

How to predict future in a world of antibody-antigen chromosomes

Zbigniew Pliszka and Olgierd Unold, Member, IEEE

Abstract—The paper deals with a representation of the antibody-antigen chromosomes. The proposed new binary decoding allows us to prove the dependence between subsequent generations of chromosomes, using quick and simple operations on chromosomes indices, instead of processing the binary strings. Some formal properties of the immune system were expressed based on this representation. A consistency theoretical proof for epistatic properties as well as exploration possibilities of a crossover operator was given.

Index Terms—Genetic algorithm, Crossover, Binary coding, Hadamard representation, Artificial Immune System.

I. INTRODUCTION

A RTIFICIAL Immune Systems (AISs) constitute currently a significant trend in the studies on biologically inspired calculations [2], [14]. Much work on AIS has concentrated on simple extraction of biological metaphors and direct application. There is very limited work on the more theoretical aspects of AIS, especially on the formal proofs of AIS algorithms [13]. A complete proof for a specifc multiobjective clonal selection algorithm using Markov chains has been given in [15]. In [1] Markov chain model of the B-cell algorithm has been developed to show a convergence proof, and also a mathematical model of the mutation operator.

Work in theoretical immunology has developed various representations for the interactions between antibody and antigen, and affinity metrics for modeling these such interactions. These antibody-antigen binding models were proposed for describing antibody cross-reactivity [5].

In this paper we attempt to model binary space, which includes both antigens and antibodies, and try to theoretically predict their further development based on knowledge of the first (initial) population. Antibody-antigen chromosomes are represented as binary, fixed-length chromosomes, using an alternative to zero-one decoding technique, called Hadamard representation.

In addition to above mentioned aim, the present paper seeks to address potential capabilities of a crossover operator. There is much criticism of the role of the crossover in evolutionary algorithm (EA) literature. Several authors [11], [3], [4] have pointed out that the crossover causes the premature convergence of the EA, i.e. the EA loses population diversity before some goal is met. Some of them argue that for problems of nontrivial size and difficulty, the contribution of crossover

O. Unold is with Institute of Computer Engineering, Control and Robotics, Wroclaw University of Technology, Wyb. Wyspianskiego 27, 50-370 Wroclaw, Poland, e-mail: olgierd.unold@pwr.wroc.pl.

978-83-60810-22-4/\$25.00 © 2011 IEEE

search is marginal [8]. Spears [10] claims that mutation is more powerful than crossover in terms of exploration, although the two operators can be treated as two forms of a searching operator. Experiments conducted by Schaffer and Eshelman [12] have been indicated that population of chromosomes manipulated by crossover contains epistatic interaction.

A consistency theoretical proof for epistatic properties as well as exploration possibilities of a crossover operator is given in this paper.

This paper extends the results of our previous study [9] by (1) using different notation that leads to a shift of the indices, (2) defining a crossover operator in H^n space, (3) introducing new property of the immune system called *Expansive system* with global range, (4) proving formal properties of a crossover operator (**Theorem 1**), (5) and supporting the states of AIS by redefined examples. In addition, some remarks on **Schema Theorem** used in Hadamard space are made.

This paper is organized as follows. Section 2 describes binary representation used in the research, next Section 3 gives some formal properties of populations in AIS. Section 4 formulates a concept of an ancestral population. Finally Section 5 concludes the paper with future works.

II. BINARY REPRESENTATION

A. Hadamard model

In the study [9] the search space $\{0,1\}^n$ was replaced by $\{-1,1\}^n$ (so called a Hadamard representation [6]). Thanks to use a new binary model the requirement of orthogonal columns pairs is omitted. Subject of this study is the following set:

$$H^{n} = \{(h_{s,n}, h_{s,n-1}, \dots, h_{s,2}, h_{s,1}) : \forall s \in \{0, 1, \dots, 2^{n} - 1\} \\ \forall i \in \{1, 2, \dots, n\} \quad h_{s,i} \in \{-1, 1\}\}$$
(1)

Its elements represent all possible binary chromosomes of equal length n, where n is a natural number higher than 1. The proposed representation has one, apparently insignificant property, which distinguishes it from the binary representation: a square of each coordinates is equaled 1. This fact draws two subsequent conclusions: the sum of the squares of coordinate of each element of the H^n space is constant and equals this space dimension, and there is no element with zero coordinates. The collection of these simple facts allows for the formulation of rules for phenotypes (indices) and development of automate methods of moving frame H^n , as well as determination of the distance (level of differentiation) between the elements of this space.

