Cortically-Inspired Spectral Clustering for Connectivity Analysis in Retinal Images
Curvature Integration

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Abstract Tree-like structures such as retinal images are widely studied in computer-aided diagnosis systems in large-scale screening programs. Despite several segmentation and tracking methods proposed in the literature, there still exist several limitations specifically when two or more curvilinear structures cross or bifurcate, or in the presence of interrupted lines or highly curved blood vessels. In this paper, we propose a novel approach based on multi-orientation scores augmented with a contextual affinity matrix, which both are inspired by the geometry of the primary visual cortex (V1) and their contextual connections. The connectivity is described with a four-dimensional kernel obtained as the fundamental solution of the Fokker-Planck equation modelling the cortical connectivity in the lifted space of positions, orientations and curvatures. It is further used in a self-tuning spectral clustering step to identify the main perceptual units in the stimuli. The proposed method has been validated on several easy and challenging structures in a set of artificial images and actual retinal patches. Supported by quantitative and qualitative results, the method is capable of overcoming the limitations of current state-of-the-art techniques.

Keywords Retinal image analysis · Contextual affinity matrix · Primary visual cortex · Spectral clustering · Perceptual grouping · Curvature

1 Introduction

1.1 Retinal Image Analysis

Diabetes, as many other systematic, cardiovascular and ophthalmologic diseases, is widespread worldwide, especially in developing countries. Diabetic retinopathy is the progressive damage to the network of tiny blood vessels in the retina and it is due to the diabetes. It is the main cause of blindness and affecting the quality of life of many people in addition to raising many healthcare and social costs. Early diagnosis and treatment is essential to reduce the financial and emotional costs tremendously. Moreover, developing automated computer-aided systems facilitate the diagnostic process for a larger population of people in a shorter time and at lower costs.

Based on several studies, the retinal vasculature is one of the easy-to-access sources of diagnostic information not only for diabetic retinopathy, but also glaucoma, hypertensive retinopathy, and other diseases,
considering their direct connection to the brain vasculature [Foracchia et al., 2001; Hubbard et al., 1999; Smith et al., 2004]. The geometrical features such as the change of vessel width, curvature, branching patterns and the fractal dimension are all considered as biomarkers for clinical studies (Bekkers et al., 2015; Chapman et al., 2002; Habib et al., 2014; Huang et al., 2015). Quantitative measurement of these features is highly dependent on correct detection and analysis of the morphologic and geometric structure of the retinal vasculature i.e. blood vessels, bifurcations and their connections.

Detection of blood vessels is often done via vessel segmentation, which is a well-studied topic in retinal image analysis (Fraz et al., 2012). The segmentation methods basically differentiate between blood vessels and background pixels, but they do not separate individual vessels from each other. Therefore, they have been used often as an initial step in tracking approaches introduced in the literature (e.g. Al-Diri et al., 2009; Bas et al., 2012; Dashtbozorg et al., 2014; De et al., 2013, 2014, 2016; Delibasis et al., 2010; Gonzalez et al., 2010; Turetken et al., 2011, 2012; Xu et al., 2011). Tracking the vessels makes it possible to investigate the features along individual vessels separately. The vasculature network constructed during tracking not only needs to be a correct global model, but it also should model the local connections between individual vessel segments at crossings and bifurcations correctly i.e., the local and global models are directly related.

Despite all the methods proposed in literature, tracking approaches are still facing some difficulties, which are either coming from imperfect segmentation and their corresponding skeletons, or they arise at crossovers and junction points, where two vessels belonging to separate trees meet or one vessel bifurcates. Any errors created during the segmentation or skeleton extraction steps propagate to the next levels and if the method is not able to resolve these issues, it results in having wrong paths. There have been several efforts in the literature for tackling these difficulties from different points of views. In addition to great performance improvements in state-of-the-art segmentation techniques (e.g. Azzopardi et al., 2015; Nguyen et al., 2013), the authors in (De et al., 2013, 2016; Turetken et al., 2011, 2012) have proposed tubularity measurement techniques and have used that as the initial step of their method. Moreover, to solve the centreline extraction problems, which is often done via morphological thinning, several modifications and rule-based post-processing methods have been proposed (Dashtbozorg et al., 2014; De et al., 2016). On the other hand, in order to find the right connections at junction points, the geometrical configuration of the junctions has been used in local and global costs followed by optimization procedures (e.g. Hu et al., 2015; Turetken et al., 2011, 2012).

In all these works, cost functions were designed in a way to avoid the abrupt change of geometrical properties (most importantly orientation) at junction points and allow a smooth transition from one vessel to the other one. The method proposed by De et al. (2016) is a digraph-based label propagation technique using the matrix-forest theorem. The digraph weight matrix is designed in such a way that it does not allow the connected filaments (vertices) to bend too much. Moreover, in the methods proposed by Cheng et al. (2014; De et al., 2013), these constraints on the geometrical properties at junction points were used to find the right connections.

In our previous work (Favali et al., 2016), we investigated the connectivity analysis in retinal images specifically at junction points, inspired by the mathematical modeling of the geometry of the primary visual cortex (V1). In contrast to the state-of-the-art techniques, the proposed approach was capable of grouping and separating the blood vessels as individual perceptual units, even though there was some information missing due to poor segmentations. It could find the right connections between small vessels and their parents, which are usually missing in the literature and removed during preprocessing, segmentation or a skeleton pruning step. It also individuated nearby parallel vessels, even with presence of a central vessel reflection. The bottleneck of this method was that it was not data-adaptive and it could not follow some of the highly curved vessels, because the introduced kernel was elongated and could not bend as much as the vessel bends at these points. This is also challenging for all the above mentioned methods, because they often do not consider data adaptivity with respect to the curvature at each point. The contextual information is usually limited to orientation, width and intensity. At points with high curvature structures, the orientation changes in a higher rate, but since the above-mentioned methods penalize this sudden change, these cases are challenging for them.

1.2 Geometry of Visual Cortex

The visual cortex is the cortical structure underlying the processing of the visual stimuli. The works by Hoffman, 1966, 1989; Koenderink and van Doorn, 1987 introduced the mathematical modelling of its functional architecture in terms of differential geometry. The study of Field et al., 1993 described the problem of context perception with psychophysical experiments, introducing the notion of association fields as the information...
integration along images that satisfy the Gestalt law of good continuation (Wagemans et al. 2012; Wertheimer, 1938). Models which take into account the structure of the cortex were proposed by (August and Zucker 2000; Mumford 1994; Williams and Jacobs 1997), where the association fields were described with the Fokker-Planck equations. In these models, different features such as orientation and curvature were considered. Then Citti and Sarti (2006) proposed a model of the association fields based on the functional organization of the primary visual cortex (V1), establishing a relation between neural mechanism and image completion. This method was later implemented by Sanguinetti et al (2008).

In this work we expand this mathematical model in order to solve the limitations found in tracking the blood vessels. We lift the images into a four-dimensional space of positions, orientations and curvatures. Then we model the connectivity with a 4D kernel described by the fundamental solution of a Fokker-Planck equation. August and Zucker (2003) described how cells in V1 are sensitive to these features. The Fokker-Planck kernel is a model of choice for the description of the cortical connectivity, since it qualitatively fits the experimental data (Sarti and Citti 2015). We will study the task of grouping using self-tuning spectral clustering techniques proposed by Zelnik-Manor and Perona (2004), an algorithm that allows to standardize the method to automatically compute the number of groups. This work presents a new application of the modeling of the visual cortex to the analysis of medical images.

