Breast Cancer Classification by Artificial Immune Algorithm based Validity Interval Cells Selection

Rima Daoudi and Khalifa Djemal
IBISC Laboratory, Evry Val dEssonne University, 91020 Evry, France

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Abstract: We present in this work an Artificial Immune System (AIS) algorithm for breast cancer classification and diagnosis. The main contribution is to select memory cells according to their belonging to a validity interval based on average similarity of training cells. The behaviour of these created memory cells preserves the diversity of original cancer learning class. All these operations allow to generate a set of memory cells with a global representativeness of the database which enables breast cancer classification and recognition. Promising results have been obtained on both Wisconsin Diagnosis Breast Cancer Database (WDBC) and (DDSM) Digital Database for Screening Mammography.

1 INTRODUCTION

Cancer is a disease in which cells become abnormal and replicate forming more cells in an uncontrolled way. Breast cancer begins in the tissues that makes the breast, cancer cells may form a mass called a tumor (Arora et al., 2008). Tumor can be benign or malignant. The correct diagnosis of breast cancer has become a major problem in the medical field since this famous type of cancer stills threatening the life of most women. Indeed, approximately one in ten women is affected by this disease in her lifetime. Although some risk reduction can be achieved through prevention, strategies in this direction can not allow the elimination of the majority of breast cancers that occur in low-income and middle-income countries. Early detection remains the main way to fight against the disease, it improves the chances of survival as well as breast cancer outcome (Daoudi et al., 2015).

There is no doubt that the evaluation and decision-making processes carried out by the experts are very important factors. However, intelligent classification algorithms also help physicians, particularly by minimizing errors of not experienced practitioners.

In this context, computerized diagnostic systems are increasingly used to directly reach the final diagnosis using artificial intelligence algorithms that perform the role of classifiers such as Neural Networks (Hagan et al., 1996),(Marcano-Cedeño et al., 2011),(Neves et al., 2015), Genetic Algorithms (Yang et al., 2013) or Support Vector Machines (Zemmal et al., 2016),(Torrents-Barrena et al., 2015). In the middle of the 90s, a new artificial intelligence approach inspired by immunology, has emerged, called Artificial Immune Systems (AIS). Several concepts of the immune response were extracted and applied as a solution to real-world science and engineering problems (De Castro and Von Zuben, 2000).

Indeed, the Artificial Immune System (AIS) is a distributed system that can perform classification, recognition and learning tasks using extraction, communication and memorization processes. Efforts made in this research focus have contributed to the emergence of several algorithms that can be classified into three large families as the natural mechanism responsible for the implementation: negative selection (Dasgupta and Majumdar, 2002), clonal selection (De Castro and Von Zuben, 2000) and artificial immune network (de Castro and Von Zuben, 2001) algorithms.

The immune network theory was proposed by Jerne in 1974 (Jerne, 1974). The hypothesis was that the immune system maintains a network of interconnected idiotypic antibodies to recognize an antigen. Negative selection is a mechanism that protects the body against the autoreactive lymphocytes. It uses the ability of the immune system to detect unknown antigens without affecting the self cells (Somayaji et al., 1998). The clonal selection theory has been proposed by Burnet in 1959 (Burnet et al., 1959). It explains how an immune response is mounted as a model of non-self antigen is recognized by the system. There

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are two processes: the recognition of the shape of the antigen and selecting the antibody specific to it. The idea is that only antibodies capable of recognizing the antigen are activated for proliferation (cloning + mutation).

Since 1959, there have been improvements of the Burnet's theory, especially on the way the antigens are recognized. But the basic principles of clonal selection and affinity maturation by hypermutation are sufficient for the purposes of artificial clonal selection algorithms.

In 2002, De Castro and Von Zuben (De Castro and Von Zuben, 2000) proposed a clonal selection based algorithm named CLONALG. The principle of this algorithm is to build an initial memory cells population and expose them to the antigens (training examples) for a number generations to develop a population of more specific memory cells to these antigens through the cloning and mutation processes.

