BIOINFORMATICS USING INTELLIGENT AND MACHINE LEARNING

A HYBRID INTELLIGENT CLASSIFIER FOR THE DIAGNOSIS OF PATHOLOGY ON THE VERTEBRAL COLUM

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Abstract: *The use of Machine Learning (ML) techniques is already widespread in Medicine Diagnosis. The use of these techniques helps increasing the efficiency of human diagnostic, which is significantly affected by the human conditions such as stress as well as the lack of experience. In this paper, integration between two ML techniques case-based reasoning (CBR) and artificial neural network (ANN) is used for the automation of the diagnosis of pathology on the vertebral column. CBR is used for indexing and retrieval. For adaptation, an untrained ANN is fed with the retrieved closest matches. Then the ANN is trained and queried with the new problem to give the adapted solution. Experiments are conducted on the vertebral column data set from University of California Irvine (UCI) machine learning repository. A comparison with several machine learning techniques used for classifying the same problem is performed. Results show that the hybridization between CBR and ANN helps in improving the classification.*

Keywords: *Computer Aided Diagnosis System, Hybrid Intelligent Classifier, Vertebral Column, Case-Based Reasoning, Artificial Neural Network.*

ACM Classification Keywords: *I.2.5 Expert system tools and techniques - Conference proceedings.*

Introduction

A hybrid intelligent system is one that combines at least two intelligent technologies. For example, combining a neural network with a fuzzy system results is a hybrid neuro-fuzzy system. Each component has its own strengths and weaknesses. Probabilistic reasoning is mainly concerned with uncertainty, fuzzy logic with imprecision, neural networks with learning, and evolutionary computation with optimization. A good hybrid system brings the advantages of these technologies together [Negnevitsky, 2005].

Case-based Reasoning (CBR) is one of the fastest growing areas in the field of knowledge-based systems. It has been used to develop many systems applied in a variety of domains, including industry, design, law, medicine, and battle planning. CBR is based on psychological theories of human cognition [Watson, 1997]. It rests on the intuition that human expertise does not depend on rules or other formalized structures but on experiences. CBR claims to reduce the effort required for developing knowledge-based systems substantially compared with more traditional artificial intelligence approaches.

An artificial neural network (ANN) is a computational model that tries to simulate biological neural networks. Neural networks are used for performing classification and clustering tasks. A neural network consists of many simple interconnected processing units called neurons. The behavior of a neural network is determined by neuron interconnections and neuron parameters. Training data are used to train a neural network to perform its desired function. Various learning algorithms have been applied to train neural networks. Back propagation is the most well-known such algorithm [Haykin, 1999].

Hybridization between neural networks and CBR may develop extra advantages to both systems. On the one hand, neural networks provide efficiency, generalization and robustness that are important features in different domains. Meanwhile, classification and clustering functions are necessary in several CBR tasks. On the other hand, CBR offers openness and modularity to the integrated system by exploiting available cases [Prentzas & Hatzilygeroudis, 2009].

In this paper a combination of the CBR and ANN is done in order to develop an intelligent classifier for the pathology on the vertebral column. The vertebral column has several major functions. It encloses the spinal cord, that delicate bundle of nerve tissue which carries nerve impulses between the brain and the rest of the body. The vertebral column also provides structural support for the chest as well as the maintenance of the posture of the body and in movement. Injuries to the vertebral column are common cause severe pain in the injured area. In severe cases, the spinal cord may be affected as well [Seymour, 1998]. Thus, facilitating an auxiliary system to medical decision supporting is important.

The developed classifier is compiled using a domain-independent CBR shell designed and developed by the author which will be reference hereinafter as (eZ-CBR). This shell integrates the CBR and ANN in one application that facilitates the processing of different domain problems in few steps. Experiments are conducted using a dataset provided by University of California, Irvine ML repository [Frank & Asuncion, 2010].

This paper is organized in five sections. The first section is this introduction. The second section gives theoretical foundations about the vertebral column and related work and the combination between CBR and ANN. The third section discusses the eZ-CBR shell; it illustrates its architecture and some implementation issues. The fourth section presents the experimental work. It discusses different dataset attributes, the conducted experiments and compares the obtained results with previous obtained results from other intelligent diagnostic systems. Finally, the fifth section concludes the work.