The structure of the paper is the following. We will start in Sect. 2 with the description of the geometry of the visual cortex and the existing tools for lifting the 2D image to the cortical space. Later an existing and a novel model of cortical connectivity are introduced. After explaining the new 4D connectivity kernel, its applicability for perceptual grouping when used in a combination with the self-tuning spectral clustering technique is explained in detail. This novel method is later validated in Sect. 3 using not only an artificial dataset consisting of curvilinear structures, but also on a set of patches selected from a public retinal dataset. The qualitative and quantitative results are further discussed in that section. Finally, the article is concluded in Sect. 4 and potential applications and future directions have been sketched.

2 Theory and Methodology

As discovered by Hubel and Wiesel (1977), V1 is one of the first layers of the visual pathway where local feature components of the visual stimulus are represented, as position, orientation, curvature, scale and movement. The cortex is organized in a hypercolumnar structure where for each point of the retinal plane there is an entire set of cells each one with a receptive field sensitive to a specific instance of these features. In Bosking et al (1997) the experimental evidence of the existence of horizontal connectivity between simple cells of different hypercolumns is presented. By injecting a chemical tracer (biocytin) and observing its propagation in the cortical layer, Bosking et al obtained experimental measures of this connectivity and showed that neurons sensitive to similar orientations are preferentially connected. Different models which consider the structure of the cortex were proposed and described in (August and Zucker 2000; Mumford 1994; Williams and Jacobs 1997), where association fields of Field et al (1993) are modelled with the Fokker-Planck equation. Besides, Citti and Sarti (2006) proposed a geometric model of the association fields based on the functional architecture of V1. A qualitative fitting of the neurophysiological data with the kernel obtained as the fundamental solution of the Fokker-Planck equation is presented by Sarti and Citti (2015). Moreover, in a quantitative analysis by Favali et al (2015), the computed kernels are compared with the experimental ones (considering the experiments of Gilbert et al (1996)) and the quantitative validations show high similarity between the connectivity kernel and the cell’s response.

2.1 Lifting the Image to the Cortical Space

A regular curve in the two-dimensional plane can be represented by $\gamma_{2D}(t) = (x(t), y(t))$. The tangent vector to the curve may be indicated as:

$$\dot{x}(t), \dot{y}(t)) = (\cos(\theta(t)), \sin(\theta(t))).$$

(1)

Based on previous studies (Citti and Sarti 2014), the two-dimensional curves can be lifted to the $(\mathbb{R}^2 \times S^1)$ space of positions and orientations $SE(2)$ using the direction of the tangent vector as:

$$\gamma_{2D} = (x(t), y(t)) \rightarrow \gamma(t) = (x(t), y(t), \theta(t))$$

(2)

where $\theta = \arctan(\frac{\gamma_2}{\gamma_1})$. Therefore, we can write the following:

$$\dot{\gamma}(t) = (\dot{x}(t), \dot{y}(t), \dot{\theta}(t)) = X_1(t) + \dot{\theta}(t)X_2(t)$$

(3)

where $X_1 = (\cos(\theta), \sin(\theta), 0)$, $X_2 = (0, 0, 1)$ are the left-invariant vector fields. The neural interpretation of this is that the lifted curves in the cortical space are the integral curves of the two vector fields $\{X_1, X_2\}$. The curvature term $\dot{\theta}(t) = \kappa(t)$ indicates the rate of change of the orientation and determines the shape of...
the curve. By defining the third vector field as the negative commutator \( X_3 = -[X_1, X_2] = -\sin \theta \partial_x + \cos \theta \partial_y \), the Lie algebra is generated by these three left-invariant (with respect to the group law of rotations and translations) vector fields as \( \text{Span}\{X_1, X_2, X_3\} \).

### 2.1.1 Orientation Score Transform

Being inspired and supported by several electrophysiological experiments, the receptive profiles of simple cells in the primary visual cortex are often interpreted as oriented Gabor filters or directional derivatives of the Gaussian filters (Citti and Sarti 2014; Daugman 1985; DeAngelis et al. 1995; Florack et al. 1992; Lee 1996). Moreover, Duits et al. (2007a,b) introduced the invertible orientation score (OS) transformation for lifting the image to the \( SE(2) \) space. The invertibility property prevents information loss during the transformation and it is guaranteed by certain requirements of the kernel used for the transformation. The cake wavelets introduced by Bekkers et al. (2014) are proper wavelets, which satisfy these criteria. Similar to the Gabor wavelets, they are quadratic anisotropic filters, but unlike these, their summed Fourier transformations cover the entire frequency domain, making them spatially scale-independent. Therefore, it is possible to disentangle the crossing and bifurcating elongated structures in a 2D image from each other regardless of their scale and without loss of image evidence. In order to construct the orientation score \( U_f(x, \theta) \), the image \( f \) is convolved with rotated and translated versions of a mother wavelet \( \psi \) as

\[
U_f(x, \theta) = (R_\theta \psi \ast f)(x) = \int_{\mathbb{R}^2} \psi(R_\theta^{-1}(y-x))f(y)dy
\]

where \( R_\theta \) is the 2D counter-clockwise rotation matrix, the overline denotes the complex conjugate and \( \ast \) denotes the convolution (Duits et al. 2007a,b).

### 2.1.2 Exponential Curves in \( SE(2) \)

As mentioned before, the curvature determines the rate of orientation change \( (\dot{\theta}(t) = \kappa(t)) \). If the parametric representation of the curves \( \gamma_{2D} = (x(t), y(t)) \) in the image is available, then by differentiating \( x \) and \( y \) once more in Eq. \[4\] we will have:

\[
(\ddot{x}, \ddot{y}) = (-\sin(\theta(t))\dot{\theta}(t), \cos(\theta(t))\dot{\theta}(t))
\]

where \( t \) is the arc-length of the curve. So the curvature can be computed as:

\[
\kappa = \dot{\theta} = \frac{\ddot{x}y - \ddot{y}x}{(\dddot{x}^2 + \dddot{y}^2)^{3/2}}.
\]

In computer vision and more specifically in retinal image analysis, several methods have been introduced for measuring the curvatures of curvilinear structures (i.e. blood vessels) (Kalitzeos et al. 2013). The classical methods that measure the curvatures locally need an initial segmentation, centreline extraction, and separation of segments located between junctions. It is then followed by fitting curves to the segments and by curvature measurement using Eq. \[6\] (Annunziata et al. 2016; Hart et al. 1999; Wilson and Cocker 2008). The drawback of all these methods is their dependency to initial preprocessing and segmentation steps, which may contain errors and missing information. More importantly, the curvature information is not available for junction points because it is not possible to fit a curve to these points where more than one elongated structure meet.

