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Adaptation of learning antigens by gene recombination in the immune system

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Abstract

The immune system is investigated as a parallel learning machine. The model is described using the perceptron and is analysed using the techniques of statistical mechanics. The relationship between gene recombination and capacity of learning antigens is considered. Although it is known that the immune system increases antibody diversity through gene recombination, our analysis shows that the total number of antigens learnt by the immune system is not affected by gene recombination. However, we find that gene recombination is effective in the adaptability of learning antigens. Our analysis is in good agreement with results of numerical simulations.

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1. Introduction

In order to recognize all unknown antigens, many varieties of antibodies exist in the immune system. It is known that this diversity of antibodies in the immune system is increased by gene recombination. There is no gene in the immune system coding for the whole of an antibody; only the parts making up an antibody are coded. An antibody molecule consists of a constant (C) region common to all antibodies and a variable (V) region, which is unique to each antibody. Furthermore, there are two or three families of the V-region gene. Gene segments are chosen from each family, and one antibody gene is formed [1].

It is believed that this gene recombination of antibody V-region genes evolved from intact V-region genes [2]. Since these intact genes are formed by an interaction with antigens, the immune system is considered to be a learning machine in the evolutionary process. Therefore, it is interesting to consider the effect that recombination has on the performance of the learning machine. How does the storage capacity of learning antigens increase by antibody diversity? Do not other effects of recombination exist? In order to answer these questions, we describe a simple model incorporating gene recombination and analyse the relationship

between gene recombination and the capacity of learning antigens using the techniques of statistical mechanics.

2. Model of the immune system incorporating gene recombination

There are two kinds of research using models for the immune system, in which the antibody diversity is investigated: formal research based on probability theory (see, e.g., [3, 4]), and research based on computer simulation using methods such as the genetic algorithm (see, e.g., [5, 6]). Most research using models which incorporate recombination is based on computer simulations. Although many models have been proposed, there is no research on the relationship between antibody diversity and gene recombination using a formal model (for a review, see [7]).

2.1. Description of the antibody incorporating gene recombination

Our study is based on a model of Farmer *et al* [8], in which strings of binary bits, 0 and 1, are used to represent both molecules and genes. The patterns of the bits represent the shapes of molecules. Same length bit strings represent antigens and antibodies. The number of complementary bits at corresponding positions represents the affinity between an antibody and an antigen. When the affinity exceeds a certain threshold it is assumed that the antibody has recognized the antigen.

We reformulate the above model. If 0 bits are replaced with -1 bits and the constant term and multiplied constant factor are ignored, the affinity M_μ^ε between the μth antibody J_i^μ and εth antigen ξ_i^ε is written as

$$M_\mu^\varepsilon = \sum_{j=1}^{l} J_j^\mu \xi_j^\varepsilon \tag{1}$$

where l is the length of the antibody and the antigen. Note that since affinity was originally defined by the number of complementary bits, the right-hand side of (1) requires a negative sign. However, for the subject considered in this paper, both definitions, positive and negative, lead to the same result.

Similar to Perelson *et al* [5], we introduce a gene recombination mechanism. Each antibody consists of segments chosen from two gene families. In this study, we assume that the two families are of the same size m and that the two segments are of the same length $l/2$, each comprising half of the antibody.

If recombination is incorporated, affinity (1) is replaced by

$$M_{\mu\nu}^\varepsilon = \sum_{i=1}^{l/2} I_i^\mu \xi_i^\varepsilon + \sum_{j=l/2+1}^{l} J_j^\nu \xi_j^\varepsilon \tag{2}$$

where I_i^μ and J_j^ν are the μth and νth gene segments selected from each gene family.

2.2. The simple perceptron for the antibody

Equation (1) can be considered to be a perceptron-type neural network model [9]. The simple perceptron is characterized as follows. The p input patterns correspond to a $p \times l$ matrix

$\xi = \left\{\xi_j^\varepsilon \pm 1, \varepsilon = 1, \ldots, p;\ j = 1, \ldots, l\right\}$. A set of couplings J is a vector with l components J_j normalized by

$$\sum_{j=1}^{l} (J_i)^2 = l. \tag{3}$$

For the εth pattern, an output of the perceptron is given by

$$O^\varepsilon = \operatorname{sgn}\left(\sum_{j=1}^{l} J_j \xi_j^\varepsilon\right) \tag{4}$$

which takes values ± 1. The perceptron learns by changing the couplings J so that this output vector O^ε agrees with a target vector $T^\varepsilon (= \pm 1)$. On the basis of geometrical consideration Cover found that the storage capacity of one perceptron is twice the number of couplings, $2l$ [10].

