Applying Distance Metric Learning in a Collaborative Melanoma Diagnosis System with Case-Based Reasoning

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Abstract. Current social habits in solar exposure have increased the appearance of melanoma cancer in the last few years. The highest mortality rates in dermatological cancers are caused for this illness. In spite of it, recent studies demonstrate that early diagnosis increases life expectancy. This work introduces a way to classify dermatological cancer with highest rates of accuracy, specificity and sensitivity. The approach is the result of the improvement of previous works that combine information of two of the most important non-invasive image techniques: Reflectance Confocal Microscopy and Dermatoscopy. Current work achieve better results than the previous systems by the use of Distance Metric Learning to the different Case Memories.

Keyword. Case-Based Reasoning, Distance Metric Learning, Collaborative Systems.

1 Introduction

Twenty-first century society exceedingly appreciates the exposure to sun rays and its artificial substitutes. An appropriate protection and not exceeding the recommended tanning times makes it a healthy habit. Despite of it, long solar exposure without protection has made the appearance of melanoma and other skin cancers increase. According to the American Cancer Society [4] although is not the most common skin cancer, it is the one that causes most deaths (a twenty percent of non-early diagnosed cases). To deal with this problem, the most important way is the use of non-invasive techniques based on images. In this field stand out: Dermatoscopy and Reflectance Confocal Microscopy [16]. The former is based on the microscopical image created with epiluminiscence and the latter makes the image with the reflectance of a coherent laser with a cell resolution.

With this paper we present a Collaborative Computer Aided System for melanoma diagnosis that uses Distance Metric Learning (DML) to improve its operation. To achieve this aim, we base our effort on solving the problems observed in our previous implemented solutions [14,15]. The main aim of this work is to improve the classification accuracy and, moreover, the specificity and sensitivity rates that are crucial for medical experts. In order to achieve this goal, we take a second step in our system, in this case working on the case memories of our sub-systems applying DML [19] to establish a new projection of the data that allows a better distance analysis. The DML approach we have used is the one proposed by Xing [18] using Convex Programming.

In our first attempt for this problem [14], we focused our effort on the combination of different diagnostic criteria to ascertain the stand out of confocal method in comparison with other techniques. We proposed the use of Case-Based Reasoning (CBR) [1] techniques in order to assist the diagnosis. The CBR is a suitable approach because it follows exactly the same procedure used by experts. Then, we use two independent CBR systems with different types of information in each one in order to obtain a shared prognostic. Moreover, we follow the medical protocol in this kind of decisions which is: to analyze whether the new case is melanocytic and, afterwards, to assess about its malignancy. Thus, combining both diagnosis allow experts to determine if the new case is Melanoma, Basal Cell Carcinoma (BCC) or a non-malignant tumor as figure 1 shows. With this first solution, we denote that due to its high precision, Confocal microscope allows medical experts to improve its prognostic
capacity making up its high economical and temporal cost and the combination of this technique with dermatoscopy allows even a better diagnostic. Despite this, the work stresses some difficulties that need to be solved. Considering the characteristics of the data, in our second proposal [15] we add a module that discovers rules from the data that are independent from the experts. Eventually, both techniques are combined to create a computer aided system that uses the two CBR modules to classify new cases and fetching obtained rules to combine the classification results. The whole process follows the medical protocol in this kind of decisions and the introduction of the rules guarantees more reliability in the integrated system because all rarities of the data are detected. Although the accuracy rates are in fact promising all these efforts are not enough in the most important study values for medical experts, the specificity and sensitivity rates. These results are crucial in medical research and need to tend to 100%.

Keeping in mind the goal of increasing the statistical results attached to false positives and negatives, we have intended to improve our work in a different manner. In this case instead of focusing our effort on improving the combination, issue accomplished with the D-module, we have worked with the case memory. Our wish has been the achievement of a better distance analysis between cases and, consequently, a more accurate classification. In this way, we have studied different pre-process techniques and, at last, we have completed our prior system (MEDIBE-II)[15] with a DML module. The decision of using DML is based on the characteristics of the domain and the improvements we want to obtain. All the details of this work and decisions will be explained in following sections.

