An Immune Algorithm Based on Danger Model

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***Abstract*— A new immune algorithm inspired from danger model is proposed. The algorithm adopts two novel mechanisms, namely variable danger zone and danger signal, which provide the algorithm with self adaptive learning in such a way that the antibodies and antigens mutual interact through a defense-offense-like manner. Several experiments are carried out to valuate the proposed algorithm. Results show that our algorithm exhibits high accuracy in solving online classification problems.**

I. Introduction

It has long been accepted among immunologists that the immune system works by discriminating self and nonself, which is called SNS (Self-NonSelf) model. Recently, however, a different theory referred to as danger model has been proposed and attracts interesting in theoretical immunology communities [1], [2]. General speaking, the danger model not only offers answers to immunological questions, it also covers many details that had not been incorporated into SNS model [2]. Although to what degree does the danger model reflect the principles of immune system is still controversial [3], what we mainly interesting in is the metaphors behind it, especially those which SNS model can not offers us, and the method of applying them in design of novel immune algorithms.

Unlike the SNS model, the danger model assumes that the recognition of danger signal rather than nonself signal is the key factor in triggering immune response. It also assumes that cells that undergoing unnatural deaths may release danger signal which covers a small area around that cell, which is called "danger zone" [4]; on the other hand, the danger signal should not be sent by healthy cells [2]. The APCs (Antigen-Presenting Cells) which receive danger signal within the danger zone are activated and co-stimulate the B-cells or helper T-cells which already have captured the antigen, i.e. received the nonself signal. Even if a B-cell or helper T-cell out of the danger zone captures the antigen, it can not be stimulated since it do not receives danger signal from any APC.

This paper present a novel immune algorithm inspired from danger theory. The concept of "danger zone" is incorporated into our model to develop and train antibody population. As its biological counterpart, the danger zone is caused by antigenic stimulation. Its radius is decreased along with immune response. The danger zone establishes a way to localize the training of antibody population, avoid the interference from distant antigens. This strategy, as far as we know, is the first attempt of introducing variable antigen activity into design of immune algorithm. In addition, two kinds of signal, i.e. antigen detection(nonself signal) and co-stimulation(danger signal) are adopted. The condition for triggering the immune response of an antibody is that it receives nonself signal and danger signal simultaneously. A suppression mechanism is adopted to control the growing of antibody population. Furthermore, clonal selection based on historical performance is used to ensure the proliferation of outstanding antibodies as well as deterioration of inferior antibodies. Based on these mechanisms a defense-offense-like manner is imposed on mutual interaction between antibody population and antigen population, which provides the algorithm with self adaptive learning capability.

II. Framework of the Proposed Algorithm

We start the discussion with a summarization of the notations and operators in our algorithm. (see Tab. I)

TABLE I
NOTATIONS AND OPERATORS USED IN THE ALGORITHM

$\mathcal{B}$	Antibody population, $\mathcal{B} = \{b_1, b_2, \cdots, b_{\lvert\mathcal{B}\rvert}\} \subseteq R^L$
$\mathcal{M}$	Memory antibodies, $\mathcal{M} = \{m_1, m_2, \cdots, m_{\lvert\mathcal{M}\rvert}\}$
$\mathcal{G}$	General antibodies, $\mathcal{G} = \{g_1, g_2, \cdots, g_{\lvert\mathcal{G}\rvert}\}$ $\mathcal{M} \cap \mathcal{G} = \emptyset, \mathcal{M} \cup \mathcal{G} = \mathcal{B}$
$\mathcal{S}$	Stimulated antibodies, $\mathcal{S} = \{s_1, s_2, \cdots, s_{\lvert\mathcal{S}\rvert}\} \subseteq \mathcal{G}$
$\mathcal{A}$	Antigen population, $\mathcal{A} = \{a_1, a_2, \cdots, a_{\lvert\mathcal{A}\rvert}\} \subseteq R^L$
$\mathrm{us}(b_i)$	Update the status of antibody b_i
$\mathrm{cs}(b_i)$	Clonal selection of antibody b_i
$\mathrm{sp}(\mathcal{B})$	Suppression within antibody population $\mathcal{B}$
$\mathrm{re}(b_i, a_j)$	Antibody b_i react to antigen a_j
$\mathrm{ud}(a_i)$	Update the danger value of antigen a_i

