

# An Antibody-Based Computing: An Application to Stable Marriage Problem

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## Abstract

Antibodies, among others, are important components of the immune system. This paper proposes using specific recognition capability exhibited by antibodies for computation, in particular, solving *stable marriage problem* which have been studied as combinatorial computational problems. Antibody-based computation is proposed by integrating the recognition capabilities of antibodies. The computation is carried out on an array form that is suitable not for only expressing stable marriage problems but for further integration to antibody microarrays.

## 1 Introduction

After Adelman pioneered DNA-based computing in his seminal work [1], many researches established that not only DNA but also other macro molecules could have computational capability comparable to DNA (e.g. [2]). Elowitz and Leibler even demonstrated that a genetic circuit may not be a dream [3,4]. Even synthetic multicellular systems have been recently studied [5], leading to synthetic biology. Possible drug production by engineering yeast [6] has given a great impact on the area. These new bio-engineering technologies have provided bioinformatics with not only new tools but systemic views.

On the other hand, post-genome era proved that sequence information of human genome alone is not sufficient, but higher knowledge of function must be revealed. Post-genome age naturally proceeds to study immune systems (as in [7]) focusing not only components such as antibodies and MHC but its systemic organization.

After the demonstration of DNA based computing by Adelman, protein based computing had been proposed by Hug and Schuler [2] and extended

by Balan and Krithivasan [8]. This paper, in a similar spirit of synthetic biology and system biology, tries to construct an information processing devices incorporating specific recognition capabilities of antibodies. Stable marriage problem [9, 10] is used as a benchmark problem for demonstrating an array format implementation of antibody-based computation.

## 2 Antibody-based Computing: An Introduction

One of the major components propelling the information processing of the immune system is the specific recognition of antigens. The immune system is capable of recognizing even artificially synthesized substances. Also, it can further classify substances into the self (those derived from the individual) and nonself. Among those bearing recognition capabilities, antibody is undoubtedly important. Further, antibodies have been studied in great detail not only in theoretical biology but in bio-engineering. Antibody-based computing directly focuses on the recognition capability and integrates it for problem solving including combinatorial problems.

### 2.1 Antibody-based computing and DNA-based computing

Similarly to the DNA-based computing, antibody-based computing utilizes complementary matching between macro molecules: antibodies. Since the computational capabilities that DNA-based computing could be inherited to antibody-based computing, we rather focus on the difference between them. Roughly said in the context of solving combinatorial problems, the difference may be clarified by the correspondence between a

complementary matching (as in *Marriage Theorem*) and a stable pairing based on preference (as in *Stable Marriage Problem*).

Affinity between antigens and antibodies can be measured and their intensities can be ordered (as formatted in an affinity matrix). That is, in contrast to **Matching**( $DNA1, DNA2$ )=1 (matched) 0 (not matched), **Affinity**( $Antigen1, Antibody2$ ) could vary from 0 (no agglutination) to 1 (highest agglutination). This difference would suggest that antibody-based computing could potentially implement error tolerance that could not be implemented on the DNA-based computing. The difference would further suggest that the antibody-based computing may be extended to a problem solver, if adaptive mechanism of the immune system realized by antibodies and their maintenance is also involved.

### 3 Solving a Combinatorial Problem

#### 3.1 Stable Marriage Problem

In a naive form, the problem assumes  $n$  men and  $n$  women with each member having preference lists to the members of opposite sex. A pair of a man  $M_i$  and a woman  $W_j$  is called a blocking pair if they are not pair in the current solution, but  $M_i$  prefers  $W_j$  to the current partner and  $W_j$  prefers  $M_i$  to the current partner as well. A matching between men and women with no such blocking pair is called *stable*.

Having stated the stable marriage problem, it would be natural to think of the algorithm for antibody-based computing. That is, the stable marriage problem (SMP) may be mapped to antigen-antibody reaction so that preference order of each person in SMP will be reflected in the affinity intensity between an antibody and an antigen. After antibodies and antigens are so arranged, the solution of SMP will emerge by observing concentration of the agglutination. It should be remarked that agglutination process could be any agglutination (not necessarily between antibodies and antigens) if their intensities are measurable and ordered.