To solve these problems, Bekkers et al. (2015) proposed a local curvature measurement technique by locally fitting exponential curves (Duits et al. 2016) to the lifted image in \( SE(2) \). The exponential curves in \( SE(2) \) are interpreted as straight lines considering the curved geometry of \( SE(2) \) and they have constant tangent vectors relative to the rotating frame \( \{X_1, X_2, X_3\} \). The tangent vectors of the exponential curve that best fit the data in the lifted image are obtained by eigensystem analysis of the Gaussian Hessian (expressed in the rotating frame). Then they directly define the curvature value of their spatial projections (Franken and Duits 2009). This approach makes it possible to assign to each location and orientation in the lifted image a curvature value, without needing explicit curve parameterizations. Such curvature maps (on \( SE(2) \)) can be projected on the plane whereby only one value of curvature value is assigned to each spatial location in the image. Finally, these 2D curvature maps can be filtered in a later stage by a vessel confidence map (as a Laplacian ridge detector) (Franken and Duits 2009) or any other vessel enhancement methods.

### 2.2 The Cortical Connectivity

We assume that the two-dimensional curve in cortical plane \( (\mathbb{R}^2) \) is lifted to a four-dimensional space of positions, orientations and curvature \( (\mathbb{R}^2 \times S^1 \times \mathbb{R}) \). This was proposed following the experiments and hypothesis by Dobins et al. (1987, 1989) that the primary visual cortex not only includes the orientation selective cells, but it is also sensitive to the curvature at each point. Thus, the lifted curve may be written as:

\[
\gamma_{2D} = (x(t), y(t)) \rightarrow \gamma(t) = (x(t), y(t), \theta(t), \kappa(t)).
\]
Similar to Eq. 3 we will have:

\[ \dot{\gamma}(t) = (\dot{x}(t), \dot{y}(t), \dot{\theta}(t), \dot{\kappa}(t)) \]

where \( \dot{\theta}(t) = \kappa(t) \). By defining two new vectors \( \{Y_1, Y_2\} \) in the 4D space as:

\[
Y_1 = X_1 + \kappa X_2 = (\cos(\theta), \sin(\theta), \kappa, 0) \quad Y_2 = (0, 0, 0, 1)
\]

we are able to write \( \dot{\gamma}(t) \) in terms of these vectors:

\[ \dot{\gamma}(t) = Y_1(t) + \dot{\kappa}(t)Y_2(t). \] (10)

In general, the solution of the following differential equation represents the curves in this lifted domain:

\[ \dot{\gamma}(t) = (\alpha_1(t)Y_1(t) + \alpha_2(t)Y_2(t))(\gamma(t)) \]

\[ \gamma(0) = (x_0, y_0, \theta_0, \kappa_0), \gamma(1) = (x_1, y_1, \theta_1, \kappa_1). \] (11)

The distribution of planes is now \( \text{Span}\{Y_1, Y_2\} \) and the Lie algebra is generated by these two vector fields. Therefore, the commutators of these vectors are as follows (with the short notation of \( \dot{\theta} = \frac{\partial}{\partial \sigma} \)):

\[
[Y_1, Y_2] = -\partial_\theta = -X_2
\]

\[
[[Y_1, Y_2], Y_1] = \sin \theta \partial_x - \cos \theta \partial_y = -X_3
\]

\[
[[Y_1, Y_2], Y_2] = 0.
\]

Fig. 1 represents the fan of integral curves of Eq. 10 in the \( SE(2) \) group for similar number of \( \kappa \) values changing with two different \( \dot{\kappa} \) rates. This figure shows how the shape of curves is dependent on the curvature value (\( \kappa \)) and its rate of change (\( \dot{\kappa} \)). The projection of both curves on 2D cortical plane represents a good model of the association fields introduced by Field et al. [1993] for modeling the cortical connectivity. The association fields (or connectivity patterns) are considered as the basis for the creation of connected boundaries in visual perception, imposing the Gestalt law of good continuity (Wagemans et al. 2012; Wertheimer, 1938).

The cortical connectivity can also be modeled by a stochastic counterpart of Eq. 10. The Markov process that results from the Brownian motion with randomly curved paths has been introduced by August and Zucker [2003]. The process is represented by the following differential equations:

\[
\begin{align*}
\dot{x}(t) &= \cos(\theta(t)) \\
\dot{y}(t) &= \sin(\theta(t)) \\
\dot{\theta}(t) &= \kappa \\
\dot{\kappa}(t) &= \sigma_\kappa dW
\end{align*}
\]

with a certain direction \( \theta \) and curvature \( \kappa \), at a specific time \( t \), then the Fokker-Planck equation describing the diffusion of the particle density will be:

\[
\frac{\partial v}{\partial t} = \frac{\sigma^2}{2} \frac{\partial^2 v}{\partial \kappa^2} - \cos \theta \frac{\partial v}{\partial x} - \sin \theta \frac{\partial v}{\partial y} - \kappa \frac{\partial v}{\partial \theta}
\]

\[ = \frac{\sigma^2}{2} \dot{Y}_{22} - Y_1 \] (14)

so that \( \dot{Y}_{22} = \partial^2/\partial \kappa^2 \). This partial differential equation means that a particle at a point \( (x, y, \theta, \kappa) \) transports in the direction of \( (\cos(\theta), \sin(\theta), \kappa, 0) \) in the 4D space. There is no transport in the \( \kappa \) direction, but the diffusion in the \( \kappa \) direction indicates the rate of transport in the \( \theta \) direction.

The non-negative fundamental solution of Eq. 14 satisfies the following equation:

\[
\frac{\sigma^2}{2} \dot{Y}_{22} \Gamma'((x, y, \theta, \kappa), (x', y', \theta', \kappa')) - \dot{Y}_1 \Gamma'((x, y, \theta, \kappa), (x', y', \theta', \kappa')) = \delta(x, y, \theta, \kappa).
\]

A good estimate of this solution is a section of fundamental solutions with \( \kappa \) fixed (\( \Gamma'_\kappa \) as a 3D kernel) symmetrized and multiplied to an exponential term which considers the closeness between two points located in the different curvature planes. Hence, this new connectivity kernel is presented as:

\[
w((x, y, \theta, \kappa), (x', y', \theta', \kappa')) = e^{-\frac{(\kappa - \kappa')^2}{\sigma^2}} \times
\]

\[ \frac{1}{2} \Gamma'_\kappa((x, y, \theta), (x', y', \theta')) + \Gamma'_\kappa((x', y', \theta'), (x, y, \theta)) \] (16)
Zelnik-Manor and Perona (2004) in which this problem has been presented in terms of dimensionality reduction of this matrix (Favali et al. 2015; Sarti and Citti 2015), often done by eigensystem analysis.

Fig. 2: The 2D projection of a set of 3D stochastic kernels for several curvature values. $\kappa = \{-0.08, -0.04, 0, 0.04, 0.08\}$ from left to right.

By this definition, considering the fact that this matrix includes information about the correct grouping, this problem has been presented in terms of dimensionality reduction of this matrix (Favali et al. 2015; Sarti and Citti 2015), often done by eigensystem analysis.

