

Classification of SD-OCT Volumes using Local Binary Patterns: Experimental Validation for DME Detection

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Abstract

This paper addresses the problem of automatic classification of Spectral Domain OCT (SD-OCT) data for automatic identification of patients with Diabetic Macular Edema (DME) versus normal subjects. Optical Coherence Tomography (OCT) has been a valuable diagnostic tool for DME, which is among the most common causes of irreversible vision loss in individuals with diabetes. Here, a classification framework with five distinctive steps is proposed and we present an extensive study of each step. Our method considers combination of various pre-processings in conjunction with Local Binary Patterns (LBP) features and different mapping strategies. Using linear and non-linear classifiers, we tested the developed framework on a balanced cohort of 32 patients.

Experimental results show that the proposed method outperforms the previous studies by achieving a Sensitivity (SE) and Specificity (SP) of 81.2% and 93.7%, respectively. Our study concludes that the 3D features and high-level representation of 2D features using patches achieve the best results. However, the effects of pre-processing is inconsistent with respect to different classifiers

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and feature configurations.

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1. Introduction

Eye diseases such as Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME) are the most common causes of irreversible vision loss in individuals with diabetes. Just in United States alone, health care and associated costs related to eye diseases are estimated at almost \$500 M [2]. Moreover, the prevalent cases of DR are expected to grow exponentially affecting over 300 M people worldwide by 2025 [3]. Given this scenario, early detection and treatment of DR and DME play a major role to prevent adverse effects such as blindness. DME is characterized as an increase in retinal thickness within 1 disk diameter of the fovea center with or without hard exudates and sometimes associated with cysts [4]. Fundus images which have proven to be very useful in revealing most of the eye pathologies [5, 6] are not as good as Optical Coherence Tomography (OCT) images [7] while dealing with DME.

Indeed, the new generation of OCT imaging, namely Spectral Domain OCT (SD-OCT) offers high resolution and fast image acquisition, producing from 27,000 to 40,000 A-scans/second with an axial resolution ranging from 3.5 μm to 6 μm [8]. Figure 1 shows one normal B-scan and two abnormal B-scans. Many of the previous works on OCT image analysis have focused on the problem of retinal layers segmentation, which is a necessary step for retinal thickness measurements [9, 10]. However, few have addressed the specific problem of DME and its associated features detection from OCT images.

A summary of the existing work can be found in Table 1. Srinivasan *et al.* [11] proposed a classification method to distinguish DME, Age-related Macular Degeneration (AMD) and normal SD-OCT volumes. The OCT images are pre-processed by reducing the speckle noise by enhancing the sparsity in a transform-domain and flattening the retinal curvature to reduce the inter-



Figure 1: Example of SD-OCT images for normal (a) and DME patients (b)-(c) with cyst and exudate, respectively.

patient variations. Then, Histogram of Oriented Gradients (HOG) are extracted for each slice of a volume and a linear Support Vector Machines (SVM) is used for classification. On a dataset of 45 patients equally subdivided into the three
 30 aforementioned classes, this method leads to a correct classification rate of 100%, 100% and 86.67% for normal, DME and AMD patients, respectively. The images that have been used in their paper, are publicly available but are already preprocessed (i.e., denoised), have different sizes for the OCT volumes, do not offer a huge variability in term of DME lesions, and some of them, without
 35 specifying which, have been excluded for the training phase; all these reasons prevent us from using this dataset to benchmark our work.

Venhuizen *et al.* proposed a method for OCT images classification using the Bag-of-Words (BoW) models [12]. The method starts with the detection and selection of keypoints in each individual B-scan, by keeping the most salient
 40 points corresponding to the top 3% of the vertical gradient values. Then, a textron of size 9×9 pixels is extracted around each keypoint, and Principal Component Analysis (PCA) is applied to reduce the dimension of every textron to get a feature vector of size 9. All extracted feature vectors are used to create

a codebook using k -means clustering. Then, each OCT volume is represented
 45 in terms of this codebook and is characterized as a histogram that captures the
 codebook occurrences. These histograms are used as feature vector to train a
 Random Forest (RF) with a maximum of 100 trees. The method was used to
 classify OCT volumes between AMD and normal cases and achieved an Area
 Under the Curve (AUC) of 0.984 with a dataset of 384 OCT volumes.

50 Liu *et al.* proposed a methodology for detecting macular pathology in OCT
 images using Local Binary Patterns (LBP) and gradient information as at-
 tributes [13]. The method starts by aligning and flattening the images and
 creating a 3-level multi-scale spatial pyramid. The edge and LBP histograms
 are then extracted from each block of every level of the pyramid. All the ob-
 55 tained histograms are concatenated into a global descriptor whose dimensions
 are reduced using PCA. Finally a SVM with an Radial Basis Function (RBF)
 kernel is used as classifier. The method achieved good results in detection OCT
 scan containing different pathology such as DME or AMD, with an AUC of 0.93
 using a dataset of 326 OCT scans.

60 Lemaitre *et al.* [14] proposed to use 2D and 3D LBP features extracted
 from denoised volumes and dictionary learning using the BoW models [15]. In
 the proposed method all the dictionaries are learned with same size of “visual
 words” ($k = 32$) and final descriptors are classified using RF classifier. The
 proposed method of this study is an extension of our previous work [14]¹. In
 65 this research, beside the comparison of 2D and 3D features and global and local
 mapping, we also compare the effects of common pre-processing steps for OCT
 data (i.e., aligning, flattening beside denoising), study the optimal configuration
 regarding the BoW approach and finally performance of different base classifiers.