The condition that the output vector O^ε agrees with the target vector T^ε, is written as

$$T^\varepsilon \sum_{j=1}^{l} J_j \xi_j^\varepsilon \geqslant 0. \tag{5}$$

Gardner calculated the storage capacity based on the condition generalized inequality (5), and has also found the same result as did Cover [11].

The simulation has been used in many studies with a genetic algorithm (see, e.g., [5, 6]). Comparing the perceptron with the genetic algorithm, although the dynamical properties such as the learning process differ, the statical properties such as the maximum capacity of learning are similar. We are interested in the maximum capacity of learning, but analytical consideration is difficult for the genetic algorithm.

2.3. Description of the immune system using the perceptron

We describe an antibody using the perceptron. For the immune system which does not incorporate recombination, an output of the μth antibody for the εth antigen is given by

$$O_\mu^\varepsilon = \operatorname{sgn}\left(M_\mu^\varepsilon\right) \tag{6}$$

with

$$\sum_{j=1}^{l} \left(J_i^\mu\right)^2 = l \qquad \text{for all} \quad \mu = 1, \ldots, m \tag{7}$$

where M_μ^ε is the affinity defined by (1). We call this system the *parallel* (P) system in this paper.

On the other hand, for the immune system with gene recombination, an output of the $\mu\nu$th antibody for the εth antigen is given by

$$O_{\mu\nu}^\varepsilon = \operatorname{sgn}\left(M_{\mu\nu}^\varepsilon\right) \tag{8}$$

with

$$\sum_{i=1}^{l/2} \left(I_i^\mu\right)^2 = \frac{l}{2} \qquad \sum_{j=l/2+1}^{l} \left(J_j^\nu\right)^2 = \frac{l}{2} \qquad \text{for all} \quad \mu, \nu = 1, \ldots, m \tag{9}$$

where $M_{\mu\nu}^\varepsilon$ is an affinity defined by (2). We call this system the *recombination* (R) system in this paper.

Throughout this paper we use N as the total gene length (i.e. the total system size) and l as one antibody gene length (i.e. one perceptron size). These N and l are related to the number m of segments in each family through

$$N = lm. \tag{10}$$

3. Calculation of the storage capacity

In this section, the storage capacity of the R-system is calculated, and for comparison, the storage capacity of the P-system is also calculated.

As mentioned previously, there are two methods in the analysis of the storage capacity of the perceptron [10, 11]. Although Cover's geometrical consideration is intuitive, it is difficult to extend it to the R-system. On the other hand, Gardner discussed this problem using the techniques of statistical mechanics [11].

In Gardner's method, inequality (5) is generalized by introducing the stability parameter κ as

$$\frac{1}{\sqrt{l}} T^{\varepsilon} \sum_{j=1}^{l} J_j \xi_j^{\varepsilon} \geqslant \kappa \tag{11}$$

where the couplings are normalized by $\sqrt{l}$. Increasing the stability parameter κ, the output of the perceptron would not be affected by the noise in the input. If a fractional volume of the space of couplings $\{J_i\}$ which fulfils inequality (11) can be defined, the storage capacity is calculable. In the present study, we employ this method of Gardner's.

When we analyse the statics of perceptron (4) using Gardner's method, each element of the target vector T^{ε} will be squared and $(T^{\varepsilon})^2 = 1$, i.e., either $T^{\varepsilon} = +1$ or -1. This shows that the choice of the target vector T^{ε} is arbitrary; however, the distribution for each ξ_i^{ε} has to be symmetrical about zero. We use the distribution defined by

$$\mathcal{P}\left(\xi_i^{\varepsilon}\right) = \tfrac{1}{2}\delta\left(\xi_i^{\varepsilon} - 1\right) + \tfrac{1}{2}\delta\left(\xi_i^{\varepsilon} + 1\right) \tag{12}$$

and assume $T^{\varepsilon} = +1$ for all ε. Therefore, the target vector T^{ε} does not appear in the following calculation.