In previous works (Favali et al. 2015, 2016; Sarti and Citti 2015) the connectivity kernel has been equivalently used as an affinity matrix describing the probability of existence of a connection between two points in the lifted domain. Similarly, the new kernel can be used for defining the affinity matrix as:

$$A_{i,j} = \omega((x_i, y_i, \theta_i, \kappa_i), (x'_j, y'_j, \theta'_j, \kappa'_j)) \quad (17)$$

Algorithm 1 Self-tuning spectral clustering algorithm:

Given a set of points $S = s_1, ..., s_n \in \mathbb{R}^d$ to cluster:

1. Define the affinity matrix $A_{i,j}$.
2. Define the diagonal matrix $D$ with $D_{i,i} = \sum_{j=1}^n A_{i,j}$ and construct the symmetric normalized graph Laplacian $L = D^{-1/2}AD^{-1/2}$.
3. Find the $C$ largest eigenvectors of $L \: x_1, ..., x_C$ and construct the matrix $X = [x_1, ..., x_C]$ where $C$ is the highest possible group number.
4. Use a gradient descent scheme to recover the rotation $R$ which best aligns $X$'s columns with the canonical coordinate system.
5. Let $Z$ be the matrix obtained after rotating the eigenvector matrix $X$ and $M_i = \max_j Z_{i,j}$. The cost function is defined as: $J = \sum_{i=1}^n \sum_{j=1}^C Z_{i,j}^2$.
6. Classify the cost of alignment for each group number and set the final group number $C_{\text{best}}$ to be the largest group number that provides the minimal cost $J_{\text{min}}$. Correspondingly, the best clustering quality $Q_{\text{clust}}$ that has a reverse relation to the alignment cost is obtained in Step 5.
7. Consider the alignment result $Z$ of the top $C_{\text{best}}$ eigenvectors and assign the points $s_i$ to cluster $c$ if and only if $\max_j (Z_{i,j}^2) = Z_{i,c}^2$.
8. Find and remove the clusters that contain less than a minimum number of cluster elements.

Unlike more basic clustering methods, as k-means, where the number of clusters and interaction distances of the nodes in the dataset must be assumed a priori, this algorithm automatically and optimally tunes these parameters. In this algorithm, which is explained step by step in Algorithm 1, we start defining our own affinity matrix that will be used in this setup. The structure of the eigenvectors is used to determine the number of groups. The cost function is evaluated from the alignment of the eigenvectors (Step 5). The best number of clusters is considered as the one which minimizes the cost function ($J_{\text{min}}$). Correspondingly, the best clustering quality $Q_{\text{clust}}$ that has a reverse relation to the alignment cost is obtained in Step 5. In the final step, the noisy elements that construct small sized groups are removed. From a neural approach, the fact that in the presence of a visual stimulus the perceptual units are defined by the emerging eigenvectors is described by Sarti and Citti (2015).

Fig. 2 represents the 2D projection on $\mathbb{R}^2$ by summation over all orientations of five different 3D stochastic kernels having different curvature ($\kappa$) values. In this figure, by increasing the absolute value of curvature, the shape of the kernel also changes and it deviates from the elongated shape.

2.3 Cortically-inspired Spectral Clustering

In modern data analysis clustering is an important research topic and many algorithms have been proposed in this area (Meila and Shi 2001; Ng et al. 2002; Perona and Freeman 1998; Shi and Malik 2000; Weiss 1999) where the eigenvectors of the graph Laplacian are used to analyse and reveal the cluster structure of the data. These techniques outperform the traditional approaches such as k-means (Von Luxburg 2007), because they do not need explicit metrics in feature space.

In our previous work (Favali et al. 2016), the problem of grouping the blood vessels in retinal images (interpreted as perceptual units) was solved by applying a semi-automatic approach based on spectral analysis of the affinity matrix. So the salient groups were obtained as the first eigenvectors corresponding to the largest eigenvalues. However a fixed threshold was defined for selecting the largest eigenvalues. In order to avoid the manual intervention, we follow the method proposed by Zelnik-Manor and Perona (2004) in which this problem is solved.

In our previous work (Favali et al. 2016), the problem of grouping the blood vessels in retinal images (interpreted as perceptual units) was solved by solving a semi-automatic approach based on spectral analysis of the affinity matrix. So the salient groups were obtained as the first eigenvectors corresponding to the largest eigenvalues. However a fixed threshold was defined for selecting the largest eigenvalues. In order to avoid the manual intervention, we follow the method proposed by Zelnik-Manor and Perona (2004) in which this problem is solved.

To conclude, we use the new affinity matrix defined based on the 4D connectivity kernel in a combination with the self-tuning spectral clustering technique, in order to find the perceptual units in the image automatically. A summary of the method is presented in Algorithm 2. It is worth mentioning that this cortically inspired affinity matrix can be augmented with other affinity matrices including information about other fea-
tatures (width, color, and so on). We assume an image \( I \in \mathbb{R}^2 \) has been given as input, and the algorithm returns the final perceptual groups in that image \( C = \{c_1, \ldots, c_K\} \), where \( K \) is the final number of clusters and \( c_i \) includes set of points in image \( I \) which belong to cluster \( i \). Fig. 3 depicts a sample application of the proposed method for clustering the perceptual units in an artificial image which includes three crossing circles with different radii and corresponding curvatures. Fig. 3a represents the original image. The second row represents the color-coded information (orientation Fig. 3b and curvature Fig. 3c) used for creating the kernel and affinity matrix. One sample level set of the 3D kernel is presented in Fig. 3d. Finally, Fig 3e shows the three detected groups in three different colors. The implementation details, validation and application of this proposed method using a set of artificial and retinal images are presented in the next section.

Algorithm 2 Proposed perceptual grouping technique for a given image \( I \in \mathbb{R}^2 \)

1. Lift the image \( I(x,y) \in \mathbb{R}^2 \) to \( U_I(x,y,\theta) \in \mathbb{R}^2 \times S^1 \) by orientation score transform (Eq. 1).
2. Calculate the curvature map \( \kappa_{\text{map}}(x,y,\theta) \) for each point in \( U_I(x,y,\theta) \) using the method proposed by Bekaerts et al.
3. Lift the image to \( \mathbb{R}^2 \times S^1 \times \mathbb{R} \) so that \( U^1_I(x,y,\theta,\kappa) = U_I(x,y,\theta) \) if \( \kappa_{\text{map}}(x,y,\theta) = \kappa \), \( \forall (x,y,\theta) \in \mathbb{R}^2 \times S^1 \).
4. Calculate all the fundamental solutions of Eq. 11 \( \mathbf{I}' \mathbf{U}(x,y,\theta,\kappa) \), \( \mathbf{I}' \mathbf{U}(x',y',\theta',\kappa') \) and \( \mathbf{I}' \mathbf{U}(x,y,\theta,\kappa) \), \( \forall \{ (x,y,\theta,\kappa), (x',y',\theta',\kappa') \} \in U_I^1 \) stochastically.
5. Calculate the final connectivity kernel \( \omega((x,y,\theta,\kappa),(x',y',\theta',\kappa')) \) for all pairs of points in \( U_I^1 \) using Eq. 10
6. Create the affinity matrix based on Eq. 17.
7. Aggregate affinity matrix with other normalized affinity matrices \( A' \) (if available) representing similarities between other contextual information (e.g. intensity, width, etc.) by \( A_{\text{final}} = (A' \odot A_{ij}) = A'_{ij}A_{ij} \); otherwise, \( A_{\text{final}} = A \).
8. Apply the automatic spectral clustering technique in Algorithm 1 for detecting the \( K \) perceptual groups in image: \( C = \{c_1, \ldots, c_K\} \).

### 3 Experiments

In this section, we present a potential application of the proposed connectivity analysis for solving the aforementioned problems in curvilinear structure tracking methods for retinal vasculature analysis (see Sect. 3.1). After explaining the material used for validating the method, the details of numerical simulation are described. Then the quantitative and qualitative results of the proposed technique are presented and discussed in detail.