This paper is organized as follows: the proposed framework is explained
 70 in Sect. 2, while the experiments and results are discussed through Sect. 3 and
 Sect. 4. Finally, the conclusion and avenue for future directions are drawn in
 Sect. 5.

¹The Document source available on Github [1]

| Ref | Diseases | | | Data size | Pre-processing | | | | Features | Representation | Classifier | Evaluation | Results |
|------|----------|-----|--------|-----------|----------------|---------|----------|----------|-------------|---------------------|------------|------------|-----------------|
| | AMD | DME | Normal | | De-noise | Flatten | Aligning | Cropping | | | | | |
| [11] | ✓ | ✓ | ✓ | 45 | ✓ | ✓ | | ✓ | HOG | | linear-SVM | ACC | 86.7%,100%,100% |
| [12] | ✓ | | ✓ | 384 | | | | | Texton | BoW, PCA | RF | AUC | 0.984 |
| [13] | ✓ | ✓ | ✓ | 326 | | ✓ | ✓ | | Edge, LBP | PCA | SVM-RBF | AUC | 0.93 |
| [14] | | ✓ | ✓ | 62 | ✓ | | | | LBP-LBP-TOP | PCA, BoW, histogram | RF | SE,SP | 87.5%, 75% |

CT

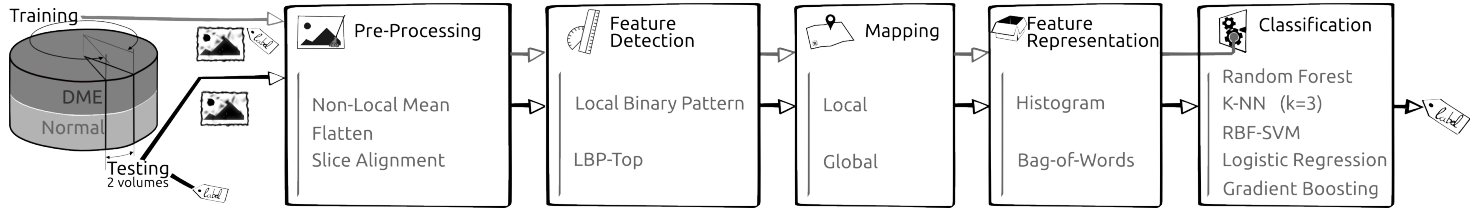


Figure 2: Our proposed classification pipeline.

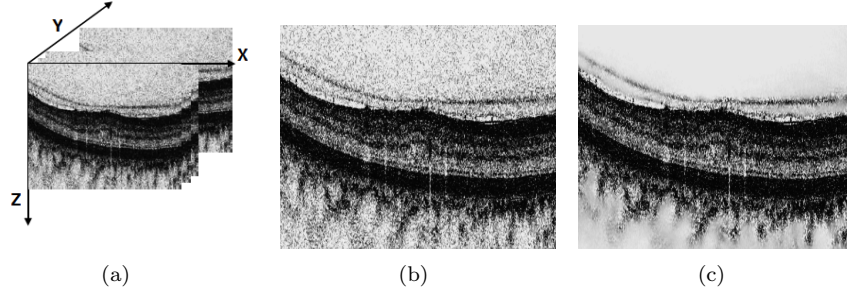


Figure 3: OCT: (a) Organization of the OCT data - (b) Original image - (c) NLM filtering. Note that the images have been negated for visualization purposes.

2. Materials and Methods

The proposed method, as well as, its experimental set-up for OCT volume
 75 classification are outlined in Fig. 2. The methodology is formulated as a standard
 classification procedure which consists of five steps. First, the OCT volumes are
 pre-processed as presented in details in Sect. 2.1. Then, LBP and LBP-TOP
 features are detected, mapped and extracted as discussed in depth in Sect. 2.2,
 Sect. 2.3, and Sect. 2.4, respectively. Finally, the classification step is presented
 80 in Sect. 2.5.

2.1. Image pre-processing

This section describes the set of pre-processing techniques which aim at
 enhancing the OCT volume. The influence of these pre-processing methods and
 their possible combinations are extensively studied in Sect. 3.

85 2.1.1. Non-Local Means (NLM)

OCT images suffer from speckle noise, like other image modalities such as
 Ultra-Sound (US) [16]. The OCT volumes are enhanced by denoising each B-
 scan (i.e. each $(x-z)$ slice) using the NLM [17], as shown in Fig. 3. NLM has
 been successfully applied to US images to reduce speckle noise and outperforms
 90 other common denoising methods [18]. NLM filtering preserves fine structures
 as well as flat zones, by using all the possible self-predictions that the image can
 provide rather than local or frequency filters such as Gaussian, anisotropic, or
 Wiener filters [17].



Figure 4: Flattening procedure: (a) original image, (b) thresholding, (c) median filtering, (d) curve fitting, (e) warping, (f) flatten image.

2.1.2. Flattening

95 Textural descriptors characterize spatial arrangement of intensities. However, the OCT scans suffer from large type of variations: inclination angles, positioning, and natural curvature of the retina [13]. Therefore, these variations have to be taken into account to ensure a consistent characterization of the tissue disposition, regardless of the location in the retina. This invariance
100 can be achieved from different manners: (i) using a rotation invariant descriptor (cf. Sect. 2.2), or (ii) by unfolding the curvature of the retina. This latter correction is known as image flattening which theoretically consists of two distinct steps: (i) estimate and fit the curvature of the Retinal Pigment Epithelium (RPE) and (ii) warp the OCT volume such that the RPE becomes flat.