3.1. Storage capacity of the R-system

For the R-system, the condition that all antigens are learnt by the immune system is written as

$$\frac{1}{\sqrt{N}} M_{\mu\nu}^{\varepsilon} \geqslant \frac{\kappa}{\sqrt{m}}. \tag{13}$$

In the analysis of the perceptron, the size l is assumed to be sufficiently large. However, in the immune system, although the antibody size is finite, m is assumed to be sufficiently large. Therefore, inequality (13) is renormalized by $\sqrt{m}$ $(=\sqrt{N/l})$.

We define the fractional volume of the space of solutions for the gene segments $\left\{I_i^{\mu}\right\}$ and $\left\{J_j^{\nu}\right\}$ which fulfils condition (13) as

$$V = \frac{1}{V^0} \int \prod_{i,\mu} \mathrm{d}I_i^{\mu}\, \delta\left(\sum_{i=1}^{l/2} \left(I_i^{\mu}\right)^2 - \frac{l}{2}\right) \int \prod_{j,\nu} \mathrm{d}J_j^{\nu}\, \delta\left(\sum_{j=l/2+1}^{l} \left(J_j^{\nu}\right)^2 - \frac{l}{2}\right) \times \prod_{\mu\nu} \left[\prod_{\varepsilon(\mu\nu)} \theta\left(\frac{1}{\sqrt{N}} \sum_{i=1}^{l/2} I_i^{\mu} \xi_i^{\varepsilon(\mu\nu)} + \frac{1}{\sqrt{N}} \sum_{j=l/2+1}^{l} J_j^{\nu} \xi_j^{\varepsilon(\mu\nu)} - \frac{\kappa}{\sqrt{m}}\right)\right] \tag{14}$$

$$V^0 = \int \prod_{i,\mu} \mathrm{d}I_i^\mu \delta \left(\sum_{j=1}^{l/2} \left(I_i^\mu\right)^2 - \frac{l}{2} \right) \int \prod_{j,\nu} \mathrm{d}J_j^\nu \delta \left(\sum_{j=l/2+1}^{l} \left(J_j^\nu\right)^2 - \frac{l}{2} \right) \tag{15}$$

where $\varepsilon(\mu\nu)$ is the index for the patterns learnt by an antibody constructed from μth and νth gene segments. The stability parameter κ in (14) appears to be a threshold parameter. Since we previously assumed $T_\varepsilon = +1$ for all ε, the difference between the threshold and the stability parameters vanishes.

We set $p_{\mu\nu}$ as the number of patterns learnt by the $\mu\nu$th antibody, i.e. $\varepsilon(\mu\nu) = \{\varepsilon(\mu\nu)_i, i = 1, \ldots, p_{\mu\nu}\}$, and assume that there is no intersection in these pattern sets,

$$\{\varepsilon(\mu\nu)_i\} \cap \{\varepsilon(\delta\gamma)_j\} = \emptyset \qquad \mu \neq \nu \quad \text{or} \quad \delta \neq \gamma. \tag{16}$$

This means that although one antibody recognizes two or more antigens, one antigen is recognized by only one of the antibodies. Since one antigen realistically can be recognized by two or more antibodies, the above assumption is unnatural. When the left-hand side of (16) is not $\emptyset$, two cases are expected in the result of the storage capacity calculation. One case is that the combination of antigens and antibodies will be optimized and the total storage capacity will increase. The other case is that one antigen is learnt from two or more antibodies and the total storage capacity will decrease. Since we are interested in the maximum capacity of learning, we consider (14) under condition (16). Although the optimization in the combination of antigens and antibodies is an interesting problem, it is not considered here and is a future issue.

We perform calculations by the replica method [12],

$$\langle\langle \log V \rangle\rangle = \lim_{n\to 0} \frac{\langle\langle V^n \rangle\rangle - 1}{n} \tag{17}$$

where $\langle\langle \cdots \rangle\rangle$ indicates the average over the quenched distribution of patterns $\left\{\xi_i^{\varepsilon(\mu\nu)}\right\}$. We introduce order parameters $q_\mu^{\alpha\beta}$ and $r_\nu^{\alpha\beta}$ as

$$q_\mu^{\alpha\beta} = \frac{2}{l} \sum_{i=1}^{l/2} I_{i,\mu}^\alpha I_{i,\mu}^\beta \qquad r_\nu^{\alpha\beta} = \frac{2}{l} \sum_{j=l/2+1}^{l} J_{j,\nu}^\alpha J_{j,\nu}^\beta \tag{18}$$