#### 3.1 Material

Two datasets have been used for validating the method. The specifications and the preparation steps of each dataset are explained in detail as follows.

##### 3.1.1 Phantom images

The set of phantom images (201 × 201) has been generated to include various rotated, curved and interrupted vessel-like structures. The orientation and curvature values in these phantom images are known. Five different groups are created to mimic possible structures that could be present in retinal images, similar to the categories proposed in our previous work [Favali et al. 2016]. These categories are (A) crossings; (B) bifurcations; (C) parallel vessels; (D) bifurcations and crossings; and (E) vessels with multiple nearby bifurcations. Each of these categories may also include challenging structures. For instance, they may be interrupted or highly curved or include small junction (crossing/ bifurcation) angles. In order to differentiate between the simple and the challenging cases for each category, we name group X as X1 if it is challenging. Fig. 6 depicts ten different phantom images (first column), two per category, together with their color-coded orientation and curvature maps (second and third columns).

The basic element used for creating these phantom images is a sine wave-like structure, which is generated with several frequencies and amplitudes and it is rotated and located at different positions depending on the target shape. By adjusting the frequency and amplitude of the waves, different curvature values can be created. In addition to the vessel-like structures, other challenging structures such as dashing and the Euler spiral have been also used to examine the strength of the method in grouping these curved structures (e.g. Fig. 6 A1).

##### 3.1.2 Retinal images

This set contains several image patches selected around junctions in the public IOSTAR dataset. The IOSTAR dataset contains images captured using scanning electron ophthalmoscope (SLO) technology. These high contrast images have a resolution of 1024 × 1024 with 45° FOV. The blood vessels, junctions and artery/vein

1 Available at: http://www.retinacheck.org/datasets
labels have been annotated for 24 images and corrected by two different experts in order to decrease the inter-user variability. Our main purpose is to emphasize the strength of the method in individualization of vessels, specifically at junction points or challenging cases, where most of the proposed methods in the literature face difficulties. Therefore, five images and their annotations are downsampled to half size 512 × 512 and in total 272 patches of 51 × 51 pixels have been selected from them. Similar to the phantom images, these patches are also categorized in five different groups (similar to the phantom images) manually depending on their structure and complexity.

The proposed method used for creating these patches is explained step by step in Algorithm 3. The first step (Step 1) is the pre-processing applied on original image \( I_o \) and its ground truth \( G \), so that the luminosity and contrast are normalized, the noise is removed and the blood vessels are enhanced. The same pre-processing technique proposed by Abbas-Sureshjani et al. (2015) for the SLO images has been applied on the green \( I_{o,g} \) and red \( I_{o,r} \) channels separately and then they are combined as
\[
I(x, y) = \sqrt{I_{o,g}^2(x, y) + I_{o,r}^2(x, y)},
\]
for all the \((x, y)\) positions in the image \( I_o \). This increases the difference between the intensity of arteries and veins.

The next step (Step 2) is the blood vessel segmentation which provides an initial estimation of the location of the blood vessels. The outcome of segmentation can be either a probability map showing the probability for each pixel to be part of a vessel or it can be a deterministic binary map, in which each pixel is labeled as a vessel (with label 1) or background (label 0). The binary map is often obtained by thresholding the probability map globally. As mentioned in Sect. 1, none of the segmentations are perfect and they may contain vessel disconnections or wrongly detected vessel pixels. In this work, we use the binary segmentations obtained by the BIMSO method proposed by Abbas-Sureshjani et al. (2015) specifically for the SLO images.

Later on (in Step 3), a set of junction locations \((\epsilon_i = \{x_i, y_i\}, i = 1, \ldots, M)\) is obtained using the BICROS method proposed by Abbas-Sureshjani et al. (2016), where \( M \) is the number of detected junctions. The obtained segmentation \( I_{seg} \) is also used as the input to the hybrid step of the BICROS method. Both these methods (BIMSO and BICROS) have been validated before using the IOSTAR dataset. The detected locations are then considered as the centre of patches with a fixed size of 51 × 51 \((s_o = 25)\). For an image \( H \in \mathbb{R}^2 \) the patch \( H'_i \) centred around junction \( \epsilon_i \) is selected as:
\[
H'_i = \{H(x, y)|x_i-s_o \leq x \leq x_i+s_o, y_i-s_o \leq y \leq y_i+s_o\}.
\]

The same operation is applied (in Step 4) on the enhanced \((I)\), segmented \((I_{seg})\) and ground truth \((G)\) images and the corresponding patches are called \( H'_i, H'_{seg,i} \) and \( G'_i \) (for all \( i, 1 \leq i \leq M \)) respectively. Fig. 4 represents a sample SLO image \( I_o \), its artery/vein ground truth \( G \) (the arteries in red and the veins in blue), enhanced \((I)\) and vessel segmented \((I_{seg})\) images, and the detected junctions \((\epsilon)\). The 51 × 51 selected patches overlaid on the hard segmentation are shown as well.

- **Algorithm 3** The pipeline for selecting the image patches from an image \( I_o \) and its ground truth \( G \)

1. Pre-processing the image, \( I_o \in \mathbb{R}^2 \).
2. Vessel segmentation \((I_{seg} \in \mathbb{R}^2)\) using the BIMSO method (Abbas-Sureshjani et al. 2015).
3. Detecting junctions using the BICROS method (Abbas-Sureshjani et al. 2016), so that \( \epsilon = \{\epsilon_1, \ldots, \epsilon_M\} \) is the set of \( M \) detected junction locations \( (\epsilon_i = \{x_i, y_i\}) \).
4. Cropping the image patches from \( I \) and \( I_{seg} \) and \( G \) around junction location \( \epsilon_i \), using Eq. (18) and obtaining \( H'_i, H'_{seg,i} \) and \( G'_i \) \((\forall 1 \leq i \leq M)\).
By obtaining the $I_{seg,i}$ it is possible to perform the connectivity analysis (Algorithm 2) only for pixels labeled as vessels. This helps in reducing the size of the affinity matrix and correspondingly the computational complexity of the spectral clustering step. The vessel locations are found as:

$$v_i = \{(x,y)|I_{seg,i}(x,y) = 1\}, \ i = 1, \ldots, M. \quad (19)$$

Therefore, for each image patch ($I'$) only at vessel pixel locations ($v_i$) the groups are obtained and the resulting clusters are compared with the vessel labels in $G'_i$. If the detected units in the image patch match the individual vessel labels in the ground truth, then it is perceived as a correct result. It is worth mentioning, in case two vessels have the same label (artery or vein) but they do not belong to the same vessel tree, they are considered as separate units during the comparison.