The main learning steps of CLONALG algorithm are:

- Generation of initial memory cells by a random selection of training examples.
- Memory cells evaluation and selection of the most representative of the antigen.
- Cloning, mutation and re-selection of the best mutated clone.
- Maintaining of diversity by the rejection of the less good memory cells and their replacement by randomly generated ones.

Compared to other clonal selection algorithms, CLONALG has low complexity and requires fewer parameters that can influence the classification accuracy (Brownlee, 2005),(Zhang, 2011). It has been successfully applied to solve various complex problems, and offers a promising precision in the field of pattern recognition.

Several studies have been published to improve the potentially negative features in the learning of CLONALG algorithm, including the exploration of the information contained in the population of mutated clones(White and Garrett, 2003), (Tasnim et al., 2014), or the generalization of memory cells(Sharma and Sharma, 2011). In (Daoudi et al., 2014), the work is to improve two limitations observed on CLONALG algorithm, the first in the way it is initialized, and the second in the selection of memory cells to be cloned to avoid rejecting cells and their replacement by randomly generated ones. The rejection step of the less competent memory cells in CLONALG is used to maintain diversity in the algorithm, but no check is made that the added random cells are better than those which are rejected. The improvements consist

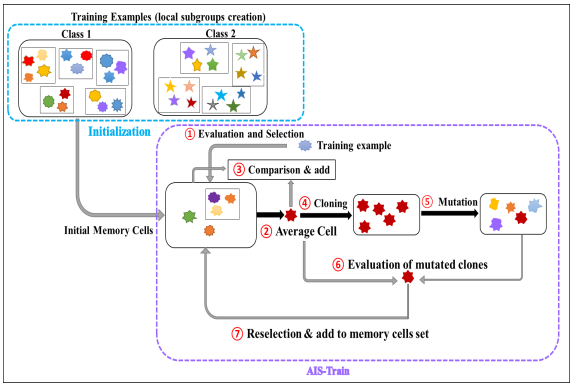

Figure 1: Cells Clonal Selection Artificial Immune System (CCS-AIS) Diagram (Daoudi et al., 2014).

in maintaining diversity by creating initial antibodies (memory cells) and new memory cells from averaged local subgroups. Diagram of CCS-AIS approach proposed in (Daoudi et al., 2014) is given in figure 1. The results significantly improves the accuracy of CLONALG. Nevertheless, we found that averaging cells operations do not adequately represent the true diversity of all examples of the class to learn. Indeed, even if the initial memory cells (antibodies) are not randomly selected, they do not often guarantee the overall representativeness of the class. In this work, we propose a method to validate these cells by using cells selection validity interval.

The rest of the paper is composed as follows: in the next section we present the databases that we used to evaluate our approach. Section 3 details the different steps of the proposed Validity Interval Cells Selection Artificial Immune System (VICS-AIS) algorithm. The results of application and the work's conclusion are given in sections 4 and 5 respectively.

2 USED DATABASES

To evaluate our proposed algorithm, we chose to apply it on two different databases the most used in the field of diagnosis of breast cancer: Wisconsin Diagnosis Breast Cancer Database (WDBC) and Digital Database for Screening Mammography (DDSM).

2.1 Wisconsin Diagnosis Breast Cancer Database (WDBC)

To evaluate our work, we chose to apply it on the Wisconsin Diagnosis Breast Cancer Database (WDBC). It was supported by Dr. William H Wolberg et al. (Wolberg and Mangasarian, 1990). WDBC consists of data from 569 breast fine needle aspirate (FNA) cases con-

taining 32 descriptive features, where the two first features correspond to a unique identification number and the diagnosis status (benign or malignant). The rest 30 features are computed from a digitized image of a FNA of a breast mass by obtaining a small drop of fluid from a breast tumor using a fine needle. With an interactive interface, active contour models are initialized near the boundaries of a set of different cells. The customized snakes are deformed to the exact shape of cells, ten features are computed for each cell and the mean value, largest value and standard error of each feature are computed for each image. The case distribution includes 357 cases of benign breast changes and 212 cases of malignant breast cancer. The descriptive features are recorded with four significant digits including:

1. Radius; 2. Texture; 3. Perimeter; 4. Area; 5. Smoothness; 6. Compactness; 7. Concavity; 8. Concave points; 9. Symmetry; 10. FracDim = fractal dimension The features are recorded with four significant digits, and since they are measured in different scales, the error function will be dominated by large-scale variables. Thus, to eliminate the effect of different levels, standardization is needed before learning.