Now we draw a overall framework for our proposed algorithm. (see Algorithm 1)

III. Learning Process of the Algorithm

Before detailing the learning process of our proposed algorithm, it's necessary to introduce the inner data structure of the antigen and antibody. Each antigen or antibody has a class label l indicating the class it belongs to. Since this paper is mainly focused on two class classification for simplicity, the value of l is then taken from $\{0, 1\}$. The label of an antigen is remain constant, whereas the label of an antibody is variable. Each antigen has a danger value indicating its activity, which

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Randomly generate $\mathcal{G}$, $\mathcal{M} \leftarrow \emptyset$;
while Stop criterion not satisfied do
    for $i \leftarrow 0$ to $|\mathcal{A}|$ do
        $\mathcal{G}$ receives signal 0 and 1 from $a_i$;
        Generate $\mathcal{S}$ which made up of antibodies receive
        signal 0 and signal 1 simultaneously;
        for $j \leftarrow 0$ to $|\mathcal{S}|$ do
            $\mathrm{us}(s_j)$;
            $\mathrm{re}(s_j, a_i)$;
        end for
        $\mathrm{sp}(\mathcal{B})$;
        $ud(a_i)$;
        for $k \leftarrow 0$ to $|\mathcal{S}|$ do
            if $s_k$ satisfies the clonal selection condition then
                $\mathrm{cs}(s_k)$;
            end if
        end for
    end for
end while
Output $\mathcal{M}$;
```

Algorithm 1: The framework of the proposed algorithm

will be decreased along with the response from antibodies. The status of an antibody is indicated by three integers: v_1, v_2, and v_3. The v_1 indicates the accumulated stimulation the antibody receives from antigens. The v_2 indicates the antibody's accumulated classification reliability. The last value v_3 indicates whether the antibody has the same label with current antigen. Several learning processes such as antibody suppression, clonal selection, and antibody reaction are both based on this three values. When an antigen is presented and stimulate antibodies, the status of each antibody may change according to their spatial locations and classification results on current antigen. Moreover, the antibody population is divided into general antibodies and memory antibodies. Any general antibody accumulates sufficient stimulation may converted to memory antibody. Memory antibodies serve as formed memory to antigen population and can be used in future classification.

The following sub-sections cover several key steps of the proposed algorithm.

A. Initialization

The algorithm starts with initializing $\mathcal{G}$ by randomly generate general antibodies. The label l of each antibody is randomly assigned. The status value v_1, v_2, and v_3 of each antibody are set to zero. The $\mathcal{M}$ is initialized as $\emptyset$.

B. Two Kinds of Signal

As mentioned above, the danger model assumes that the immune system does not react to foreigner but to danger maker. However, "no reaction" does not means "no detection". In fact, the danger serves as a co-stimulation signal, which we call "signal 1"; and the perceiving of the foreign antigens is called "signal 0". Antibodies receive both signal 0 and signal 1 are said to be stimulated (see Fig.1). When an antigen is presented, all general antibodies receive signal 0 from it. Precisely speaking, general antibodies can perceive the appearance of current antigen ag by calculating the affinity between them and that antigen:

$$\mathit{affinity}(b_i, ag) = \|b_i - ag\| \tag{1}$$

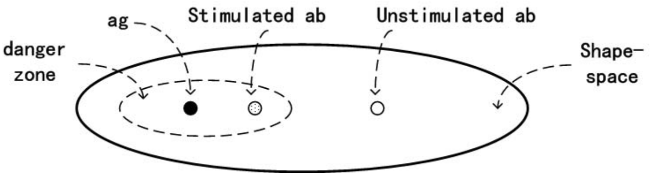


Fig. 1. The two kinds of signal. Every general antibody receives signal 0. But only those within danger zone can receive signal 1, which are said to be stimulated by current antigen.

Unlike the signal 0, signal 1 only received by antibodies within the danger zone created by ag, which is defined as:

$$D = \{p | \mathit{affinity}(p, ag) \leq ag.danger\} \tag{2}$$

The antibodies receives signal 0 and signal 1 are stimulated and allowed to change their status values (see Algorithm 2).