The paper is organized as follows. Section 2 describes related works. Section 3 describes the new tool obtained by the combination of the different modules. In section 4, experimentation is presented and the performance is analysed. Finally, section 5 summarizes the conclusions and further work.

2 Related Work

The present work tries to classify new dermatological cases using the combination of different kinds of decisions. In the last years, the application of ensemble methods and collaborative systems have increased significantly. One of the most relevant lines is to improve clustering using ensembles [3]. There are also works to allow the classification using data of different complexity [2] and with different types of medical information [7]. In contrast to these approaches and the presence of several works focused on studying the melanoma domain from individual approaches such as in [6], there are not works to classify melanoma in a collaborative way that follow the medical roles and use independent CBR classifiers. We are working with two different points of view (confocal and dermatoscopic) from which we select the best classification from one of the systems depending on different criteria. These characteristics do not allow to talk about an Ensemble Learning system but the combination idea is similar enough to the one used in this kind of methods which combine the decisions from different systems to build a more reliable solution using the individual ones [12].
can be summarized [5] in: 1) Bagging, 2) Boosting and 3) Stacking. And the most common voting methods [10] are: 1) Plurality, 2) Contra-Plurality, 3) Borda-Count and 4) Plurality with Delete. All of them are based on the number of votes of a class (plurality). With all this information and attending to the medical necessities, the collaborative model is a good method for this kind of classification. In spite of it, the concrete characteristics of the domain [13] make necessary a method different from the classical ensemble ones. We are using different attributes of the same data in each system, then the independence of the data is guaranteed, in contrast to the standard Bagging. Analyzing the classification attributes, the vote method should be based on plurality but with some arrangements requested by medical researchers, who weight more the information from Confocal Microscopy. Once we have experimented the protocol used by experts, we would like to improve it by using rules to do a better system combination.

In previous works, we have used clustering in order to discover new patterns on the medical domain [17] and we detected particular behaviours on the data. These characteristics guarantee a correct classification of the new patients when certain conditions in the attributes of the case were detected. Thus, bearing in mind that the main goals are the improvement of the classification and to minimize the false negatives situations, we created the D-Rule module. This module preprocesses the input data and creates a set of rules to help the whole classifier. Despite of using a similar idea of [9], we preprocess the data in a non-based interval way, where concrete values are detected and encapsulated in a rule. Moreover, our rules do not depend ones on each other and attributes are analysed independently.

In the field of Distance Metric Learning (DML) the methods could be divided into four families [11]. The first two are based on the supervision of the method. In this case, we have supervised and unsupervised DML. The last two families are based on a more concrete classification and are the DML methods based on Support Vector Machines and the ones that use Kernel methods. In our case and attending to the problem characteristics, we are working in the Supervised DML family [18]. With this methods we try to keep close all the data points within the same classes, while separating all the data points from different classes far apart. Even these techniques had been used and tested in clustering and retrieval, there are not literatures that applies it in a CBR environment.

3 Improving a Combination of CBR Systems in Dermatological Cancer

In this section, we want to describe the incremental improving of a basic classification system that tends to a complete Decision Support System for melanoma diagnosis. First of all, we describe the simple combination of CBR systems using the medical protocol. Then, we introduce the D-Rule module which through a preprocess algorithm obtain a better combination. And, in a third step we study the possibility of a projection of the original data in order to better classify the cases according to its similitude. At last, we show the result of the whole system.

3.1 Basic Combination of CBR Systems

Based on the medical protocol described in section one (shown at Fig. 1), we have developed a Collaborative Computer Aided System for melanoma diagnosis. In this way we have implemented an independent CBR system for each possible decision that uses the knowledge extracted from the Dermatoscopy and the Reflectance Confocal Microscopy image data. As a combination protocol, we follow in this case the same that medical experts implement in the daily diagnostic work [14].

