Segmentation of Doppler optical coherence tomography signatures using a support-vector machine

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Abstract: When processing Doppler optical coherence tomography images, there is a need to segment the Doppler signatures of the vessels. This can be used for visualization, for finding the center point of the flow areas or to facilitate the quantitative analysis of the vessel flow. We propose the use of a support-vector machine classifier in order to segment the flow. It uses the phase values of the Doppler image as well as texture information. We show that superior results compared to conventional simple threshold-based methods can be achieved in conditions of significant phase noise, which inhibit the use of a simple threshold of the phase values.

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1. Introduction

Optical coherence tomography (OCT) has nowadays become an established biomedical imaging modality [1]. The transition from time-domain to Fourier-domain OCT enabled the imaging of full 3D volumes with high resolution [2–5]. Nowadays, these volumes can be recorded within fractions of a second due to the great sensitivity that is achieved with state-of-the-art systems [6–12]. One main area of application lies in ophthalmology as OCT allows for the non-invasive imaging of the different layers of the retina with unprecedented resolution [13]. A promising functional extension of OCT is Doppler OCT (DOCT) [1], which might help for early diagnosis of major retinal diseases as perfusion is highly affected by pathologies. This has already been shown with Laser Doppler velocimetry for several diseases [14–16]. DOCT as contrast enhancement might as well reduce the number of invasive fluorescein angiograms. There are several variants of measuring and contrasting blood flow with OCT. Quantitative information is provided for example by phase resolved DOCT which extracts flow information by measuring the phase shift between adjacent A-scans [17,18]. This induced phase shift is related to the axial velocity component of moving scatterers, such as red blood cells. Potential applications of DOCT in ophthalmology include the quantitative measurement of flow within 3D volumes [19–22], the visualization of vessels and capillary networks [23–27], or the determination of total retinal blood flow [28]. Also, due to the high-speed advantage of FDOCT, pulsatile flow dynamics can be followed over time within single retinal vessels [29–33]. An important step for quantifying flow is the segmentation of the flow area from bulk tissue. In phase difference or Doppler tomograms, Doppler flow is mapped to a different phase difference range than bulk tissue that exhibits no motion. It can, therefore, in principle be easily segmented from the image histogram [21]. Other approaches use statistical image processing [23] or filtering in the spatial frequency domain by either applying a spatial carrier frequency [24] or by using the induced spatial frequency shift of the moving structure per se [25,34]. Finally, resonant Doppler imaging used the effect of fringe washout for segmentation of moving structures from bulk tissue [35].

Histogram-based image segmentation is a classic problem in image processing. A huge amount of literature exists that deals with various variants of histogram-based image segmentation (see e.g. the recent work by Sen et al. and citations therein [36]). Even though the Doppler information is present in the histogram of the Doppler OCT image, histogram-based methods cannot be readily applied, as the contribution of the flow in the histogram is so small that it does not lead to distinct modes in the histogram (see Fig. 1).

Furthermore, phase noise present in the system makes a clear distinction difficult, as phase values that indicate flow are also present in the area of bulk tissue. Phase noise stems from mechanical vibrations of the system, scanner jitter and the shot-noise limited detection of the OCT system.

Kolbitsch et al. [21] recently presented an investigation of threshold-based histogram methods. They suggested calculating the probability of a phase value representing flow with a Gaussian shaped histogram filter. This basically meant that a high phase value (positive or negative) had a high probability of representing flow. Then they applied a large median filter on the mask followed by thresholding and used the final mask to extract Doppler signatures. However, the adjustment of the filter edges had to be done manually which is tedious and there is no objective measure that determines the optimal parameters. In addition, by using only the phase values of the image, the capability of the filter to remove bulk tissue is limited due to the presence of phase noise.
It is desirable in quantitative Doppler analysis to have a method available that is capable of segmenting Doppler flow according to objective measures, with the properties of being exact at the vessel boundaries, not being influenced by fringe-washout and phase wraps and which is capable of minimizing the influence of phase noise on the segmentation error. If the goal is to contrast the flow, like in angiography, the conditions can be slightly relaxed.

