engineering at Akita University in 1990 and a Doctorate from Tokyo Institute of Technology in 1995. Between 1995 and 1997 he was a Postdoctoral Fellow at the Centre for Vision Research in York University of Canada. He was a Research Associate at Tokyo Institute of Technology between 1997 and 2000. In 2000 he moved to Toyama University, where he is now an Associate Professor of computer Engineering.