In our work the WDBC database is normalized in the range [0, 1] according to the following equation:

$$x_i = \frac{x_i^o - x_{min}}{X_{max} - x_{min}} \quad (1)$$

Where x_{min} is the minimum of the data X for all i, x_{max} is the maximum of the data X for all i, x_i^o is the original i^{th} data of data X, and x_i the normalized feature value.

2.2 Digital Database for Screening Mammography (DDSM)

The digital database for screening mammography (DDSM) was assembled by a group of researchers from the University of South Florida and was completed in 1991(Heath and Bowyer, 2000). It comprises 2620 cases collected from the hospital, "Massachusetts General Hospital" (MGH), the University "Wake Forest University" (WFU) and the hospital "Washington University of St. Louis School of Medicine" (WUSTL). DDSM has been widely used by the scientific community in the field of breast cancer diagnosis; it has the advantage of using the same standardized lexicon by the American College of Radiology (ACR) in the BI-RADS (Breast Imaging-Reporting And Data System). Different patient records were made as part of breast cancer screening and were classified into three cases: normal cases (no lesions) benign, and malignant cases. Each file is composed of four views that contain the external oblique (MLO) and craniocaudal (CC) of each breast. These files are also provided with data annotations by radiologists. These annotations are used to describe the various lesions present in the images such as the number and type of anomalies (microcalcifications / masses), the biopsy result (Benin / malignant), the location of lesions, etc. In this work, we only deal with the case of masses (not microcalcifications). Sub-database of DDSM was created consisting of 242 masses: 128 benign and 114 malignant. These examples will be partitioned (in the same way that the WDBC database) into training and test examples.

The description of breast masses is a very important step, three new descriptors: the Skeleton End Point (SEP), Protuberance selection (PS) and the Spiculated Mass Descriptor (SMD) were proposed in ((Sellami-Masmoudi et al., 2009), (Cheikhrouhou et al., 2011) and (Kachouri et al., 2012)) respectively, which were compared to 19 other features proposed in the literature ((Daoudi et al., 2014)). In this work, all of the 22 features are used to evaluate the performance of the proposed VICS-AIS classifier.

3 PROPOSED AIS ALGORITHM BASED VALIDITY INTERVAL CELLS SELECTION (VICS-AIS)

We propose in this work a method for validating the memory cells by using a validity interval for improving breast cancer recognition. This validity interval is based on the standard deviation of average similarities of all training cells, more particularly of the relevant class. As we mentioned in section 1, the created memory cells in (Daoudi et al., 2014) which are used in classification do not often ensure a good representation of all original cells of the different training classes (benign and malignant). To improve the representativeness of theses training cells, we propose to determine a validity interval allowing the selection of more efficient memory cells. By using a validity interval we garantee a better deversity for the set of memory cells, and we have less identical cells that may slow down the training process. This proposed solution is composed of three main steps. The first one consist in determining the validity interval of selection, the second step concerns the selection of initial memory cells using validity interval presented in the first step. The last step is the global AIS training system.

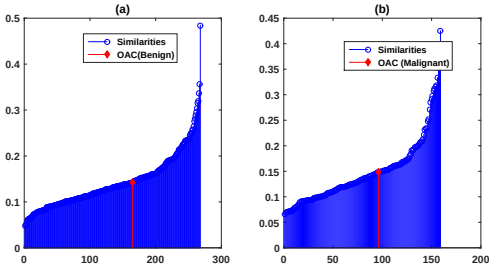

Figure 2: Histogram of similarities between the overall average cell (OAC) and training examples of Benign class (a) and Malignant class (b).

