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

Guillaume Lemaître[1,a,*], Mojdeh Rastgoo[1,a,*], Joan Massich[1,*], Carol Y. Cheung[c], Tien Y. Wong[c], Ecosse Lamoureux[c], Dan Milea[c], Fabrice Mériaudeau[1], Désiré Sidibé[1]

[a] *ViCOROB, Universitat de Girona, Campus Montilivi, Edifici P4, 17071 Girona, Spain*
[b] *LE2I UMR6306, CNRS, Arts et Métiers, Univ. Bourgogne Franche-Comté, 12 rue de la Fonderie, 71200 Le Creusot, France*
[c] *Singapore Eye Research Institute, Singapore National Eye Center, Singapore*

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

☆Document source available in GitHub [1]

*Corresponding author

Email addresses: `g.lemaitre58@gmail.com` (Guillaume Lemaître), `mojdeh.rastgoo@gmail.com` (Mojdeh Rastgoo), `joan.massich@u-bourgogne.fr` (Joan Massich)

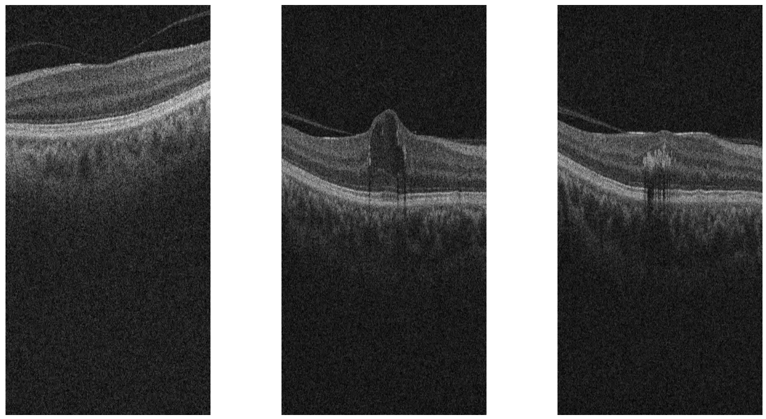
and feature configurations.

Keywords: Diabetic Macular Edema, Optical Coherence Tomography, DME, OCT, LBP

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. 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]. 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 higher resolution and fast image acquisition; it can produce $27,000$ 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 interpatient variations. Then, Histogram of Oriented Gradients (HOG) are extracted



(a) Normal (b) DME-cyst (c) DME-exudate

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

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 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 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 points corresponding to the top 3% of the vertical gradient values. Then, a texton of size 9×9 pixels is extracted around each keypoint, and Principal Component Analysis (PCA) is applied to reduce the dimension of every texton 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 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.

Liu *et al.* proposed a methodology for detecting macular pathology in OCT images using Local Binary Patterns (LBP) and gradient information as attributes [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 obtained 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.

The proposed method, which is an extension of our previous work [1], is based on LBP features to describe the texture of OCT images and dictionary learning using the BoW models [14]. We propose to extract 2D and 3D LBP features from OCT images and volumes, respectively. The LBP descriptors are further extracted from the entire sample or local patches within individual samples. In this research beside the comparison of 2D and 3D features, we also compare the effects of common pre-processing steps for OCT data (i.e., noise removing, aligning, flattening), study the optimal configuration regarding the BoW approach in conjunction with different base classifiers.

This paper is organized as follows: the proposed framework is explained in Sect. 2, while the experiments and results are discussed in Sect. 3. Finally, the conclusion and avenue for future directions are drawn in Sect. 6.

Table 1: Summary of the state-of-the-art methods.