We, therefore, present an approach that yields more robust results with respect to phase noise and multiple scattering by the combination of several descriptive features of the flow areas. It is based on a support-vector machine (SVM) classifier, which is a supervised learning method. The improved results come at the cost of requiring representative training data. However, as will be pointed out in the paper, the choice of training data is straightforward. We apply the method to circumpapillary DOCT scans and to do 3D retinal angiography which is described in section 3.2.

2. Methods

An SVM is a decision machine that transforms training data to some multi-dimensional space and finds the hyperplane with the highest margin, i.e. the largest distance to the samples, as a decision boundary [37]. Normally, the SVM is used for binary classification problems although there are extensions that allow for multiclass classification [37]. The key idea is that several features can be combined for classification, i.e. in our case for describing flow. The optimal hyperplane after training then separates the bulk tissue from the flow. After this phase the learned SVM can be readily applied to new data sets. We combine features of the phase values of the DOCT image with texture features that can be calculated after histogram equalization. This is described in more detail in the following paragraphs.

2.1. Histogram equalization

The histogram of the Doppler image can be seen as a probability density function over the phase values after appropriate normalization. From this, the cumulative distribution function (CDF) can be calculated which is defined as

\[ F(x) = P(X \leq x), \quad -\infty \leq x \leq \infty, \]

where \( P(X \leq x) \) denotes the probability that the random variable \( X \), the density of which is represented by the appropriately normalized histogram, takes on values smaller or equal \( x \). Histogram equalization aims at linearizing the CDF. Normally, this is a standard tool in order to increase the contrast in images. In cases of images with narrow histograms and relatively few gray levels, the equalization has the effect of increasing the visual graininess, which is usually not desired. In the case of Doppler OCT images, we can profit from this effect to separate flow from surrounding tissue. At first, we mask the Doppler image by using the intensity image in order to remove the noise floor and to only have tissue and flow information present in the data. We achieve this by first median filtering the intensity image.
with a filter of size 3x3 in order to reduce the noise. Then we threshold it and use it as a mask for the DOCT image. The threshold value was chosen empirically such that it cuts-off the noise and keeps the structure of interest. The application of histogram equalization now leads to an increase of graininess in the area of bulk tissue and maps the flow values of the vessels to constant values. An example DOCT image is shown in Fig. 2(a). Figure 2(b) shows the same image after histogram equalization.

The effect of the histogram equalization now allows for the separation of the flow from bulk tissue by using an image filter that quantifies the “randomness” of data. Texture filters, which can be used for this are e.g. an entropy filter, standard deviation filter or range filter that quantify, as their name suggests, the entropy, standard deviation and range of values within a certain window. This directly gives us an important and robust feature for segmentation of the vessel flow without additional preprocessing steps like local normalization for example. Areas of flow are thus characterized by a low value of “randomness” after histogram equalization, whereas the bulk tissue is characterized by a high value. This can be seen in Fig. 2(c) where the background below and above tissue had been filled with noise before the application of the entropy filter.

2.2. Support vector machine

We use a 1-norm, soft-margin SVM with a Gaussian radial basis function kernel in order to be able to model non-linear separation boundaries. The SVM is trained on training data and can then be applied to new data sets. Due to the presence of phase noise, we cannot expect that our segmentation problem provides us with perfectly separable training data which is why we use a soft-margin SVM that allows for some misclassified data points. The 1-norm, soft margin SVM hereby is less sensitive to outliers than the 2-norm, soft-margin SVM and the problem can be formulated as follows [37]

\[
\begin{align*}
\text{minimize}_{w,b,\xi} & \quad \frac{1}{2}\|w\|^2 + C \sum_{n=1}^{N} \xi_n, \quad C > 0 \\
\text{subject to} & \quad y_n (w^T \phi(x_n) + b) \geq 1 - \xi_n, \quad n = 1, \ldots, N \\
& \quad \xi_n \geq 0, \quad n = 1, \ldots, N
\end{align*}
\]
In the above equation, the training samples are denoted by \((x_i, y_i)_{i=1\ldots N}\), where \(y_i \in \{-1,1\}\) denotes the class the sample belongs to. The decision function is given by \(f(x) = w^T \Phi(x) + b\) where \(w\) is a vector of coefficients, \(b\) is a constant and \(\Phi\) is a fixed feature space transformation. However, this feature space transformation does not have to be explicitly specified as it is sufficient to calculate the scalar product in the feature space to solve the optimization problem (see e.g. [37], for details). This is efficiently achieved by the definition of appropriate kernels. We use a Gaussian radial basis function kernel, i.e.

