The Thirteenth International Symposium on Artificial Life and Robotics 2008(AROB 13th '08),
B-Con Plaza, Beppu, Oita, Japan, January 31-February 2, 2008

Antibody-Based Computing

Kouji Harada † and Yoshiteru Ishida ‡

† ‡ *Department of Knowledge-Based Information Engineering,*
Toyohashi University of Technology,
Tenpaku, Toyohashi, 441-8580, Japan
(Tel : 81-532-44-6885; Fax : 81-532-44-6873)
(Email address){† harada, ‡ ishida}@tutkie.tut.ac.jp

Abstract: An application of the antibody's flexible recognition (i.e. multi-reactivity) to antigenic epitopes to a combinatorial computing is just getting started. The present study discusses an antibody-based computation algorithm to solve a combinatorial problem: the stable marriage problem. The problem supposes n men and n women, and each person ranks all members of the opposite sex in a strict order of preference. Under a given preference lists, to detect all stable n couples including no affair pairs means to solve this problem. In a proposed algorithm, a man and a woman are replaced with an antigenic epitope and an antibody respectively and a man (woman)'s preference to a woman (man) is re-scaled as strength of a binding affinity between an epitope to the man and an antibody to the woman. Under these settings, we demonstrate how a parallel progression of immune reactions solve the stable marriage problem

Keywords: Antibody, Epitope, Affinity, DNA Computing, The stable marriage problem

I. INTRODUCTION

Nowadays, imaginative yet pragmatic parallel computing methods are developing, of which DNA computing by Adleman is distinguished. He operated DNA strands by typical biotechnological instruments, cataphoresis and applications of some enzymes, and he demonstrated being able to derive in parallel solution paths of Hamilton path problem [1].

One feature of DNA is the one-to-one binding of a single strand DNA and its complimentary strand enabling a certain type of combinatorial computing. In some sort of combinatorial problems represented by a directed graph, an arc does not associate with its weight. The most popular example is Hamilton path problem, to which DNA-computing scheme first applied. In those problems, DNA's one-to-one binding feature is well-suited to coding those problem settings. However, in the other type of combinatorial problems supposing a weighted arc between vertices (e.g. the stable marriage problem [2], representing weighted arcs by one-to-one binding-based biomaterials, such as DNA strands would not be easy and hence the representation would become unnatural.

Looking cautiously around objective world, we would notice there are biomaterials appropriate for representing a weighted arc between vertices. Those are "antibody'" and "antigenic epitope (or just epitope)". Because an antigenic epitope which is a binding partner of antibody is not always determined on one-to-one level, but rather a group level [3]. An antibody shows different binding affinity against different antigenic epitopes.

Hitherto, some seminal works discussing feasibility of the antibody-based computation have been presented [4][5][6]. The present work also discusses feasibility of an antibody-based parallel computing method. By way of example, we propose an algorithm for solving the stable marriage problem.

A proposed algorithm utilizes the difference of a binding affinity between an antibody and an antigenic epitope.

The stable marriage problem [2] can be expressed by a bipartite graph. An instance of the stable marriage problem involves n men and n women, and each person ranks all members of the opposite sex in strict order of preference. A matching M (which is n couples of a man and a woman) may have a so-called "blocking pair", in which a man "m" and a woman "w" are not matched together such that m prefers w to his current partner and w prefers m to her current partner. A particular matching not including any blocking pair is called "stable" matching. To seek all stable matchings under a given preference lists means to solve the problem.

In a proposed solution algorithm of the stable marriage problem, a man and a women are replaced with an antigenic epitope and an antibody respectively, and a man(woman)'s preference to a woman(man) is represented as a binding affinity between an antigenic epitope to the man and an antibody to the woman.

The present paper demonstrates a proposed algorithm is able to find in parallel all stable matchings in a given instance.

II. Antibody-Based Solution Algorithm of the Stable Marriage Problem

1. Representation of a Man and Woman by Immuno-Agents

In the setting of the stable marriage problem, a man group **m** and a woman group **w**,

m = {m*1*, m*2*, ……. , m*n*},
w = {w*1*, w*2*, ……….., w*n*}.

are given. Here, m*i* and w*j* represents *i* th man in the group **m** and j th woman in the group **w**, respectively.

The setting of the stable marriage problem is mapped to a biochemical system equipped with a set of antibodies and antigenic epitopes. Here a man and a woman are put into a couple of antigenic epitopes and a couple of antibodies, respectively. When an antigenic epitope and an antibody are respectively symbolized as "e" and "Ab", we define the *i* th man and *j* th woman as {e(i), e'(i)} and {Ab(j), Ab'(j)} respectively (Fig. 1).

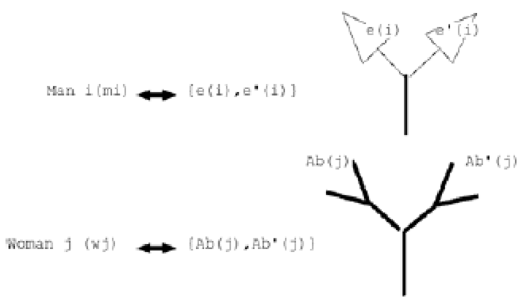

Fig. 1: Representation of a man and a woman by a couple of antigenic epitopes and a couple of antibodies.

