# **Review of Artificial Immune System Research**

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**Abstract** – Artificial immune system (AIS) is a metaphorical computational intelligence system developed using ideas and theories extracted from biological immune system. It is a growing area of research attempts to bridge the divide between immunology and engineering, it exploits the mechanisms of the natural immune system including functions, principles and models in order to develop problem solving techniques. AIS is offering great diversity of problem solving algorithms and techniques. It is one of the attracting fields, which notably succeed in convincing researchers to start investigating and developing real-world models to non-linear engineering problems applied to different applications such as anomaly detection, classification, machine learning, clustering etc.

In spite of those great properties of AIS, researchers continue arguing that AIS research does not yet reach the quality and importance of the other computational intelligence techniques like neural networks, DNA computation, evolutionary algorithms, swarm intelligence and fuzzy logic systems, and they admitted that the time has come to try to define the role that AIS can play and the type of applications and algorithms that will allow its potential to be realized.

This conceptual paper is providing detailed review on AIS research focusing on the main frameworks which are considered as milestones in AIS research history, it also provides suggestions extracted from deep study on different conceptual researches on how this rich research area can be improved and reach the equal importance and level of the other computational intelligence techniques.

Index Terms— Artificial Immune System, Computational Intelligence Systems, Immune System, Adaptive immune System, Innate Immune System.

#### **1** INTRODUCTION

ooking closely at research related to modelling and designing solutions for real-life problems it can easily be

concluded that in the near future human knowledge will become more important in system modelling as a suitable replacement to classical mathematical modelling. Those systems based on human knowledge are called computational intelligent systems [1]. In the last few years, it is evident that great increase and interest in modelling using computational intelligence systems inspired by nature and particularly from human biology which clearly has achieved notable success, among these systems we can mention artificial neural networks, DNA computation, evolutionary algorithms, swarm intelligence, artificial immune systems and fuzzy logic systems [1][2][3][4].

Biology over years is considered a rich source of inspiration for modelling and designing solutions to real world complex problems. In fact, creating intelligent systems and nontraditional approaches inspired by nature and biology has been of interest to scientists and researchers for quite long time. Meanwhile, it is clearly recognized that it is not possible to mathematically model all engineering and real world problems using traditional methods [1][3][5].

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AIS is relatively new branch of computational intelligence techniques that offer powerful and robust information processing capabilities. It is a steadily progressing technique inspired by biological immune system [6][7][8][9].

The next section of this paper provides a review on AIS research taking into consideration the suggestions and ideas from AIS researchers on how to improve this intelligent research area.

Section three provides a summarized review on recent researchers regarding the development of the AIS research.

Section four provides the way forward collected from suggestions extracted from literature beside suggestions proposed in this paper, while section five provides conclusion.

#### 2 Review of AIS Research

Two directions of research employed jointly to accentuate the AIS field, which are mathematical and computational techniques. Although many deep investigations have been conducted to better understand the principles of human immune system but still the field not totally understood [10], later in this paper, we will see valuable suggestions from different researchers to help make maximum benefit from AIS theory.

AIS is a very attractive computational intelligence, it offers a variety of paradigms that can be adapted to computational tasks [11][12], it is robust, decentralized and error tolerance. These great properties provide researchers with powerful information processing and problem solving ideas [13][14]. AIS possess great diversity of applications, techniques and models [7][15], so algorithms and techniques have been applied to

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wide range of applications such as information security, machine learning, fault diagnosis, data mining, clustering, classification, learning, image processing and robotics [14][16][17][18].

When reviewing AIS literature, it is noticed that number of conceptual frameworks are used frequently in building AIS models for different engineering applications. This section will provide detailed review literature to the AIS research generally with close focus on the most important researches and key developments.

Two generations of AIS can be found in literature, first generation which is relying only on simplified immune models and its algorithms have often shown considerable limitations when applied to realistic applications. It uses simplistic models of immunology as the initial inspiration, for example negative and clone selection. In contrast the second generation is more complicated and utilizes interdisciplinary collaboration to develop a deeper understanding of the immune system and hence produce more complex models. Because of the limitations of the first generation, the second generation of AIS is emerging, using models derived from cutting-edge immunology, such as Dendritic Cell Algorithm (DCA). Both generations of algorithms have been successfully applied to variety of traditional and complex engineering problems, including anomaly detection, pattern recognition, optimization and robotics [13].