In a more concrete way we can observe that the system binds the output of two Case-Based Reasoning (CBR) systems [1]. CBR performs the same resolution procedure that experts: solving new cases through the comparison of previous experiences. In a general way, the CBR life cycle can be summarized in the next four steps: 1) Retrieving the most similar cases from the case memory with the assistance of a similarity function, 2) Adapting the retrieved solutions to build a new solution for the new case, 3) Revising the proposed solution and 4) Retaining the useful knowledge generated in the solving process if it is necessary. An important point to highlight is that experts want to understand how decisions are made and this is one of the characteristics of CBR systems. Each one of the CBR systems has an independent case memory filled from the previously diagnosed injuries through the confocal and the dermatoscopy studies respectively. These two parts are completely independent and at the end of its work they put on its vote for the best classification according to their specific data. With this separate ballots, the system creates the final diagnosis (Solution) and, if proceeds, saves the new case in one of the case memories or in both.

The first option tested, as a decision process to perform a diagnosis, represents exactly the logical scheme used by the experts who mainly focus the interest on confocal diagnosis and, only if it is non conclusive they use the dermatological one. Therefore, the selection of the threshold values used to perform this decision and defined by medical experts are crucial to achieve a good performance. All this characteristics are described in the algorithm (Fig. 2).
Let $c_{\text{new}}$ be the new input case.
Let $\text{best}_{\text{confocal}}$ be the most similar case using the confocal CBR.
Let $\text{best}_{\text{dermatoscopical}}$ be the most similar case using the dermatoscopical CBR.
Let $\text{distance}(c_i, c_j)$ be the distance between two cases $c_i$ and $c_j$ performed by the normalized Euclidean distance.
Let $\text{threshold}_{\text{confocal}}$ be the minimal value to accept two cases as similar from the confocal point of view.
Let $\text{threshold}_{\text{dermatoscopical}}$ be the minimal value to accept two cases as similar from the dermatoscopical point of view.
Let $\text{class}(c)$ be the class of the case $c$.

if $\text{distance}(c_{\text{new}}, \text{best}_{\text{confocal}}) < \text{threshold}_{\text{confocal}}$ then
  \[ \text{return class}(\text{best}_{\text{confocal}}) \]
else
  if $\text{distance}(c_{\text{new}}, \text{best}_{\text{dermatoscopical}}) < \text{threshold}_{\text{dermatoscopical}}$ then
    \[ \text{return class}(\text{best}_{\text{dermatoscopical}}) \]
  else
    \[ \text{return class}(\text{best}_{\text{confocal}}) \]
\[ \text{Fig. 2.} \] Algorithm to diagnose a new case using the confocal and dermatoscopical criteria with plain combination.

Let $A$ be the set of all attributes of the medical domain.

forall attributes in $A$ do
  Let $A_i$ be the attribute $i$ of the set $A$.
  Let $V$ be the all possible values of attribute $A_i$.
  forall values in $V$ do
    if $\exists V_j \mid \text{class is unique for all cases in training set}$ then
      CreateRule ($A_i, V, j, \text{class}$)
\[ \text{Fig. 3.} \] Algorithm to generate rules in the D-Rule system.

3.2 Rule-Based Combination of CBR Systems

This module is based in the analysis of the training data in order to obtain a set of rules. These rules summarize the data complexity in the case memory. The main goal is to represent the existing gaps in the data space with no information associated, in order to advise the classifier in this sense. On the same way, when the correct classification is guaranteed with a high reliability, an alert to the following classifiers is sent, if a set of characteristics in the input data is detected.

In our domain, it is quite usual that from a certain discrete value of an attribute, the variation of the final decision on the classification does not change. So, the intervals proposed in [9] have been eliminated and clear-cut zones affected always in the same way have been created. These zones are summarized in one or more rules. The algorithm followed to generate the rules (Fig. 3) shows that we use all possible values of an attribute to analyze the input data. One of the advantages found in the medical domain is that the attributes are well delimited, so it is difficult to find a new case with a different value of the predefined ones in the domain. The module output is a set of if-then-else rules which quantity depends on the data complexity and varies with the different types of classification (Melanoma, Melanocytic or BCC).