where α and β $(=1, \ldots, n)$ are replica indices. In the calculations, we assume replica symmetry,

$$q_\mu^{\alpha\beta} \to q_\mu \qquad r_\nu^{\alpha\beta} \to r_\nu. \tag{19}$$

By a standard procedure (see, e.g., [13]), we find

$$\frac{\langle\langle \log V \rangle\rangle}{N} = \operatorname*{extr}_{\{q\},\{r\}} \frac{G}{n} \tag{20}$$

where G is represented by

$$\begin{aligned} \frac{1}{n} G(\{q_\mu\}, \{r_\nu\}) = {} & \sum_{\mu\nu} \alpha_{\mu\nu} \int \mathrm{D}y \log H \left(\frac{\kappa + y\sqrt{(q_\mu + r_\nu)/2}}{\sqrt{1 - (q_\mu + r_\nu)/2}} \right) \\ & + \frac{1}{2m} \sum_\mu \left[\frac{1}{2} \log(1 - q_\mu) + \frac{1}{2(1 - q_\mu)} \right] \\ & + \frac{1}{2m} \sum_\nu \left[\frac{1}{2} \log(1 - r_\nu) + \frac{1}{2(1 - r_\nu)} \right] \end{aligned} \tag{21}$$

$$\mathrm{D}y = \frac{\exp(-y^2/2)}{\sqrt{2\pi}} \mathrm{d}y \qquad H(x) = \int_x^\infty \mathrm{D}y \tag{22}$$

and $\alpha_{\mu\nu}$ is the storage ratio, $\alpha_{\mu\nu} = p_{\mu\nu}/N$. We derive the saddle point equations, $\partial G/\partial q_\mu = 0$ and $\partial G/\partial r_\nu = 0$, from (21),

$$\sum_{\nu} \frac{\alpha_{\mu\nu}}{[1-(q_\mu+r_\nu)/2]^2} \int_{-\kappa}^{\infty} \mathrm{D}y(\kappa+y)^2 = \frac{1}{m(1-q_\mu)^2} \tag{23}$$

$$\sum_{\mu} \frac{\alpha_{\mu\nu}}{[1-(q_\mu+r_\nu)/2]^2} \int_{-\kappa}^{\infty} \mathrm{D}y(\kappa+y)^2 = \frac{1}{m(1-r_\nu)^2}. \tag{24}$$

According to Gardner's consideration [11], the maximum storage capacity is determined by taking the limits $q_\mu \to 1$ and $r_\nu \to 1$ in (23) and (24). However, if these limits are not taken simultaneously, either (23) or (24) will diverge to infinity. Taking the limits simultaneously, we find

$$\sum_{\nu} \alpha_{\mu\nu} = \left[m \int_{-\kappa}^{\infty} \mathrm{D}y(\kappa+y)^2 \right]^{-1} \tag{25}$$

$$\sum_{\mu} \alpha_{\mu\nu} = \left[m \int_{-\kappa}^{\infty} \mathrm{D}y(\kappa+y)^2 \right]^{-1}. \tag{26}$$

Furthermore, taking the limit $\kappa \to 0$ in (25) and (26) gives rise to

$$\sum_{\nu} \alpha_{\mu\nu} = \frac{2}{m} \qquad \sum_{\mu} \alpha_{\mu\nu} = \frac{2}{m}. \tag{27}$$

Therefore, the total storage ratio of the entire R-system is given by

$$\sum_{\mu\nu} \alpha_{\mu\nu} = \sum_{\mu} \left(\sum_{\nu} \alpha_{\mu\nu} \right) = \sum_{\mu} \frac{2}{m} = 2. \tag{28}$$

3.2. Storage capacity of the P-system

On the other hand, in the calculation for the P-system, we assume that there is one family and the segment length is equal to the antibody length l. The storage ratio of one antibody is

$$\alpha_\mu = \frac{p_\mu}{N} = \frac{2l}{N} = \frac{2}{m}. \tag{29}$$

Since antibodies do not interact with each other, the total storage ratio of the entire P-system is given by

$$\sum_{\mu} \alpha_\mu = 2. \tag{30}$$

Therefore, the total storage capacity is the same in the R-system and P-system.