#### 3.2 Mapping a stable marriage problem to antibody-based computing

As stated above, mapping a combinatorial

problem to antibody-based computing can be done by composing antigens-antibodies compounds corresponding to a problem entity. Antibodies and antigens for a compound corresponding to a particular individual will be determined by considering her (his) preference list over men (women).

Landshtainer's ABO blood group system [11] may be most familiar and yet simple example. His blood type system is based on antigens (as agglutinogen) on red blood cells and antibodies (as agglutinin) in the blood serum. **Table 1** shows agglutinogen and agglutinin of each blood type. Affinity between antibody and antigen is shown in **Table 2**. **Table 3** indicates the well-known incompatible transfusion among the blood type A, B, AB, and O.

**Table 1.** Landsteiner's ABO Blood Group System

Blood Type	A	B	AB	O
Antigen (agglutinogen)	A	B	A, B	None
Antobody (agglutinin)	$\beta$	$\alpha$	None	$\alpha, \beta$

**Table 2.** Affinity Matrix. Circle indicates that the antibody-antigen reaction would occur if the antibodies in the column meet with antigens in the row.

Antigen	A	B
Antibody		
$\alpha$ (anti-A)	○	
$\beta$ (anti-B)		○

**Table 3.** Agglutination when the blood type in the column is transfused with the blood type to the row. Circle indicates that the blood type of the column when transfused to that of the column would agglutinate.

Blood Type	A	B	AB	O
A		○		○
B	○			○
AB	○	○		⊙
O				

In this example, we map the relation the woman  $W_i$  (the man  $M_i$ ) prefers the man  $M_j$  (the woman  $W_j$ ) to other to the relation that if the blood of  $W_i$  ( $M_i$ ) would be agglutinate when the blood of  $M_j$  ( $W_j$ ) were transfused. That is, if the woman  $W_i$  prefers the man  $M_j$  most the blood type should be so assigned that the type for  $W_i$  comprises of antibody  $AbW_i$  and antigen  $AgW_i$ ; and that for  $M_j$  of antibody  $AbM_j$  and antigen  $AgM_j$  and the affinity  $\mathbf{Aff}(AbW_i, AgM_j)$  are highest.

For the trivial case when the preference lists of men and women are as in **Table 4**, simple assignment would suffice: a man to type A and another man to type B; for the woman who like a man with type A to type B and for another woman type A (**Fig. 1**). It should be noted that assignment to A for two men and to B for two women would not work, since the assignment does not reflect the preference of men and women.

In a nontrivial preference list shown in **Table 5**, one assignment would be type O to  $M_1$  and  $W_1$ , type A to  $M_2$ , and type B to  $W_2$  (**Fig. 2**) For other two preference lists (with the graph topologically different from those shown Figs. 1 and 2), it is not possible to map the blood type with the above correspondence, and other compounds should be synthesized for realizing the preference lists.

These examples suggest a scheme for synthesizing antigen-antibody compounds that realize mapping from given preference lists to the compounds. If the woman  $W_i$  prefers the man  $M_j$  to other men, the compound corresponding to  $W_i$  contains antibody  $AbW_i$  and the compound corresponding to  $M_j$  contains antigen  $AgM_j$  that satisfies  $\mathbf{Aff}(AbW_i, AgM_j)$  highest among other  $AgM_j$  ( $j=1\dots n$ ).

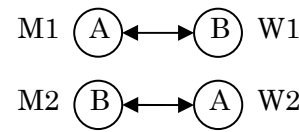
If  $M_j$  is the second in the preference list of  $W_i$ , then  $\mathbf{Aff}(AbW_i, AgM_j)$  must be second highest and so on.  $AgM_j$  must realize orders from women  $W_k$  other than  $W_i$ , hence the affinity  $\mathbf{Aff}(AbW_k, AgM_j)$  must realize the order accordingly. (If  $AgM_j$  alone cannot realize the order, then new antigen realizing the order must be added to the corresponding compound. In fact, the above example also suggests that compounds can be composed of a set of antigens and a set of antibodies.) Constraints for selecting antibodies and antigens for a compound corresponding to a person can be summed up as follows:

- $\mathbf{Aff}(AbW_i, AgM_j) > \mathbf{Aff}(AbW_i, AgM_k)$  if the woman  $W_i$  prefers  $M_j$  to  $M_k$  in her preference list for all  $W_i \in W$ , and for all distinct pairs  $M_j, M_k \in M$ ; and
- $\mathbf{Aff}(AbM_i, AgW_j) > \mathbf{Aff}(AbM_i, AgW_k)$  if the man  $M_i$  prefers  $W_j$  to  $W_k$  in his preference list for all  $M_i \in M$ , and for all distinct pairs  $W_j, W_k \in W$ .

