

ARTIFICIAL IMMUNE SYSTEM: ALGORITHMS AND APPLICATIONS REVIEW

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ABSTRACT

“Artificial immune system” also known as immune computation, is a fast developing research area in the computational intelligence community. As a kind of computational intelligent system, artificial immune system (AIS) are inspired by the information processing mechanism of biological immune system. During past two decade researchers aiming to develop immune based models and technique to solve complex computational or engineering problem. This work present a survey of existing AISs models and algorithm with a focus on the last 20 years and some application of artificial immune system.

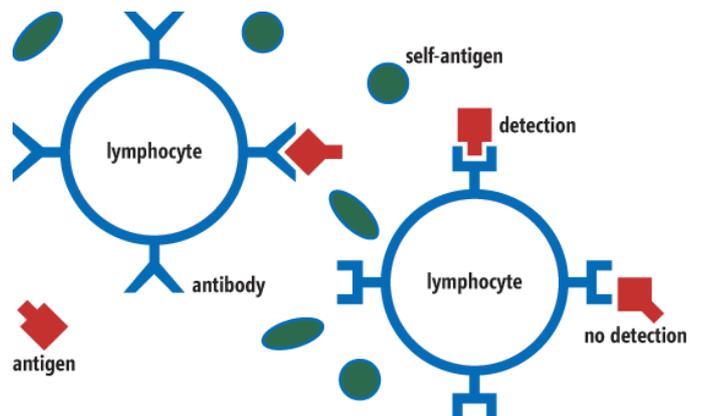
Keywords

Artificial Immune System, Clonal Selection, Negative Selection, Dendritic Cell, Artificial Immune Network.

1. INTRODUCTION

In artificial intelligence, artificial immune systems are a class of computationally intelligent, rule based machine learning systems inspired by the principals and processes of the vertebrate immune system. The function of a biological immune system is to protect the body from foreign molecules known as antigens. It has great pattern recognition capability that may be used to distinguish between foreign cells entering the body (non-self or antigen) and the body cells (self). Immune systems have many characteristics such as uniqueness, autonomous, recognition of foreigners, distributed detection, and noise tolerance (Castro and Zuben, 1999). Inspired by biological immune systems, Artificial Immune Systems have emerged during the last two decade. They are incited by many researchers to design and build immune-based models for a variety of application domains. Artificial immune systems can be defined as a computational paradigm that is inspired by theoretical immunology, observed immune functions, principles and mechanisms (Castro and Timmis, 2003). This report investigates the different AIS computational paradigms and introduces different AIS models and techniques developed in the literature since the work of Dasgupta et al. (2003). The studied models are mainly based on the immune network theory, clonal selection principles and negative selection mechanisms. The rest of this report is organized as follows: Section 2 presents a theoretical background of the immune systems; Section 3 presents an overview of the existing AIS models and algorithms

that are developed based on the immune system principles Section 4 presents case studies; Section 5 highlights directions for future work and forms the conclusion of this work; section 6 highlights application of artificial immune system.



2. BACKGROUND OF IMMUNE SYSTEM

The immune system is a host defense system comprising many biological structures and processes within an organism that protects against disease. To function properly, an immune system must detect a wide variety of agents, known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue. In many species, the immune system can be classified into subsystems, such as the innate immune systems versus the adaptive immune systems, or humeral immunity versus cell-mediated immunity. In humans, the blood-brain barrier, blood-cerebrospinal fluid barrier, and similar fluid-brain barriers separate the peripheral immune system from the neuro-immune system, which protects the brain.

Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer.

INNATE IMMUNE SYSTEM

Antigen's or foreign molecules that successfully enter an organism meet the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of micro-organisms, when damaged, injured or stressed cells send out alarm signals, many of which (but

not all) are recognized by the same receptors as those that recognize pathogens. Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way. This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms.

ADAPTIVE IMMUNE SYSTEM

The adaptive immune system evolved in early vertebrates and allows for a stronger immune response as well as immunological memory, where each pathogen is "remembered" by a signature antigen. The adaptive immune response is antigen-specific and requires the recognition of specific "non-self" antigens during a process called antigen presentation. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is maintained in the body by "memory cells". Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it.