Z. Pliszka is with Wroclaw Public Library, Sztabowa 95, 53-310 Wroclaw, Poland.

At the beginning, we determined the order of the indexing of points in H^n and their four representations, which we will use alternating (see Table I).

TABLE I Indexing and representation of points in H^n space.

Element's symbol	Decimal representation	Binary representation	Hadamard representation
r_0	0	(0,0,,0,0,0)	(1, 1,, 1, 1, 1)
r_1	1	$(0,0,\ldots,0,0,1)$	(1, 1,, 1, 1,-1)
r_2	2	$(0,0,\ldots,0,1,0)$	(1, 1,, 1,-1, 1)
r_3	3	(0,0,,0,1,1)	(1, 1,, 1,-1, -1)
:	:	:	:
$r_{2^{n}-3}$	$2^n - 3$	$(1,1,\ldots,1,0,1)$	(-1,-1,,-1, 1,-1)
$r_{2^{n}-2}$	$2^n - 2$	$(1,1,\ldots,1,\ 1,\ 0)$	(-1,-1,,-1,-1, 1)
$r_{2^{n}-1}$	$2^n - 1$	(1,1,,1, 1, 1)	(-1,-1,,-1,-1,-1)

The number of points included in H^n is equal to $|H^n| = 2^n$. For each element in the binary representation there are numerous functions transforming the elements of this representation to the elements of the Hadamard representation and inversely (see [9]).

Index s of the element r_s having a binary representation $(b_{s,n}, \ldots, b_{s,1})$ and the Hadamard representation $(h_{s,n}, \ldots, h_{s,1})$, and equal to the value of the decimal representation, can be calculated from one of the formulas:

$$ID(r_s) = s = \sum_{t=1}^{n} 2^{t-1} b_{s,t} = \sum_{t=1}^{n} 2^{t-2} (1 - h_{s,t})$$
 (2)

In cases of doubt, we will use the function symbol $ID(r_s)$, otherwise the sign of the index s will be used.

B. The distance in H^n

The distance of two points

 $r_t = (h_{t,n}, h_{t,n-1}, \dots, h_{t,2}, h_{t,1})$ and $r_k = (h_{k,n}, h_{k,n-1}, \dots, h_{k,2}, h_{k,1})$ in H^n space is measured according to the following equation:

$$\forall r_t, r_k \in H^n$$
 $w(r_t, r_k) = n - \frac{1}{4} \sum_{i=1}^n (h_{t,i} + h_{k,i})^2$ (3)

The distance defined in that way will always be a nonnegative integer, which will tell us on how many coordinates in Hadamard representation the values differ (exactly as in the binary representation) (see Table I). In addition, H^n space with the w distance determined in this way is metric and has many interesting properties (proved in [9]). For example, there is an algorithmic method for construction a table of distances between any elements from the H^n space (without calculating the distance between elements). Bearing in mind that the space H^n contains 2^n elements, and the space H^{n+1} contains $2^{n+1} = 2 \cdot 2^n$, the distance table W_{n+1} of dimesion $2^{n+1} \times 2^{n+1}$ is to be obtained form the table W_n of dimension $2^n \times 2^n$ according to the following formula:

$$\langle W_n \rangle \xrightarrow{\mapsto} \left\langle \begin{array}{cc} W_n & \langle W_n + 1 \rangle \\ \langle W_n + 1 \rangle^T & W_n \end{array} \right\rangle,$$

where +1 means addition to each element of the table a value of 1, and W_n^T the transpose of a matrix W_n . The number situated on the cross of the k-row with the t-column corresponds to $w(r_k, r_t)$ distance. Exceptionally, for the purposes of this algorithm, we assume that $W_0 = \langle 0 \rangle$, because, as already mentioned, the spaces H^n where n > 1 are considered in this study. The distance table for n = 4 is presented in Table II.