A related point to consider is that the same patch selection approach can be applied on a full sized lifted image, avoiding lifting each patch separately and results in skipping Steps 1, 2 and 3 of Algorithm 2. Therefore, if we assume that the full sized image $I$ is lifted to $U'_I(x,y,\theta,\kappa) \in \mathbb{R}^2 \times S^1 \times \mathbb{R}$, then the cropped patch at location $\epsilon_i (i = 1, \ldots, M)$ is defined as:

$$U'_{I,i}(x,y,\theta,\kappa) = \{U'_I(x,y,\theta,\kappa)|x_i - s_{\theta} \leq x \leq x_i + s_{\theta}, \ y_i - s_{\theta} \leq y \leq y_i + s_{\theta}\}. \quad (20)$$

In order to lift the retinal images, considering the Gaussian profile of the blood vessels (shown in Fig. 5) and the fact that the blood vessels have a darker intensity compared to the background, the real part of the negative OS response ($-U_I(x,y,\theta)$) is used for obtaining the orientation (see Sect. 2.1.1). Because of the quadratic property of the cake wavelets, the real part of the transformation performs as a vessel ridge detector. Moreover, for each location the response may be different from zero in more than one orientation layer; therefore, the orientation at which the maximum response is obtained is assigned to each location. It means the dominant orientation $\theta_d$ at location $(x,y)$ is defined as

$$\theta_d = \arg \max_{\theta \in [0, \pi]} Re(-U_I(x,y,\theta)).$$

In order to evaluate the curvature map for each location $\kappa_{map}(x,y)$ an altered version of the method described in Sect. 2.1.2 is used. Aforementioned, the curvature measurement is based on the eigensystem analysis of the Gaussian Hessian in the lifted domain. Moreover, a confidence measurement $s_\sigma(x,y,\theta)$ is used...
that the depicted confidence and curvature maps are of a sample SLO image of the IOSTAR dataset. Note orientation (e), confidence (f) and curvature (g) maps have been used in the lifted domain as well. Therefore, we altered the method to a multi-scale approach. To have been used in the lifted images, starting from Step 4. The orientation and curvature values of these images are available from the beginning. The last two columns of Fig. 6 represent two different clustering results per image (two images per category). For each image, two kernels have been used for obtaining the affinity matrix: the new kernel (adaptive, based on the curvature at each point); and the kernel used in our previous work (Favali et al, 2016). This helps in highlighting the importance of including additional contextual information for connectivity analysis. Moreover, for these phantom images, no additional affinity matrices have been used for calculating the final affinity matrix as proposed in Step 7 of Algorithm 2, so $A_{final} = A$. Each color in the final results represents one detected unit. The parameter $\kappa$ used in these simulations is 0.01 for the 3D kernel (Favali et al, 2016) and 0.001 for the 4D one. As seen in this figure, the new method is capable of grouping the elongated, rotated and curved structures despite disconnections, high curvature points or small crossing angles. It not only differentiates well between curved crossing structures, but also groups the bifurcations within the main parent structure so that they construct one unique unit.

3.2 Numerical Approximations of the Kernel

In Sect. 2.2 it is described how the cortical connectivity can be modelled by the stochastic counterpart of Eq. 10. The kernel is numerically estimated with the Markov Chain Monte Carlo method (MCMC) (Robert and Casella 2013). The system in Eq. 13 can be approximated by:

$$\begin{align*}
&x_{s+\Delta s} - x_s = \Delta s \cos(\theta), \\
y_{s+\Delta s} - y_s = \Delta s \sin(\theta), & s \in 1, \ldots, H \\
&\theta_{s+\Delta s} - \theta_s = \Delta s \kappa \\
&\kappa_{s+\Delta s} - \kappa_s = \Delta s N(0, \sigma_{\kappa})
\end{align*}$$

(22)

where $H$ is the number of steps of the random path and $N(0, \sigma_{\kappa})$ is a generator of numbers taken from a normal distribution with mean 0 and standard deviation of $\sigma_{\kappa}$. The stochastic path is obtained from the estimate of the kernel as the average of their passages over discrete volume elements, solving this finite difference equation $n$ times (Sarti and Citti 2015). The affinity matrix described in Eq. 17 is evaluated from this kernel.

3.3 Validation

3.3.1 Phantom images

To validate the method using the phantom images, the method presented in Algorithm 2 is directly applied on the lifted images, starting from Step 3. The orientation and curvature values of these images are available from the beginning. The last two columns of Fig. 6 represent two different clustering results per image (two images per category). For each image, two kernels have been used for obtaining the affinity matrix: the new kernel (adaptive, based on the curvature at each point); and the kernel used in our previous work (Favali et al, 2016). This helps in highlighting the importance of including additional contextual information for connectivity analysis. Moreover, for these phantom images, no additional affinity matrices have been used for calculating the final affinity matrix as proposed in Step 7 of Algorithm 2, so $A_{final} = A$. Each color in the final results represents one detected unit. The parameter $\kappa$ used in these simulations is 0.01 for the 3D kernel (Favali et al, 2016) and 0.001 for the 4D one. As seen in this figure, the new method is capable of grouping the elongated, rotated and curved structures despite disconnections, high curvature points or small crossing angles. It not only differentiates well between curved crossing structures, but also groups the bifurcations within the main parent structure so that they construct one unique unit.

Fig. 5: The intensity of a sample image patch ($I'_i$, shown in the $xy$ plane) is projected to the $z$ coordinate to depict the Gaussian profile of a sample blood vessel.

This final curvature map is used in Step 3 of Algorithm 2. The scales we used for our SLO images are $\{1.5, 2.5, 3.5\}$ in pixels. Fig. 4 represents the color-coded orientation $\theta$, confidence $c$ and curvature $\kappa$ maps of a sample SLO image of the IOSTAR dataset. Note that the depicted confidence and curvature maps are related to one single scale $\sigma = 1.5$, and the absolute curvature value is shown.

by Bekkers et al (2015) based on blob detection via the Laplacian computed in the plane orthogonal to the tangent direction. The method performs the best when the scale of the Gaussian filters ($\sigma$) matches the vessel width. By using a single scale, the curvature values are accurate only for the vessels which their width match the used scale. Since the blood vessels in retinal images have different widths, using a multi-scale approach helps in covering various vessel widths available in the image and getting more accurate results. The idea is similar to the multi-scale feature extraction step of the BIMSO segmentation method (Abbasi-Sureshjani et al, 2015), since there the Gaussian filters have been used in the lifted domain as well. Therefore, we altered the method to a multi-scale approach. To do so, confidence and curvature maps have been obtained for several scales ($s$) in the $xy$ plane ($\theta$), $\sigma_i (x, y, \theta)$, $i = 1, \ldots, n$. Then the final curvature map is constructed by assigning to each pixel the curvature value that corresponds to the scale at which the largest confidence value has been obtained, i.e. $\forall (x, y, \theta) \in \mathbb{R}^2 \times \mathbb{S}^1$:

$$\kappa_{map}(x, y, \theta) = \arg\max_{\sigma_i \in \{\sigma_1, \ldots, \sigma_n\}} \kappa_{map}(x, y, \theta).$$

(21)
Fig. 6: Samples of phantom images in different categories. From left to right, the images in each category represent: stimulus, the orientation map, the curvature map and the clustering result with the previous (Favali et al. 2016) and the new kernel. The color of the curvature maps are scaled between the maximum and minimum values of the curvature in each image.
3.3.2 Retinal patches

To validate the method on retinal image patches, 272 image patches with a fixed size of $51 \times 51$ pixels have been examined semi-automatically. The number of patches processed per group is presented in the second column of Table 1. For these patches, we define an additional affinity matrix to include the intensity of vessel pixels as a Gaussian weighting. The values of this affinity matrix for each pair of pixels ($e_i$ and $e_j$) in patch $k$ is calculated as follows:

$$A'_{ij} = e^{-\frac{(f_i - f_j)^2}{\sigma_{int}^2}}$$  \hspace{1cm} (23)

where the intensity values ($f_i$ and $f_j$) are obtained from the preprocessed image patch ($I_k$) at corresponding locations and the $\sigma_{int}$ parameter controls the effectiveness of the intensity similarity. This affinity matrix is normalized (between 0 and 1) and then it is included in the final affinity matrix at Step 7 of Algorithm 2.