4. Adaptability of learning antigens

Let us write (27) in the matrix form

$$MA = 0 \tag{31}$$

where A is a (m^2+1)-dimensional vector represented by $A = {}^t(\alpha_{11}, \alpha_{12}, \ldots, \alpha_{mm-1}, \alpha_{mm}, 1)$ and M is a $2m \times (m^2+1)$ matrix. The following example is that of matrix M for the case of $m = 3$:

$$M = \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & -2/3 \\ 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 & 0 & -2/3 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & -2/3 \\ 1 & 0 & 0 & 1 & 0 & 0 & 1 & 0 & 0 & -2/3 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 & 1 & 0 & -2/3 \\ 0 & 0 & 1 & 0 & 0 & 1 & 0 & 0 & 1 & -2/3 \end{pmatrix}. \tag{32}$$

Since the rank of matrix M is $2m-1$ and the number of storage ratios $\alpha_{\mu\nu}$ is m^2, the number of linear independent solutions of (31) is given by

$$m^2 - \operatorname{rank} M = m^2 - (2m-1) = (m-1)^2. \tag{33}$$

Therefore, $(m-1)^2$ storage ratios of m^2 are arbitrary under the condition $\alpha_{\mu\nu} \geqslant 0$, and take different values. The other storage ratios are not arbitrary but take different values. When comparing the number of arbitrary storage ratios with the number of all storage ratios, we find

$$\lim_{m\to\infty} \frac{(m-1)^2}{m^2} = 1. \tag{34}$$

Therefore, when the number of segments belonging to one gene family m is sufficiently large, almost all antibodies are arbitrary regarding the number of antigens which can be learnt. It is considered that the R-system has adaptability in the storage capacity of learning antigens as compared to the P-system.

5. Consideration for the finite-size antibody

In the preceding calculation for the P-system, the perceptron size l was assumed to be sufficiently large. However, the antibody gene length is finite. On the basis of geometrical consideration, Cover calculated the storage capacity of the finite-size perceptron [10]. In the l-dimensional space, the probability P that p patterns can be discriminated into two groups is

$$P(l, p) = 2^{1-p} \sum_{k=0}^{l-1} \binom{p-1}{k} \tag{35}$$

where (:) is the binomial coefficient. In particular, in the limit $l \to \infty$, (35) becomes the step function that takes the value 1 if $p \leqslant 2l$ and zero otherwise. Therefore, $p = 2l$ is the maximum capacity of the storage patterns.

For the P-system, the storage capacity for each perceptron can be evaluated. We set $\hat{p}$ as the total number of learnt patterns and $\hat{p}_\mu$ as the number of patterns assigned to each perceptron, that is,

$$\hat{p} = \sum_{\mu=1}^{m} \hat{p}_\mu. \tag{36}$$

We assume that when all perceptrons have learnt the assigned patterns, the entire system has learnt all the patterns. Therefore, the probability P_{P} that the P-system will learn $\hat{p}$ patterns is given by

$$P_{\mathrm{P}}(N, m, \hat{p}_1, \ldots, \hat{p}_\mu) = \prod_{\mu=1}^{m} P(N/m, \hat{p}_\mu). \tag{37}$$

In particular, when all $\hat{p}_\mu$ are equal to $\hat{p}/m$, (37) takes the highest probability for $\hat{p} = 2N$. This is because $P(N/m, \hat{p}_\mu)$ behaves as a linear function of $\hat{p}_\mu$ near $\hat{p}_\mu = 2N/m$. Then (37) is rewritten as

$$P_{\mathrm{P}}(N, m, \hat{p}/m, \ldots, \hat{p}/m) = P^m(N/m, \hat{p}/m). \tag{38}$$

Figure 1 shows the curves for the probability $P_{\mathrm{P}}(N, m, \hat{p}/m, \ldots, \hat{p}/m)$, (38), for various m. When m becomes large, the maximum storage capacity of the P-system decreases from $2N$. On the other hand, for the R-system, it is difficult to apply geometrical analysis to the finite-size antibodies.