\[
k(x_i, x_j) = \Phi(x_i) \Phi(x_j) = \exp(-\gamma \|x_i - x_j\|^2), \gamma > 0,
\]

where \(\gamma\) determines the radius of the kernel. \((\xi_i, \alpha_i)_{i=1\ldots N}\) denote so-called slack variables that allow for some misclassified labels and, finally, the box constraint \(C\) controls the trade-off between the penalty introduced by the parameters \(\xi_i\) and the margin. The parameters that need to be determined for training of the SVM are the parameter of the kernel function \(\gamma\) and the value of the box constraint \(C\). These settings directly influence the generalization capability of the SVM from the training data to unseen data that is to be segmented. When applying the SVM to unseen data, e.g. a point \(z\), the actual classification is given by \(\text{sign}(f(z))\), which denotes the side of the decision surface, the point \(z\) is mapped to.

For solving the optimization of the SVM given in Eq. (1) and Eq. (2) we use sequential minimal optimization [38]. It breaks up the quadratic minimization problem that has to be solved into smaller problems, resulting in a significant speed-up in training of the SVM (less than a minute on i7 CPU 920 at 2.67 GHz with 6GB Ram - Bioinformatics toolbox of Matlab 7.9).

In this paper, we follow the standard solution to the problem of finding the optimal parameters \(\gamma\) and \(C\) by doing an extensive search of the parameter space with 10-fold cross-validation, consisting of a raw search of the parameter space followed by a fine one [39]. We included some multiple scattering as background in the evaluation of the performance of the current parameter setting during the cross-validation. Omitting it, would have led the SVM to perfectly segment the flow areas, but as a result of overfitting it would have also segmented all the multiple scattering components as belonging to the flow areas, which is exactly what we would like to avoid. After finding the optimal parameters, we do not include the multiple scattering in the final training of the SVM as it would only decrease the separability of the data. It should be noted, however, that several schemes exist that can be employed to speed up the parameter search (see e.g. [40]).

The features that we use for training of the SVM are the phase, the average phase within a [3,3]-window [41] as well as the entropy within a [5,5]-window and within a [9,9]-window, calculated from the averaged image. This means that our training vector has the dimensions \(N \times 4\) where \(N\) stands for the amount of training data (pixels) used.

In general, the windows should be as small as possible for the segmentation of the boundaries of the flow area to be as exact as possible. However, we found it necessary to include also the entropy in a window of size 9 in order to correctly segment flow with phase wraps or fringe washout. The abrupt transitions between properly resolved and phase wrapped flow areas appear as edges in the evaluation windows. This yields high entropy if calculated with a window size of 5, eventually leading to misclassifications if this is the only entropy feature used.

Of course, the window size affects the size of the flow areas that can be segmented. The largest window size gives the minimum size of the flow areas the filter is sensitive to. The size of the window is a relative number that has to be compared to the oversampling factor (OF) which is defined in Eq. (3). However, we found that the aforementioned features lead to very good segmentations for the whole range of OFs that we investigated.
3. Results

The optical setup and settings that were used for all our experiments has already been described elsewhere [33]. Before processing the DOCT images, we corrected the images for background motion by using a histogram based algorithm [11].