105 Our correction is similar to the one of Liu *et al.* [13]: each B-scan is thresholded using Otsu's method followed by a median filtering to detect the different retina layers (see Fig 4(c) and Fig 4(b)). Then, a morphological closing and opening is applied to fill the holes and the resulting area is fitted using a second-order polynomial (see Fig. 4(d)). Finally, the scan is warped such that the curve
110 becomes a line as presented in Fig. 4(e) and Fig. 4(f).

2.1.3. Slice alignment

The flattening correction does not enforce an alignment through the OCT volume. Thus, in addition to the flattening correction, the warped curves of each B-scan are positioned at the same altitude in the z axis.

2.2. Feature detection

In this research, we choose to detect simple and efficient LBP texture features with regards to each OCT slice and volume. LBP is a texture descriptor based on the signs of the differences of a central pixel with respect to its neighboring pixels [19]. These differences are encoded in terms of binary patterns as in Eq. (1):

$$LBP_{P,R} = \sum_{p=0}^{P-1} s(g_p - g_c)2^p, \quad s(x) = \begin{cases} 1 & \text{if } x \geq 0 \\ 0 & \text{otherwise} \end{cases}, \quad (1)$$

where g_c , g_p are the intensities of the central pixel and a given neighbor pixel, respectively; P is the number of sampling points in the circle of radius R .

Ojala *et al.* further extended the original LBP formulation to achieve rotation invariance at the expense of limiting the texture description to the notion of circular “uniformity” [19]. Referring to the coordinate system defined in Fig. 3(a), the LBP codes are computed on each $(x-z)$ slice, leading to a set of LBP maps, a map for each $(x-z)$ slice.

Volume encoding is later proposed by Zhao *et al.* by computing LBP descriptors in three orthogonal planes, so called LBP-TOP [20]. More precisely, the LBP codes are computed considering the $(x-z)$ plane, $(x-y)$ plane, and $(y-z)$ plane, independently. Thus, three sets of LBP maps are obtained, one for each orthogonal plane.

In this research, we consider rotation invariant and uniform LBP and LBP-TOP features with various sampling points (i.e., $\{8, 16, 24\}$) with respect to different radius, (i.e., $\{1, 2, 3\}$). The number of patterns ($LBP_{\#pat}$) in regards with each configuration is reported in Table 2.

Table 2: Number of patterns ($LBP_{\#pat}$) for different sampling points and radius ($\{P, R\}$) of the LBP descriptor.

| | Sampling point for a radius ($\{P, R\}$) | | |
|---------------|--|-------------|-------------|
| | $\{8, 1\}$ | $\{16, 2\}$ | $\{24, 3\}$ |
| $LBP_{\#pat}$ | 10 | 18 | 26 |

Table 3: Size of a descriptor for an SD-OCT volume. d denotes the number of slices in the volume, N the number of 2D windows, and N' the number of 3D sub-volumes, respectively.

| | Global mapping | Local mapping |
|---------|-----------------------------------|------------------------------------|
| LBP | $d \times LBP_{\#pat}$ | $(N \times d) \times LBP_{\#pat}$ |
| LBP-TOP | $1 \times (3 \times LBP_{\#pat})$ | $N' \times (3 \times LBP_{\#pat})$ |

2.3. Mapping

The mapping stage is used to partition the previously computed LBP maps to later extract the final descriptor as presented in the next section. For this work, two mapping strategies are defined: (i) *global* and (ii) *local* mapping.

The size of the feature descriptor is summarized in Table 3.

Global mapping considers to extract the final descriptors from the 2D feature image for LBP and 3D volume for LBP-TOP. Therefore, for a volume with d slices, the *global*-LBP mapping will lead to the extraction of d elements. While the *global*-LBP-TOP represents the whole volume as a single element. The *global* mapping for 2D images and 3D volume is shown in Fig. 5(a) and 5(b).

Local mapping considers to extract the final descriptors from a set of $(m \times m)$ 2D patches for LBP and a set of $(m \times m \times m)$ sub-volumes for LBP-TOP. Given N and N' the total number of 2D patches and 3D sub-volumes respectively, the *local*-LBP approach provides $N \times d$ elements, while *local*-LBP-TOP provides N' elements. This mapping is illustrated in Fig. 5(c) and 5(d).

2.4. Feature representation

Two strategies are used to describe each OCT volume texture.