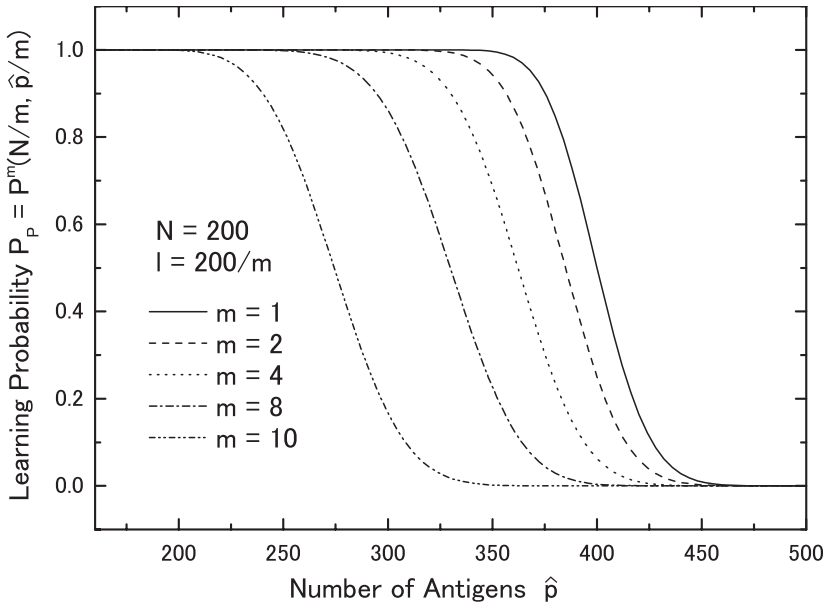

Figure 1. Learning probability of the P-system, P_P. The number of segments in each family is $m = 2$, 4, 6, 8 and 10; the length of the entire system is $N = 200$; the length of an antibody is $l = 200/m$.

6. Numerical simulations

In this section, the correctness of the preceding analysis is checked by numerical simulations. The learning rule used in the simulation for the P-system is

$$J_i^\mu(t + \Delta t) = J_i^\mu(t) + \eta T^\varepsilon \xi_i^\varepsilon \tag{39}$$

when $T^\varepsilon M_\mu^\varepsilon < \kappa$, where η is the learning rate, and the couplings are not changed when $T^\varepsilon M_\mu^\varepsilon \geqslant \kappa$. This rule is known as the perceptron learning rule [9]. For the R-system, we extend (39) and the learning rule is given by

$$\begin{aligned} I_i^\mu(t + \Delta t) &= I_i^\mu(t) + \eta T^\varepsilon \xi_i^\varepsilon \\ J_j^\nu(t + \Delta t) &= J_j^\nu(t) + \eta T^\varepsilon \xi_j^\varepsilon \end{aligned} \tag{40}$$

when $T^\varepsilon M_{\mu\nu}^\varepsilon < \kappa$ and the couplings are not changed when $T^\varepsilon M_{\mu\nu}^\varepsilon \geqslant \kappa$. In the simulations, we set $\eta = 0.0001$ for both systems.

The simulation procedure for the P-system (or for the R-system) is as follows:

(a) Randomly generate the couplings J_i^μ (or I_i^μ and J_j^ν) which satisfy condition (7) (or (9)).
(b) Randomly generate the antigens ξ^ε according to distribution (12).
(c) Assign each antigen to one of the antibodies.
(d) Choose one antigen and compute affinity (1) (or (2)) with the assigned antibody.
(e) Change the couplings according to learning rule (39) (or (40)).
(f) Repeat (d) and (e) for all antigens.
(g) Return to (d) and iterate this procedure, if there remains an antigen not learnt.