Theoretical Foundations

Vertebral Column The spine (or backbone) is a column of 26 bones called vertebrae that extend in a line from the base of the skull to the pelvis. This is referred to as the "spinal column" or "vertebral column". The spinal column provides the main support for the upper body, allowing humans to stand upright or bend and twist, and it protects the spinal cord from injury [Seymour, 1998]. Figure 1 shows a front and side views of the vertebral column.

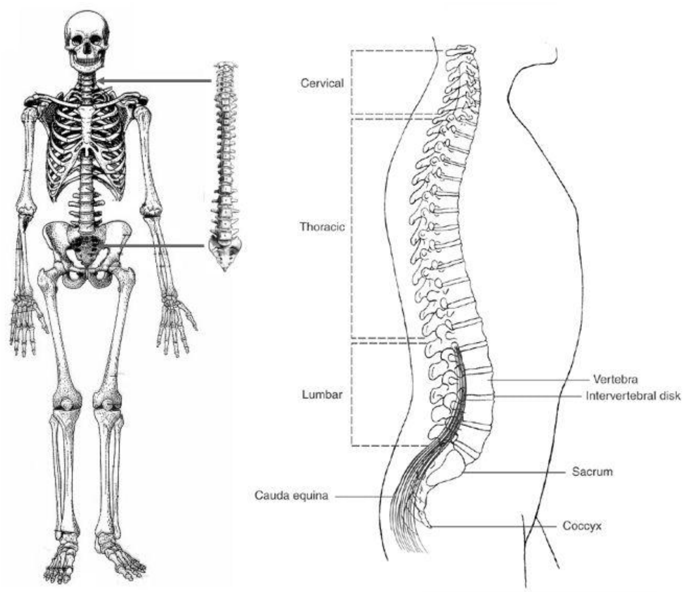


Fig. 1: The Vertebral Column

The lower part of the back holds most of the body's weight. Even a minor problem with the bones, muscles, ligaments, or tendons in this area can cause pain when a person stands, bends, or moves around. The disk which is a flat round plate like structure separates the bones that make up the spinal column. It is a fibrous structures filled with a pulpy, gelatinous matter. It functions as shock absorbers for the spine. Disc-related injuries to the back can be associated with deformation of the discs, including bulging and rupturing of the discs. Less often, a problem with a disc can pinch or irritate a nerve from the spinal cord, causing pain that runs down the leg, below the knee.

The most common examples of pathologies of the vertebral column are disc hernia and spondylolisthesis that cause intense pain. A herniated disc may occur suddenly in an event such as a fall or an accident, or may occur gradually with repetitive straining of the spine. When a herniated disc occurs, the space for the nerves is further diminished, and irritation of the nerve results. Spondylolisthesis is a condition in which a break in both sides of the ring allows the body of the vertebra to slip forward. Spondylolisthesis results from repetitive extension of the back (bending backward). This causes weakness in the rings of the lumbar vertebrae, eventually leading to a break (fracture) in a ring [Lepori, 2011]. Figure 2 shows examples of pathologies of the vertebral column with focus on herniated disc and spondylolisthesis.

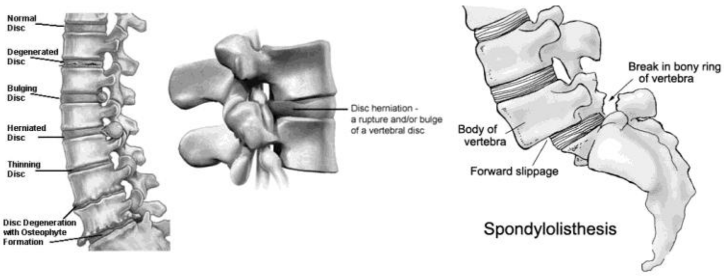


Fig. 2: Examples of Disk Problems

Related Work ML algorithms are already used in many medical diagnosis applications; however the use of them in diagnosis of Orthopedics is rare. This is due to the knowledge elicitation problem where there is a lack of clinical numeric values that describe the pathologies of the orthopedics. Some efforts have been explored in the following paragraphs which are based on the dataset provided by UCI [Frank & Asuncion, 2010] which is built by Dr. Henrique da Mota during a medical residence period in the Group of Applied Research in Orthopedics (GARO) of the Centre Médico-Chirurgical de Réadaptation des Massues, Lyon, France [Frank & Asuncion, 2010].