CLONAL SELECTION

The concept of clonal selection was introduced by the Australian doctor FRANK MACFARLANE BURNET in 1957. The theory is used to explain basic response of adaptive immune system to antigenic stimulus. It establishes the idea that only those cells capable of recognizing an antigen will proliferate while other cells are selected against. Clonal selection operates on both B and T cells. B cells, when their antibodies bind with an antigen, are activated and differentiated into plasma or memory cells. Prior to this process, clones of B cells are produced and undergo somatic hyper mutation. As a result, diversity is introduced into the B cell population. Plasma cells produce antigen-specific antibodies that are work against antigen. Memory cells remain with the host and

Promote a rapid secondary response (Castro and Timmis, 2003).

NEGATIVE SELECTION

Negative selection is a mechanism to protect body against self-reactive lymphocytes. It utilizes the immune system's ability to detect unknown antigens while not reacting to the self-cells. During the generation of T-cells, receptors are made through a pseudo-random genetic rearrangement process. Then, they undergo a censoring process in the thymus, called the negative selection. In this process, T-cells that react against self-proteins are destroyed and only those that do not bind to self-proteins are allowed to leave the thymus. These matured T-cells then circulate throughout the body performing immunological functions and protecting the body against foreign antigens (Somayaji et al., 1997).

IMMUNE NETWORKS THEORY

The immune Network theory has been introduced by Jerne (1974). The main idea was that the immune system maintains an idiotypic network of interconnected B cells for antigen recognition. These cells interconnect with each other in certain ways that lead to the stabilization of the network. Two B cells are connected if the affinities they share exceed a certain threshold, and the strength of the connection is directly proportional to the affinity they share.

3. ARTIFICIAL IMMUNE SYSTEM: ALGORITHMS

The Clonal Selection Algorithm

In artificial immune system, **clonal selection algorithms** are a class of algorithms inspired by the clonal selection theory of acquired immunity that explains how B and T lymphocytes improve their response to antigens over time called affinity maturation. These algorithms focus on the Darwinian attributes of the theory where selection is inspired by the affinity of antigen-antibody interactions, reproduction is inspired by cell division, and variation is inspired by somatic hyper mutation. Clonal selection algorithms are most commonly applied to optimization and pattern recognition domains.

The Algorithm, The clonal selection theory has been used as inspiration for the development of AIS that perform computational optimization and pattern recognition tasks. In particular, inspiration has been taken from the antigen driven affinity maturation process of B-cells, with its associated hyper mutation mechanism. These AIS also often utilize the idea of memory cells to retain good solutions to the problem being solved. In de Castro and Timmis' book, they highlight two important features of affinity maturation in B-cells that can be exploited from the computational viewpoint. The first of these is that the proliferation of B-cells is proportional to the affinity of the antigen that binds it, thus the higher the affinity, the more clones are produced. Secondly, the mutations suffered by the antibody of a B-cell are inversely proportional to the affinity of the antigen it binds. Utilizing these two features, de Castro and Von Zuben developed one of the most popular and widely used clonal selection inspired AIS called CLONAL'G, which has been used to perform the tasks of pattern matching and multi-modal function optimization.

When applied to pattern matching, a set of patterns, *S*, to be matched are considered to be antigens. The task of CLONALG is to then produce a set of memory antibodies, *M*, that match the members in *S*. This is achieved via the algorithm outlined below.

Input : *S* = set of patterns to be recognized, *n* the number of worst elements to select for removal

Output: *M* = set of memory detectors capable of classifying unseen patterns

Begin

Create an initial random set of antibodies, *A*

Forall patterns *in S* **do**

Determine the affinity with each antibody in *A*

Generate clones of a subset of the antibodies in *A* with the highest affinity.

The number of clones for an antibody is proportional to its affinity

Mutate attributes of these clones to the set *A*, and place a copy of the highest Affinity antibodies in *A* into the memory set, *M*

Replace the *n* lowest affinity antibodies in *A* with new randomly generated antibodies

End

3.2 Negative Selection Algorithm

The Biology The process of deleting self-reactive lymphocytes is termed clonal deletion and is carried out via a mechanism called negative selection that operates on lymphocytes during their maturation. For T-cells this mainly occurs in the thymus, which provides an environment rich in antigen presenting cells that present self-antigens. Immature T-cells that strongly bind these self-antigens undergo a controlled death (apoptosis). Thus, the T-cells that survive this process should be unreactive to self-antigens. The property of lymphocytes not to react to the self is called immunological tolerance.