Ref	Diseases			Data size	Pre-processing				Features	Representation	Classifier	Evaluation		
	AMD	DME	Normal		De-noise	Flatten	Aligning	Cropping				Sensitivity (SE)	Specificity (SP)	AUC
[11]	✓	✓	✓	45	✓	✓		✓	HOG		linear-SVM	86.7%,100%,100%		
[12]	✓		✓	384					Texton	BoW, PCA	RF			0.984
[13]	✓	✓	✓	326		✓	✓		Edge, LBP	PCA	SVM-RBF			0.93
[15]		✓	✓	62	✓				LBP-LBP-TOP	PCA, BoW, histogram	RF	87.5%	75%	

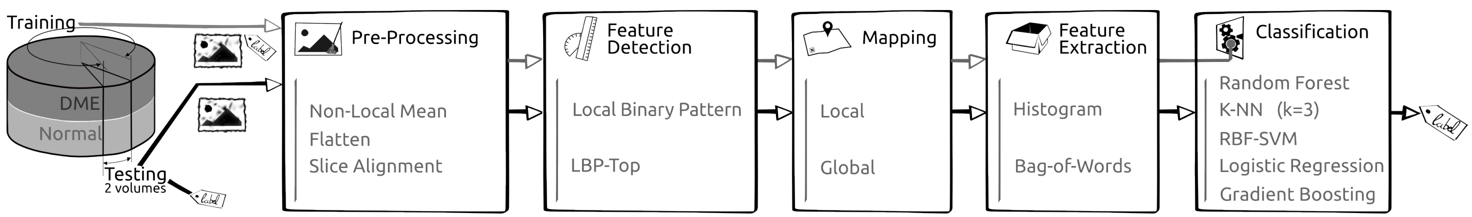
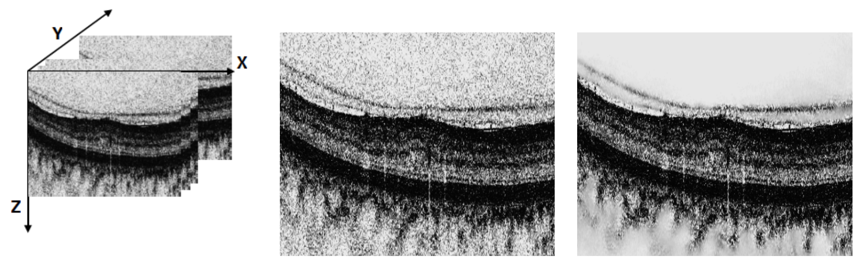


Figure 2: Our proposed classification pipeline.



(a) (b) (c)

Figure 3: OCT: (a) Organization of the OCT data - (b) Original image - (c) NL-means 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 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 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. 3.3-**??**.

2.1.1. Non-Local Means (NL-means)

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 NL-means [17], as shown in Fig. 3. NL-means has been successfully applied to US images to reduce speckle noise and outperforms other common denoising methods [18]. NL-means 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].

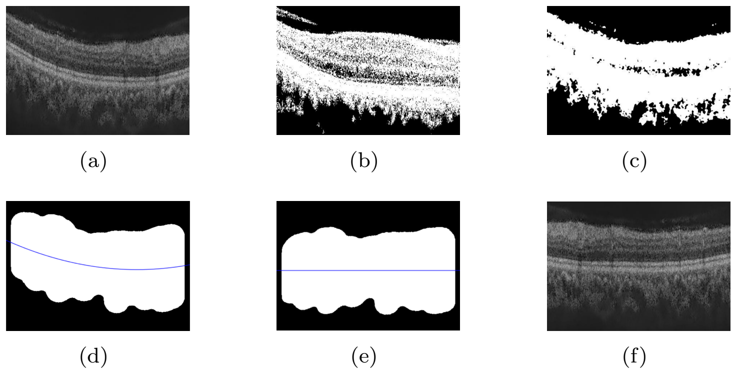


Figure 4: Flattening procedure: (a) original image, (b) thresholding, (c) median filtering, (d) curve fitting, (e) warping, (f) flatten image.

2.1.2. Flattening

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 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.

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 becomes a line as presented in Fig. 4(e) and Fig. 4(f).

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

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.