[Neto & Barreto, 2009] reported results from a performance comparison among some standalone ML algorithms Support Vector Machine (SVM), Multiple Layer Perceptron (MLP) and Generalized Regression Neural Network (GRNN) and their combinations in ensembles of classifiers. They used the same dataset to benchmark the performance. They evaluated the learning strategies in the classification modules according to their ability in discriminating patients as belonging to one out of three categories: Normal, Disk Hernia and Spondylolisthesis.

[Mattos & Barreto, 2011] introduced two novel ensemble models built using Fuzzy Adaptive Resonance Theory (FA) and Self Organizing Map (SOM) Neural Networks as base classifier. They used the vertebral column dataset provided by UCI [Frank & Asuncion, 2010] to compare three proposed strategies that convert these two unsupervised learning to supervised learning to be applied for the vertebral column classification task. Choosing the appropriate parameters for training base classifiers, for each classification task, was tackled using a metaheuristic approach. The vertebral column dataset was one of ten datasets which were used as for comprehensive performance evaluation in order to compare the ART in Ensembles and Multiple SOM Classifiers in Ensembles variants built from standard supervised classifiers.

[Neto et al., 2011] incorporated the reject technique to the diagnosis of pathologies on the Vertebral Column. The reject option proposes a novel method to learn the reject region on complex data. They applied their technique on the same UCI dataset and compared it with several ML techniques.

Combination of CBR and ANN In case-based reasoning (CBR) systems expertise is embodied in a library of past cases, rather than being encoded in classical rules. Each case typically contains a description of the problem, plus a solution and/or the outcome. The knowledge and reasoning process used by an expert to solve the problem is not recorded, but is implicit in the solution [Aamodt & Plaza, 1994]. Whenever, a new input case has to be dealt with, the case-based system performs inference in four phases known as the CBR cycle: retrieve, reuse, revise and retain. Figure 3 summarizes the CBR cycle.

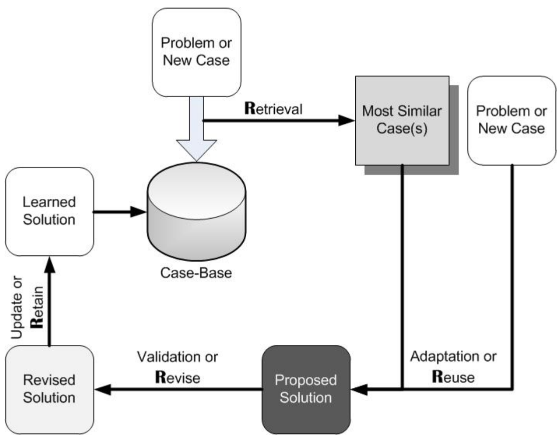


Fig. 3: The CBR Cycle

The retrieval phase retrieves from the case base the most relevant stored case or cases to the new case. The retrieval phase depends on indexing and similarity metrics. Indexing enables the efficient retrieval of relevant cases from the case base, thus limiting the search time. Similarity metrics assess the relevance of the retrieved cases to the new case. A simple approach to similarity assessment is the nearest neighbor matching [Kolodner, 1993]. Weights may be assigned to case features to denote feature importance in similarity assessment.

Adapting the most relevant retrieved case to meet the requirements of the new case is an important process due to the fact that retrieval involves partial matching. Adaptation focuses on differences between the most relevant case and the new case. Various adaptation methods have been developed such as substitution, transformation and derivational replay [Kolodner, 1993]. Adaptation can be a complex and time-consuming task usually requiring domain-dependent knowledge and sometimes user intervention [Kolodner, 1993]. There are some developed techniques have been developed to automatically acquire adaptation knowledge. Other techniques decrease the need for adaptation by retrieving cases that are easier to adapt. However, case adaptation is in many ways the Achilles' heel of CBR [Watson, 1997].