In the work [9] the definition of the polar points was introduced. Two points r_t and r_k in H^n are called polar points if and only if for each coordinate these points have opposite values.

$$\forall j \in \{1, \dots, n\} \qquad h_{t,j} = -h_{k,j}$$

According to the formula (3), the distance between polar points is constant and equals $w(r_t, r_k) = n$. Some other properties of polar points were given in [9].

C. Crossover in H^n

Any two points from H^n can be provided in accordance with the definition (1) as:

$$r_t = (r_{t,n}, r_{t,n-1}, \dots, r_{t,2}, r_{t,1})$$
$$r_k = (r_{k,n}, r_{k,n-1}, \dots, r_{k,2}, r_{k,1})$$

Assuming that c is the position of the cutting operation in a crossover counted from the right, fulfilling the inequality $0 \le c \le n$, we define the operation of the crossing-over an element r_t with an element r_k after the locus c as follows (note that crossover operator corresponds to 1-point-crossover):

$$K(\{r_t, r_k\}, c) \mapsto \{(r_{t,n}, r_{t,n-1}, \dots, r_{t,c+1}, r_{k,c}, r_{k,c-1}, \dots, r_{k,1}), (r_{k,n}, r_{k,n-1}, \dots, r_{k,c+1}, r_{t,c}, r_{t,c-1}, \dots, r_{t,1})\}$$

The newly received elements belong to the H^n and can be symbolically represented:

$$r_s = (r_{t,n}, r_{t,n-1}, \dots, r_{t,c+1}, r_{k,c}, r_{k,c-1}, \dots, r_{k,1})$$
(4)

$$r_q = (r_{k,n}, r_{k,n-1}, \dots, r_{k,c+1}, r_{t,c}, r_{t,c-1}, \dots, r_{t,1})$$
(5)

Now, the operation of the crosover can be written as

$$K(\{r_t, r_k\}, c) \mapsto \{r_s, r_q\},\tag{6}$$

where the indices s and q can be taken from the formulas ([9]):

$$s = t - (t \mod 2^c) + (k \mod 2^c)$$
 (7)

$$q = k - (k \mod 2^c) + (t \mod 2^c) \tag{8}$$

III. PROPERTIES OF ARTIFICIAL IMMUNE SYSTEM IN H^n SPACE

This section depicts some properties of AIS, in which antibody-antigen chromosomes are represented using Hadamard encoding. Introduced properties are illustrated by the examples based on the content of Table II.

 r_{15} r_0 r_1 r_2 r_3 r_4 r_5 r_6 2 2 2 2 r_7 r_8 r_9 r_{10} r_{11} r_{12} r_{13} r_{14} r_{15}

A. Radius of tolerance

A radius of tolerance R is understood as the border value enabling a mutual recognition of elements in H^n space.

Two elements $x, y \in H^n$ recognize or do not tolerate each other if the distance between them is higher than the radius of tolerance.

$$w(x,y) > R \tag{9}$$

where R complies with the inequality: $0 \le R \le n$. Elements $x, y \in H^n$ complying the weak inequality

() (D

$$w(x,y) \le R \tag{10}$$

will be described as not recognizing or tolerating each other. **Example 0**

In the examples considered here we use the H^4 space, whose distance tables are presented in Table II. Moreover, for all the demonstrated examples we assume the value of the radius of tolerance R = 2.