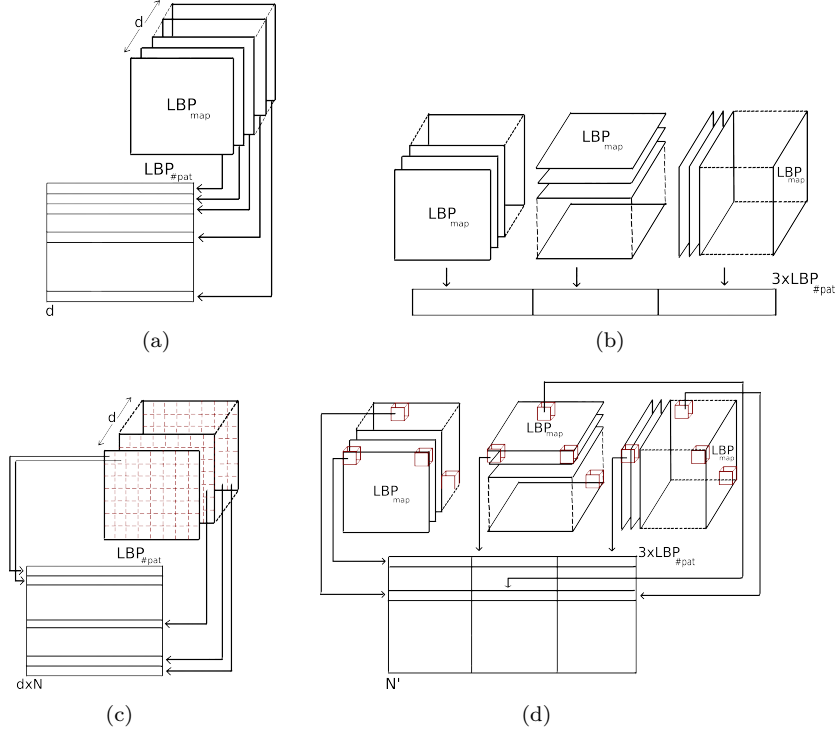


Figure 5: Graphical representation of the feature extraction: (a) extraction of LBP for global mapping - (b) extraction of LBP-TOP for global mapping - (c) extraction of LBP for local mapping - (d) extraction of LBP-TOP for local mapping.

Low-level representation The texture descriptor of an OCT volume is defined as the concatenation of the LBP histograms with the *global*-mapping.

The LBP histograms are extracted from the previously computed LBP maps (see Sect. 2.2). Therefore, the LBP-TOP final descriptor is computed

160 through the concatenation of the LBP histograms of the three orthogonal planes with the final size of $3 \times LBP_{\#pat}$. More precisely, an LBP histogram is computed for each set of LBP maps (x - z) plane, (x - y) plane, and (y - z) plane, respectively. Similarly, the LBP descriptor is defined through concatenation of the LBP histograms per each (x - z) slice

165 with the final size of $d \times LBP_{\#pat}$.

High-level representation The concatenation of histograms employed in the low-level representation in conjunction with either *global*- or *local*-mapping

can lead to a high dimensional feature space. For instance, *local*-mapping results to a size of $N \times d \times LBP_{\#pat}$ for the final LBP descriptor and $N' \times LBP_{\#pat}$ for the final LBP-TOP descriptor. High-level representation simplifies this high dimensional feature space into a more discriminant lower space. BoW approach is used for this purpose [15]. This model represents the features by creating a codebook or visual dictionary, from the set of low-level features. The set of low-level features are clustered using k -means to create the codebook with k clusters or visual words. After creating the codebook from the training set, the low-level descriptors are replaced by its closest word within codebook. The final descriptor is a histogram of size k to represent the codebook occurrences for a given mapping.

2.5. Classification

Classification corresponds to the mapping of a set of inputs \mathbf{x} into a set of categorical outputs \mathbf{y} using a linear or non-linear function $f(\cdot)$. In supervised learning methods, this function is defined by providing a training set of N samples \mathbf{x}_{tr} with their associated labels \mathbf{y}_{tr} . In order to make a comparative study, five different classifiers are used: (i) k -Nearest Neighbor (NN), (ii) Logistic Regression (LR) [21], (iii) Random Forest (RF) [22], (iv) Gradient Boosting (GB) [23, 24], and (v) Support Vector Machines (SVM) [25, 26]. Details regarding the parameters used in our experiments are provided in Sect. 3.

3. Experiments

A bundle of experiments composed of three experiments is designed to test the influence of the different blocks composing our framework in comparison to our previous work [14]. These experiments are designed in order to investigate the effects of the (i) optimal number of words, (ii) different pre-processing steps, and (iii) different classifiers. Table 4 reports the experiments which have been carried out in [14] as a baseline and outlines the complementary experimentation here proposed. The reminder of this section details the common configuration

| | | Actual | |
|-----------|----|---------------------|---------------------|
| | | A+ | A- |
| Predicted | P+ | True Positive (TP) | False Positive (FP) |
| | P- | False Negative (FN) | True Negative (TN) |

Figure 6: Confusion matrix with true and false positive detected samples (TP, FP) in the first row, from left to right and the false and true negative detected samples (FN, TN) in the second row, from left to right.

parameters across the experiments, while the detailed explanations are presented in the following subsections.

All the experiments are performed using our own dataset (see Sect. 3.1) and are reported according to the validation (see Sect. 3.2). In all the experiments, LBP and LBP-TOP features are extracted using both *local* and *global*-mapping for different sampling points of 8, 16, and 24 for radius of 1, 2, and 3 pixels, respectively. The partitioning for *local*-mapping is set to (7×7) pixels patch for 2D LBP and $(7 \times 7 \times 7)$ pixels sub-volume for LBP-TOP.

3.1. SERI-Dataset

This dataset was acquired by the Singapore Eye Research Institute (SERI), using CIRRUS TM (Carl Zeiss Meditec, Inc., Dublin, CA) SD-OCT device. The dataset consists of 32 OCT volumes (16 DME and 16 normal cases). Each volume contains 128 B-scan with resolution of 512×1024 pixels. All SD-OCT images are read and assessed by trained graders and identified as normal or DME cases based on evaluation of retinal thickening, hard exudates, intraretinal cystoid space formation and subretinal fluid.