3.1 Validity Interval of Selection

From training cells, we calculate an overall average cell (OAC), then we determine its similarity (Sim) with all the examples of the training class. We calculate the statistical characteristics: the mean, variance and standard deviation.

Similarity is the measure of match between the antigen (training example) and a memory cell. In our work, and as the attribute values of the used databases are real, it is determined using the Euclidean distance (ED) calculated by:

$$ED(OAC, Training\_Example) = \sqrt{\sum_{i=1}^{n}(x_i - y_i)^2} \quad (2)$$

with $OAC = x_1,..,x_n$ and $Training\_Example = y_,..,y_n$, and n is the database dimension.

$$Sim(OAC, Training\_Example) = 1 - ED \quad (3)$$

The average similarity of the class (Sim_moy) is the average of similarities of OAC with all instances of the class. Figure 2 shows an example of the similarities between the overall average cell (OAC) and training examples of each class (left: Benign,right: Malignant) of WDBC database. The figure illustrates the diversity of training examples of each class, which we must select the right memory cells representative of the same diversity.

Subsequently, we calculate the standard deviation σ of the similarities of each class by the equations:

$$\sigma = \sqrt{\frac{1}{M}\sum_{i=1}^{M}(x_i - \bar{x})^2} \quad (4)$$

With $\bar{x}$ = The average similarity of the class (Sim_moy), and M: the total number of training data.

The Validity Interval (VI) of each training class is determined by:

$$VI = Sim\_moy \pm \sigma = [Sim\_moy - \sigma, Sim\_moy + \sigma] \quad (5)$$

This interval will be used to validate the selected clones to reach all final memory cells pool.

3.2 Initial Memory Cells Selection using Validity Interval (VI)

In this step, the creation of the initial memory cells for each training class is performed in the same manner as in (Daoudi et al., 2014), i.e. from averaged local subgroups of training examples. The aim is to create initial cells representing all the data to learn, instead of randomly selecting cells not necessarily representative of the class.

After creating the initial memory cells $(MC_1,..,MC_N)$, we compute the average similarity of each one with all the Training examples $(TE_1,..,TE_M)$.

with N: the number of initial memory cells (NB_{MC_i}).

$$Sim\_moy(MC_i) = \frac{1}{M}\sum_{j=1}^{M} Sim(MC_i, TE_j) \quad (6)$$

- If $Sim\_moy(MC_i) \in VI$; MC_i is kept in the initial memory cells set.
- Otherwise, it will not be considered.

3.3 AIS Training System

In this step, the training of the artificial immune system is made. Average cells are created and added to the set of the final memory cell as has been described in (Daoudi et al., 2014), but with an additional condition.

Indeed, the memory cells (medium or mutated clones) will be added to the memory cells only if their average similarities are in the validation interval (VI) of the relevant class.

- If $Sim\_moy(Cell) \in VI$; add $Cell$ to final memory cells. (Cell= Average cell or mutated clone).
- Otherwise, reject Cell.

In this way we enable the generation of memory cells with an overall representativeness of each class to learn. General diagram of VICS-AIS proposed algorithm is given in Figure 3

At the end of a defined number of iterations (fixed by the user), we dispose of a set of global memory cells for each training class. These cells will be used in the test phase to determine the class of each sample to be classified. The application results of our approach for breast cancer diagnosis are presented in the following section.