The Algorithm Negative selection algorithms are inspired by the main mechanism in the thymus that produces a set of mature T-cells capable of binding only non-self-antigens. The first negative selection algorithm was proposed by Forrest *et al* (1994) to detect data manipulation caused by a virus in a computer system. The starting point of this algorithm is to produce a set of self-strings, S , that define the normal state of the system. The task then is to generate a set of detectors, D , that only bind/recognize the complement of S . These detectors can then be applied to new data in order to classify them as being self or non-self, thus in the case of the original work by Forrest *et al*, highlighting the fact that data has been manipulated. The algorithm of Forrest *et al* produces the set of detectors via the process outlined in below.

Input : S_{seen} = set of seen known self-elements

Output: D = set of generated detectors

Begin

Repeat

Randomly generate potential detectors and place them in a set P

Determine the affinity of each member of P with each member of the self-set S_{seen}

If at least one element in S recognizes a detector in P according to a recognition threshold,

Then the detector is rejected, otherwise it is added to the set of available detectors D

Until stopping criteria has been met

End

3.3 Artificial Immune Network Models

The Biology In 1974, Jerne proposed an immune network theory to help explain some of the observed emergent properties of the immune system, such as learning and memory. The premise of immune network theory is that any lymphocyte

receptor within an organism can be recognized by a subset of the total receptor repertoire. The receptors of this recognizing set have their own recognizing set and so on, thus an immune network of interactions is formed. Immune networks are often referred to as idiotypic networks. In the absence of foreign antigen, Jerne concluded that the immune system must display a behavior or activity resulting from interactions with itself, and from these interactions immunological behavior such as tolerance and memory emerge.

The Algorithm

Input : S = set of patterns to be recognized, nt network affinity threshold,

ct clonal pool threshold, h number of highest affinity clones, a number of

new antibodies to introduce

Output: N = set of memory detectors capable of classifying unseen patterns

Begin

Create an initial random set of network antibodies, N

Repeat

For all patterns in S do

Determine the affinity with each antibody in N

Generate clones of a subset of the antibodies in N with the highest affinity. The number of clones for

An antibody is proportional to its affinity

Mutate attributes of these clones to the set A , a and place h number of

The highest affinity clones into a clonal memory set, C

Eliminate all elements of C whose affinity with the antigen is less than a predefined threshold ct

Determine the affinity amongst all the antibodies in C and eliminate those antibodies whose affinity with each

Other is less than the threshold ct

Incorporate the remaining clones of C into N

End

Determine the affinity between each pair of antibodies in N and eliminate all antibodies whose affinity

is less than the threshold nt

Introduce a random number of randomly generated antibodies and place into N

End until a stopping criteria has been met

End

3.4 DENDRITIC CELL

The Biology Polly Matzinger explains how the clonal selection theory placed the antigen-specific cells of adaptive immunity (most notably the T helper cell) at the center of the decision of whether or not to initiate an immune response. This decision was achieved through the deletion of the self-reacting lymphocytes, so that responses will only be initiated against non-self. It was discovered, however, that T helper cells themselves require a co-stimulatory signal from non-antigen-specific APCs in order to initiate an effective adaptive immune response. As a consequence, it could not be assured that immunity only be directed against non-self, as APCs express on their surfaces both self and non-self-antigens. Matzinger proposed the danger theory in 1994, which has gained much popularity amongst immunologists in recent years as an explanation for the development of peripheral tolerance (tolerance to agents outside of the host). The danger theory states that APCs are themselves activated via an alarm: danger signals. These activated APCs will then be able to provide the necessary co-stimulatory signal to the T helper cells that subsequently control the adaptive immune response. The danger signals are emitted by ordinary cells of the body that have been injured due to attack by pathogen. For example, the intra-cellular contents released due to uncontrolled (necrotic) cell death could provide such signals. These signals are detected by specialized innate immune cells called dendritic cells that seem to have three modes of operation: immature, semi-mature and mature. In the dendritic cells immature state it collects antigen along with safe and danger signals from its local environment such as: (PAMPS) and inflammatory cytokines. The dendritic cell is able to integrate these signals to decide whether the environment is safe or dangerous. If safe the dendritic cell becomes semi-mature and upon presenting antigen to T-cells the dendritic cell will cause T-cell tolerance. If dangerous the dendritic cell becomes mature and causes the T-cell to become reactive on antigen-presentation. **The Algorithm** Danger theory is a relatively new addition to the field of immunology, and thus danger theory inspired algorithms are still in their infancy. Green smith et al with the dendritic cell algorithm (DCA), which introduced the notion of danger signals, safe signals and pathogen associated molecular patterns signals which all contribute to the context of a data signal at any given time. This context is integrated via a process inspired by the role of dendritic cells (a specialized APC of the innate immune system). This removes the need to define what self is, but adds the necessity to define the danger, safe and PAMP signals.