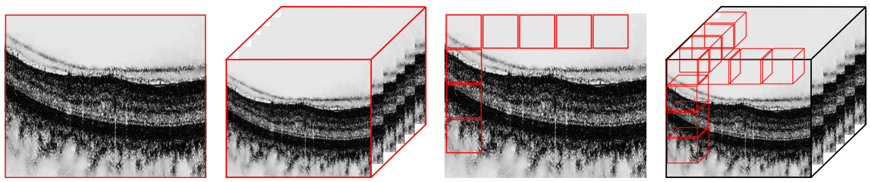
2.2. Feature detection

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):

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

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]. Volume encoding is later proposed by Zhao *et al.* by computing LBP descriptors in three orthogonal planes, so called LBP-TOP [20].

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.



(a) (b) (c) (d)

Figure 5: *Global* (a)-(b) and *local* (c)-(d) mapping for LBP and LBP-TOP features (2D B-scan and 3D volume, respectively).

2.3. Mapping

The mapping stage is used to partition the previously computed feature images 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.

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.

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 detected LBP images (see Sect. 2.2). Therefore, the LBP-TOP final descriptor is computed through the concatenation of the LBP histograms of the three orthogonal planes with the final size of $3 \times LBP_{\#pat}$. Similarly, the LBP descriptor is defined through concatenation of the LBP histograms per each slice 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 lead to a high dimensional feature space. For instance, *local*-mapping results to a size of $N \times d \times LBP_{\#path}$ for the final LBP descriptor and $N' \times LBP_{\#path}$ 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 [14]. 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, each of the training example is represented as a histogram of size k. The histogram is obtained by calculating the frequency of occurrences of each of the k words in the extracted features from the training example.

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

An experimental suit composed of three experiments is designed to test the influence of the different blocks composing our framework in comparison to our previous work [15] (baseline). Table 3 summarizes the different aspects of each experiment as well as the baseline [15].

Lemaitre *et al.* [15] proposed to pre-process the volumes using NL-means denoising without any flattening or aligning. Then local and global mapping LBP and LBP-TOP features were extracted and BoW approach with fixed codebook size of 32 words were used as a high representation of the feature. Finally the RF classifier was used to classify the the volumes. This framework was tested using two datasets of Duke and SERI and was compared to the proposed method of Venhuizen *et al.* [12]. The obtained results highlighted the discriminative power of LBP descriptors and showed that the proposed framework outperforms the others. However while comparing the obtained results using the two dataset of SERI and Duke, substantial difference were observed. This was attributed to the fact that the volumes in Duke dataset were provided with embedded pre-processing steps.

Considering the conclusion drawn from our baseline, three experiments are designed in order to investigate the effects of (i) optimal number of words, (ii) different pre-processing steps, and (iii) different classifiers. These experiments are defined such as:

- Experiment #1 is intended to find the optimal number of words (unlike [15]) and its effect with respect to different configurations (pre-processing which consists of denoising, flattening, and aligning along different mapping).

- Using the optimal number of words for high level representation of the features, experiment #2 investigates the performance of different configurations and classifiers.

- Finally experiment #3 is defined to investigate the benefits of different configurations and performance of different classifiers on low level represented features.

The detail explanation of each experiment is presented in the following subsections while the reminder of this section details the common configuration parameters across the three experiments.

All the experiments are performed using our own dataset SERI. Acquisition details regarding SERI is reported in Sect. 3.1. For all the experiments, LBP and LBP-TOP features are extracted for different sampling points of 8, 16, and 24 for radius of 1, 2, and 3, respectively. As previously mentioned, the *local*- and *global*-mapping strategies are used. The partitioning for *local*-mapping is set to (7×7) patch for 2D LBP and $(7 \times 7 \times 7)$ sub-volume for LBP-TOP.