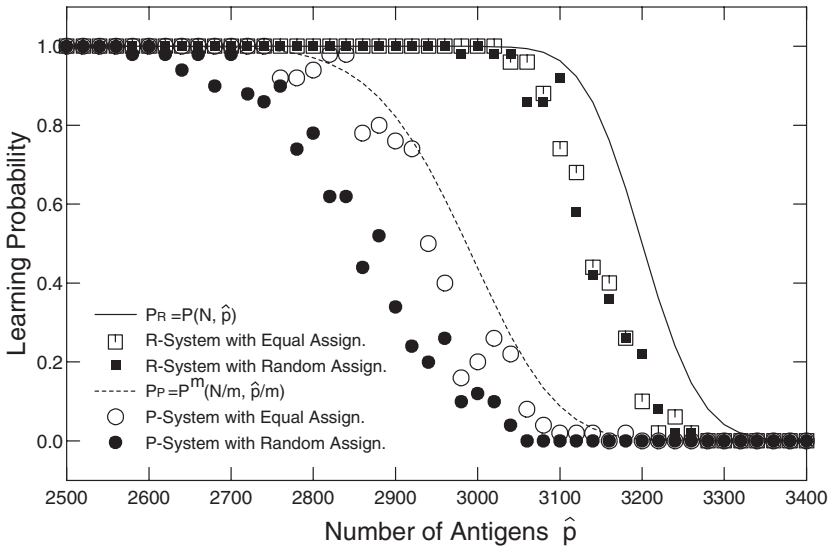

Figure 2. Results of the numerical simulations for the learning probability against the number of antigens. The length of an antibody is $l = 200$; the length of a segment is 100; the number of segments in each family is $m = 8$.

Each trial is terminated after 5000 iterations and the number of trials in which all antigens are learnt are counted as successes. We performed 50 trials for a fixed $\hat{p}$. Then, we defined the learning probability for $\hat{p}$ as

$$\text{the learning probability} = \frac{\text{number of successes}}{\text{number of trials } (=50)}. \tag{41}$$

Figure 2 shows the results of the learning probability against the number of antigens. Figure 3 shows the average number of learnt antigens for various m. We performed simulations for the case where the number of antigens assigned to each antibody, $\hat{p}_\mu$ or $\hat{p}_{\mu\nu}$, is random, and for the case where it is equal. Random assignment yields a somewhat realistic simulation in terms of learning an antigen which encounters an antibody at random.

For the R-system, figure 3 shows that the average number of learnt antigens is close to $2N$ and it is independent of m. Therefore, we anticipate that the entire system has similar properties to one perceptron with size N. Then, the probability P_{R} that the R-system will learn $\hat{p}$ patterns is assumed to be

$$P_{\mathrm{R}}\,(N, m, \hat{p}) = P(N, \hat{p}). \tag{42}$$

Although m becomes large, the maximum storage capacity of the R-system is still $2N$. Figures 2 and 3 show good agreement with (42) for both random and equal assignments. The storage capacity of each antibody can be arbitrary and they need not be the same.

On the other hand, for the P-system, the simulation for equal assignment shows agreement with the probability P_{P}, (38). However, the simulation of random assignment yields a lower probability than that of equal assignment. Since an antibody assigned a greater number of antigens has a low probability of learning, the total storage capacity will decrease. Therefore, gene recombination is effective in increasing the adaptability to learning antigens.

Figure 4 shows the results of the simulations in which all gene lengths of the entire system were the same, and the length of the antibody gene was changed. All simulations show good agreement with (42) in that the storage capacity is independent of m and proportional to N.

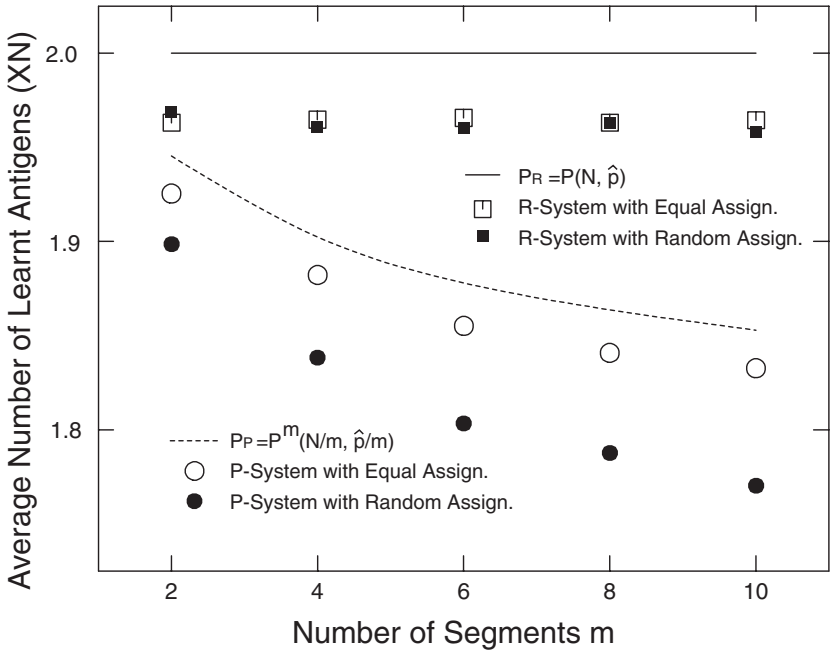

Figure 3. Results of the numerical simulations for the average number of learnt antigens. The number of segments in each family is $m = 2$, 4, 6, 8 and 10; the length of an antibody is $l\ (=N/m) = 200$; the length of a segment is 100.