3.2. Validation

All the experiments are evaluated in terms of Sensitivity (SE) and Specificity (SP) using the Leave-One-Patient Out Cross-Validation (LOPO-CV) strategy, in line with [14]. SE and SP are statistics driven from the confusion matrix (see Fig. 6) as stated in Eq. (2). The SE evaluates the performance of the classifier

with respect to the positive class, while the SP evaluates its performance with respect to negative class.

$$SE = \frac{TP}{TP + FN} \quad SP = \frac{TN}{TN + FP} \quad (2)$$

The use of LOPO-CV implies that at each round, a pair DME-normal volume
215 is selected for testing while the remaining volumes are used for training. Subsequently, no SE or SP variance can be reported. However, LOPO-CV strategy has been adopted despite this limitation due to the reduced size of the dataset.

Table 4: The outline and summary of the performed experiments. \sim indicate that common configuration applies.

| | Dataset | Pre-processing | Features | Mapping | Representation | Classification | Evaluation |
|---|---------|----------------|---|-------------------------------|--------------------|-------------------------|------------------------|
| Common: | SERI | NLM | LBP,LBP-TOP $P = \{8, 16, 24\}$ $R = \{1, 2, 3\}$ | | | | LOPO-CV SE, SP |
| Baseline [14]: Goal: Evaluation of features, mapping and representation | + Duke | \sim | \sim | <i>global</i> <i>local</i> | BoW Histogram | RF | + comparison with [12] |
| Experiment#1: Goal: Finding the optimum number of words | \sim | + F + F+A | \sim | <i>global</i> <i>local</i> | BoW $k \in K$ | LR | +ACC, F1-score (F1) |
| Experiment#2: Goal: Evaluation of different pre-processing for high-level features | \sim | +F +F+A | \sim | <i>global</i> <i>local</i> | BoW optimal k | 3-NN RF SVM GB | \sim |
| Experiment#3: Goal: Evaluation of different pre-processing for low-level features | \sim | +F +F+A | \sim | <i>global</i> | Histogram | 3-NN RF SVM GB | \sim |

3.3. Experiment #1

This experiment intends to find the optimal number of words and its effect
220 on the different configurations (i.e., pre-processing and feature representation),
on the contrary to [14], where the codebook size was arbitrarily set to $k = 32$.

Several pre-processing strategies are evaluated: (i) NLM, (ii) a combination
of NLM and flattening (NLM+F), and (iii) a combination of NLM, flattening,
and aligning (NLM+F+A). LBP and LBP-TOP descriptors are detected us-
225 ing the default configuration. Volumes are represented using BoW, where the
codebook size ranging for $k \in \{10, 20, 30, \dots, 100, 200, \dots, 500, 1000\}$. Finally,
the volumes are classified using LR. The choice of this linear classifier avoids
that the results get boosted by the classifier. In this manner, any improvement
would be linked to the pre-processing and the size of the codebook.

230 The usual build of the codebook consists of clustering the samples in the
feature space using k -means (see Sect. 2.4). However, this operation is rather
computationally expensive and the convergence of the k -means algorithm for all
codebook sizes is not granted. Nonetheless, Nowak *et al.* [27] pointed out that
randomly generated codebooks can be used at the expenses of accuracy. Thus,
235 the codebook are randomly generated since the final aim is to asses the influ-
ence of the codebook size and not the performance of the framework. For this
experiment, the codebook building is carried out using random initialization us-
ing k -means++ algorithm [28], which is usually used as a k -means initialization
algorithm.

240 For this experiment, SE and SP are complemented with ACC and F1 score
(see Eq. (3)). ACC offers an overall sense of the classifier performance, and F1
illustrates the trade off between SE and precision.

The complete set of all ACC and F1 graphics can be found at [1]. In order
to illustrate the impact of the dictionary size, Fig. 7 illustrates the ACC and
245 F1 graph for a particular case. In this figure, the classification performance of
local-LBP features extracted from the NLM +F configuration is illustrated.

Appendix A - Table 6 shows the results obtained for the optimal dictionary
size.

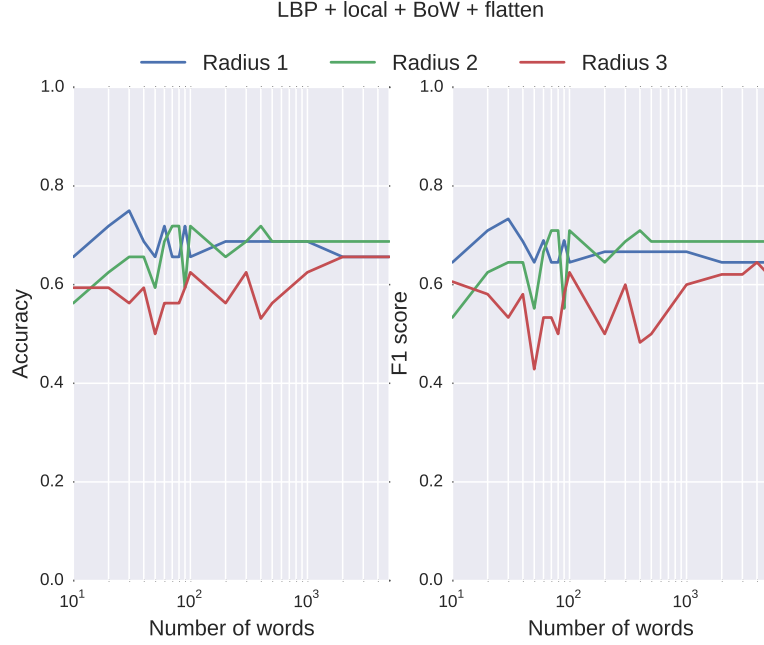


Figure 7: The performance of LR with NLM+F pre-processing for different P and R .

$$ACC = \frac{TP + TN}{TP + TN + FP + FN} \quad F1 = \frac{2TP}{2TP + FP + FN} \quad (3)$$

3.4. Experiment #2

250 This experiment explores the improvement associated with: (i) different pre-processing methods and (ii) using a larger range of classifiers (i.e., linear and non-linear), for the features from the high-level representation.

