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Learning ensemble classifiers for diabetic retinopathy assessment

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ABSTRACT

Diabetic retinopathy is one of the most common comorbidities of diabetes. Unfortunately, the recommended annual screening of the eye fundus of diabetic patients is too resource-consuming. Therefore, it is necessary to develop tools that may help doctors to determine the risk of each patient to attain this condition, so that patients with a low risk may be screened less frequently and the use of resources can be improved. This paper explores the use of two kinds of ensemble classifiers learned from data: fuzzy random forest and dominance-based rough set balanced rule ensemble. These classifiers use a small set of attributes which represent main risk factors to determine whether a patient is in risk of developing diabetic retinopathy. The levels of specificity and sensitivity obtained in the presented study are over 80%. This study is thus a first successful step towards the construction of a personalized decision support system that could help physicians in daily clinical practice.

1. Introduction

Diabetes Mellitus (DM) is a disease currently attaining over 400 million people around the world [1]. Its incidence is constantly growing, and it is expected to affect 10% of the world's population by 2040. It is considered one of the main global causes of death, overcoming other diseases like HIV/AIDS, tuberculosis and malaria [2], [3]. It has been estimated that 46% of the people attained by this illness are never properly diagnosed and treated [4]. Furthermore, DM may lead to many health complications such as kidney failure, amputation and blindness.

Diabetic retinopathy (DR) is a disease characterized by a progressive damage of the retina. Many factors are related to the development of DR, like the period of diabetes evolution, genetic factors and metabolic control density [5]. Diabetic retinopathy appears when diabetes harms the blood vessels. In a first stage, the arteries in the retina weaken and begin to leak, forming small, dot-like hemorrhages. These leaking vessels often from deposits of lipoproteins (exudates) in the retina, which produces a blur vision. A second complication is the growth of new weak blood vessels that break and leak blood into the eye, harming the macula so the retina cannot project images to the brain. The result is a loss of sight. Consequently, DR is the most serious ophthalmic condition induced by DM if it is not detected early and properly treated [6], [7].

As DR is a main cause of vision loss among people suffering from diabetes, all these patients must be periodically screened in order to detect signs of retinopathy development in an early stage. The screening process consists in taking an image of the eye fundus, which is analyzed by expert ophthalmologists for signs of microaneurisms or exudates. Fig. 1 shows an eye of a healthy person on the left, and an eye with diabetic retinopathy on the right. The central dark circle of the eye is the macula. Small red or yellow spots can be seen near the macula on the eye in the right, corresponding to microaneurisms and hemorrages. Yellow bigger spots in the peripheral retina are exudates.

Early and frequent screening of diabetic patients reduces the chance of blindness and decreases the overall load on the health care centres [8]. However, as the number of diabetic patients is very large and it is continually increasing, it is already very resource-

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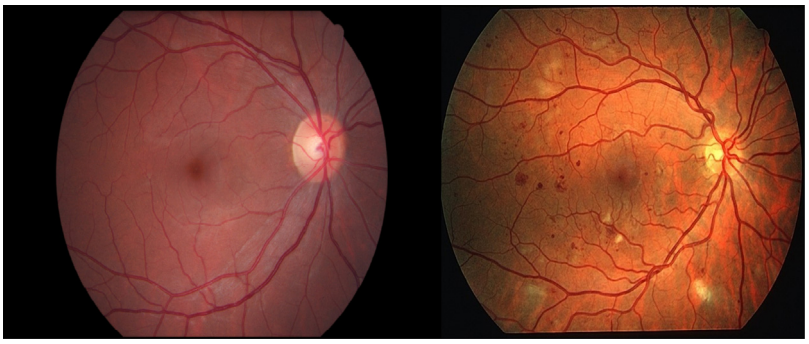

Fig. 1. Normal eye (left), versus eye with signs of diabetic retinopathy (right).

consuming to perform a yearly screening to all of them (which is the frequency recommended by international medical associations such as the American Diabetes Association, [9], the American Academy of Ophthalmology and the Royal College of Ophthalmologists, [10].