```
$g_i.v_1 \leftarrow g_i.s_1 + 1$;
if $g_i.l = antigen.l$ then
    $g_i.v_3 = 1$;
else
    $g_i.v_3 = -1$;
end if
$g_i.v_2 \leftarrow g_i.v_2 + g_i.v_3$;
```

Algorithm 2: $\mathrm{us}(g_i)$ used to update the status of antibody

C. Antibody Reaction and Antigen Defense

In addition to updating status, stimulated antibodies also react to current antigen. The intensity of such reaction is inversely proportional to the affinity between the antibody and current antigen ag:

$$\mathit{reactivity}(s_i, ag) = 1 - \mathit{affinity}(s_i, ag)/ag.danger \tag{3}$$

That is, the antibodies which closer to ag have stronger reactivity against it. Stimulated antibodies react to ag independently according to their reactivity:

$$s_i = s_i + s_i.v_3 \times \mathit{reactivity} \times (ag - s_i) \tag{4}$$

From equation 4 we can find that the stimulated antibodies which have same label with ag(i.e. $v_3 = 1$) will run forward it; whereas those which have different label with ag($v_3 = -1$) will run backward it (see Fig. 2). Equation 3 and 4 form the reaction operator $\mathrm{re}(b_i,\mathit{antigen})$.

In our model, we adopt variable antigen danger value. Such strategy , like natural immune system, can be seen as both result of reaction of antibody against antigen and result of defense of antigen against antibody (see Fig. 2). In fact,

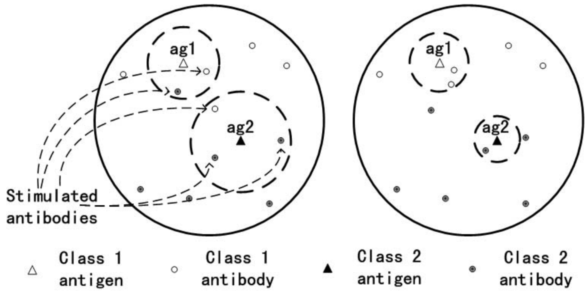


Fig. 2. Antibody reaction. Left: before stimulation; Right: after stimulation. The stimulated antibodies with $v_3 = 1$ run forward the antigen; those with ($v_3 = -1$) run backward the antigen. The danger value of antigen $ag2$ decreases more than that of $ag1$ since it stimulates more antibodies.

considering that the danger value represents the activity of an antigen, it's reasonable to assume that the more antibody stimulated by an antigen, the more its activity decreased due to immune reaction. On the other hand, the decreasing of danger value can be seen as an antigen's self-protection strategy since there will be less antibodies stimulated and response to it in the future due to the decreasing of danger value (note again that only general antibodies within danger zone can be stimulated by current antigen). Based on these considerations, we design algorithm 3 to update the danger value of antigen ag.