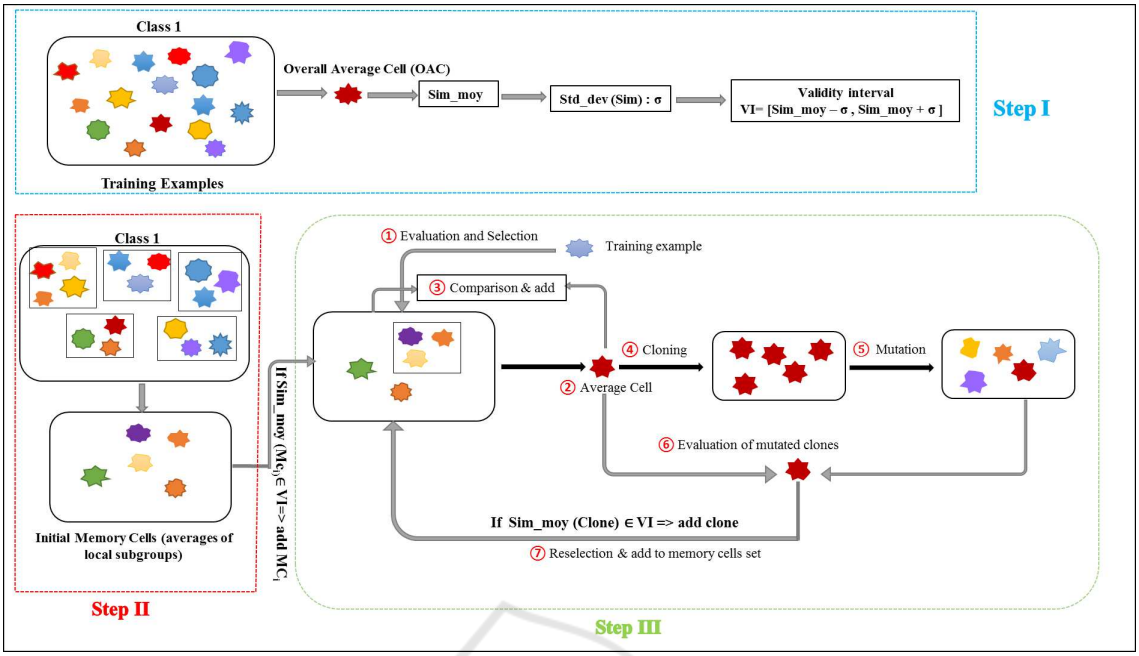

Figure 3: Diagram of VICS-AIS composed of Step I: Validity interval Creation for selection (VI), Step II: initial memory cells selection using (VI) and Step III: AIS training system.

4 EXPERIMENTAL RESULTS

The overall results of this research are given in this section. First we present the parameters used in evaluation, then all achieved tests are given and discussed in subsequent sections.

4.1 Algorithm Parameters

We present in this section all of the parameters used in our evaluations of the VICS-AIS approach on both WDBC and DDSM databases.

4.1.1 Number of Initial Memory Cells

The initial memory cells population must be consistent enough to properly represent the learning database. At the same time, the number of these cells should not be very great because it affects the speed of the algorithm. The number of initial memory cells of each class (NB_{MC_i}) which is also the number of local sub-groups is randomly determined by the equation:

$$NB_{MC_i} = round(rand(\frac{X}{3}, \frac{X}{2})) \quad (7)$$

With X the total number of training examples of a given class.

4.1.2 Number of Clones

The number of clones of each memory cell is calculated proportionally to its similarity value by the following equation:

$$NB_{Clones} = round(\beta * Sim) \quad (8)$$

Where β is a cloning factor fixed by user. In our work, β was set to 5 experimentally.

4.1.3 Range of Mutation

The mutation interval of each clone is inversely proportional to its similarity value. I.e, the larger similarity value is, the less the interval of change is wide. Thus, the mutation value is randomly selected between [Sim-1,1-Sim]. Table 1 summarizes all the parameters used in the evaluation of the proposed VICS-AIS approach:

Table 1: Used parameters in evaluation.