Artificial Neural Network (ANN) is an information processing paradigm that is inspired by the way biological nervous systems, such as the brain, process information. It is composed of massively parallel computing systems consisting of an extremely large number of simple processors with many interconnections. ANN models attempt to use some organizational principles believed to be used in the human [Bishop, 1995]. The back-propagation algorithm has emerged as the workhorse for the design of a special class of layered feed-forward networks known as multilayer perceptrons (MLP). A multilayer perceptron has an input layer of source nodes and an output layer of neurons (i.e., computation nodes); these two layers connect the network to the outside world. In addition to these two layers, the multilayer perceptron usually has one or more layers of hidden neurons, which are so called because these neurons are not directly accessible. The hidden neurons extract important features contained in the input data [Bishop, 1995]. Neural networks also have some disadvantages such as the required training time may be extensive and convergence to an acceptable solution is not always assured, the initialization of weights may play an important role in the training process leading to different solutions, and the determination of neural network topology (such as finding the required number of hidden nodes) is done on a trial-and error approach [Prentzas & Hatzilygeroudis, 2009].

Neural networks are usually combined with CBR to perform tasks such as indexing, retrieval and adaptation. In this way, appealing characteristics of neural networks such as parallelism, robustness, adaptability, generalization and ability to cope with incomplete input data are utilized.

eZ-CBR Shell

eZ-CBR shell is designed using object-oriented paradigm. So the entire shell is consisted of interacting objects which are grouped into three main parts the input part, the processing part which deals with the CBR process, and the output part. The input part deals with domain definition and loading different files required for building a CBR application. The CBR process part has all the necessary classes and functions required to complete the CBR process. The output part is responsible for writing the output.

Case Representation eZ-CBR shell applies object-oriented techniques for representing cases [Bergmann et al., 2005]. Such representations are particularly suitable for complex domains in which cases with different structures occur. The case in eZ-CBR shell is represented by a list of attributes. The list is dynamically allocated so the case can be represented with any number of attributes. The attribute type is lately bound to its actual type using polymorphism. The case itself can be one of the attributes in the attribute list. Figure 4 shows the case structure class diagram along with different classes that constitute the case class.