Some studies [11], [12] have argued that a high percentage of diabetic patients could be safely screened every 2 or 3 years, because their medical condition indicates that they are very unlikely to develop DR. These results coincide with those of a local study developed at *Sant Joan de Reus University Hospital* (SJRUH), which observed that just a 9% of diabetic patients develop DR. Detecting which patients do not need a screening, could permit more frequent screening of the patients that have a higher risk of DR. This may result in an improvement of the usage of Ophthalmology service resources without reducing the quality of health care.

The Ophthalmology unit of SJRUH has been collecting detailed information on the screening of thousands of diabetic patients in the area of Reus (Tarragona, Spain) for several years. This database is highly valuable, as it is very uncommon for a hospital to collect and store systematically such accurate data about the patients' condition on each visit to the medical centre. Expert ophthalmologists analyzed these data to identify the components of the *Electronic Health Record* (EHR) that are more relevant in the assessment of the risk of developing DR [13]. As a result of this study, nine numerical and categorical attributes were selected as the key factors to be taken into account when determining whether a diabetic patient is likely to have DR.

At this point, the main aim of our study is to explore the feasibility of using different *machine learning* (ML) techniques to build computational models based on the values of the attributes available in the EHR (without the need of an image). Such a classification model, given the data of a patient, can assess the personalised risk level of developing DR and, therefore, can help the physician to decide the best screening time. Those patients with a high risk should be screened more frequently, whereas those with a low risk could be safely screened again in 2–3 years.

In this paper, we study whether the use of ensemble classification techniques based on uncertainty models may lead to a good classification accuracy for the problem of risk assessment of DR based on EHR data. Specifically, *fuzzy random forests* (FRF) and *dominance-based rough set balanced rule ensemble* (DRSA-BRE) are applied to the data of SRJUH. The numerical attributes have been discretized before the analysis. FRF and DRSA-BRE are particularly appropriate for dealing with uncertain data, providing qualitative classification rules which are easier to understand by medical physicians than rules referring to particular numerical values. The classification models constructed by these techniques assign a relevance measure to each of the classification rules, which may also be a highly valuable information for the doctors. Both techniques are examples of *ensemble* methods, in which a group of classifiers is built and the final prediction for a particular patient is made taking into account the opinions of all the classifiers.

The rest of the paper is organized as follows. Section 2 presents the background and the related work on risk-prediction models for DR. It also includes a brief introduction to FRF and DRSA-BRE followed by reviews of their medical application. Section 3 explains how the dataset was constructed, which are the attributes included in this study and how the numerical ones were discretized. It also explains how the FRF and DRSA-BRE models have been applied for DR detection. Section 4 presents and discusses the experimental results on the use of the two classification learning techniques on these data. Conclusions and an outline of the future lines of research are presented in Section 5. The article ends with Appendix A and B with a detailed definition of FRF and DRSA-BRE, respectively.

2. Background and related works

This section begins with related works on diabetic retinopathy detection, which are mainly focused on the computational analysis of the images obtained from the eye fundus (and not on the physical and clinical features of the patient, as in this work). After that, the two studied rule induction methods are presented: fuzzy random forests and dominance-based rough set balanced rule ensembles. A brief review of medical applications of these methods is also included.

2.1. Diabetic retinopathy detection

Research on DR detection has mainly focused on the automatic analysis of the eye images. Currently researchers are studying how to extract signs of DR from images taken from the eye fundus. Several computer vision techniques have been used to build models for the detection of these signs. There exists a medical definition of 5 levels of severity of DR. Some works consider only the distinction between normal eyes and eyes with lesions, while other works try to differentiate the 5 categories according to the number, size and shape of different types of lesions (microaneurysms, hemorrhages and exudates). There are mainly two kinds of computer vision approaches: those based on the classical procedure of feature extraction and classification, and those based on the use of advanced neural networks.

As a recent example of the feature extraction approach, Saleh and Eswaran (2012) presented a system for the detection of microaneurysms and hemorrhages. In this work, first a morphological pre-processing stage extracted and removed the optic disc from the image. Then, depending on the illumination disparity, the background of the image was removed so that the resulting image contained only the blood vessels and the microaneurysms and hemorrhages. Finally, the image was classified using the geome-

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