All the pre-processing stages are evaluated (NLM, NLM+F, and NLM+F+A). In this experiment, the codebooks for the BoW representation of LBP and LBP-
 255 TOP features are computed using regular k -means algorithm which is initialized using k -means++, where k is chosen according to the findings of *Experiment #1*. Finally, the volumes are classified using k -NN, RF, GB, and SVM. The k -NN classifier is used in conjunction with the 3 nearest-neighbors rule to classify the test set. The RF and GB classifier are trained using 100 un-pruned trees, while

260 SVM classifier is trained using an RBF kernel and its parameters C , and γ are optimized through grid-search.

Complete list of the obtained results from this experiment are shown in Appendix A - Table 7. Despite that highest performances are achieved when NLM+F or NLM+F+A are used, most configurations decline when applied with
265 extra pre-processing stages. The best results are achieved using SVM followed by RF.

3.5. Experiment #3

This experiment replicates the *Experiment #2* for the case of low-level representation of LBP and LBP-TOP features extracted using *global*-mapping.

270 The obtained results from this experiment are listed in Appendix A - Table 8. In this experiment, flattening the B-scan boosts the results of the best performing configuration. However, its effects is not consistent across all the configurations. In terms of classifier, RF has a better performance than the others despite the fact that the highest SP is achieved using SVM.

275 4. Results and discussion

This section summarizes the results obtained from Sect. 3 (extensive results can be found in Appendix A) and extends the discussion. Table 5 combines the obtained results from Sect. 3 with those reported by Lemaitre *et al.* [14], while detailing the frameworks configurations. This table sorts the achieved
280 performances with SE higher than 55%, in a descending manner.

The obtained results indicate that expansion and tuning of our previous framework improves the results. From *Experiment #1*, tuning the codebook size leads to an improvement of 6% in terms of SE (see Table 5 at line 7 and 13). Furthermore, the fine tuning of our framework (see Sect. 2) also leads to
285 an improvement of 6% in both SE and SP (see Table 5 at line 1 and 13). Our framework also outperforms the proposed method of [12] with an improvement of 20% and 36% in terms of SE and SP, respectively.

Note that although the effects of pre-processing are not consistent through all the performance, the best results are achieved with NLM +F and NLM
290 +F+A configurations as pre-processing stages. In general, the configurations presented in *Experiment #2* outperform the others, in particular the high-level representation of locally mapped features with an SVM classifier. Focusing on the most desirable radius and sampling point configuration, smaller radius and sampling points are more effective in conjunction with local mapping, while
295 global mapping benefit from larger radius and sampling points.

5. Conclusions

The work presented here addresses automatic classification of SD-OCT volumes as normal or DME. In this regard, an extensive study is carried out covering the (i) effects of different pre-processing steps, (ii) influence of different
300 mapping and feature extraction strategies, (iii) impact of the codebook size in BoW, and (iv) comparison of different classification strategies.

While outperforming the previous studies [14, 12], the obtained results in this research showed the impact and importance of optimal codebook size, the

potential of 3D features and high level representation of 2D features while ex-
tracted from local patches. The strength of SVM classifier while used along
BoW approach and RF classifier while used with global mapping. In terms
of pre-processing steps, although the highest performances are achieved while
alignment and flattening were used in the pre-processing, it was shown that
the effects of these extra steps are not consistent for all the cases and do not
guaranty a better performance.

Several avenues for future directions can be explored. The flattening method
proposed by Liu *et al.* flattens roughly the RPE due to the fact that the RPE is
not segmented. Thus, in order to have a more accurate flattening pre-processing,
the RPE layer should be pre-segmented as proposed by Garvin *et al.* [29]. In
this work, the LBP invariant to rotation was used and the number of pattern
encoded is reduced. Once the data are flattened, the non-rotation invariant
LBP could be studied since this descriptor encode more pattern. In addition to
LBP, other feature descriptors can be included in the framework to complement
LBP.

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Conflict of interest statement

The authors declare no conflict of interest.

Appendix A Complementary results for *Experiment #1* & *#2* & *#3*

Table 6: Experiment #1 - Optimum number of words for each configuration as a result of LR Classification, for high-level feature extraction of *global* and *local*-LBP, and *local*-LBP-TOP features with different pre-processing. The pre-processing includes: NF, F, and F+A. The achieved performances are indicated in terms of ACC, F1, SE, and SP