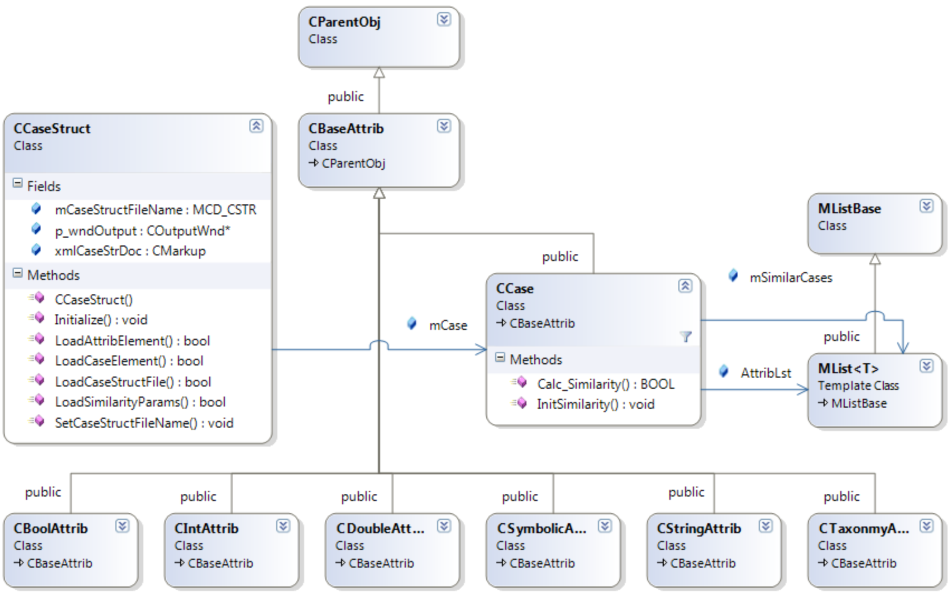


Fig. 4: The Case Structure Class Diagram in eZ-CBR Shell

Similarity is always used for describing something like "closely related". Similarity measures for such object-oriented representations are often defined by the general scheme: The goal is to determine the similarity between two objects, i.e., one object representing the case (or a part of it) and one object representing the query (or a part of it). This similarity is called object similarity (or global similarity). The object similarity is determined recursively in a bottom up fashion, i.e., for each simple attribute, a local similarity measure determines the similarity between the two attribute values, and for each relational slot an object similarity measure recursively compares the two related sub-objects. Then the similarity values from the local similarity measures and the object similarity measures, respectively, are aggregated (e.g., by a weighted sum) to the object similarity between the objects being compared [Bergmann & Stahl, 1998]. The similarity between a query, I and a case, J of a class C is defined as the sum of the similarities of its constituent features multiplied by their relevance weights as described in Equation 1.

$$Sim_C(I,J) = \sum_{i=0}^{n} w_i \times sim_i(I_i,J_i) \quad with \sum_{i=0}^{n} w_i = 1 \qquad (1)$$

Where w_i is the feature relevance weight and sim_i is the local similarity measure (i.e. feature specific similarity measure).

Case Retrieval eZ-CBR shell uses similarity based retrieval with K-Nearest Neighbor algorithm. The following is the retrieval steps employed by the process.

- For a given a query case instance, calculate the distance between the query-instance and all the case-base bases using the similarity measures as described before;
- Sort the distance and determine nearest neighbors based on the minimum distance;
- Determine parameter K = number of nearest neighbors. The K value is configured by the user;
- Gather the category of the nearest neighbors;
- Use simple majority of the category of nearest neighbors as the prediction value of the query instance.

Adaptation eZ-CBR shell employs feed-forward back-propagation artificial neural network [Bishop, 95] to adapt the retrieved cases to the solution. The following is a list of steps during the adaptation process that are required to be conducted for each query case.

- For each query case, get the most similar cases from the retrieval process;

- Prepare the attributes of the most similar cases to feed them as input for an initialized feed-forward back-propagation neural network;
- Configure the neural network topology by determining the number of hidden layers and number of neurons in each layer;
- Train the network using back propagation;
- When converging is done, query the network with the query case;
- Collect the neural network output which is the adapted solution for the selected query;
- Repeat for other queries.

Configuration of the neural network is done through configuration parameters which define the number of hidden layers and number of neurons in each layer in addition to the training parameters such as learning rate, momentum, maximum number of epochs and the desired accuracy. The number of the hidden layers and the number of neurons in each layer are set to an arbitrary value at the beginning, then to find out how many hidden neurons are required trial and error approach can be employed.

The Vertebral Column Experiments

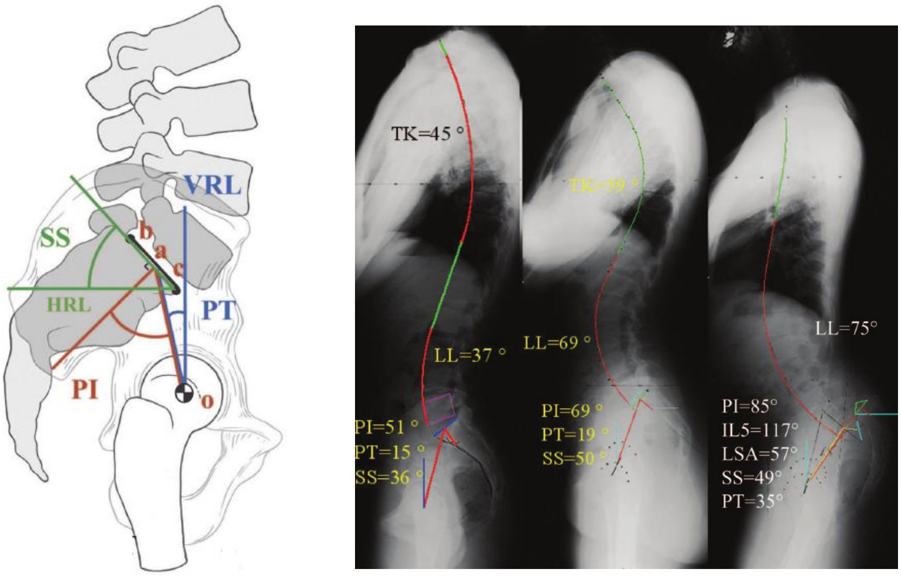
UCI Vertebral Column Data Set The data set has been organized in two different but related classification tasks. The first task is for classifying patients as belonging to one out of three categories: Normal, Disk Hernia or Spondylolisthesis. For the second task, the categories Disk Hernia and Spondylolisthesis were merged into a single category labeled as Abnormal. Table 1 shows the two tasks.