Hart and Timmis [19] categorize AIS application engineering into three classes: anomaly detection, optimization and classification. Considering key works and the progress of AIS in last decade, it is important to assess the contributions of this important field into application areas to which it has been applied. Hart and Timmis argue that AIS should contain features and properties that are not present in other paradigms to be considered a successful and useful field. As a way forward this paper proposes three suggestions for the researchers to get most benefit from AIS, which are:

- Focus on innate immune system and cooperative solutions between both innate and adaptive immune systems;
- 2- Consider combining AIS with other intelligent systems to overcome individual limitations;
- 3- Develop more models on one of the AIS important features, i.e. life-long learning feature.

Although AIS techniques have great success in modelling solutions to real-world problems, Dasgupta [7] argues that still there are some open issues, he mentioned uniqueness and usability of each model needs to be determined as the most important issues. Dasgupta mentioned some aspects to be addressed in order to make the AIS a real-world problem solving technique [7]:

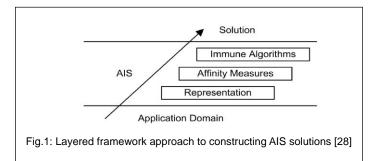
- Needed some improvement in the AIS algorithms efficiency;
- Enhancement of the representation;
- Researchers on AIS should start introducing new other immune mechanisms;
- Developing a unified architecture for AIS modeling.

Twycross and Aickelin [20] argued that AIS need to be built based on much more biologically-realistic models, and instead of building AISs based on the complex human adaptive immune system, AISs should draw inspiration from relatively simpler organisms which possess only innate immune systems, even if we must build AISs which incorporate adaptive immune system it should combine innate mechanisms as well since there is no organism with only an adaptive immune system. Also they argued that AIS need to be based around more sophisticated systemic models of the immune system than those currently employed [20].

Timmis et al. in [21] see AIS as one of the genuine interaction between immunology, mathematics and engineering so the field of AIS can easily be driven a true interdisciplinary biological inspiration mechanism. According to [21] there is more attention from researchers to inspire ideas from biological immune system, so AIS is becoming a more interdisciplinary topic where we have both researchers focusing on biological aspects and others on the engineering aspects. This paper concur with a number of researchers, Forrest and Beauchemin [22], Andrews and Timmis [23], Stepney et al. [24], Bersini [25], Timmis [26] and Cohen [27] concluding that engaging AIS engineers with the immunological modelling scientists are very useful for both communities [21].

Forrest and Beauchemin [22] present a conceptual paper reviewing agent based models (ABM) techniques as they applied to immunology, and argue that there is still a question about the usefulness of using agent based AIS models in understanding the natural immune system. The research paper [22] proposed a comprehensive framework for agent based models, this framework then used to create specialized models for particular applications.

De Castro & Timmis [28] proposed a generic layered approach of immune system inspired engineering solutions. As shown in Figure 1 this framework identifies the components that need to be address in the designing and deploying AIS solution, which are: representation, affinity measures and immune algorithms.



This layered framework demonstrates the general structure of most AIS, and being used frequently to describe the main AIS types. The layered framework takes the application domain of the AIS as its starting point, followed by three layers to be considered before the required AIS is engineered. These layers are: component representations which shows how the components of the system to be represented, affinity measures shows how the interactions between the components of the system are measured and quantified, and then immune algorithms which shows how the components of the systems are going to interact.

Twycross and Aickelin [29] proposed a conceptual framework for AIS incorporating properties and key roles of innate immune system, this will provide a forward step in developing more integrated AIS models.

De Castro and Timmis [15] propose a conceptual structure for modelling and engineering AIS, with the general basis of representing and modelling immune organs, cells and organs.

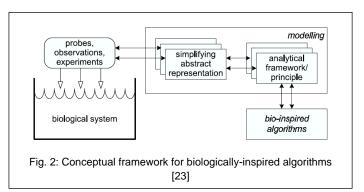
Elhag et. al. [24] also proposed a set of general-purpose algorithms to govern the dynamics of the AIS.