Note that the set of the antibody and that of the epitope must be selected as they satisfy the previously given man and woman's preference lists. Concretely if m*i* ranks w*j* k th in the m*i*'s preference order, the selected antigenic epitipe e'(i) must satisfy ranking k th on the strength of the binding affinity to Ab'(j) (Table.1). Likewise, if w*i* ranks m*j* k th in the w*i*'s preference order, the selected antibody Ab(i) must satisfy ranking k th on the strength of the binding affinity to e(j) (Table.2). Also for any i,j (i,j=1 ….. n), let the strength of the binding affinity between Ab(i) and e'(j) or Ab'(i) and e(j) be zero.

Table.1: Correspondence between each man's preference to *n* different women and each epitope's binding affinity to *n* different antibodies

Preference (Affinity) \ Man (Antigen)	m*1* (e'(1))	…	m*i* (e'(i))	…
1	w*1* (Ab'(1))	…	…	…
2	w*4* (Ab'(4))	…	…	…
3	w*2* (Ab'(2))	…	…	…
⋮	…	…	…	…
k	…	…	W*k* (Ab'(j))	…
⋮	…	…	…	…
n	…	…	…	…

Table.2: Correspondence between each woman's preference to *n* different men and each antibody's binding affinity to *n* different epitopes

Preference (Affinity) \ Woman (Antigen)	w*1* (Ab(1))	…	w*i* (Ab(i))	…
1	m*1* (e(1))	…	…	…
2	m*4* (e(4))	…	…	…
3	m*2* (e(2))	…	…	…
⋮	…	…	…	…
k	…	…	m*j* (e(j))	…
⋮	…	…	…	…
n	…	…	…	…

2. Blocking Pair

If a matching *M* is to be stable, any two couples in *M* does not include a "blocking pair". This session proposes an immune reaction-based scheme to detect if a blocking pair exists between surveyed two couples. Our scheme is devised to be able to detect a blocking pair by a formation of an antibody-epitope complex. In the scheme, we have to arrange a definite layout of an antibody and an epitope corresponding to each man and woman in surveyed two couples. Taking two couples:(m*2*-w*4*, m*3*-w*1*) for example, we show our scheme to detect a blocking pair when w*4* and m*3* is an affair relationship. The first step is to prepare antibody-epitope pair corresponding to each couple and to arrange them in a certain layout. In Fig. 2(a), on the first couple: m*2*-w*4*, the epitope e(2) corresponding to m*2* who is not surveyed is grounded, and the antibody Ab(4) in {Ab(4), Ab'(4)} corresponding to the surveyed w*4* is binded chemically to the grounded epitope e(2). By the same token, on the second couple: m*3*-w*1*, the antibody Ab'(1) corresponding to w*1*, who is not surveyed is grounded and the eqitope e'(3) in {e(3), e'(3)} corresponding to the surveyed m*1* is binded chemically to the grounded antibody Ab'(1). If the m*4* and m*3* is an affair relationship, Ab(4) is likely to bind e(3) rather than the present binding partner e(2), at the same time e'(3) is likely to bind Ab'(4) rather than the present binding partner Ab'(1). Therefore, Ab(4) and e'(3) disengage themselves from their present binding partners: e(2) and Ab'(1), and they bind together then form an antibody-epitope complex: {Ab(4)-e(3), Ab'(4)-e'(3)} (Fig. 2(b)).

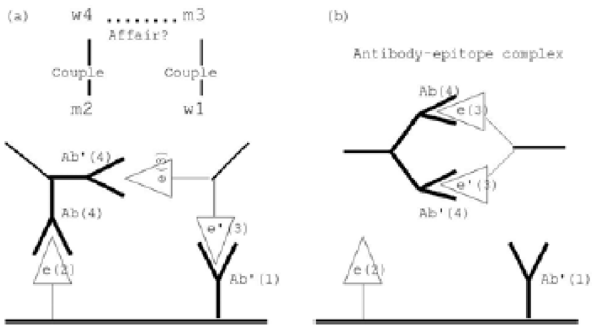

Fig. 2: (a) Arrangement of antibody-epitope pairs corresponding to the surveyed two couples: m*2*-w*4* and m*3*-w*1* to detect if a relationship between m*3* and w*4* is a blocking pair. (b) Formation of an antibody-epitope complex when a relationship of m*3* and w*4* is a blocking pair.

If the above-mentioned arrangement is applied to any two couples, we can easily know through detection of an antibody-epitope complex if the surveyed two couples has a blocking pair. In other words, if an immune complex is not detected, we can find the surveyed two couples is "stabl'".

3. Algorithm

This section explains an immune reaction-based algorithm of the stable marriage problem. As the problem supposes *n* persons to each sex, the total number of matching mounts to factorial of *n*. For a matching *M*, a choice of a surveyed couple is ${}_nC_2 \times 2$ patterns. The factor "2" considers two possible blocking pairs in two couples.