B. Self-aggression

System $B_k \subseteq H^n$ undergoes self-aggression if elements x, y occur, which recognize each other and belong to this system.

$$\exists x, y \in B_k : w(x, y) > R \tag{11}$$

Example 1

In H^4 the systems undergoing self-aggression are for example:

 $B_8 = \{r_0, r_1, r_2, r_4, r_8, r_3, r_5, r_6\} \text{ where } w(r_1, r_6) = 3$ $B_4 = \{r_3, r_5, r_6, r_9\} \text{ where } w(r_6, r_9) = 4$

System $B_k \subseteq H^n$ is free of self-aggression if any two elements belonging to this system do not recognize themselves.

$$\forall x, y \in B_k \quad w(x, y) \le R \tag{12}$$

Example 2

Free systems of self-aggression, when R = 2: $B_5 = \{r_0, r_1, r_2, r_4, r_8\}$ $B_3 = \{r_3, r_5, r_6\}$ $B_2 = \{r_0, r_1\}$ Let us notice that system B_2 is free of self-aggression also when R = 1.

Systems undergoing self-aggression have elements (chromosomes) dispersed in the space under consideration, systems free of self-aggression are centered around a certain element (chromosome) and we have a suspicion that this is a local extremum for many used objective functions.

C. Dazzling distance set

A dazzling distance set of a system $B_k \subseteq H^n$ is a set of points of H^n recognized by any point of B_k .

$$P(B_k) = \{ z \in H^n : \exists x \in B_k \land w(x, z) > R \}$$
(13)

Example 3

For $B_3 = \{r_3, r_5, r_6\}$ from the **Example 2** the dazzling distance set is:

$$P(B_3) = \{r_1, r_2, r_4, r_8, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}\}$$

If B_k undergoes self-aggression then some points belonging to B_k simultaneously belong to $P(B_k)$, which means that

$$B_k \cap P(B_k) \neq \emptyset$$

because, according to (11) there is a pair of points $x, y \in B_k$ that w(x, y) > R and $y \in H^n$, what gives (13).

Example 4

The system $B_4 = \{r_3, r_5, r_6, r_9\}$ from the **Example 1** is in such a state:

$$P(B_4) = \{r_1, r_2, r_4, r_6, r_7, r_8, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}\}$$

and we have:

$$B_4 \cap P(B_4) = \{r_6, r_9\} \neq \emptyset$$

Otherwise, if B_k is free of self-aggression, then B_k and $P(B_k)$ are disjunctive sets, which can be presented as follows:

$$B_k \cap P(B_k) = \emptyset \tag{14}$$

since, according to (12), any two elements $x, y \in B_k$ satisfy the inequality $w(x, y) \leq R$, which contradicts (13).

 TABLE II

 The distance table between any elements in H^4 .

Example 5

 B_3 (described in **Example 2** and **3**) is free of self-aggression, for which identity occurs:

$$B_3 \cap P(B_3) = \emptyset$$

D. Complete system

System B_k is complete if its dazzling distance set contains its whole completion $\overline{B_k} = H^n \backslash B_k$.

$$\overline{B_k} \subseteq P(B_k) \tag{15}$$

Example 6

The conditions of the complete system are fulfilled by $B_7 = \{r_0, r_1, r_2, r_3, r_4\}$, for which following identities occur:

$$P(B_7) = \{r_3, r_4, r_5, r_6, r_7, r_8, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}, r_{15}\}$$
$$\overline{B_7} = \{r_5, r_6, r_7, r_8, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}, r_{15}\},$$

Thus, a relation occurs:

$$\overline{B_7} \subseteq P(B_7)$$

The statement, that we are dealing with a complete system, gives us confidence that in many problems we control the entire space under consideration, using only a certain part of the elements (chromosomes) of that space. In many issues, the important task to deal with is to set the minimum complete systems (i.e. which contain the smallest number of elements) for a given space.

E. Balanced system

System B_k is balanced if at the same time it is a system free of self-aggression, and complete. System B_k satisfies the equality

$$\overline{B_k} = P(B_k)$$

The relationship $\overline{B_k} \subseteq P(B_k)$ we have from the definition of a complete system (see (15)). Inverse relationship $\overline{B_k} \supseteq P(B_k)$, we get as a request from two facts: $P(B_k) \subseteq H^n = B_k \cup \overline{B_k}$, as well as B_k as a system free of self-aggression satisfies (14), and therefore $\overline{B_k} \supseteq P(B_k)$.