Table 1: UCI Vertebral Column Data Set Classification

Task	Task 1			Task 2	
Classification	Normal (NO)	Disk Hernia (DH)	Spondylolisthesis (SL)	Normal (NO)	Abnormal (AB)
No. of Patients	100	60	150	100	210

Each patient is represented in the data set by six biomechanical attributes derived from the shape and orientation of the pelvis and lumbar spine (in this order): pelvic incidence, pelvic tilt, lumbar lordosis angle, sacral slope, pelvic radius and grade of spondylolisthesis.

Figure 5A [Labelle et al., 2005] describes graphically some of the above attributes. Pelvic incidence (PI) is defined as an angle subtended by line (oa), which is drawn from the center of the femoral head to the midpoint of the sacral endplate and a line perpendicular to the center of the sacral endplate. The sacral endplate is defined by the line segment (bc) constructed between the posterior superior corner of the sacrum and the anterior tip of the endplate at the sacral promontory. For the case when the femoral heads are not superimposed, the center of each femoral head is marked, and a connecting line segment will connect the centers of the femoral heads. The pelvic radius will be drawn from the center of this line to the center of the sacral endplate. Sacral slope (SS) is defined as the angle subtended by a horizontal reference line (HRL) and the sacral endplate line (bc). Pelvic tilt (PT) is defined as the angle subtended by a vertical reference line (VRL) originating from the center of the femoral head (o) and the pelvic radius (oa). It is positive when the hip axis lies in front of the middle of the sacral endplate [Labelle et al., 2005]. Lordosis angle is the bigger sagittal angle between the sacrum superior plate and the lumbar vertebra superior plate or thoracic limit. The grade of spondylolisthesis is the percentage level of slipping between the inferior plate of the fifth lumbar vertebra and the sacrum [Neto et al., 2011].



(A) The Pelvic Morphology Parameters

(B) Illustrative Cases of two Normal Adults and one subject with Spondyloptosis

Fig. 5 [Labelle et al., 2005]

The association between PI and spondylolisthesis has been reported in many cases [Labelle et al., 2005]. As shown in Figure 5B, the normal case on the left has a pelvic incidence angle within normal limits, while the normal case in the middle has a PI value above normal. The case on the right has a developmental spondyloptosis. It can be clearly seen that the normal spine adjusts to pelvic morphology: the greater the PI, the greater will be SS and/or PT, and consequently, the greater will be the lumbar lordosis as the spine adjusts to maintain a stable posture [Labelle et al., 2005].

The Experiments Two major experiments have been conducted to automatically classify patients. Each major experiment represents a task. So, eZ-CBR has built one ternary classifier for task 1 and one binary classifier for task 2. In both experiments the data set has been randomly split into two parts one used for training and one for testing the results. Also, the classifier is tested when the entire data set has been used for training and the same number of queries has been tested. Each experiment has its own retrieval and adaptation parameters. Some of ANN learning parameters have been adjusted by trial and error, and they remain constant in all runs of both experiments. These parameters are the learning rate (0.9), the momentum (0.7), the maximum number of epochs (25,000) and the mean square error (0.0001). Table 2 and Table 3 show different parameters for each major experiment for task 1 and task 2 respectively.

Table 2: Task 1 Automatic Ternary Classification Experiment

Runs		**Run 1**	**Run 2**	**Run 3**	**Run 4**
Number of training cases		270	310	230	310
Number of Query cases		40	40	80	80
Training : Testing		13 : 87	N/A	25 : 75	N/A
Retrieval K Nearest Neighbor		40	40	30	40
ANN Adaptation	No. of Neurons in Input Layer	6	6	6	6
	No. of Neurons in Output Layer	3	3	3	3
	No. of Neurons in Hidden Layer(s)	6, 6	6, 6	6, 6	6, 6
	Accuracy %	±85%	±90 %	±84%	±88%