Parameter	Value
Similarity	1- Euclidean distance
NB_{Clones}	$\beta * Sim$
β (Cloning factor)	5
Mutation	Rand($sim-1, 1-sim$)
NB_{MC_i}	$rand(\frac{X}{3}, \frac{X}{2})$
k (Local subgroup size)	$\frac{X}{NB_{MC_i}}$

After presenting the parameters used for the evaluation of the approach that we proposed to improve the clonal selection, we present in the next section the application results of VICS-AIS (Validity Interval Clonal Selection Artificial Immune System). The algorithm VICS-AIS aims to enhance the diversity of the CCS-AIS algorithm (Daoudi et al., 2014). Indeed, to improve the overall representativeness of the training data and preserve good diversity in the algorithm, we proposed to use a validity interval for each class to learn based on the statistical characteristics of the latter.

4.2 Classification Results

Based on the parameters set in the previous section, this work uses four-fold cross validation to evaluate the performance of the proposed approach. We shared our databases into four equal parts, and used three parts, for training and one for testing at each evaluation. After 1,2 5 and 10 generations (iterations) of the algorithm, the memory cells generated at the end of training are used in evaluation. The average of 10 successive runs is taken as the end result of an evaluation. Tables 2 and 3 present the classification results obtained by the VICS-AIS method on WDBC and DDSM databases are respectively, for the different number of generations.

Table 2: Classification results on WDBC database.

Generations	(%) Train $\pm\sigma$	(%) Test $\pm\sigma$
1	96.96 $\pm$0.85	94.18 $\pm$1.32
2	97.80 $\pm$0.30	94.75 $\pm$1.05
5	98.55 $\pm$0.32	95.48 $\pm$0.90
10	98.95 $\pm$0.16	97.58 $\pm$0.22

Table 3: Classification results on DDSM database.

Generations	(%) Train $\pm\sigma$	(%) Test $\pm\sigma$
1	94.55 $\pm$1.40	94.64 $\pm$0.87
2	94.70 $\pm$1.60	94.91 $\pm$1.12
5	95.54 $\pm$0.56	95.18 $\pm$0.80
10	96.66 $\pm$0.20	95.76 $\pm$0.39

On WDBC database, proposed VICS-AIS algorithm obtained 97.58% classification accuracy after 10 generations, compared to CCS-AIS which provided 96.80%. On DDSM database, the final classification result after 10 generations of VICS-AIS algorithm was 95.76%, while CCS-AIS algorithm reached 94.98%. We also noticed a rapid learning of the VICS-AIS algorithm with respect to CCS-AIS, and this is thanks to the good selection of appropriate memory cells, and elimination of redundant or identical cells. So we can say that the proposed approach has contributed to the improvement of CCS-AIS algorithm.

Since the VICS-AIS algorithm is an improvement CCS-AIS algorithm, we present in Figure 4 a comparison between the two approaches in terms of average similarities of both Benign and Malignant classes of WDBC database (because it is more consistent than the base DDSM). The average similarities of final memory cells obtained by the two approaches are calculated and compared with the average similarity of the original cells of the database. we also present a comparison between these values and between the validity intervals of each approach in table 4.

The validity intervals of final memory cells obtained by CCS-AIS algorithm on both benign and malignant classes are narrower than those of the memory cells obtained by our approach (table4). From figure 4, we can observe that average similarities of final memory cells of VICS-AIS are nearest to the average similarities of training WDBC database for benign and malignant classes, unlike average similarities of CCS-AIS memory cells which are smaller. From these obtained results, we can say that the proposed VICS-AIS method is effective. Indeed, the introduction of validity interval in the algorithm allowed a global representation of the diversity of training data, which is important to avoid local minima and ensures a more accurate classification.

4.3 Comparative Study

In this section, we provide a comparative study between the approach we proposed, and some clonal selection algorithms of the literature (including CCS-AIS) that we have implemented. We applied each algorithm on the two databases (WDBC and DDSM) using the same parameters listed in table 1. The results of each application for 10 generations are listed in table 5.