The group labels are automatically compared with the clustering results. In case two vessels with similar labels in the ground truth image (artery or vein) belong to separate vessel trees (parents), they get a different label. In addition, the operator performs a final check to control the final results. Two criteria are used to evaluate the performance. One is the Correct Detection Rate (CDR%) as defined in our previous work [Favali et al. 2016]. This criterion represents the percentages of correctly grouped patches among all examined cases. The second criterion is $Q_{\text{clust}}$ defined in Step 6 which measures the alignment quality of Algorithm 1. As mentioned in Algorithm 1, the best number of clusters is the one which minimizes the defined cost function or maximizes the quality ($0 \leq Q_{\text{clust}} \leq 1$). This criterion represents how well aligned the elements of each group are. These two performance values have been measured for all the patches and presented in the last two columns of Table 1 for each category separately.

During the experiments the parameters used in numerical simulations and the calculation time of different parts of the experiments (excluding the patch preparation steps of Algorithm 3) have been recorded. Several parameters are involved in creating the kernel. Some of them are determined automatically based on the available information in the data and others need to be set manually. The first set includes the size of the kernel in $x$ and $y$ dimension ($n_x$ and $n_y$ respectively). The other one is the number of discrete curvature values ($n_k$), which for each the 3D kernel is created. Considering the step size as 1 pixel, $n_x$ and $n_y$ are determined by the difference between maximum and minimum coordinates of the vessel locations in $x$ and $y$ directions. Similarly, considering the step size of 0.05 for discrete curvature values, $n_k$ is obtained by division of the difference between maximum and minimum of the available curvature values in the patch over the step size. Moreover, the number of steps $H$ used in generating the random paths is set automatically as one third of the patch size. The second set of parameters is set manually. The number of discrete orientations ($n_o$), number of iterations in the Monte-Carlo simulation (n) and $\sigma_k$ (used in Eq. 16) were set to 18, 100000 and 1 respectively and kept constant for all the cases. The other parameters are presented in Table 1 for each category separately and for all the cases (in mean ± standard deviation format).

Table 1: The number of analyzed patches, the parameters used during numerical simulation and the measured performance values per category and in total.

| Group | Size | Parameters | Performance |
|-------|------|------------|-------------|
|       |      | $\sigma_o$ | $\sigma_{int}$ | $Q_{\text{clust}}$ | $t_{\text{disc}}$ | $t_{\text{kernel}}$ | $t_{\text{affinity}}$ | $t_{\text{cluster}}$ |
| A     | 16   | 0.0079 ± 0.0024 | 0.2532 ± 0.0013 | 0.8125 ± 0.0056 | 2750 ± 2043 |
| B     | 42   | 0.0011 ± 0.0027 | 0.2966 ± 0.0026 | 0.7143 ± 0.0079 | 2993 ± 2241 |
| C     | 48   | 0.0031 ± 0.0044 | 0.2512 ± 0.0093 | 0.8542 ± 0.0078 | 2993 ± 2241 |
| D     | 31   | 0.0038 ± 0.0047 | 0.2578 ± 0.0016 | 0.7742 ± 0.0094 | 2993 ± 2241 |
| E     | 19   | 0.0025 ± 0.0041 | 0.2690 ± 0.0046 | 0.7368 ± 0.0087 | 2993 ± 2241 |
| A1    | 9    | 0.0018 ± 0.0024 | 0.2574 ± 0.0037 | 0.6667 ± 0.0756 | 2993 ± 2241 |
| B1    | 23   | 0.0004 ± 0.0010 | 0.2951 ± 0.0054 | 0.6522 ± 0.0987 | 2993 ± 2241 |
| C1    | 41   | 0.0030 ± 0.0044 | 0.2993 ± 0.0078 | 0.8537 ± 0.0097 | 2993 ± 2241 |
| D1    | 27   | 0.0040 ± 0.0048 | 0.2552 ± 0.0018 | 0.8148 ± 0.0094 | 2993 ± 2241 |
| E1    | 18   | 0.0021 ± 0.0038 | 0.2926 ± 0.0018 | 0.7222 ± 0.0967 | 2993 ± 2241 |
| All   | 274  | 0.0031 ± 0.0087 | 0.2750 ± 0.0072 | 0.7602 ± 0.0942 | 2993 ± 2241 |

For recording the calculation times the whole process has been divided into four steps: the discretization step before creating the kernel; creating the kernel for several curvature values; creating the affinity matrix and the spectral clustering step. The times are called $t_{\text{disc}}$, $t_{\text{kernel}}$, $t_{\text{affinity}}$ and $t_{\text{cluster}}$ respectively, and they are affected by several parameters including the number of vessel pixels in each patch ($|v_i|$, $i = 1, \ldots, M$), the number of discrete orientations ($n_o$), curvatures ($n_k$) and the dimension of the kernel in $x$ and $y$ dimensions ($n_x$ and $n_y$). To consider these effects, the weighted average of calculation times for each image patch is obtained, so that the weight for each timing is defined as the product of the affecting parameters. It worthy mentioning that since the final number of clusters ($C_{\text{best}}$) is determined by comparison among the clustering costs of several cluster sizes ($C$), $t_{\text{cluster}}$ is additionally affected by the number of examined cluster sizes ($n_c = 20$ for all the cases), so the final clustering time is divided by
\( t_c \). Thus weighted timings are calculated as:

\[
\begin{align*}
\tau_{\text{disc}} &= \frac{1}{N} \sum \tau_{\text{disc},i} n_{x,i} n_{y,i} n_{o,i} / \sum n_{x,i} n_{y,i} n_{o,i} \\
\tau_{\text{kernel}} &= \frac{1}{N} \sum \tau_{\text{kernel},i} n_{x,i} n_{y,i} n_{o,i} / \sum n_{x,i} n_{y,i} n_{o,i} \\
\tau_{\text{affinity}} &= \frac{1}{N} \sum \tau_{\text{affinity},i} |v_i|^2 / \sum |v_i|^2 \\
\tau_{\text{clust}} &= 1/n_c \sum (\tau_{\text{clust},i}) |v_i|^2 / \sum |v_i|^2 
\end{align*}
\]

(24)

where \( i \) and \( N \) indicate the patch number and total number of patches respectively. It is worth mentioning that the size of the affinity matrix for patch \( i \) is \(|v_i|^2\). These weighted times and their normal average over all patches per step are presented in Table 2.

Table 2: The weighted and normal mean of the processing time of each step in analyzing retinal patches.

| \( \tau_{\text{disc}} \) (s) | \( \tau_{\text{kernel}} \) (s) | \( \tau_{\text{affinity}} \) (s) | \( \tau_{\text{clust}} \) (s) |
|--------------------------|--------------------------|--------------------------|--------------------------|
| mean(s)                  | 0.06                     | 43.26                    | 17.86                    | 0.86                     |
| weighted mean (s)        | 0.06                     | 60.64                    | 17.73                    | 1.06                     |

A set of sample results for various kinds of patches is depicted in Fig. 7. In this figure, the first column shows the cropped patch from the artery/vein ground truth image. The second column depicts the color-coded normalized intensity values taken from the pre-processed image. As seen in these figures, the variation of intensity is too much even for small children vessels belonging to one parent vessel. The third and fourth columns represent the color-coded orientations and curvature values. Finally, the last column represents the clusters found in each patch, each shown in an individual color. The presented results, parameters and timings are discussed in the next section.