The spot size of the laser beam on the retina was 14.7 µm. The radius of the circular scans was 2.1 mm which means a lateral width of the B-scans of 13.2 mm. The Doppler images of Fig. 3 and 4 have an OF of 3.34. We defined the OF as follows

\[ \text{OF} = \frac{w \cdot N}{d}, \]  

where \( w \) is the spot size, \( N \) is the number of sampling points and \( d \) is the width of the tomogram. We compare our method with a segmentation by a Gaussian mixture model (GMM) as it is a systematic expansion of the work of Kolbitsch et al. [21] that allows for better comparison than manually defined thresholds. The GMM is optimized by using an expectation-maximization algorithm [42], which we initialize with the results of k-means clustering [37]. The phase is taken from the DOCT image that had been averaged with a [3,3]-kernel as this increases the separability of flow and bulk tissue. As already mentioned, training data is chosen such that it includes the flow appearances that are to be expected, i.e. flow in both directions, phase wraps and fringe washout. As we do not want to \textit{a priori} prefer flow to background or vice versa, we use the same amount of training data for the background and the flow in order to have a balanced data set for the SVM, which is a binary classification problem. The GMM models three Gaussians, the flow in both directions and the background, which is why we use the same amount of data for each flow direction as for the background in order to get the same prior probabilities for the three classes. Of course, the training data is from a different scan than the one that is to be segmented. An exemplary histogram together with the resulting GMM is visualized in Fig. 3, showing the results for training data taken from the volume which is discussed in section 3.2. The results of the two investigated segmentation procedures for the image in Fig. 2 can be seen in Fig. 4. Figure 4(a) shows the segmentation result of the SVM-based procedure and Fig. 4(b) shows the result of applying the GMM. In both cases, we have first calculated a mask of values that are segmented as flow. From this mask we have removed connected components with less than 50 pixels in order to remove small clutter from the segmentation results. The final mask was used to paint in the results.

Choosing 50 pixels for the size of the connected components is an empirical value. The flow areas that we segmented were all much bigger than 50 pixels and this size consistently gave good results in our experiments.

The segmentation that is achieved by the SVM is more homogenous and less susceptible to scatter. This is visualized in Fig. 5(a) showing a close-up of the area in the orange box in Fig. 4(a). Figure 5(b) shows the same area of the result shown in Fig. 4(b). The blue part in the middle of the segmented flow in Fig. 5 denotes missing values due to fringe-washout.
The GMM basically gives two thresholds that are used for segmenting the data. It is clear that changing these thresholds can influence the registration result. However, it is not possible
to segment more of the flow without including more noise or, vice versa, to reduce the amount of noise without undersegmenting the flow areas.

In order to further illustrate the properties of the SVM, we have repeated a grid search just using the average phase and the entropy in a window of size 9x9 of the same training data used for the training of the SVM that was applied in Fig. 4(a) and Fig. 5(a). Using two features allows us to visualize the feature space in 2D. The result is shown in Fig. 6. Figure 6(a) shows the 2D visualization of the grid search result ($\gamma = 360, C = 45$). Figure 6(b) shows the application of the resulting SVM to the same area that is shown in Fig. 5. The segmentation is not as precise at the borders of the flow areas as in Fig. 5(a) because only two features are used. The position of the hyperplane might seem counter-intuitive because it does not seem to perfectly separate flow and bulk tissue. Therefore, we manually picked settings that let the SVM adapt very well to the training data (Fig. 6(c), $\gamma = 1/2, C = 8$). However, it can be seen in Fig. 6(d) that this SVM does not generalize very well to unseen data as it is overfitted which results in oversegmentation of the flow areas.

![Figure 6](image.png)

Fig. 6. Result of training and applying SVM using just two features. Black line denotes decision surface ($f(x) = 0$). (a) 2D feature space with decision boundary obtained after training with parameters $\gamma$ and $C$ as obtained by grid search. (b) Resulting segmentation on the same part that is shown in Fig. 5. (c) Feature space with seemingly better separating decision surface obtained by manual parameter settings that (d) shows the problem of oversegmentation due to overfitting as illustrated by the arrows. Area shown in (d) is the same as in (b). Support vectors are the data points that determine the position of the decision boundary after optimization.

### 3.1. Connection between oversampling factor and segmentation accuracy

The phase noise present in the Doppler images changes with the OF [43]. A higher OF means less phase noise. It is therefore of interest to investigate the generalization performance of SVMs on data with an OF different from the training data.