Input : S = set of data items to be labelled safe or dangerous

Output: D = set of data items labelled safe or dangerous

Begin

 Create an initial population of dendritic cells (DCs), D

 Create a set to contain migrated DCs, M

Forall data items in S do

 Create a set of DCs randomly selected from D , P

Forall DCs in P do

 Add data item to DCs collected list

 Update danger, PAMP and safe signal concentrations

 Update concentrations of output cytokines

 Migrate the DC from D to M and create a new DC in D if concentration of co-stimulatory

 Molecules is above a threshold

End

End

Forall DCs in M do

 Set DC to be semi-mature if output concentration of semi-mature cytokines is greater than mature cytokines,

 Otherwise set as mature

End

Forall data items in S do

 Calculate number of times data item is presented by a mature DC and a semi-mature DC

 Label data item a safe if presented by more than semi-mature DCs than mature DC's,

 Otherwise label as dangerous

 Add data item to labelled set M

End

End

4. CASE STUDY

Some experiments were carried out in order to test some of the existing AIS algorithms and explore their capabilities. The ClonalG and the aiNet were chosen for this case study and tested on a cancer data set. The data set consisted of

693 instances and the number of attributes was 12. The predicted output of this dataset represents the recurrence status where the value one as an output indicates the possibility of the patient getting the cancer again in the future. The results of the two experiments are discussed in the following sections.

Experiment No. 1: ClonalG Algorithm In this experiment, the ClonalG algorithm was tested against the cancer dataset. Initially, the dataset was normalized to unity before being fed to the algorithm. Once the data was normalized a percentage of the samples was chosen at random and removed from the data set. This then became the sample that the detectors were trained on. The basic steps of ClonalG as presented in Castro and Zuben (2002) are as follows:

1. Initialization: Create an initial random population of individuals (P)
2. Antigenic presentation: for each antigenic pattern, do:
 - a. Affinity evaluation: present it to the population P and determine its affinity with each element in the population P;
 - b. Clonal Selection and expansion: select n1 highest affinity elements of P and generate clones of these individuals proportionally to their affinity with the antigen: the higher the affinity, the higher the number of copies and vice-versa;
 - c. Affinity maturation: mutate all these copies with a rate inversely proportional to their affinity with the input pattern: the higher the affinity, the smaller the mutation rate and vice-versa. Add these mutated individuals to the population P and reselect the best individual to be kept as the memory m of the antigen presented;
 - d. Metadynamics: replace a number n2 of individuals with low affinity by (randomly generated) new ones;
3. Cycle: repeat Step 2 until a certain stopping criterion is met. The above algorithm was coded in Matlab and obtained from Delahunty and Callaghan (2004), with the stopping criterion set at 500 detectors. Once the data in the data set was normalized a percentage of the self-samples was chosen at random and removed from the data set. This then became the sample that the detectors were trained on. For all test runs, the accuracies were found unacceptably

low and varied according to the test tolerance value. It was noticed that by increasing the threshold value, the accuracy results were improved and vice versa. All of the parameters were varied in the following way without significant effect in the results except for the test tolerance:

1. The number of detectors for the training stage was varied from 500 → 2000
2. The size of training samples was varied from 50 → 500
3. The number of final detectors for the testing phase was varied from 300 → 700
4. The test tolerance value was varied from 0.6 → 1.0

Table 1 highlights the effect of the test tolerance value change on the accuracy, sensitivity, and specificity of the algorithm.

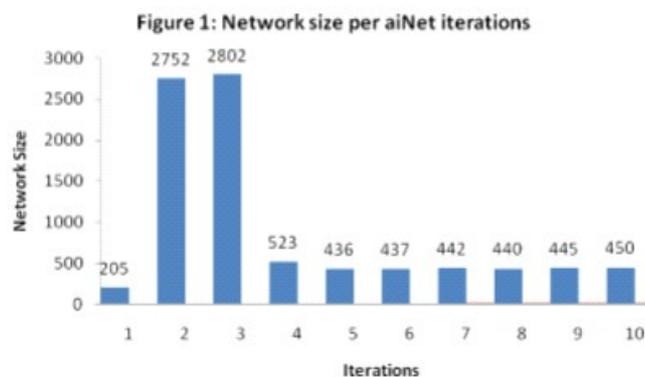
Table 1: Test results

Test Tolerance value	Accuracy	Sensitivity	Specificity
0.6	31.4574	0.9772	0.0084
0.7	35.0649	0.9406	0.0781
0.8	40.1154	0.7945	0.2194
0.9	54.1126	0.6712	0.4810
1.0	63.4921	0.4886	0.7025