```
$var \leftarrow (|\mathcal{S}| + 1)^{k_1}$;
$ag.danger \leftarrow ag.danger/var$;
```

Algorithm 3: $\mathrm{ud}(ag)$ used to update the danger of antigen

D. Suppression Between Antibodies

We control the growing of antibody population through suppression mechansim. The suppression is divided into two independent processes. One is the suppression between stimulated antibodies in $\mathcal{S}$; the other is suppression between memory antibodies in $\mathcal{M}$. The intensity of suppression between any two antibodies is inversely proportional to their mutual affinity.

Precisely speaking, for any two stimulated antibodies s_i and s_j, the one with lower affinity to current antigen will be deleted with probability p_1 calculated by:

$$p_1 = \left(1 - \frac{\mathit{affinity}(s_i, s_j)}{2 \times \mathit{antigen.danger}}\right)^{k_2} \tag{5}$$

Where k_2 is adjustable parameter controls the intensity of suppression between stimulated antibodies. Similarly, For any two memory antibodies m_i and m_j which are included in the danger zone, the one with lower affinity to current antigen will be deleted with probability p_2 calculated by:

$$p_2 = \left(1 - \frac{\mathit{affinity}(m_i, m_j)}{2 \times ag.danger}\right)^{k_3} \tag{6}$$

Where k_3 is adjustable parameter controls the intensity of suppression between memory antibodies. Algorithm 4 depicts the whole suppression process(see also Fig. 3).

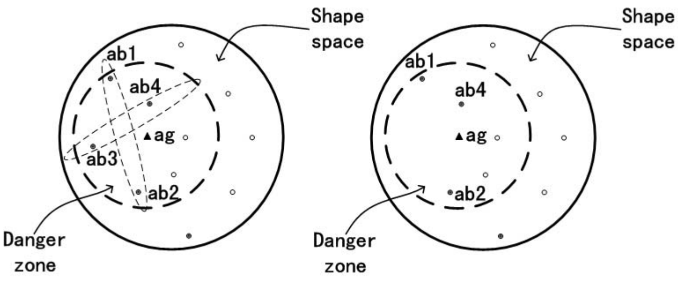


Fig. 3. Suppression between antibodies. Antibodies $ab1$ and $ab2$ are randomly grouped into a pair; $ab3$ and $ab4$ are randomly grouped into another pair. Since $ab1$ and $ab3$ have relative lower affinity against current antigen, they are deleted with probability calculated according to formula 5 or 6. Finally, $ab3$ is deleted, whereas $ab1$ survives.

```
randomly group $\mathcal{S}$ into pairs;
for all pairs do
    calculate $p_1$ according to equation 5;
    if $random < p_1$ then
        delete the one with lower affinity to antigen;
    end if
end for
randomly group $\mathcal{M}$ into pairs;
for all pairs do
    calculate $p_2$ according to equation 6;
    if $random < p_2$ then
        delete the one with lower affinity to antigen;
    end if
end for
```

Algorithm 4: The suppression operator $\mathrm{sp}(\mathcal{B})$

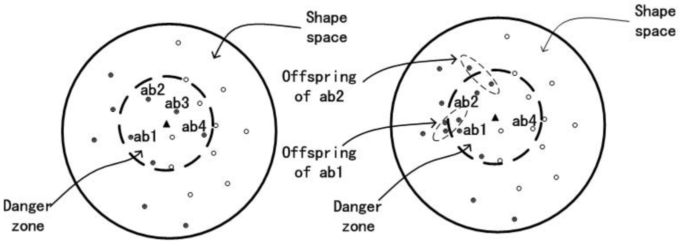


Fig. 4. The clonal selection process

E. Clonal Selection

The clonal selection is adopted as aid for proliferation of outstanding antibodies and deterioration of incapable antibodies. So that we need first bring forward a measurement to decide whether an antibody is outstanding or incapable. We achieve this by introducing two positive threshold value, namely T_1 and $T_2 (T_2 \leq T_1)$. Only when the v_1 of a general antibody reaches T_1 can it enter the clonal selection process. Then, according to the v_2 of that antibody, one out of three operations will be implemented on it:

1) If $s_2 \geq T_2$, convert it to memory antibody and clone it, all clones go through mutation.
2) If $rel \leq -T_2$, invert its label, reset its status to zero.
3) If $|rel| < T_2$, delete it with possibility p. Where $p =$

$1 - (|v_2|/T_2)^2$.

The adoption of clonal selection makes us measure the potential of any antibody from the point of view of historical performance. If the v_1 reaches T_1 but v_2 still below T_2, that means the antibody alternately recognize(stimulated by) antigens with different class label. In other word, the antibody has low classification reliability, then it is reasonable to let it release the chance of proliferation. Algorithm 5 depicts the process of clonal selection(see also Fig. 4).