Example 7

This time let us assume that $B_5 = \{r_0, r_1, r_2, r_4, r_8\}$ (B_5 is taken from the Example 2). For such a system the following identities are fulfilled:

$$P(B_5) = \{r_3, r_5, r_6, r_7, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}, r_{15}\}$$

$$\overline{B_5} = \{r_3, r_5, r_6, r_7, r_9, r_{10}, r_{11}, r_{12}, r_{13}, r_{14}, r_{15}\}$$

and

$$\overline{B_5} = P(B_5)$$

F. Extensive system

We call $B_k \subseteq H^n$ an extensive system if each crossing-over of its elements results in offspring, which also belongs to this system.

$$\forall x, y \in B_k \subseteq H^n \quad \forall c \in \{0, 1, \dots, n\} \quad K(\{x, y\}, c) \subseteq B_k$$

Example 8

The examples of the extensive systems are presented below:

$$B_{2} = \{r_{0}, r_{1}\}$$
$$B_{4} = \{r_{0}, r_{1}, r_{2}, r_{3}\}$$
$$H^{4}$$
$$B_{1} = \{r_{0}\}$$

To check the extensibility of B_2 and B_4 systems, equations (7) and (8) can be used. It can be noticed that both the singleton system and any H^n space, as a whole, are extensive systems.

G. Expansive system

A system B_k is expansive if it possesses elements (not necessary different), which after a crossing-over produce elements out of the system.

$$\exists x, y \in B_k \subseteq H^n \quad \exists c \in \{0, 1, \dots, n\}: \quad K(\{x, y\}, c) \not\subset B_k$$

Example 9

Let us assume $B_9 = \{r_0, r_1, r_2\} \subseteq H^4$. Assuming in equations (6) (7) and (8) fore c = 1, t = 1, k = 2 we have:

$$K(\{r_1, r_2\}, 1) \mapsto \{r_0, r_3\} \not\subset B_9$$

due to the element $r_3 \notin B_9$.

H. Expansive system with global range

We say that the expansive system $B_k \subseteq H^n$ is global in range, if each element from the completation of B_k can be obtained only as a result of crossing-over of its elements and offsprings.

Example 10

Note that the set of elements $B_{11} = \{r_0, r_{15}\}$ is the expansive system with global range. These two elements are sufficient to be the ancestors of all space H^n . And more generally, any system consisting of two polar points, is a expansive system with global range (proof to be found below).

Definition 1

An *initial* or *primary population* is a set of chromosomes (elements) from the H^n space, which receives an evolutionary process (or program) input. We assume that all elements of such a set take part in the first selection process for the parent pool.

Definition 2

We say that the population is *ancestral*, if all its elements can be obtained from a primary population as a result of the assembling only crossing-overs.

Note that this definition does not reject the elements created by the assembly of other operations (for example, mutation or inversion) on the initial population, but it requires the existence of the potential emergence of such elements by submitting only the crossing-overs of the initial population and its posterity. In this case, we also have the ancestral population.

IV. ANCESTRAL POPULATION

Theorem 1

The whole space H^n is the ancestral population if and only if there are the elements in the primary population P, which have the following properties:

for each position (locus), we have two elements from P having different (in terms of dual opposing) values.

Proof

 \Rightarrow (proof by contradiction)

Suppose that for the initial population $P \subseteq H^n$ there is the locus $l \in \{1, n\}$, with the property that all elements from P have one value (in the case of binary representation, for example 0, and Hadamard representation 1). Then, according to formulas (4) and (5), the value of the position l will not change, regardless of the choice of parental pairs, the choice of the value c as a point of crossing-over, and the number of crossing-over operations. So we had no opportunity to receive elements with the value on position l different, than the one which have all the elements of P. And that means that we do not receive as a result of crossing-overs the elements from H^n with the opposite value (from our example is a binary value 1 or Hadamard value -1) to be set in position l in the space P. This would contradict the assumption that all space H^n is the ancestral population. Thus, the implication in this direction is true.