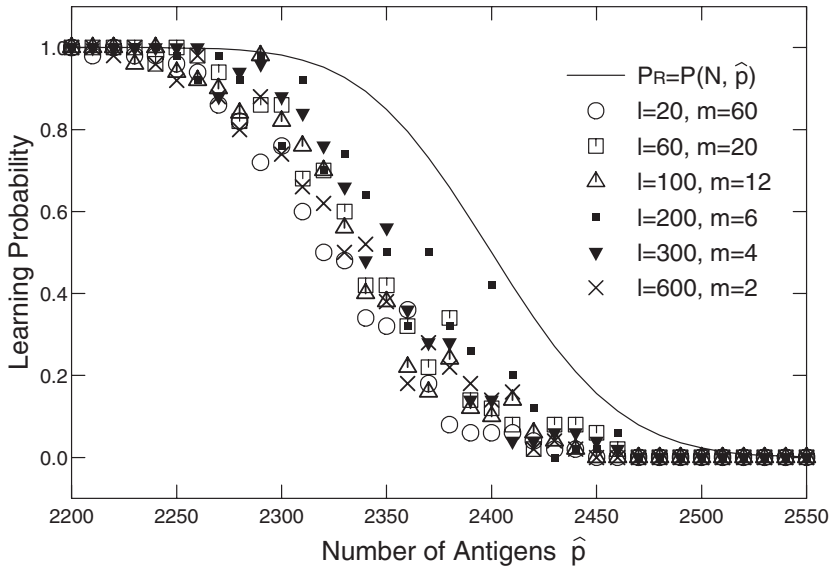

Figure 4. Results of the numerical simulations for the learning probability against the number of antigens. All lengths of the entire system are the same, $N = 1600$; the length of an antibody varies between $l = 20$, 60, 100, 200, 300 and 600.

7. Conclusion

The model discussed in this paper does not necessarily express the natural immune system correctly, since the model is greatly simplified. However, compared with the artificial neural network model, it is of interest in the aspect of the system size and the adaptability of learnt patterns. In the neural network model, since the number of neurons can be sufficiently large, the system is stabilized and has robust properties such as noise tolerance. The simple perceptron can learn only linearly separable tasks. However, inseparable tasks are also learnable with a multilayer structure of neurons. In the immune system, the size of an antibody is finite and inaccuracy arises in learning. This will cause further performance degradation if the number of antibodies increases. Moreover, the multilayered structure cannot be incorporated. Therefore, we infer that, in the process of evolution, gene recombination is incorporated, by which the inaccuracy in learning decreases and adaptability increases.

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References

[1] Tonegawa S 1983 *Nature* **302** 575
[2] Janeway C A Jr 1993 *Sci. Am.* **269** (3) 72
[3] De Boer R J and Perelson A S 1993 *Proc. R. Soc.* B **252** 171
[4] Percus J K, Percus O E and Perelson A S 1993 *Proc. Natl Acad. Sci. USA* **90** 1691
[5] Perelson A S, Hightower R R and Forrest S 1996 *Res. Immunol.* **147** 202
[6] Takumi K and Hogeweg P 1998 *J. Theor. Biol.* **192** 309
[7] Perelson A S and Weisbuch G 1997 *Rev. Mod. Phys.* **69** 1219
[8] Farmer J D, Packard N H and Perelson A S 1986 *Physica* D **22** 187
[9] Minsky M L and Papert S A 1969 *Perceptrons* (Cambridge, MA: MIT Press)
[10] Cover T 1965 *IEEE Trans. Electron. Comput.* **14** 326
[11] Gardner E 1988 *J. Phys. A: Math. Gen.* **21** 257
[12] Mézard M, Parisi G and Virasoro M A 1987 *Spin Glass Theory and Beyond* (Singapore: World Scientific)
[13] Nishimori H 2001 *Statistical Physics of Spin Glasses and Information Processing* (Oxford: Oxford University Press)