```
**if** $|b_i.v_2| < T_2$ and $random < 1 - (|b_i.v_2|/T_2)$ **then**
    delete $b_i$;
**else if** $b_i.v_2 \leq -T_2$ **then**
    $b_i.l \leftarrow -b_i.l$;
    $b_i.v_1 \leftarrow 0$;
    $b_i.v_2 \leftarrow 0$;
**else**
    Clone $b_i$;
    Mutate each clone of $b_i$;
    Convert $b_i$ to memory antibody;
**end if**
```

Algorithm 5: Clonal selection operator cs(b_i)

The size of clones is calculated by following formula:

$$size = \lfloor (mc - 1) \times \frac{b_i.v_2 - T_2}{T_1 - T_2} + 1 \rfloor \tag{7}$$

Note that for b_i that can takes part in cloning, $T_2 \leq b_i.v_2 \leq T_1$, then from equation 7 we have $0 \leq size \leq mc$. So the parameter mc represents the maximum size of clones.

IV. SIMULATIONS

In this section, we present experiments for illustrating the learning process as well as evaluating the classification accuracy of our proposed method.

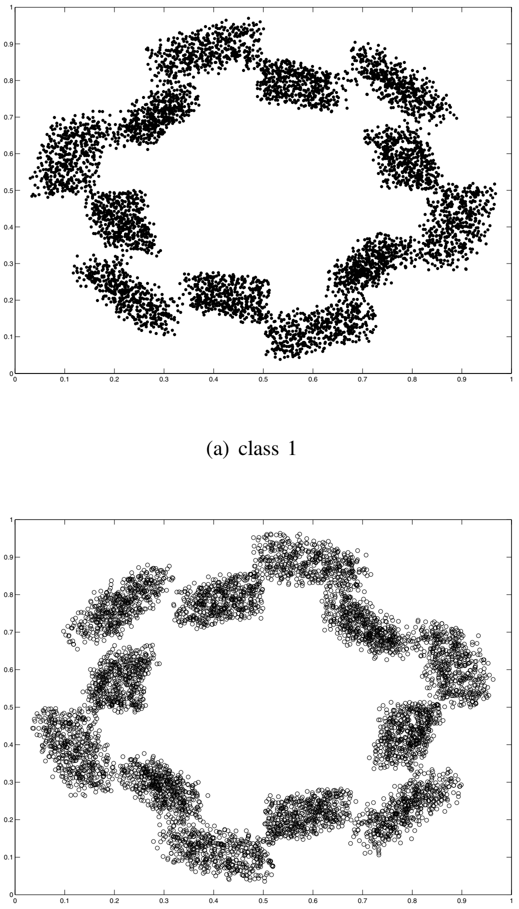
A. Artificial Data

T_1	T_1	$iniSize$	$iniDV$	mc	k_1	k_2	k_3
6	4	10	0.02	4	1.5	0.5	1.5

TABLE II

PARAMETER SETTINGS OF THE EXPERIMENT BASED ON ARTIFICIAL DATA

The artificial data set contains 12000 antigens in 2-dimensional unit square. The antigens are averagely divided into two classes which are highly not linearly separable(see Fig. 5). Our objective is to obtain an antibody population with controlled size that can correctly classify and represent the topology of original antigens in each class. The parameter settings are listed in Table.II, where the $iniSize$ indicates the initial size of general antibody population; the $iniDV$ represents the initial danger value of antigens. The stop criterion is defined as over 30000 generations(a quarter of antigen population size) there is no antibody stimulated.



(a) class 1

(b) class 2

Fig. 5. The antigen population. Left: class 1 antigens; right: class 2 antigens. Each class contains 9000 antigens. The two classes are highly not linear separable.

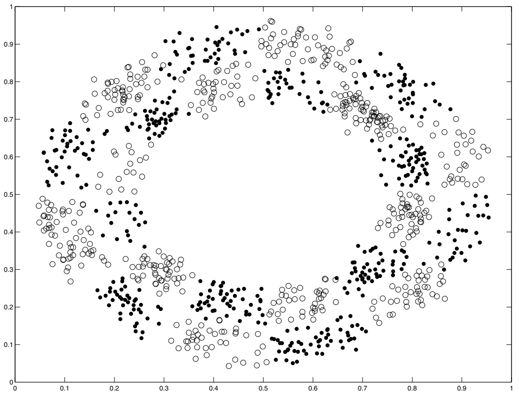


Fig. 6. The final memory antibody population. The dots represent class 1 antibodies; the circles represent class 2 antibodies.

Fig. 6 shows the final memory antibody population. The learning process lasts 486965 generations. The final memory

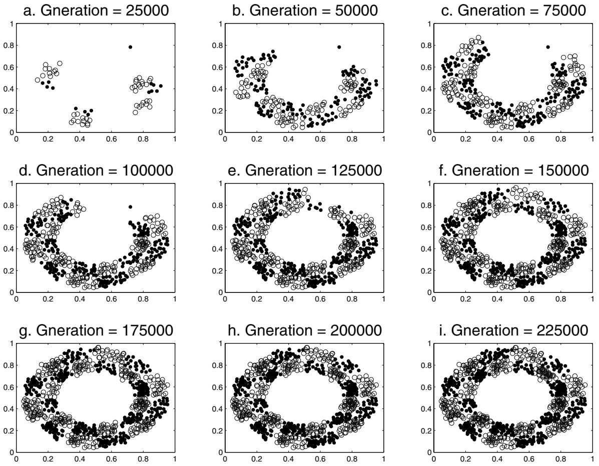
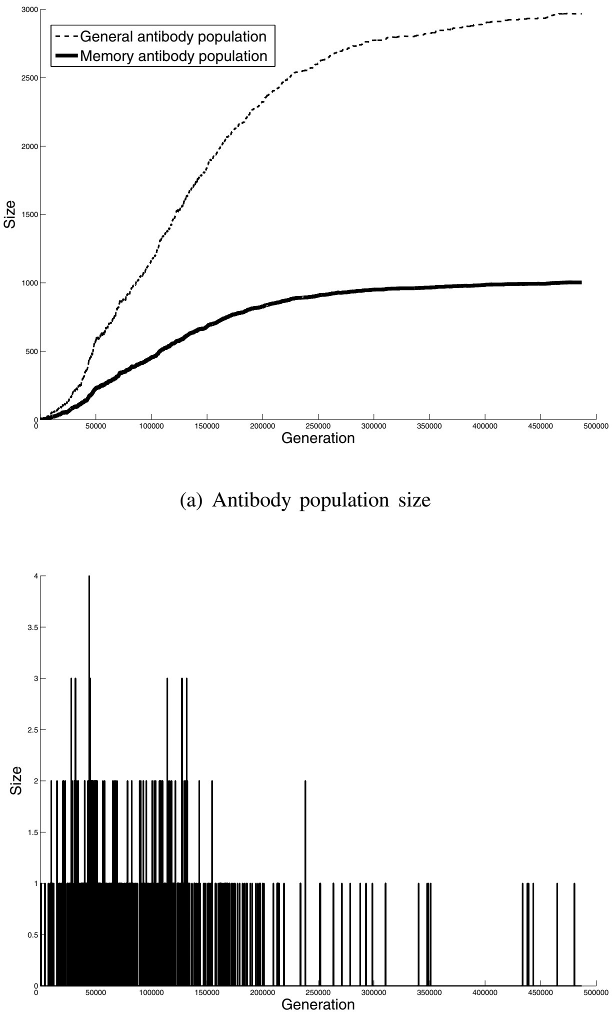


Fig. 7. The memory antibody population in early phases. The dots represent class 1 antibodies; the circles represent class 2 antibodies.