The three experiments are evaluated using Leave-One-Patient Out Cross-Validation (LOPO-CV) strategy. At each round, a pair DME-normal volume is selected for testing while the remaining volumes are used for training. The use of this method implies that no variance in terms of Sensitivity (SE) and Specificity (SP) can be reported. Despite this limitation, LOPO-CV has been employed due to the small size of the dataset. All the experiments are evaluated in terms of SE and SP, which 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.

$$SE = \frac{TP}{TP + FN} \qquad SP = \frac{TN}{TN + FP} \tag{2}$$

Only in experiment #1, beside SE and SP additional metrics such as Accuracy (ACC) and F1-score (F1) are applied. ACC is used to have an overall sense of the classifier performance and F1 is used to see the trade off between SE and precision.

$$ACC = \frac{TP + TN}{TP + TN + FP + FN} \qquad F1 = \frac{2TP}{2TP + FP + FN} \tag{3}$$

Predicted		Actual A+	Actual A-
	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.

3.1. SERI-Dataset

This data was acquired by the Singapore Eye Research Institute (SERI), using CIRRUS TM (Carl Zeiss Meditec, Inc., Dublin, CA) SD-OCT device. The datasets consist 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.

Table 3: The outline and summary of the performed experiments. $\sim$ indicate that common configuration applies.

	Dataset	Pre-processing	Features	Mapping	Representation	Classification	Evaluation
Common:	SERI	NL-means	LBP,LBP-TOP $P = \{8, 16, 24\}$ $R = \{1, 2, 3\}$				LOPO-CV SE, SP
Baseline [15]: **Goal: Evaluation of features, mapping and representation**	+ Duke	$\sim$	$\sim$	*global* *local*	BoW Histogram	RF	+[12]
Experiment#1: **Goal: Finding the optimum number of words**	$\sim$	+ F + F+A	$\sim$	*global* *local*	BoW $k \in K$	LR	+ACC, F1
Experiment#2: **Goal: Evaluation of different pre-processing for high-level features**	$\sim$	+F +F+A	$\sim$	*global* *local*	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	$\sim$	*global*	Histogram	3-NN RF SVM GB	$\sim$

3.2. Experiment #1

In order to determine the optimal size of the codebook when using BoW, this experiment evaluates several codebook sizes on SERI dataset.

Several pre-processing strategies are evaluated: (i) NL-means, (ii) a combination of NL-means and flattening, and (iii) a combination of NL-means, flattening and aligning. LBP and LBP-TOP descriptors are detected using the default configuration. Volumes are represented using BoW, where the codebook size ranging for $k \in \{10, 20, 30, \cdots, 100, 200, \cdots, 500, 1000\}$. 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.

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 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, the codebook are randomly generated since the final aim is to asses the influence of codebook size and not the performance of the framework. For this experiment, the codebook building is carried out using random initialization k-means++ algorithm [28], which is usually used as a k-means initialization algorithm.

Figure 7 shows the ACC and F1 score graphs obtained for a single case[1] in [1], while the optimal number of words for all the configurations are reported in a compact manner in Appendix A - Table 5.

3.3. Experiment #2

After studying the impact of the codebook size in Sect. 3.3, this experiment explores the improvement associated with: (i) different pre-processings, and (ii) using larger range of classifiers (i.e. linear and non-linear) for high represented features.