Experiment No. 2: AINet Algorithm, The aiNet algorithm discussed in the previous sections is a well-known technique for clustering and data compression. The aiNet algorithm can be divided into two main stages. First, it performs the clonal selection principle and affinity maturation interactions similar to the clonal selection algorithm ClonalG, to produce the network of antibodies. In the second stage, the Minimal Spanning Tree (MST) is built on the antibody network, where each edge is looked at in relation to its neighbors. The inconsistent edge, whose weight is significantly larger than the average of nearby edge weights on both sides of the edge to be discarded, leading to the data partition into clusters.

In this experiment, the aiNet algorithm has been tested against the same cancer dataset used in the previous experiment then the simulation results are presented. The Matlab code is developed by Castro and Zuben (2000) which has been reported in AISWeb. The 692 samples from the cancer dataset were subdivided into two clusters. For the training purpose, the aiNet parameters were set as follows:

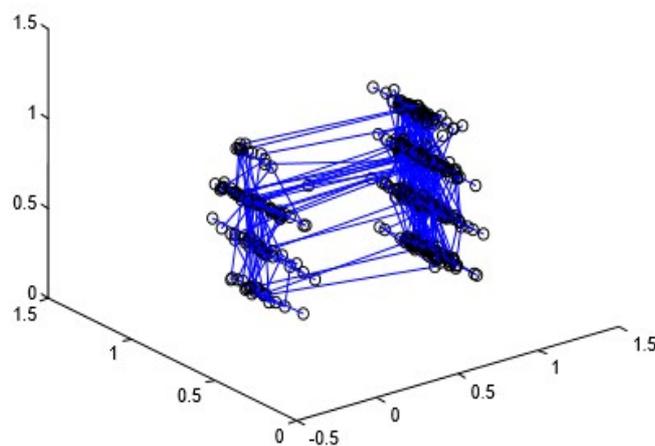
- The suppression threshold = 0.2
- The pruning threshold = 1.0
- Number of best matching cells to be selected (n) = 4
- Clone number multiplier (N) = 20
- Percentile amount of clones to be re-selected = 10%
- The stopping criterion is a fixed number of generations = 10.



The results show that the aiNet algorithm has successfully determined two clusters for the tested data. Figure 1 illustrates the network size per aiNet iterations. The algorithm starts from the fifth iteration to produce almost the same number of nodes. The resulting network contains an average of 442 cells, reducing the data set size to 64% of its original complexity (size). Figure 2 depicts the application of aiNet algorithm to the cancer dataset, where Figures 2(a), (b), (c) and (d) illustrate the Minimal spanning tree, clusters analysis, network dendrogram and the final network structure respectively.

Beside the aiNet capability of reducing redundancy and describing immune network structure, including data distribution and clustering, it has some drawbacks. These include its high number of user-defined parameters and its high computational cost per iteration $O(m^2)$, with relation to the number of memory antibodies (m) (Castro and Zuben, 2001).