antibody population contains 1003 memory antibodies, among which 479 antibodies belong to class 1 and 524 antibodies belong to class 2; hence the compression ratio is 8.36%. From Fig6 we can find that the evolved antibodies can well represent the areas in which both class of original antigens reside, and that the boundary of closer different classes is clear. In fact, in terms of inner-class antigens, the proposed algorithm works as 'data compressor'; in terms of inter-class, the proposed algorithm plays role as a cluster.

We use the original data set to test the classification performance of our algorithm. The final correct classification rate is 88.83%. considering that the data set is highly not linear separable and the quantity of antigens which reside close to overlapping areas is considerable(see Fig. 5), this performance is acceptable.

Fig.7 shows the memory antibody population in former 225000 generations. The algorithm behaves as incremental learning: gradually stimulated by different antigens, the randomly initialized antibodies undergo clonal selection and suppression, eventually grows into matured antibodies. As shown in Fig.7 and Fig.8(a), the learning process can be divided into two distinct phases: the shaping phase and the maturating phase. At the former 250000 generations, the memory antibody population is gradually shaped as the rough topology of original antigens. The population increases fast in this phase. When the shaping is finished, the population enters the maturating phase. The maturating lasts 200000 generations in which the population size is increases slowly. Fig.8(b) shows the number of stimulated antibodies in different generations, from which we can find that the stimulation of antigens to antibodies is decreases along with the decreasing of danger value. At the former shaping phase, the danger value of antigen is relative large, there is more antibodies stimulated by danger zones, both the clonal selection and antibody suppression are frequent. The general topology of antibody population is formed in this phase. At the maturating phase, the danger value of antigen is small, there is less antibodies stimulated, so the clonal selection and antibody suppression is sparse. The diversity of antibody number in different areas is formed in this phase.



(a) Antibody population size

(b) Stimulated antibodies size

Fig. 8. The size of memory antibody population and stimulated antibodies during the learning process. The sampling frequency is 50 generations.

B. Real Problem

T_1	T_1	$iniSize$	$iniDV$	mc	k_1	k_2	k_3
6	4	100	1.5	3	0.08	3.6	5

TABLE III

PARAMETER SETTINGS USED IN EXPERIMENT BASED ON PIMA INDIANS DIABETES DATA SET

The follow experiment is based on Wisconsin Breast Cancer Database taken from the University of California at Irvine(UCI) Machine Learning Repository [11]. The original

Method	Reported accuracy(%)
C4.5 [5]	94.74
RIAC [6]	94.99
LDA [7]	96.80