To use this module we follow, mainly, the same scheme as in the basic approach using the best retrieved cases but adding the information provided by the rules. It allows the possibility of selecting automatically and better the best diagnosis. The logic process followed, as a combination, is the one described in Fig. 4.

3.3 Application of Distance Metric Learning to the Case Memories

We would like to learn a metric that keep close all the data points from the same class and, at the same time, separate as far as possible the data points from different classes. This metric can be obtained
Let $c_{\text{new}}$ be the new input case  
Let $\text{best}_{\text{confocal}}$ be the most similar case using the confocal CBR  
Let $\text{best}_{\text{dermatoscopical}}$ be the most similar case using the dermatoscopical CBR  
Let $\text{distance}(c_i, c_j)$ be the distance between two cases $c_i$ and $c_j$ performed by the normalized Euclidean distance  
Let $\text{numRules}_{\text{confocal}}$ be the number of rules carried out by $\text{best}_{\text{confocal}}$  
Let $\text{numRules}_{\text{dermatoscopical}}$ be the number of rules carried out by $\text{best}_{\text{dermatoscopical}}$  
Let $\text{class}(c)$ be the class of the case $c$  
if $\text{numRules}_{\text{confocal}} > \text{numRules}_{\text{dermatoscopical}}$ then  
\hspace{1em} return $\text{class}(\text{best}_{\text{confocal}})$  
else  
\hspace{1em} if $\text{numRules}_{\text{confocal}} < \text{numRules}_{\text{dermatoscopical}}$ then  
\hspace{2em} return $\text{class}(\text{best}_{\text{dermatoscopical}})$  
else  
\hspace{3em} if $\text{distance}(c_{\text{new}}, \text{best}_{\text{dermatoscopical}}) < \text{distance}(c_{\text{new}}, \text{best}_{\text{confocal}})$ then  
\hspace{4em} return $\text{class}(\text{best}_{\text{dermatoscopical}})$  
else  
\hspace{5em} return $\text{class}(\text{best}_{\text{confocal}})$  

Fig. 4. Algorithm to diagnose a new case using the confocal and dermatoscopical criteria and combining the results by rules.

from several methods but the one we have chosen is the one proposed by Xing [18]. In this approach we learn a global distance metric that minimizes the distance between pairs of data included in the equivalence constraints and data pairs from the inequivalence constraints are separated. To obtain this metric we apply the following process:

We have a set of data points $C = \{x_1, x_2, \ldots , x_n\}$ where $n$ is the number of samples, each $x_i \in \mathbb{R}^m$ is a vector where $m$ is the number of features. Then, the distance metric is the matrix $A \in \mathbb{R}^{m \times m}$ and the distance between the data points expressed by
\[
d_A^2(x, y) = \| x - y \|_A^2
\]
So if we establish the equivalence constraint as
\[
S = \{x_i, x_j \mid x_i \text{ and } x_j \text{ belong to the same class}\}
\]
and the inequivalence set as
\[
D = \{x_i, x_j \mid x_i \text{ and } x_j \text{ not belong to the same class}\}
\]
we have to obtain $A$ that
\[
\min_{A \in \mathbb{R}^{m \times m}} \sum_{(x_i, x_j) \in S} \| x_i - x_j \|_A^2
\]
and
\[
A \preceq 0 \sum_{(x_i, x_j) \in D} \| x_i - x_j \|_A^2 \geq 1
\]

Once we have obtained this matrix $A$, we could work with the metric to establish the distance between our cases. The calculations to obtain $A$ could be done by different ways. In our case, we have focused our attention on Convex Programming [8] that provides an easy way.
3.4 Rule-Based Combination of CBR Systems with Distance Metric Learning
application to its Case Memories

The final approach used in this paper is to apply the DML techniques to the different case memories of each CBR system and then run these systems combining its results using the module based on preprocessing generated rules. This process is shown in figure 5. As we could see in this scheme we have two CBR modules one for confocal data and the other for the dermatoscopic one. For each one of these modules we have applied the Xing DML technique [18] in order to better distinguish among similar cases. The final classification is obtained through the most similar cases retrieved from each module and selected using the preprocessed rules.