In experiment 1, where the classifier seeks three outputs normal, disk herniated, or spondyloptosis the used neural network had two hidden layers each one had six neurons while the output layer had three neurons each one was responsible for one class. In run 1 and 3, the data set was randomly split into two parts the largest part was used for the training of the eZ-CBR while the smallest part was used in testing. The number of K closest matches was set to an arbitrary value also obtained by trial and error. The level of accuracy gained in these runs was approximately 85%. In run 2 and run 4, the entire data set was used for training and the same testing part was used. In these runs, where exact match in the retrieval process is likely to happen, the obtained accuracy was approximately 89%.

Table 3: Task 2 Automatic Binary Classification Experiment

Runs		**Run 1**	**Run 2**	**Run 3**	**Run 4**
Number of training cases		270	310	230	310
Number of Query cases		40	40	80	80
Training : Testing		13 : 87	N/A	25 : 75	N/A
Retrieval K Nearest Neighbor		60	60	60	60
ANN Adaptation	No. of Neurons in Input Layer	6	6	6	6
	No. of Neurons in Output Layer	1	1	1	1
	No. of Neurons in Hidden Layer(s)	6	6	6	6
	Accuracy %	±85%	±98%	±86%	±93%

In experiment 2, the used neural network only had one neuron in the output layer responsible for the binary classification. Only one hidden was used. The same splitting of the data set has been performed like experiment 1. In run 1 and 3, where a part of the data set was used in the training, the accuracy obtained was approximately 86% while in run 2 and 4 where the entire data set was used in the training; the obtained accuracy was approximately 95%.

Results Comparison [Neto & Barreto, 2009] reported results from a performance comparison among some standalone ML algorithms Support Vector Machine (SVM), Multiple Layer Perceptron (MLP) and Generalized Regression Neural Network (GRNN) the accuracy obtained was 82%, 83%, and 75% for each of the used algorithms respectively. After ensemble these classifiers they become C-SVM, C-MLP and C-GRNN, and reached 94%, 88%, and 81%. [Mattos & Barreto, 2011] tested the same data set on several developed ensemble classifiers built using built using Fuzzy Adaptive Resonance Theory (FA) and Self Organizing Map (SOM) Neural Networks as base classifier. Average accuracy obtained during their experiments was approximately 83%. [Neto et al., 2011] incorporated the reject technique to classifiers based on SVM with different kernels, and they could reach average approximate accuracy of 85%.

Excluding the high accuracy obtained from eZ-CBR during the experiments in which the entire data set was used of the training, eZ-CBR obtained average approximate accuracy is 85% which is almost the same accuracy obtained from other ML techniques.

Conclusion

In this paper a hybrid CBR and ANN classifier is developed for the classification of the pathology on vertebral column. The application is developed using eZ-CBR shell. eZ-CBR shell is a hybrid case-based reasoning and neural network tool that is developed by the author. The developed classifier is successful up to ±85% in classification of abnormal Pelvic Morphology patients. The obtained accuracy is almost the same accuracy obtained by other researchers who classified the same data set using other ML algorithms.

eZ-CBR shell shows a great potential in the hybridization between CBR and NN systems. CBR and NN are similar in that they perform the same kind of processing: given a problem, finding a solution with respect to the previous problems encountered. In the case of the CBR, this is done with a step-by-step symbolic method whereas in the case of the NNs, this is done with some numeric method. But, from an external point of view, the processes remain essentially the same. CBR and ANN are complementary on several points. On the kind of data they can handle, CBR deals easily with structured and complex symbolic data while ANN deal easily with numeric data. Therefore, a system able to deal with both kinds of representations would be suitable. On the way the problem space is represented, it is often difficult for a neural network to learn special cases, because of an over-generalization. On the opposite, a CBR system can easily deal with these special cases. Thus a combined system shows good generalization capabilities.

As for future research, an automated topology configurator needs to be added in the eZ-CBR shell in the adaptation part. Instead of adjusting ANN topology and learning parameters using trial and error technique, another ML may be incorporated to automatically optimize the ANN topology and learning parameters. Such ML algorithm may be an evolutionary algorithm that will be able to search for the optimum ANN topology without users' intervention.

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