| Features | Pre-processing | {8, 1} | | | | | {16, 2} | | | | | {24, 3} | | | | |
|-----------------------|----------------|--------|------|------|------|-----|---------|------|------|------|-----|---------|------|------|------|-----|
| | | ACC% | F1% | SE% | SP% | W# | ACC% | F1% | SE% | SP% | W# | ACC% | F1% | SE% | SP% | W# |
| <i>global</i> -LBP | | | | | | | | | | | | | | | | |
| | NF | 81.2 | 78.5 | 68.7 | 93.7 | 500 | 62.5 | 58.0 | 56.2 | 62.5 | 80 | 62.5 | 62.5 | 62.5 | 62.5 | 80 |
| | F | 71.9 | 71.0 | 68.7 | 75.0 | 400 | 68.7 | 66.7 | 62.5 | 75.0 | 300 | 68.7 | 66.7 | 62.5 | 75.0 | 300 |
| | F+A | 71.9 | 71.0 | 68.7 | 75.0 | 500 | 71.9 | 71.0 | 68.7 | 75.0 | 200 | 75.0 | 68.7 | 68.7 | 68.7 | 500 |
| ----- | | | | | | | | | | | | | | | | |
| <i>local</i> -LBP | | | | | | | | | | | | | | | | |
| | NF | 75.0 | 75.0 | 75.0 | 75.0 | 70 | 65.6 | 64.5 | 62.5 | 68.7 | 90 | 62.5 | 60.0 | 56.2 | 68.7 | 30 |
| | F | 75.0 | 73.3 | 68.7 | 81.2 | 30 | 71.8 | 61.0 | 68.7 | 75.0 | 70 | 62.5 | 62.5 | 62.5 | 62.5 | 100 |
| | F+A | 75.0 | 69.0 | 62.5 | 81.2 | 40 | 71.9 | 71.0 | 68.7 | 75.0 | 200 | 68.7 | 66.7 | 68.7 | 62.5 | 10 |
| ----- | | | | | | | | | | | | | | | | |
| <i>local</i> -LBP-TOP | | | | | | | | | | | | | | | | |
| | NF | 68.7 | 68.7 | 68.7 | 68.7 | 400 | 75.0 | 75.0 | 75.0 | 75.0 | 500 | 71.9 | 71.0 | 68.7 | 75.0 | 60 |
| | F | 68.7 | 68.7 | 68.7 | 68.7 | 300 | 68.7 | 66.7 | 62.5 | 75.0 | 50 | 75.0 | 76.5 | 81.2 | 68.7 | 80 |
| | F+A | 75.0 | 73.3 | 68.7 | 81.2 | 100 | 75.0 | 73.3 | 68.7 | 81.2 | 90 | 75.0 | 69.0 | 62.5 | 81.2 | 70 |

Table 7: Experiment #2 - k -NN, SVM, RF, and GB classification with BoW for the *global* and *local* LBP and *local* LBP-TOP features with different pre-processing. The optimum number of words were selected based on experiment #1. The most relevant configurations are shaded. The configurations which their performances declines with additional pre-processing are shaded in light gray while those with the opposite behavior are shaded with darker gray color. The highest results which are specified in Table 5 are highlighted in **bold**.

| k-NN | | | | | | | | SVM | | | | | |
|---------------|----------------|-------------------|------|--------------------|------|--------------------|------|-------------------|------|--------------------|------|--------------------|------|
| Features | Pre-processing | {8, 1} | | {16, 2} | | {24, 3} | | {8, 1} | | {16, 2} | | {24, 3} | |
| | | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% |
| global-LBP | | | | | | | | | | | | | |
| | NF | 43.7 | 93.7 | 43.7 | 87.5 | 43.7 | 62.5 | 68.7 | 87.5 | 62.5 | 62.5 | 50.0 | 56.2 |
| | F | 43.7 | 56.2 | 50.0 | 75.0 | 62.5 | 56.2 | 56.2 | 56.2 | 56.2 | 75.0 | 56.2 | 68.7 |
| | FA | 56.2 | 62.5 | 43.7 | 81.2 | 68.7 | 56.2 | 56.2 | 68.7 | 68.7 | 68.7 | 56.2 | 75.0 |
| local-LBP | | | | | | | | | | | | | |
| | NF | 75.0 | 87.5 | 50.0 | 68.7 | 43.7 | 43.7 | 75.0 | 93.7 | 50.0 | 75.0 | 56.2 | 56.2 |
| | F | 56.2 | 56.2 | 50.0 | 50.0 | 50.0 | 43.7 | 81.2 | 93.7 | 68.7 | 68.7 | 68.7 | 75.0 |
| | FA | 56.2 | 43.7 | 50.0 | 75.0 | 50.0 | 62.5 | 75.0 | 93.7 | 75.0 | 68.7 | 68.7 | 68.7 |
| local-LBP-TOP | | | | | | | | | | | | | |
| | NF | 56.2 | 75.0 | 56.2 | 75.0 | 62.5 | 56.2 | 81.2 | 87.5 | 75.0 | 100 | 56.2 | 75.0 |
| | F | 62.5 | 43.7 | 37.5 | 68.7 | 43.7 | 62.5 | 81.2 | 81.2 | 75.0 | 68.7 | 81.2 | 68.7 |
| | F+A | 56.2 | 56.2 | 68.7 | 50.0 | 43.7 | 62.5 | 62.5 | 75.0 | 68.7 | 75.0 | 62.5 | 81.2 |
| RF | | | | | | | | GB | | | | | |
| Features | Pre-processing | 8 ^{riu2} | | 16 ^{riu2} | | 24 ^{riu2} | | 8 ^{riu2} | | 16 ^{riu2} | | 24 ^{riu2} | |
| | | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% |
| global-LBP | | | | | | | | | | | | | |
| | NF | 68.7 | 93.7 | 43.7 | 62.5 | 50.0 | 68.7 | 56.2 | 50.0 | 37.5 | 31.2 | 50.0 | 43.7 |
| | F | 56.2 | 50.0 | 56.2 | 75.0 | 50.0 | 75.0 | 50.0 | 56.2 | 56.2 | 75.0 | 43.7 | 62.5 |
| | FA | 68.7 | 50.0 | 56.2 | 62.5 | 62.5 | 56.2 | 56.2 | 50.0 | 68.7 | 50.0 | 43.7 | 75.0 |
| local-LBP | | | | | | | | | | | | | |
| | NF | 81.2 | 81.2 | 62.5 | 56.2 | 56.2 | 56.2 | 75.0 | 62.5 | 68.7 | 87.5 | 50.0 | 75.0 |
| | F | 56.2 | 81.2 | 62.5 | 68.7 | 68.7 | 62.5 | 68.7 | 75.0 | 50.0 | 75.0 | 50.0 | 62.5 |
| | FA | 68.7 | 62.5 | 62.6 | 68.7 | 43.7 | 43.7 | 56.2 | 50.0 | 68.7 | 56.2 | 50.0 | 50.0 |
| local-LBP-TOP | | | | | | | | | | | | | |
| | NF | 68.7 | 62.5 | 68.7 | 81.2 | 68.7 | 68.7 | 37.5 | 68.7 | 62.5 | 81.2 | 62.5 | 50.0 |
| | F | 50.0 | 62.5 | 62.5 | 62.5 | 43.7 | 75.0 | 50.0 | 56.2 | 43.7 | 62.5 | 50.0 | 62.5 |
| | F+A | 50.0 | 62.5 | 81.2 | 87.5 | 50.0 | 68.7 | 56.2 | 62.5 | 81.2 | 68.7 | 75.0 | 68.7 |