In order to investigate this, we recorded different series of circumapapillary scans with oversampling ratios of 2.23, 3.34, 4.45 and 5.57 from a single subject. For each scan we have chosen training data representing flow in both directions, including phase wraps and fringe washout, and trained the SVM using the aforementioned extensive grid search [39]. We have then manually segmented two flow areas on a different slice than the one from which the training data was chosen and segmented these areas with the different SVMs. The presented flow areas were chosen as they exhibit all the characteristic cases that we can expect when
dealing with Doppler data. This means flow in opposite axial directions, phase wraps and fringe washout. With the manual segmentations the segmentation accuracy was quantified as the ratio of correctly classified points to all data points. In addition, multiple scattering components were again included in the evaluation in order to check if this part is correctly segmented as background. Also, we included a rim of 10 pixels around the manual segmentation of the flow areas, otherwise oversegmentation might lead to a classification accuracy of 100%. The results can be seen in Table 1.

Table 1. Results of applying SVM to scans with different OF

| Training | 2.23 | 3.34 | 4.45 | 5.57 |
|----------|------|------|------|------|
| 2.23     | 0.94 (0.95) | 0.94 | 0.95 | 0.95 |
| 3.34     | 0.92 | 0.94 (0.95) | 0.95 | 0.95 |
| 4.45     | 0.90 | 0.92 | 0.94 (0.97) | 0.95 |
| 5.57     | 0.88 | 0.91 | 0.93 | 0.96 (0.95) |

The values on the diagonal in Table 1 indicate the classification accuracy for applying the SVM to the chosen flow areas in a different scan but with the same OF as the one from which the training data was taken. The numbers in parentheses on the diagonal denote the results of the 10-fold cross validation of the grid search with final parameter settings. It can be seen that an SVM that is trained with data of a low OF generalizes better to higher OF than the other way round. This means that an SVM, which is trained with a high OF might be overfitted when applied to data of a lower OF. This apparently is not the case when the SVM is applied to data with a higher OF than the training data as increasing the OF increases the separability of the data. This is the reason why it may still be well segmented by an SVM which had been trained with data of a lower OF.

In order to visualize the effect of applying a SVM to data with a different OF than the training data, Fig. 7 shows the segmentation results for the two flow areas that were investigated for the following set of training and evaluation OF: Fig. 7(a): 2.23/2.23, Fig. 7(b): 2.23/5.57, Fig. 7(c): 5.57/2.23, Fig. 7(d): 5.57/5.57, where the first number indicates the OF of the training data and the second number the one of the evaluation data. Although all registration results show reasonably good results, it can be seen that the best segmentation result is indeed obtained on the diagonal where training and evaluation data have the same OF. In Fig. 7(b), it can be seen that the SVM that was trained on more noisy features than

Fig. 7. Images visualizing the effect of applying the SVM to data with a different OF than the training data. (a) 2.23/2.23, (b) 2.23/5.57, (c) 5.57/2.23, (d) 5.57/5.57. Red parts denote segmented flow areas. White bars denote scale bars: (a) horizontal: 150 µm, vertical: 50 µm, (b) horizontal: 120 µm, vertical: 50 µm.
present in the target image, tends to oversegment the data, i.e. it also segments the parts under
the flow area on the right that actually represent multiple scattering components. The reverse
effect can be seen in Fig. 7(c) where the SVM that was trained on data with less noisy features
undersegments the flow, not segmenting the noisier flow borders. In practice, it is therefore
advisable to train an SVM for every OF that is used. Once this is done, the SVM can be
applied to any new data set of the same OF for segmentation.