4 Experimentation

This section describes the data extracted from images and analyzes the results of the experiments performed through sensitivity and specificity rates.

4.1 Testbed

One of the main difficulties in the classification of injuries in melanoma domain is the huge amount of information that new technologies are able to collect and the ignorance about how they are interrelated [13]. The most used techniques to gather information from tissue are the dermoscopic and the confocal analysis. Confocal microscope is the most precise and the one that medical experts consider as world class.

Nevertheless, a negative point is that the confocal analysis is a long and expensive test, so the number of available cases is limited. Due to this situation, the data set used in this work is composed only by 150 instances of suspicious lesions. All instances contain information related to confocal and dermatoscopic images and the histology corroborated diagnosis. Attending to the considerations of the
medical experts that have created this set, it includes enough cases from each kind of illness to be representative of the domain. Then, in medical terms it is an appropriated case memory for this study. Detailing the instances, dermatological information has forty-one fields and confocal microscopy, due to its higher resolution, contributes with data from eighty-three different attributes.

### 4.2 Experimentation Framework

We have tested the classification accuracy of the platform proposed with a basic decision combination, with the use of rules obtained through the use of preprocessing algorithms and with the application of DML to the original data. In addition, we tested the accuracy of the two independent CBR systems (one for confocal data and another for dermatoscopy). This information is complemented with the analysis of the sensitivity and the specificity for the different cases. In the case of the plain combination platform, the medical consensus is to use 0.5 as confocal threshold and double of the distance between new case and best confocal case as dermatological one. All the CBR systems used in experimentation are configured with one-nearest neighbour algorithm with normalized Euclidean distance as retrieve function. This experiment framework has been tested applying a leave-one-out to the original data to obtain the average accuracy of those systems.

### 4.3 Results and Discussion

Analyzing these results, table 1 shows the accuracy rate to classify new injuries. This analysis is done in the three possible classes (Melanoma, Melanocytic and BCC) and using only confocal image, only dermoscopic image, both images with rules, without them, and with the DML module. The results obtained highlight two points: firstly, the techniques added to the basic combination of systems achieve better classification results than the plain combination or the independent systems. In a second term we could observe that the results using the whole system have the highest possible accuracy. On the other hand, tables 2 and 3 summarize the results of analyzing the statistics from the point of view of specificity and sensitivity, the most important values for medical experts. Analyzing the results from the more basic systems, we could see that it is more reliable to do a prognosis of real negative cases than the positive ones. This happens because data sets are unbalanced, what means that, they have different number of cases of each type because data sets represent a real situation: there are more

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healthy people than ill people. Despite of it, the use of the combination of both types of images with the help of preprocessing obtained rules allows an important increase of sensitivity and specificity rates (in addition to improve the accuracy). It is important to highlight that, using the DML technique in order to better classify the new cases, we accomplish the desire of medical experts that is to avoid false negatives. This situation is shown with the 100% sensitivity and specificity for all the types of classification.

5 Conclusions and Further Work

As medical experts explain, early melanoma diagnosis is one of the main goals in dermatology. The diagnosis process with non-invasive techniques is complex because of the data typology. With our current work we have proposed a platform to aid experts through this diagnostic process in order to improve its classification results. The proposal combines information from techniques based on images through a combination algorithm based on experts’ experiences. In addition, we use preprocessed rules in order to improve this combination and Distance Metric Learning to better analyze the distance between cases. After the result analysis of testing melanoma data sets, we can conclude that the incremental solutions to the problem allows an optimal classification even in specificity and sensitivity rates. These results also highlight that we have reached our ceiling with this data set. This situation makes us think about some important future challenges. The first of this is the obtaining of new data in this domain. Our previous works in data characterization of the domain shown that the new techniques used by medical experts generate high volumes of data. One of the main goals is to start using this data establishing relationships between it and extracting clear patterns of its characteristics. So, we will need to work with those huge amounts of data in order to process them previous to start classification processes.

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References