Table 8: Experiment #3 - Classification results obtained from low-level representation of global LBP and LBP-TOP features with different pre-processing. Pre-processing steps include: NF, F, F+A. Different classifiers such as RF, GB, SVM, and k -NN are used. The most relevant configurations are shaded. The configurations which their performances declines with additional pre-processing are shaded in light gray while those with the opposite behavior are shaded with darker gray color. The highest results which are specified in Table 5 are highlighted in **bold**.

| Features | Pre-processing | k -NN | | | | | | SVM | | | | | |
|-------------------|----------------|------------|------|-------------|-------|-------------|------|------------|------|-------------|------|-------------|-------|
| | | {8, 1} | | {16, 2} | | {24, 3} | | {8, 1} | | {16, 2} | | {24, 3} | |
| | | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% |
| $global$ -LBP | | | | | | | | | | | | | |
| | NF | 37.5 | 50.0 | 25.0 | 50.0 | 37.5 | 68.7 | 56.2 | 62.5 | 56.2 | 43.7 | 56.2 | 68.7 |
| | F | 62.5 | 50.0 | 56.2 | 75.0 | 62.5 | 68.7 | 75.0 | 68.7 | 62.5 | 62.5 | 62.5 | 68.7 |
| | FA | 56.2 | 50.0 | 56.2 | 75.0 | 62.5 | 68.7 | 75.0 | 68.7 | 62.5 | 62.5 | 62.5 | 68.7 |
| $global$ -LBP-TOP | | | | | | | | | | | | | |
| | NF | 31.2 | 93.7 | 37.5 | 100.0 | 37.5 | 81.2 | 62.5 | 75.0 | 62.5 | 93.7 | 56.2 | 87.5 |
| | F | 50.0 | 56.2 | 56.2 | 75.0 | 56.2 | 62.5 | 68.7 | 75.0 | 43.7 | 68.7 | 68.7 | 56.2 |
| | F+A | 75.0 | 43.7 | 56.2 | 43.7 | 68.7 | 50.0 | 68.7 | 62.5 | 62.5 | 56.2 | 56.2 | 68.7 |
| Features | Pre-processing | RF | | | | | | GB | | | | | |
| | | 8^{riu2} | | 16^{riu2} | | 24^{riu2} | | 8^{riu2} | | 16^{riu2} | | 24^{riu2} | |
| | | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% | SE% | SP% |
| $global$ -LBP | | | | | | | | | | | | | |
| | NF | 43.7 | 62.5 | 43.7 | 62.5 | 56.2 | 75 | 43.7 | 43.7 | 43.7 | 37.5 | 37.5 | 31.25 |
| | F | 56.2 | 56.2 | 68.7 | 62.5 | 62.5 | 68.7 | 25 | 56.2 | 50.0 | 43.7 | 25.0 | 43.7 |
| | F+A | 65.2 | 56.2 | 50.0 | 50.0 | 56.2 | 68.7 | 43.75 | 62.5 | 62.5 | 50.0 | 31.2 | 31.2 |
| $global$ -LBP-TOP | | | | | | | | | | | | | |
| | NF | 56.2 | 68.7 | 68.7 | 87.5 | 68.7 | 81.2 | 68.7 | 68.7 | 75.0 | 50.0 | 56.2 | 43.7 |
| | F | 56.2 | 62.5 | 81.2 | 68.7 | 81.2 | 81.2 | 56.2 | 62.5 | 62.5 | 68.7 | 68.7 | 81.2 |
| | F+A | 68.7 | 62.5 | 75.0 | 68.7 | 75.0 | 81.2 | 56.2 | 43.7 | 62.5 | 62.5 | 75.0 | 75.0 |

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