Wang et. al. [5] proposed a new complex AIS, in which complex representation is used as extension of binary representation and incorporated complex representation into AIS. The proposal also shows that the binary values cannot alone describe pattern recognition problems in real-life problems [5].

Tarakanov and Dasgupta [6] present a mathematical model based on the antigen-antibody bindings which is one of the great features of the immune system as a highly distributed adaptive learning system. The protein binding is represented as a mathematical abstraction for key biophysical mechanisms of proteins' behavior. Research shows that even simple variants of immune system networks incorporates main properties of immune response [6].

Andrews and Timmis [23] consider that the majority of AIS models are based on two theories which are Burnet clonal selection theory [30] and Jerne immune network theory [31]. By investigating the state of current thinking among immunologists today, Andrews and Timmis [23] found that certain immune system concepts, such as self-non-self discrimination, are not agreed upon among all researchers. In this paper, it is identified that possible inspiration ideas for AIS can be gained from immune system models especially new models. More theoretical understanding is required since work to date in the realm of AIS has mainly concentrated on what other paradigms do, such as simple optimization and learning. Therefore, attention should not only be paid to the potential of the immune system as inspiration, but also other systems with which the immune system interacts, in particular the immune, neural and endocrine systems. This will pave the way for a greater understanding of the role and function of the immune system and develop a new breed of immune inspired algorithms [23][32].

Mishra and Bhusry [33] present a research paper which reviewed major works in the area of AIS. It has been observed that most of AIS research focused on only three algorithms, i.e. clonal selection algorithms, negative selection algorithm and artificial immune networks. So writers encourage computer scientists and engineers to evolve new models and algorithms. Stepney et al. [24] argue that the next biological inspired computational intelligence systems should develop more sophisticated biological models. Writers also argue that these bioinspired algorithms are best developed in multidisciplinary conceptual framework as a sophisticated biological models. In this important document Stepney et al. present a conceptual framework in which biologically-inspired models and algorithms can be developed and analyzed, this unique framework is shown in Figure 2 below [24][29].



Irun Cohen [27] introduces the concept of computational strategy which immune system uses to carry out its functions in protecting human body. Author invites immunologists to enlist computational scientists to help engineers and practitioners to organize, study and manipulate the enormous amounts of data have obtained by experimenting immune system. Also see that immune computation should influence the technologies used by immunologists in modeling immune system [27]. Forrest and Beauchemin [34] provide a comprehensive review on modelling approaches in immune system inspired systems and highlight different ways of modeling immune system. Within this conceptual paper, the authors focus more on agent based modelling where cells might be represented as individual distributed agents. Authors argue that Agent Based Models (AM) might be more appropriate tool for modelling immunology due to the ease of incorporating knowledge into the model that might not be easily expressed mathematically [21]. Cohen model [35] is considered as one of the substantial models of the immune system. It presents immune system as complex, reactive and adaptive system whose role is to maintain stability to human body, this is not concur with the classical view that sees the main functions of immune system as defence mechanism against pathogen and self-non-self discrimination system. Cohen's immune theory was able to highlight a number of ideas for inspiration that are not presented in the main algorithms of immune system like clonal selection and immune network algorithm [23].

Timmis et al. in [36] agreed with Mishra and Bhusry [33], on that many research papers that AIS technique are much more than engineering systems inspired by the immune system and they suggest that there is a great chance for both immunology and engineering to learn from each other and start working together in an interdisciplinary manner. They also argue that AIS is becoming a more interdisciplinary topic where people are working more on the biological aspects and others on the engineering aspects. So more time need to be spend to develop abstract computational models of the immune system and work closer with immunologists to better understand the biology behind the system.

Greensmith et al. [13] argued that there is a massive change in AIS research, the change is the obvious move to secondapproach of AIS followed by theoretical studies of AIS and

IJSER © 2020 http://www.ijser.org computational immunology. The change in focus of the field suggests that, as the characterization of the second-generation approaches improves, they will increase in popularity and may eventually dominate the field. Like any discipline, the future of AIS research are not clear, given that AIS algorithms are still evolving. As our knowledge of immunology increases, at some point in the future we may have the grounding and computational resources to build full, biologically accurate computational immune systems, based on both the innate and adaptive systems and their numerous cell types [13].