3.2. 3D retinal angiography

The presented algorithm can also be applied to a whole volume in order to extract the flow
information present in the data. We recorded a volume of a healthy subject with a size of 3.5
mm x 3.5 mm and an OF of 3.34 covering the optic nerve head. In this region, there are areas
exhibiting large flow values that only appear as arcs in DOCT tomograms due to strong fringe
washout. It is difficult to find the optimal settings with a grid search in this case. Not
including examples of these arcs as flow values in the grid search leads to parameter settings
that do not segment these parts of the flow. Including them however, leads to parameter
settings that oversegment the flow areas and include a lot of multiple scatter and phase noise
in the segmentation. The grid search is not able to strike a compromise between the two
results. But knowing the results of the two aforementioned grid searches, near to optimal
settings can be found by choosing parameters that lie somewhere in the middle of the two
results while keeping in mind that the margin can be influenced by the box constraint \(C\). Of
course, it can be argued that the flow areas that are only visible as arcs do not contain useful
information, anyway. Our aim was, however, to visualize all the available information that is
present in the data. Because of this, we did not include the entropy in a window of size 9 as
the arcs would be averaged out.

![Fig. 8. 3D angiography, (a) Result with proposed approach, (b) Result after using GMM for segmentation. Note the increased amount of segmentation error in (b) as compared to (a) indicated by the arrows. Size of volume: 3.5x3.5x1.7 mm. For 3D color rendering see associated video (Media 1).](image1)

![Fig. 9. Top view of volumes shown in Fig. 8, (a) Result with SVM based approach, (b) Result with GMM. Arrows indicate areas of better performance of SVM based approach. For 3D color rendering see associated video (Media 2).](image2)
The resulting segmentation is shown in Fig. 8(a) (Media 1) where it is compared to the result of the GMM trained on the same data which is shown in Fig. 8(b) (Media 1). Again, connected components with less than 50 pixels have been removed to reject clutter. Still, it can be seen that the SVM based procedure achieves a segmentation that includes less noise while achieving a higher amount of detail. This can be better seen in the top view which is shown in Fig. 9 (Media 2). Figure 9(a) (Media 2) again shows the result of the SVM based procedure and Fig. 9(b) (Media 2) shows the result of applying the GMM.

4. Discussion

The use of a sliding window for calculation of the average phase and the entropy limit the size of the flow areas that can be segmented. Methods like scatter [44] or phase variance [45] operate on a pixel-by-pixel basis laterally and are, therefore, able to segment capillaries. Yet, these methods rely on high lateral oversampling and did not prove to be useful for achieving exact flow segmentations in our settings. In addition, they are prone to segmenting multiple scattering.

The presented method has great potential for facilitating the analysis of time-course Doppler data, e.g. in circumpapillary Doppler OCT scans. In this case, a method capable of reliably and objectively segmenting the flow greatly facilitates the quantitative perfusion analysis. We believe that our method is an important step in the direction of automated flow extraction and characterization.

Multiple scattering is a stochastic process. It can therefore happen that parts of it have the same features as the flow area it stems from. This may lead to misclassifications as can be seen in the red square in Fig. 3(a). However, this is a problem for all the methods that do not consider the shape of the resulting segmentation. Thus, it might be solved by regularizing the shape of the resulting segmentation, thus favoring a smooth outline of the flow. In this case, one would need to have access to the posterior probabilities of the SVM. For this purpose, an algorithm by Platt might be used that maps the SVM outputs into probabilities by training the parameters of an additional sigmoid function [46]. Also, a relevance vector machine might be used [37].

In order to achieve a good classification by the SVM, the training data has to be chosen carefully. In contrast to a simple GMM, the SVM is not generative and needs labeling of the training data by the user. Therefore, care has to be taken that the training data chosen is representative and contains as little errors as possible, e.g. by including bulk tissue in the training data of the flow. Due to phase noise, the data cannot a-priori be assumed to be separable. Therefore we have chosen a soft-margin classifier, i.e. some misclassification during training is allowed.

5. Conclusion

We have presented a method that is capable of segmenting flow in standard phase-resolved Doppler OCT images under conditions of considerable phase noise that prevent the use of a simple threshold filter. The optimal separating hyperplane between bulk tissue and flow values is learned by a support vector machine classifier that takes spatial information around the pixels into account. After training, the SVM can be readily applied to new data sets. We compared our method to a segmentation achieved by employing a GMM that had been trained on the same data and could show that the results of the proposed method show less segmentation error, especially in areas of multiple scattering. It, therefore, presents a further step towards a fully automated analysis of Doppler data.

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