NEFCLASS [8]	95.06
Optimized-LVQ [9]	96.70
Big-LVQ [9]	96.80
AIRS [9]	97.20
Supervised fuzzy clustering [10]	95.57

TABLE IV

PREVIOUS RESULTS ON BREAST CANCER DIAGNOSIS PROBLEM.

database contains 699 instances, each instance has 9 numeric-valued attributes. Since there are 16 instances that contain missing attribute values, we only use the rest 683 instances for our experiment. The instances are divided into 2 classes: class 0(tested benign) contains 444(65.0%) instances; class 1(tested malignant) contains 239(35.0%) instances. We apply 10-fold cross-validation for 20 times. In each time, the mean classification accuracy on both training sets and validating sets are calculated, then the final accuracy is obtained by averaging all the 20 results. The attributes are normalized in the unitary hypercube $[0, 1]^9$ using the min-max normalization. Table III lists the parameter settings used in this experiment.

The breast cancer diagnosis is a widely used benchmark problem among machine learning community, and several previous results have been reported. Some well-known methods and their results are listed in Table IV. These methods are all use 10-fold cross-validation which is the same setting used in our experiment. Although there are some other studys that also attain well performance, they used different validation settings and are ignored in Table IV.

Table V summarizes the result of our experiment. The overall average accuracy on training set is 97.46%; and the overall average accuracy on validation set is 96.84%. It turns out from Table V that the obtained memory antibodies can well represent the original antigens. Comparing with several previous results on this dataset, our algorithm exhibits compititive classification capacity.

	worst	best	mean	std.
Training set	97.20%	98.10%	**97.46%**	6.1e-4
Validation set	96.49%	97.66%	**96.84%**	2.3e-3

TABLE V

CLASSIFICATION ACCURACY OF EXPERIMENT BASED ON WISCONSIN BREAST CANCER DATABASE

V. CONCLUSION

An adaptive learning immune algorithm is proposed in this paper. Our method is based on the essential elements of danger theory, which is a newborn promising theoretical immunology model. We evaluate our method through several experiments. Primary results show that our method exhibits strong capacity in online two class classification. Most of the work in this paper is experimental, so the next step will be a thorough theoretical study. We plan to analyze the correlation between parameters and to what degree does each parameter affect the classification performance, and to study the rules of how to choose parameter settings to obtain an optimal performance.

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