By comparing the results, it is easily noticeable that the VICS-AIS algorithm has the best classification rate on both WDBC and DDSM databases. Another important point which illustrates the effectiveness of improvements in CCS-AIS algorithm is the standard deviation (σ). Indeed, the VICS-AIS algorithm has smaller values of σ, which means that it is the most accurate approach. It was reduced by 0.3% on WDBC database and 0.39 % on the DDSM database. Learning the 10 generations of VICS-AIS is also the fastest among the approaches listed in Table 5, thanks to the good selection of memory cells, and elimination of repetitive cells due to the cloning and the mutation operators.

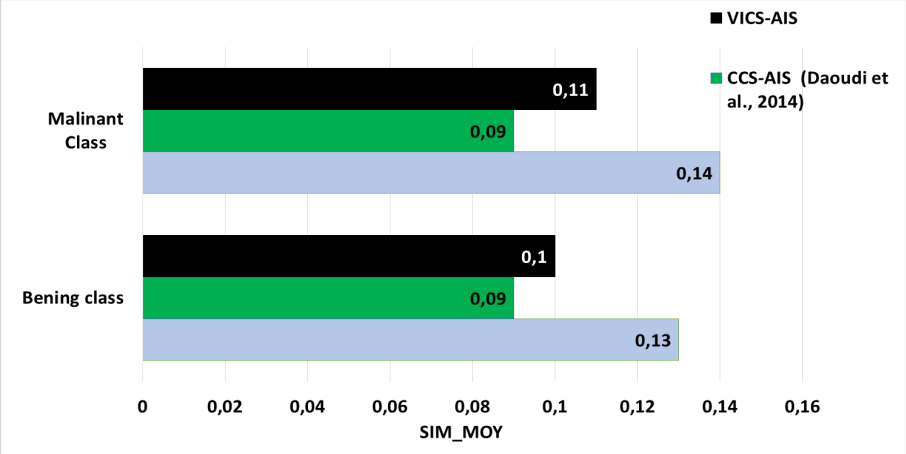

Figure 4: Comparison between average similarities values of WDBC database and final memory cells of CCS-AIS algorithm and our approach.

Table 4: Comparison of Validation Intervals and average similarities values of WDBC database with final memory cells of CCs-AIS algorithm and our approach.

	(%) VI (B)	VI (M)	Sim_moy (B)	Sim_moy (M)
WDBC	[0.08,0.19]	[0.08,0.20]	0.13	0.14
CCS-AIS(Daoudi et al., 2014)	[0.06,0.12]	[0.06,0.13]	0.09	0.09
VICS-AIS	[0.08,0.12]	[0.08,0.14]	0.10	0.11

Table 5: Comparison of classification results.

Algorithm	(%) WDBC	(%) DDSM
CLONALG (De Castro and Von Zuben, 2002)	89.86± 4.45	85.15± 6.46
AIRS (Watkins et al., 2004)	90.30± 1.36	89.15± 1.88
CLONAX (Sharma and Sharma, 2011)	93.40± 2.23	92.25± 1.47
MF-AIS (Daoudi et al., 2013)	95.03± 0.50	94.91± 0.61
CCS-AIS (Daoudi et al., 2014)	96.80± 0.52	94.98± 0.78
VICS-AIS (This Study)	97.58± 0.22	95.76± 0.39

5 CONCLUSION

The objective of this work is to provide help to the experts for a second opinion for breast cancer diagnosis. In this aim, we presented in this paper an artificial immune algorithm based validity interval for memory cells selection (VICS-AIS). The proposed approach selects the memory cells according to their belonging to a validity interval based on average similarity to ensure global representation of the diversity of the data to learn. The main contributions that we brought and that justify the improved results are :

- Improvement of initialization, by creating specific initial memory cells for each learning class, and selection of the most representative among these cells.
- Creation of potential memory cell for cloning and mutation.
- Use of a validity interval of selection to improve the overall representativeness and preserve good diversity of learning data.

The obtained results on WDBC and DDSM databases show a great performance of the classifier. Based on this work, we can say that the introduction of validity intervals in the training of AIS algorithms is effective to properly represent the true diversity of the training data, and guarantee good quality memory cells.

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