### 3.4 Discussion

Based on the results presented in the previous section, the main advantage of the new method is that by including the curvature information as an additional contextual information, the kernel adapts itself naturally according to the available data. If the curvature is high, the kernel rotates as well, otherwise it finds a closer path to the points which are collinear with respect to the reference point. In both datasets, the bifurcations are grouped with the parent vessel, but at crossovers with small crossing angles, despite their similar appearance to junctions, the vessels are totally separated. The main reason is that the curvature at junction points is high (because of sudden change of orientation), while for crossings the orientation for individual vessels changes only slightly (in most of the cases). This is advantageous not only in differentiating between junctions and crossings, but also in separation of arteries from veins or crossing tree structures from each other. Fig. 8 shows the clustering results for two retinal patches obtained using the new kernel and the previously introduced kernel by Favali et al. (2016). This helps in depicting the differences between the two methods visually.

As presented in Fig. 7, the intensity is a less informative feature compared to the geometrical features because of its large variation within a small neighborhood; however, in some cases, it is a good local criterion differentiating arteries from veins. Thus it is also included in the final affinity matrix with a smaller effect (using a relatively large \( \sigma_{\text{int}} \)).

Some examples of the limitations of the method in clustering the phantom and retinal patches are represented in Fig. 9 and 10 respectively. For phantom cases, the presence of very high curvature combined with the co-circularity and co-linearity of vessels does not allow to obtain a good clustering result. Considering other features, as the intensity, could be helpful in solving this problem. However, as shown in the top row of Fig. 10, the feature of intensity is not useful for correct clustering. In this image, one of the bifurcations has been assigned as a vessel crossing the other one because it is almost orthogonal to its parent vessel; while the other crossing vessel has been wrongly clustered as a bifurcation. In the bottom row, one of the small bifurcations is totally missing in the segmentation and the other small one is not clustered with its parent vessel because of lack of information.

The statistical analysis on the parameters used during numerical simulations is presented in Table 1. Based on these results the curvature diffusion constant parameter (\( \sigma_k \)) changes in a small range for simple and challenging cases per group, except for category A and A1, considering the fact that the number of available challenging patches in category A is small compared to the others. The \( \sigma_{\text{int}} \) parameter has a small variation as well. Therefore, it is reasonable to use the mean value in general for examining new patches in each group. It is worth mentioning that all the patches examined in this work have been selected from retinal images with the same resolution and respective pixel size. If the pixel size increases or decreases, the \( \sigma_k \) controlling the size of
Fig. 7: Samples of retinal patches in different categories. From left to right, the images in each category represent: artery/vein vessel ground truth, intensity, orientation, curvature and clustering results. The color of the curvature maps are scaled between the maximum and minimum values of the curvature in each image patch.
Fig. 8: Comparison between clustering results obtained using the connectivity kernel introduced in this work and the one proposed by Favali et al. (2016). From left to right: artery/vein vessel ground truth, intensity, orientation, curvature and clustering results with the previous and the new kernels.

Fig. 9: From left to right: the stimuli (a), the orientation maps (b), the curvature maps (c) and the clustering results with the new kernel (d).

Fig. 10: Wrong clustering results on two retinal patches. From left to right: the artery/vein ground truth, vessel intensity, orientation, curvature and clustering results.
the 3D kernel needs to be increased or decreased accordingly. It is also important to mention that compared to previous work, the eigensystem analysis is fully automatic in this work, due to the use of self-tuning spectral clustering. Therefore, no additional parameters need to be tuned for this step.

Qualitative and quantitative results indicate the better performance of the method on all kinds of retinal patches and challenging structures. Compared to the previous work (Favali et al., 2016), the CDR% performance values have changed for some groups. There are two main reasons. On one hand, in the previous work, the CDR% was calculated for 20 patches per group; while in this work each group is categorized into two groups depending on the available structure and also the number of patches per group is different. On the other hand, in this work we evaluated the performance with the assumption that the bifurcations need to be grouped with the main parent vessel, while in previous work, due to use of one elongated kernel, the assumption was to have at least two separate units depending on the bifurcation angle. Another minor difference is that the dataset has changed and the patches have been selected from a different set of retinal images. Therefore, it is not fair to make a one-by-one comparison to the previous results.

Last but not least point is about the computation times. The codes are implemented in Matlab and the times are measured on an Apple Macbook Air, Intel Core i7, 1.7 GHz processor and 8GB of memory. The most time consuming step as presented in Table 2 is the calculation of several 3D kernels. The number of kernels depends on the number of discrete curvature values ($n_o$) existing in the data, and the computation time as mentioned before depend on its size. The next most time consuming part is the calculation of the affinity matrix which is performed per pair of points. The weighted average times are good indicators of the complexity of each step. Although they are still relatively small, they can be improved both from hardware and implementation points of view.

4 Conclusion

In this work a new method for analyzing the connectivities in images containing elongated, rotated and curved structures is proposed. The new connectivity model is inspired by the geometry of the primary visual cortex, where the connectivity between all the lifted points into the four-dimensional space of positions, orientations and curvatures is represented by a 4-dimensional kernel. We use a set of artificial images and retinal patches to identify perceptual units in these figures, showing that this can be considered as a good quantitative model for their constitution and in general for the law of good continuation. Including the geometrical contextual properties in addition to local features, such as intensity, makes the method very robust against different kinds of variations and missing information which could exist in clinical images. We analyze different challenging cases that are very informative for clinical studies and we show how the proposed method is successful in solving the problem of grouping, also for blood vessels with high curvature. That was a limitation in the previously proposed method (Favali et al., 2016) and many of the state-of-the-art techniques. Moreover, the mechanism used of the self-tuning spectral clustering allows to standardize the method, automatically computing the number of groups.

In this work, the method is examined only on small patches to reduce the computational complexity. However, as mentioned before, this can easily be improved from implementation and hardware points of view. In addition, by replacing the self-tuning spectral clustering step with label propagation methods or using the affinity matrix in an optimization framework (e.g. integer programming), the constitution of the entire vasculature network in full retinal images becomes more feasible and much easier. Another limitation of the method arises when wrong information is provided as the input of the method; then the failure is natural. If the measured curvature or orientations are not accurate enough, then the method fails. Therefore, it is essential to validate the curvature and orientation measurement methods in advance.

The proposed method has a great potential in discrimination and separation of arteries from veins in retinal images and, in a general view, separation of all the tree structures crossing each other in the vasculature network. Most of the segmentation or artery/vein separation methods are local, pixel-based techniques which do not take into account the global connectivity of the blood vessels in the network. By including this global connectivity criterion, most of the errors and wrong detections will be eliminated and the problem of missing information will be handled appropriately. This is a potential extension and application of the method which will be investigated in future work. Additionally, it is important to investigate the relation between the $\sigma_\kappa$, controlling the size of the kernel, and the vessel widths.

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