Dasgupta and the team in their comprehensive review [37] argued that recently, the immune system has drawn significant attention to as a potential source of inspiration for novel approaches to solve complex computational problems and its great features offer rich metaphors for its artificial counterpart. For the AIS to gain more attention and to become more valuable in problem solving, and unlike other engineering systems, AISs require both immunology and engineering to learn from each other through working in an interdisciplinary manner. A collaborative effort of several interdisciplinary research scientists has produced a prolific amount of immune inspired algorithms by extracting or gleaning useful mechanisms from the immune system theories, processes and elements [37].

According to Zhang and Yunfang [32], AIS algorithms have mainly been developed in an ad-hoc manner, with particular applications in mind. This may question the usefulness and may mean that theoretical justification for the use of AIS has mostly been lacking. The theoretical work done so far merely constitutes the first steps towards developing a more rigorous underpinning to the area, and therefore it is clearly that more remaining work is to be done. Writers see that much work on AIS has concentrated only on simple extraction of metaphors and direct application. Despite the creation of a framework for developing AIS, it still lacks significant formal and theoretical underpinning. AIS have been applied to a wide variety of problem domains, but a significant effort is still required to understand the nature of AIS and where they are best applied. Freitas and Timmis [38] outline the need to consider carefully the application domain when developing AIS. They review the role AIS have played in the development of a number of machine learning tasks including classification and optimization. However, they clearly pointed out that there is a lack of appreciation for possible inductive bias within algorithms and positional bias within the choice of representation and affinity measures [32].

Last in this review, and looking to the comprehensive revisions of Timmis and his team in [26] and [39], they concluded that AIS is lacking thought regarding the application areas of AIS, lacking theoretical work and limited view of immune system, and also lacking the proposal and development of a general framework to design AIS. Comparing to other computational intelligence or soft computing paradigms, such as artificial neural networks, evolutionary computation and fuzzy systems, it is clear that there is presence of well described set of components and/or mechanisms with which to design such algorithms. He then proposed a framework which need more work in terms of formalization from a mathematical viewpoint and augmentation in terms of new shapes spaces and development of new algorithms [32][39].

### 3 Recent Researches on AIS Development

Recent researches on AIS development are also seeing AIS as a very promising and effective study area with obvious limitations and very big room of improvement. Several review papers have discussed the slow advances in AIS and proposed improvement strategies through novel and simpler AIS models, as well as the importance of developing a unified architecture for integration of existing models.

According to [40], several reviews have discussed advances in the field of AIS on a qualitative perspective. In this work, Haider et al investigated main questions about AIS research from a quantitative perspective, results shown that the field has been growing ever since it was established for the past couple of decades. Writers encouraged external scientists not only engineers to entertain the challenges presented by AIS, but also to be a benchmark for scientific domain analyses [40]. Mishwa et al in their research in [41] proved that the hybrid techniques used are more effective than their parent techniques, and arguing that AIS for detection research area could see a massive growth through the support of additional immune aspects such as gene libraries and Idiotypic networks. Generally writers concluded that the research on the HIS is not comprehensive and there will be many more theories needed, they are certain that the performance and capability of network IDS design based on this understanding will improve.

Karin, Fister JR and Fister are encouraging AIS researchers to further extract inspiration from the components and processes from the immune system for creating effective and powerful computational systems. They are also considering that the possibilities of extracting useful metaphors and constructing new AIS theories are wide-open. They insisted that, a significant number of concepts could be used in the development of AIS in the near future, some of those concepts are clonal expansion, affinity maturation, cross-reactivity, epitope, idiotope, paratope, B-cell and BCR, T-cell and TCR, network structure, dynamics and meta-dynamics [42].