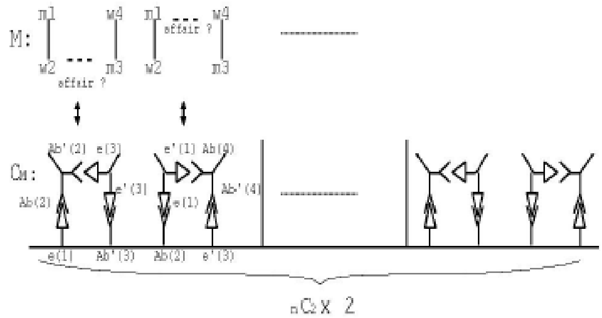

Fig. 3: ${}_nC_2 \times 2$ antigen-epitope pairs correspond to every combination of two couples in *M*, and they are arranged in a single horizontal row

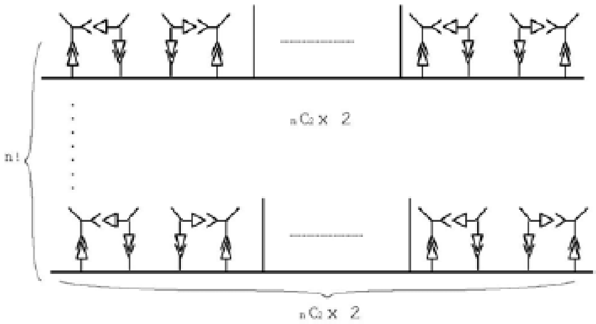

Fig. 4: All C_M s are prepared.

The first operation to find all stable matchings in a given instance is to prepare ${}_nC_2 \times 2$ antigen-epitope pairs corresponding to every combination of two couples in *M* and arrange them in a single horizontal row (Fig. 3). This arrangement on a matching *M* represents a solution candidate of the stable marriage problem and let it be symbolized by C_M. The second operation is to prepare all of C_M to every matching *M* and arrange them (Fig. 4). This operation prepares all solution candidates, and this experiment's preparation is completed. The last operation is to find all stable matchings. To do this operation, we just wait all antibody-epitope reactions proceeding in parallel come to the end. As already explained in the last section, in a certain arrangement C_M to a matching *M* including blocking pairs, an antibody and an epitope corresponding to a couple with an affair relationship finally forms a antibody-epitope complex. Therefore C_M of not producing any antibody-epitope complex represent "stable matching" and they are solutions of the stable marriage problem (Fig. 5).

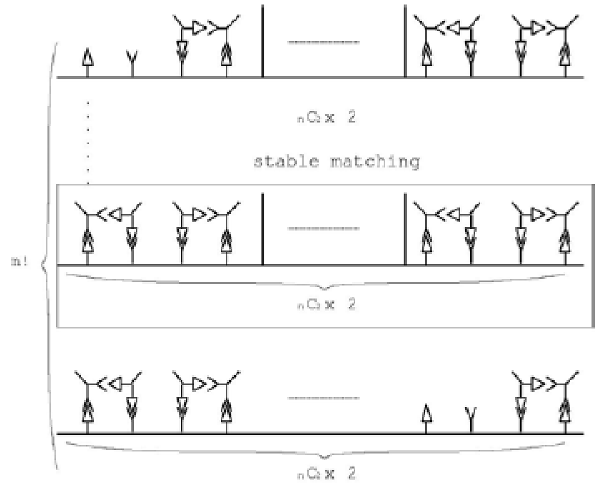

Fig. 5: A particular C_M of not forming any antibody-epitope complexes represents a "stable" matching

III. CONCLUSION

In order to demonstrate the multi-reactivity between an antibody and an epitope is appropriate for finding a particular relationship in many-to-many and weighted relationships, by way of example we have proposed the antibody-epitope reaction based solution algorithm of the stable marriage problem. This proposed algorithm is able to find in parallel all stable matchings if all solution candidates are previously prepared. However, some problems are still left. A major problem is that a scheme to prepare all solution candidates in parallel is not established. Thus, it remains possible that operations to prepare the solution candidates become a bottleneck of the proposed algorithm. Although we might be able to apply ideas of the combinatorial chemistry for preparing the solution candidates with fewer steps, this problem is an issue for the future.

ACKNOWLEDGMENTS

This study has been supported by the Grant-in-Aid for Young Scientists (B) No.18700293 of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) from 2006 to 2008. We are grateful for their support.

REFERENCES

[1] Adleman LM (2004), Molecular Computation of Solutions To Combinatorial Problems. Science 266 11: 1021-1024
[2] Gusfield D and Irving RW (1989), The Stable Marriage Problem. The MIT Press
[3] Smith DJ, Forrest S, Hightower RR et al (1997), Deriving shape space parameters from immunological data. J Theor Biol 189 2:141-150
[4] Ishida Y (2008), An Antibody-Based Computing: An Application to Stable Marriage Problem. J AROB in press
[5] Balan MS, Krithivasan K and Sivasubramanyam Y (2002), Peptide Computing - Universality and Complexity. Proc. of DNA7, LNCS 2340:290-299
[6] Balan MS and Krithivasan K (2004), Parallel computation of simple arithmetic using peptide-antibody interactions. Bio Systems 76:303-307