[1] `http://tinyurl.com/jeczfh6`

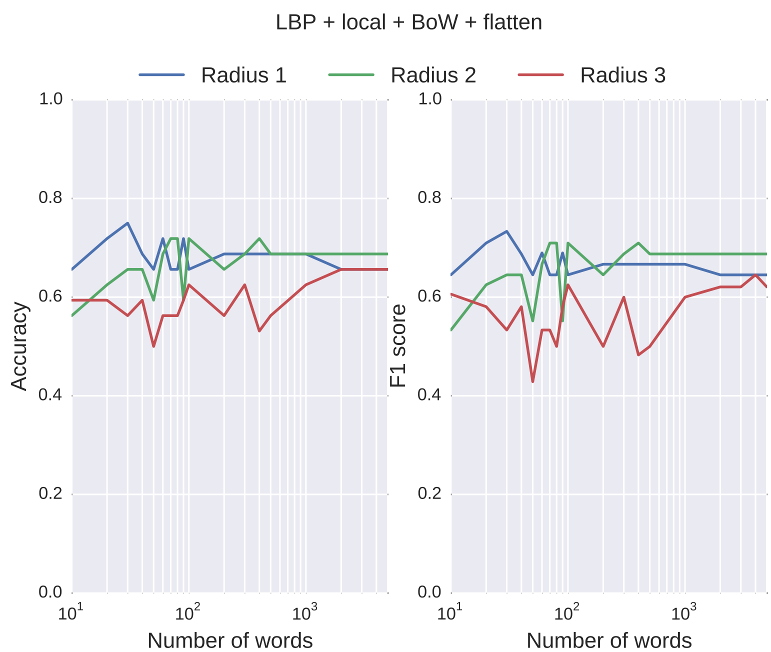


Figure 7: The performance of LR with NL-means+F pre-processing for different P and R.

Similar pre-processing strategies to the previous experiment are evaluated (NLM, NLM+F, and NLM+F+A). In this experiment the codebooks for the BoW representation of LBP and LBP-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. Regarding the classification strategies, k-NN classifier is trained by considering the 3 nearest neighbor. The RF and GB classifier are trained using 100 un-pruned trees, while SVM classifier is trained with 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 6, while the most relevant configurations are shaded and the highest results are highlighted in **bold**.

3.4. Experiment #3

This experiment replicates the *Experiment #2* for the case of low-level represented features from the volumes.

The same pre-processing strategies (NLM, NLM+F, and NLM+F+A) are investigated. LBP and LBP-TOP descriptors are detected using the default configuration. Volumes are represented using low-level feature representation of the *global* mapping. Finally, the volumes are classified using k-NN, RF, GB, and SVM, similarly to *Experiment #3*. The obtained results from this experiment are listed in Appendix A - Table 7.

4. Results

Table 4 represents a summary and comparison of the obtained results from experiment #2 & #3 with respect to the baseline. The complete list of obtained result regarding each experiment can be found in Appendix A (see Table 5, 6, and 7). This table illustrates the highest 26 performances from highest to lowest considering their achieved SE and SP. The related experiment, choice of pre-processing, type and configuration of the features, choice of mapping and representation, choice of classifier, and finally if required size of codebook is illustrated in this table.

Table 4: Summary of all the results. The best results for each experiment are denoted in bold.

Line	Experiment	Evaluation		Pre-processing	Feat. Detection				Mapping	Feat. Representation	Classifier	#words
		SE	SP		Type	$\{8,1\}$	$\{16,2\}$	$\{24,3\}$				
1	#2	81.2	93.7	NLM+F	LBP	✓			local	High	SVM	30
2	#2	75.0	93.7	NLM+F+A	LBP	✓			local	High	SVM	40
3	#2	75.0	93.7	NLM	LBP	✓			local	High	SVM	70
4	#2	75.0	100	NLM	LBP-TOP		✓		local	High	SVM	500
5	#2	81.2	87.5	NLM	LBP-TOP	✓			local	High	SVM	400
6	#2	81.2	87.5	NLM+F+A	LBP-TOP		✓		local	High	RF	90
7	#2	81.2	81.2	NLM	LBP	✓			local	High	RF	70
8	#3	81.2	81.2	NLM	LBP-TOP			✓	global	Low	RF	
9	#2	81.2	81.2	NLM+F	LBP-TOP	✓			local	High	SVM	300
10	#3	81.2	81.2	NLM+F+A	LBP-TOP			✓	global	Low	GB	
11	#3	81.2	81.2	NLM+F	LBP-TOP			✓	global	Low	RF	
12	#2	75.0	87.5	NLM	LBP	✓			local	High	k-NN	70
13	Lemaitre *et al.* [15]	75.0	87.5	NLM	LBP	✓			local	High	RF	32
14	Lemaitre *et al.* [15]	75.0	87.5	NLM	LBP-TOP		✓		global	Low	RF	
15	#2	68.7	93.7	NLM	LBP	✓			global	High	RF	500
16	#3	75	81.2	NLM+F+A	LBP-TOP			✓	global	Low	RF	
17	#2	68.7	81.2	NLM	LBP-TOP		✓		local	High	RF	500
18	#3	62.5	93.7	NLM	LBP-TOP		✓		global	Low	SVM	
19	#3	68.7	87.5	NLM	LBP-TOP		✓		global	Low	RF	
20	#3	68.7	81.2	NLM	LBP-TOP				global	Low	RF	
21	#3	75.0	75.0	NLM	LBP-TOP				global	Low	RF	
22	#3	68.7	75.0	NLM+F	LBP-TOP	✓			global	Low	SVM	
23	#3	56.2	75.0	NLM	LBP			✓	global	Low	RF	
24	#3	56.2	75.0	NLM+F	LBP		✓		global	Low	k-NN	
25	#3	56.2	75.0	NLM+F+A	LBP		✓		global	Low	k-NN	
26	Venhuizen *et al.* [12]	61.5	58.8									