Mishrad and Husry [33] in their survey paper which highlighted the recent applications of AIS, are agreeing that AIS models have accomplished tremendous achievements in many application areas, but there are still many theoretical problems exist, and they are proposing the following solutions:

- The work should focus on expansion and advancement of the algorithms not only on the applications as been noticed now,
- Further analyze such as convergence and advancement of unified framework is needed,
- Consider combining different techniques of soft computing that includes neural network, genetic algorithm, and fuzzy logics.
- More study requires for resolving complicated real world situations and applying them to more challenging application areas like classification and future prediction problems.

According to Hang and the team [43], AIS research recently has drifted away from more biologically appealing models to biological details, such as DCA. They argued that there are powerful algorithms that have already arisen and can arise when more than two of the different approaches are hybridized or new HIS theory is proposed.

## 4 The Way Forward

Looking closely to the AIS research after decades of research and after hundreds of papers and conferences, and not ignoring those great conceptual frameworks and ideas and theories in literature, it may be the right time to take a deeper look and assess AIS research contributions generally and to find new ideas allowing this field to go forward and be fully exploited since we don't noticed many instances of AIS applications applied to real world problems or being used in industry.

As a way forward, AIS researchers should start following some steps in order to make the AIS a real world problem solving technique and to eventually agreed that this research area are worth comparing it with other successful theories and disciplines.

The adaptive immune system does not act independently to eliminate foreign invaders; both innate and adaptive immunity work together for the ultimate goal of protecting human body. Moreover, intensive research on biological immune system prove that the innate immunity occupied central role in the immune response and innate immunity plays a crucial role in the activation of the adaptive immune response [28][44][45][46]. Since no organism with only adaptive immune system, some research urges that there is no sense to build AIS with no innate immune capabilities [33]. In literature both systems are covered widely but in many cases they characterized as two separate subsystems, this view does not reflect the wide perspective describing the immune system as a parallel distributed system composing of great number of cells, organs and molecules cooperate and interact for the ultimate goal of protecting human body, So the innate and adaptive systems interplay provides human body that high level of comprehensive protection [13][15][21][47].

It is important also to note that innate and adaptive immune systems operate over a typical different timescales. The innate immune system started the immune response instantly or after a very short time and take a small time scale reacting to invasion, unlike adaptive immune system which operates over a longer time period, and initiate a reaction after long period of time some times in days [21].

Although literature focused in decades on adaptive immune mechanism, but recently intense research has appreciated and highlighted the importance of the central role of innate immunity in the natural immune system response mechanism, this is being reflected in AIS research with many models and frameworks having both innate and adaptive subsystems.

Computational intelligence techniques have shown notable success recently when applying single technique at a time, but it is proved that modelling hybrid systems working cooperatively is more effective in solving complex real world problems. Integrating different learning and adaptation techniques is very useful for overcoming individual limitations and weaknesses. This trend is one of the most intensively growing areas in recent years, and it has contributed effectively in the developments of a large number of intelligent system [2][33][48][49].

Second suggestion is to combine theories and algorithms from AIS and other intelligent systems in a single system. Hybrid intelligent systems utilize the main characteristics of various soft computing methods and techniques like artificial neural networks, fuzzy logic system, artificial immune systems, evolutionary computation and genetic algorithms [48][49].

Researchers generally have explored combining two different computational intelligent techniques, in literature we can find many models with this combination providing solutions to very complex real world problems. Combining AIS with any of the intelligent techniques is improving the quality of those combined systems since we avoid single limitations and we add strengths of two techniques together in a single solution.

In literature we have found tens of hybrid systems combining AIS functions and theories with other soft-computing techniques. For example Hajela et al. [50] in their early solution combined AIS ideas with genetic algorithms, they used immune networks to improve the convergence of genetic algorithms for design. Nasaroui et al. [51] proposed a fuzzy AIS model, which uses a fuzzy set to model the area of influence of each B-cell, which makes it more robust to noise.

Vargas et al. [52] presented an immune learning classifier network named CLARINET for autonomous navigation by combining the strengths of learning classifier systems, evolutionary algorithms, and an immune network model.

Xian et al. [53] proposed a novel intrusion detection method that optimizes the objective function of unsupervised fuzzy k-means clustering based on clonal selection algorithm.