**Table 4.** A trivial preference list for two by two stable marriage problem.

	M1	M2
W1	2	1
W2	2	1

	W1	W2
M1	2	1
M2	2	1

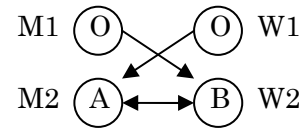


**Fig. 1.** A blood type assignment reflecting the preference

**Table 5.** A non-trivial preference list for two by two stable marriage problem.

	M1	M2
W1	1	2
W2	2	1

	W1	W2
M1	1	2
M2	2	1



**Fig. 2.** A blood type assignment reflecting the preference

### 3.3 Solving a stable marriage problem with an array format

An illustrative example with Landsteiner's blood group suggests the following algorithm to solve SMP with an array format. In the array, row  $i$  and column  $j$  correspond to the compound for man  $i$  (i.e.  $AbM_i$  and  $AgM_i$ ) and that for woman  $j$  (i.e.  $AbW_j$  and  $AgW_j$ ). In other word, at the cross-point  $ij$ , two antigen-antibody reactions between  $AbM_i$  and  $AgW_j$  (reflecting man  $i$ 's preference) and between  $AbW_j$  and  $AgM_i$  (reflecting

woman  $j$ 's preference) will take place.

Under the assumption that the concentration observed at each cross-point is proportional to both  $\mathbf{Aff}(AbM_i, AgW_j)$  and  $\mathbf{Aff}(AbW_j, AgM_i)$ , the array can find a stable matching by selecting one cross-point with highest concentration from each row and column. This matching is certainly stable one, for suppose otherwise there must be a blocking pair  $M_k$  and  $W_l$  such that  $\mathbf{Aff}(AbM_k, AgW_l) > \mathbf{Aff}(AbM_k, AgW_{p(M_k)})$  and  $\mathbf{Aff}(AbW_l, AgM_k) > \mathbf{Aff}(AbW_l, AgM_{p(W_l)})$  where  $p(M_k)$  denotes a partner of  $M_k$  in the current matching. Then both concentration at the cross-point  $kl$  is higher than those of  $kp(M_k)$  and those of  $lp(W_l)$  reflecting the affinities.

Although obtaining a stable matching shows some computational power, it can be solved in  $O(N^2)$  time where  $N$  is the size of men (and women). Gale and Shapley have invented a well-known algorithm for giving stable matchings for man-oriented matching or woman-sided one [9]. By further assuming that the concentration observed at a cross-point can reflect the amount of antibodies imposed, the array is capable of obtaining any stable matching in the array from the man-oriented (man optimal and woman pessimal) matching to the woman-oriented (woman optimal and man pessimal) one. By equally increasing all the antibodies  $AbM_i$  ( $i=1..n$ ) (or equivalently antigens  $AgW_j$   $j=1..n$ ), from a unit to  $\alpha$  the matching would become close to the man-oriented one. Similarly, increase of  $AbW_i$  ( $i=1..n$ ) will bias the matching towards the one of woman-oriented one. Since there are many variants of the stable marriage problem, which are NP-hard, devising the array for solving these problems is a challenging problem. Another challenge is to devise the array as a component of problem solver that can deal with not only a particular problem but with similar problems, as the immune system has done.

## 4 Conclusion

We have shown that antibodies, a macro molecule of the immune system, with a specific recognition capability can be used for computation as a macromolecule DNA is used for DNA computing. Focusing on a stable marriage problem, and extending ABO blood group system, it is shown that the antibody-based computation will be implemented on

an antibody microarray.

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