5. Discussion

In this research, first the effects of required number of words with respect to different feature configuration and pre-processing was investigated in experiment #1. The obtained results from this experiment indicated that commonly less umber of words is required when higher number of sampling points and radius ($\{P, R\} = \{24, 3\}$) are used. Considering the mapping stage it was observed that the number of words decreases for *local*-LBP in comparison with *global*-LBP. Concerning different pre-processing steps, opposite to the initial expectation, it was observed that the influence of this step is not substantial nor consistent over all the obtained results.

Similar performances concerning different pre-processing was observed in experiment #2. In fact, most configurations decreased in performance while flattening or flattening and aligning were added to denoising in pre-processing step (i.e. light shaded configurations in Appendix A - Table 6). However the configurations with the highest performances, achieved better results when flattening or flattening and alignment were added to the pre-processing. These configurations are highlighted in dark shades in Table 6. Regarding the feature configuration, high representation of locally mapped feature descriptors with smaller radius and number of sampling points achieved better performances. In terms of choosing a classifier, SVM provided the best results, followed by RF.

By analyzing the effects of pre-processing for low represented features, similar conclusions were drawn. Although flattening the B-scans boosted the performance of the best performing configurations, the effect was not consistent across all the configurations. In Appendix A - Table 7, the most relevant configurations are shaded and the highest results are highlighted in **bold**. Concerning the feature configurations opposite to experiment #2, larger radius and number of sampling points obtained better results and in general LBP-TOP had a better performance in comparison to LBP. In terms of classifier, RF had a better performance than others but the highest SP was achieved using SVM.

Finally analyzing all the results as it is illustrated in Table 4, it is clear that just optimizing the codebook size without additional pre-processing step improves the results (compare line 7 (experiment #2) and line 13 (baseline)). The obtained results indicated that the highest results were achieved while flattening and flattening and alignment was added in the pre-processing step using high representation of locally mapped LBP features (compare the first five lines). These results also outperformed the baseline. In general with respect to the highest 10 performances (all outperforming the baseline), high representation of locally mapped features with SVM classifier outperformed other configurations. Considering the desirable radius and sampling points as it was concluded before, smaller radius and sampling points is effective for local mapping while global mapping benefits from larger radius and sampling points.

6. 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 (i) the effects of different pre-processing steps, (ii) the influence of different mapping and feature extraction strategies, (iii) the impact of the codebook size in BoW, and (iv) the comparison of different classification strategies.

While outperforming the previous studies [15, 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 extracted 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.

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Conflict of interest statement

The authors declare no conflict of interest.

Appendix A Completed list of results obtained from experiment #1 & #2 & #3

Table 5: 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#
global-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
local-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
local-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 6: Experiment #3 - k-NN and SVM 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 the previous experiment.

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	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

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	**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 7: Experiment #4 - 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.

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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