Fu et al. [54] proposed a hybrid artificial immune network which uses the swarm learning of particle swarm optimization to speed up the convergence of artificial immune system. Gan et al. [55] proposed a technique that combines the simple representation method of gene expression programming and the advantage of clonal selection algorithms.

Danzhen et al. [56] introduced a fuzzy artificial immune network (FaiNet) algorithm for load classification. It consists of three parts: the artificial immune network learning algorithm, the minimal spanning tree algorithm, and the classification algorithm based on fuzzy C-means algorithm [48].

Mu-Chun Su et al. [57] presented an on-line learning neurofuzzy system which was inspired by parts of the mechanisms in immune systems. It illustrates how an on-line learning neuro-fuzzy system can capture the basic elements of the immune system and exhibit some of its appealing properties.

Bateni et al. [58] presented a new automated alert correlation approach which employs fuzzy logic and artificial immune system to discover and learn the degree of correlation between two alerts and uses this knowledge to extract the attack scenarios.

Shamshirband et al. [59] introduces a bio-inspired method, namely the cooperative based fuzzy artificial immune system

IJSER © 2020 http://www.ijser.org (Co-FAIS). It is a modular based defense strategy derived from the danger theory of the human immune system. The agents synchronize and work with one another to calculate the abnormality of sensor behavior in terms of context antigen value (CAV) or attackers and update the fuzzy activation threshold for security response.

Shin & Kuan [60] proposed an evolutionary multi-objective optimization algorithm that applies the concept of biological immune system as an alternative algorithm for solving Pareto engineering optimization problems. The optimization algorithm developed and presented in this paper uses the cycle of affinity-maturation principle in the immune system that contains the repeated activation, proliferation and differentiation.

In [61] Yang Liu proposed a neuro-immune inspired computational framework and its applications to a machine visual tracking system.

We also encourage computer scientists and engineers to use features and properties that are not present in other paradigms and to evolve new immune system models and algorithms, this will guarantee improvement in the AIS algorithms efficiency. Also, we encourage AIS researchers to develop more models on one of the AIS important features like memory or discrimination.

We also concur with many researchers including Timmis et al. [36] that there is a great chance for both immunological modelling scientists and engineers to learn from each other and start working together in an interdisciplinary manner, so researchers could focus on biological aspects while engineers focus on engineering and problem solving aspects and work closer with immunologists to better understand the biology behind the system.

The next suggestion is concur with Stepney et al. [24] that the researchers should start developing more sophisticated biological models so AIS research will be based on more sophisticated models of the immune system than those currently employed.

In our last suggestion we do agree with [7] that the uniqueness and usability of each single AIS model needs to be determined, so each algorithm find the enough time to scale well. We also encourage developers to consider building their AIS research on well-known developed AIS architectures and frameworks, this will also help enhancing those architectures.

# 5 Conclusion

Biological immune system is a very powerful intelligent system it is also a very complex interdisciplinary paradigm. A relatively new computational intelligence system called artificial immune system created from the biological immune system and inspired by the great features of the immune system like anomaly detection, recognition of foreigners, adaptability, imperfect detection, memory, multi layered, diversity, dynamic learning, autonomy, optimization, parallel detection and others. Researchers heavily used AIS metaphor to model and design solutions to complex engineering problems especially in anomaly detection, optimization and classification. Since immune system itself is a very successful protection system, artificial immune system is used frequently in computer and network security applications especially IDS.

In this paper we carefully reviewed the AIS research in which we noticed great achievements that AIS has accomplished in complex engineering problem although still there is a big room of improvements especially in AIS algorithms and models. This paper also reflects the important opinions of the AIS researchers on the progress of this rich research field. Many researchers argue that the research of AIS has open issues still need to overcome in order to become a real world problem solving technique, those issues are like the importance of the research to be unique and the need for it to be effective in solving complex real world problems. The researchers have agreed generally in some aspects as a way forward, like:

- Working on new other immune mechanisms;
- Using cooperative frameworks incorporating innate immunity not only adaptive immune system;
- Using hybrid intelligent systems composing AIS and one of the soft computing techniques like fuzzy logic or neural network;
- Immunologists and computational scientists need to work together to improve the research of AIS.

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