 \Leftarrow

In the proof of equivalence in the other direction, we use the Restore Pattern using Crossovers (RPC) Algorithm (see Algorithm 1). Let the pattern W be an arbitrary element in space H^n . Meeting the objectives of **Theorem T1**, irrespective of the value that we are going to set to fixed, but any position (locus) c of the pattern W, we will always find a chromosome in the initial population with a value at that position of searched pattern W. This assures us that the inner loop **L1** always ends up with a variable *found* with a value of true. This, in turn, runs a block **BL1**, which carries the crossingovers and, possibly, newly formed chromosomes attach to the pool taking part in further operations. The algorithm assumed that the offspings replace parents. In a case when offsprings join to the current population and parents would remain in it, a block **BL1** should look like:

begin of BL11

 $G := first_element_from(K({G,B[i]},c))$ $B := B \cup K(K({G,B[i]},c),c)$ maks := maks + 2

end of BL11

And in a case when we want do attach to the pool the element matching the pattern, a block **BL1** should look like:

```
begin of BL12

G := first\_element\_from(K({G,B[i]},c))

B := B \cup {G}
```

Algorithm 1 RPC Algorithm

Input: n {the length of chromosome}

W[1,..,n] {the table containing the pattern of the chromosome}

j {the number of chromosomes in a population}

PB[1,..,j][1,..,n] {the table of tables containing the chromosomes of the initial population}

Definition:

B[1,..,j+2n][1,..,n] {the table of tables containing the chromosomes of the current population}

begin

 $B := BP \{ \text{insert BP into the first n-positions of } B \}$ maks := ic := nG := B[1]repeat i := 0found := **false** repeat begin of L1 i := i + 1if W[c] = B[i][c] then found := true end if end of L1 **until** (found or (i = maks)) if found then begin of BL1 $G := first_element_from(K({G,B[i]},c))$ $B := (B \setminus K(\{G, B[i]\}, c)) \cup K(\{G, B[i]\}, c)$ end of BL1 end if c := c - 1**until** ((not found) or (c = 0)) **Output:** if found then G else false end if

maks := maks + 1 end of BL12

end

The function first_element_from() returns, according to (6), chromosom resulting from crossing-over, having at locus c a value equals to the value of the pattern at the same position (see (4) and (5)).

Summing up, since the RPC Algorithm, meeting the objectives-led part of the Theorem, is able from the initial population—using only crossing-overs—create any element from the space H^n , so H^n is the ancestral population.



Fig. 1. Exemplary ancestral population with the primary population h_0 and h_7 .

End of Proof

At the end, as a conclusion of the above **Theorem 1** let us write, without any proof, convenient Theorem in applications: **Theorem 2**

If a primary population $P \subseteq H^n$ contains the pair of polar points, then the whole space H^n is an ancestral population.

For example, having two polar points h_0 and h_7 as a primary population from H^3 we are able after four crossovers obtain all 8 points from the space in question, according to **Theorem 2** (see Figure 1). More crossover operations are needed when using natural selection and random points of crossing.

At this point, it seems natural to mention the **Schema Theorem** [7], one of the fundamental theorems of genetic algorithms. The **Theorem 1** shows that, if not all space H^n is the ancestral population, there must be positions (perhaps one such a position) in all chromosomes of the initial population, having the same value (locus). Thus, we should look for aboveaverage schemes at those positions. Crossover operation is only possible to duplicate chromosomes with such a chosen scheme. Changes of this trend can only be caused by other operations (for example, mutation or inversion). Given that the vast majority of models considered, crossing is an operation with a much greater likelihood of occurrences in relation to other operations, reducing the quantity or even just reducing the growth of occurrences in the next population will be proportionately less likely.