Figure 2(a): Minimal Spanning Tree



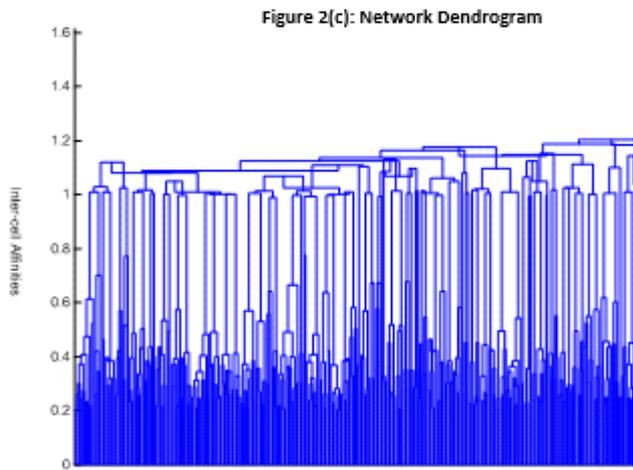
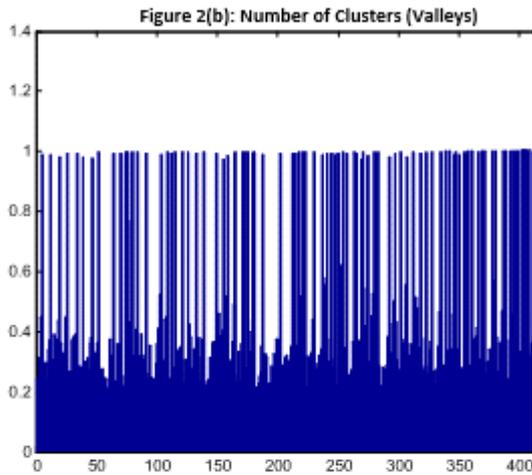
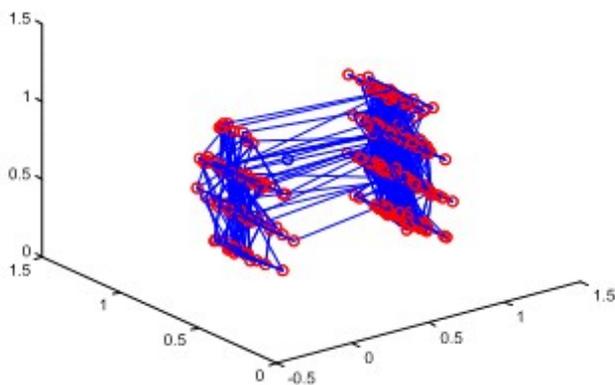


Figure 2(d): Final Network Structure



CONCLUSIONS

An overview of the Artificial Immune Systems field including a background on the main ideas and concepts of AIS and the recent advances in the literature have been presented in this survey. This has provided a motivation to continue exploring the AIS field and contribute to the development of the new AIS models and techniques. A case study was carried out to demonstrate how the AIS approaches can be employed in dealing with real world problems and for achieving different data analysis tasks. Two experiments were conducted to test the ClonalG and aiNet algorithms respectively against a cancer dataset. In the first test, the results obtained for accuracy were unacceptably low and more improvements required for getting better outcomes. On the other hand, a correct classification was achieved in the aiNet test by detecting successfully the number and shape of the clusters for the tested dataset. Researchers have explored the main features of the AIS mechanisms and exploited them in many application areas. Based on their aspects, some of the AIS techniques have been found to be more suitable for certain application areas compared to other AIS approaches. This survey found that negative selection models and algorithms were widely used in fault detection and computer security applications utilizing the self/non-self-recognition aspect. Alternatively, the artificial immune network approaches were used in clustering, classification, data analysis and data mining applications. The clonal selection models were used mostly for optimization problems. Although AIS models have achieved great successes in various application domains, there are still some theoretical issues that need to be further explored such as the development of unified frameworks, convergence, and scalability. The developments of the artificial immune systems would benefit not only from the inspiration of biological immune principles and mechanisms, but also hybridization with other soft computing paradigms, such as neural networks, fuzzy logic, and genetic algorithms. They could also be further studied and applied to more challenging application areas and to solve complex real world problems.

5. SOME APPLICATION OF ARTIFICIAL IMMUNE SYSTEM:

•Robotics:

- Behavior arbitration mechanisms.
- Emergence of collective behavior.

• Control:

- Identification, synthesis and adaptive control.
- Sequential control.

• Optimization:

- Restrict, multimodal and combinatorial.

• Neural Network Approaches:

- Similarities and differences.
- Associative memory.

- Growing Boolean competitive network.

• Anomaly Detection:

- Computational security.
- Negative selection.
- DNA-based negative selection.
- Image inspection.
- Image segmentation.
- Time series novelty detection.

• Agent-Based Approaches:

- Computational security.
- Intelligent buildings.
- Adaptive noise neutralization.

• Learning:

- Pattern recognition.
- Concept learning.
- The Baldwin effect.
- Generation of emergent properties.

• Inductive Problem Solving:

- Finite-State Automaton.
- Genetic Programming.

• Pattern Recognition:

- Generic approaches.
- Spectra recognition.

• Computer Models:

- Cellular Automaton, Multi-Agent and Disease Processes.

• Other Applications:

- Open Webserver coordination.
- Scheduling.
- Data Mining.
- Classifier systems.
- Sensor-based diagnosis.
- Evolution of gene libraries.
- Self-identification processes.

- A Simulated Annealing model of diversity.
- The reflection pattern in the immune systems.

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