Introduced concepts allow us to distinct and classify different populations, what is more to penetrate into the potential future directions of their evolution (states reachable, unreachable, etc.) regardless of the selected crossover algorithms, selection of parents, or the elimination of individuals. And then, we should be able to compare the genetic algorithms in terms of efficiency and optimization.

Comparing the two algorithms, we need to ensure comparability of the population, on which we conduct experiments. It is obvious that the same algorithm, e.g. over the population of the class of expansive systems, has a chance of finding new solutions in successive generations, but over the populations form extensive class, after reviewing the current population, better solutions are no longer found.

V. CONCLUSIONS AND FUTURE WORK

The introduced Hadamard representation allows us to prove the dependence between subsequent generations of binary chromosomes encoding antibody and antigen space. Some properties of this representation were pointed out, which allows for quick and simple operations on chromosomes indices, instead of processing the binary sequences. The main contributions of this paper are to introduce new property of the immune system called *Expansive system with global range*, and to prove for epistatic properties as well as exploration possibilities of a crossover operator. Some remarks on Schema Theorem over $\{-1, 1\}^n$ space were also made.

Future research will show to what extent the Hadamard chromosomes are exploitable.

REFERENCES

- [1] Clark E., Hone A., Timmis J. (2005), A Markov Chain Model of the B-cell Algorithm, In: LNCS 3627, Springer, 318–330.
- [2] Dasgupta D. (1999), Artificial Immune Systems and their Applications, Springer-Verlag, Berlin, Heidelberg.
- [3] Fogel, D., Atmar, J. W. (1990), Comparing genetic operators with Gaussian mutations in simulated evolutionary processes using linear systems, Biological Cybernetic, 63: 111–114.
- [4] Forest, S., Javornik, B., Smith, R.E., Perelson, A.S. (1993), Using genetic algorithms to explore pattern recognition in the immune system, Evolutionary Computation, 1: 191–211.
- [5] Freitas A., Timmis J. (2007), Revisiting the Foundations of Artificial Immune Systems for Data Mininig, IEEE Trans. Evol. Comp. 11(4) 521– 540.
- [6] Hadamard J. (1893), Résolution d'une Question Relative aux Déterminants, Bull. Sci. Math. 2(17), 240–246.
- [7] Holland J. (1975), Adaptation in Natural and Artificial Systems, University of Michigan Press, Ann Abor.
- [8] Park, K., Carter, B. (1994), On the effectiveness of genetic search in combinatorial optimization, Tech. Report BU-CS-94-010, Computer Sci. Department, Boston University.
- [9] Pliszka Z., Unold O. (2010), Metric Properties of Populations in Artificial Immune Systems, In: Proceedings of the International Multiconference on Computer Science and Information Technology (AAIA'10), Wisla, Poland, 113–119.
- [10] Spears, W. M. (1992), Crossover or mutation?, D. Whitley ed., Proc. Of the 2-nd Foundations of Genetic Algorithms Workshop, Morgan Kaufman, 221–237.
- [11] Spears, W.M. (1994), Simple population schemes, In: Proc. Of the 1994 Evolutionary Programming Conference, Word Scientific: 296–317.
- [12] Schaffer, J. D., Eshelman, L. J. (1991), On crossover as an evolutionary viable strategy, Proceedings of the Fourth International Conference on Genetic Algorithms, La Jolla, CA: Morgan Kaufmann, 61–68.
- [13] Timmis J., Hone A. N. W., Stibord T., Clark E. (2008), *Theoretical Advances in Artificial Immune Systems*, Theoretical Computer Science, Vol. 403, Issue 1, 11–32.
- [14] Wierzchoń S.T. (2001), Sztuczne Systemy Immunologiczne. Teoria i zastosowania, Akademicka Oficyna Wydawnicza EXIT, Warszawa (in Polish).
- [15] Villalobos-Arias M., Coello Coello C. A., Hernandez-Lerma O. (2004), Convergence Analysis of a Multiobjective Artificial Immune System Algorithm, In: LNCS 3239, Springer, Berlin, Heidelberg, 226–235.