A Variational Method for Geometric Regularization of Vascular Segmentation in Medical Images

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Abstract—In this paper, a level-set-based geometric regularization method is proposed which has the ability to estimate the local orientation of the evolving front and utilize it as shape induced information for anisotropic propagation. We show that preserving anisotropic fronts can improve elongations of the extracted structures, while minimizing the risk of leakage. To that end, for an evolving front using its shape-offset level-set representation, a novel energy functional is defined. It is shown that constrained optimization of this functional results in an anisotropic expansion flow which is useful for vessel segmentation. We have validated our method using synthetic data sets, 2-D retinal angiogram images and magnetic resonance angiography volumetric data sets. A comparison has been made with two state-of-the-art vessel segmentation methods. Quantitative results, as well as qualitative comparisons of segmentations, indicate that our regularization method is a promising tool to improve the efficiency of both techniques.

Index Terms—Anisotropic propagation, blood vessel segmentation, energy optimization, shape analysis, surface evolution.

I. INTRODUCTION

VESSEL segmentation is one of demanding applications that has received a considerable attention [1]. It is important for evaluation of vascular abnormalities (such as stenoses and plaques) and also has applications for surgical planning.

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The vast majority of methodologies for robust extraction of vascular structures are mainly based on features extracted from image content. Multiscale analysis of second derivatives is widely used for enhancement or detection of curvilinear structures in 2-D and 3-D medical images [2]–[8]. Although these have proved to be useful for enhancement of line features, the final output of such procedures is not a direct segmentation of the input image. Skeleton-based methods [9], [10] are algorithms in which subsequent 2-D slices of vessels are resolved using tubular shape priors for ridge detection. Recently another tracking methodology was proposed by Tyrrell et al. [11] using 3-D cylindroidal superellipsoids and local regional statistics to extract topological information from microvasculature networks. These methods are shown to be robust against noise, however, their explicit parametrical shape priors are too exclusive, in case of complex vessel boundaries. Another series of publications using statistical mixture modeling coupled with expectation-maximization algorithm include [12]–[14]. These are histogram based and, therefore, need an accurate parametrical estimation or nonparametric modeling [15] of involved probability density functions.

Recently, a number of surface evolution level-set-based algorithms for vessel segmentation have been developed. A combinational method is proposed by Gazit et al. [16], which uses Haralick edge detector, Chan–Vese minimal variance functional and geodesic active contours. Also, capillary active contours was invented by Yan et al. [17], a method that is based on the capillary force acting on the free fluid surface. Another level-set-based method introduced in [18], is an algorithm for artery–vein separation with a couple of level set functions, where the front speed is a heuristic composition of three different factors determined by image gradient, histogram and a vessel enhancement filter’s response. A front evolution technique is proposed by Jackowski et al. [19] that is based on wave propagation in oriented domains.

Some other methods are concerned with basic challenges using surface evolution for vessel segmentation. Lorigo et al. [20] proposed the use of active contours with co-dimension two utilizing the curvature of the underlying 3-D curve [21] for smoothing. From the practical point of view, this is computed as minimum magnitude surface principal curvature of e-level set. This is still too restrictive to allow extended elongations: in a common seeding or thresholding initialization scenario, evolution starts from the inside of vascular structures and extends over the thin lower contrast parts. In such a procedure, the “tips” of the evolving surface experience higher smoothness constraint since the magnitude of surface minimum principal curvature is high exactly at such structures. In fact, one basic
Fig. 1. (a) Portion of a TOF-MRA 1.5 Tesla data set, the arrow indicates a damaged pattern of a thin vessel. (b) Same portion in 3 Tesla indicates a smooth vascular pattern.

limitation of free curvature-based evolution is that the surface always shrinks to zero. Other state-of-the-art vessel segmentation techniques include flux maximizing flows [22], [23]. They offer a multiscale computing scheme for robust estimation of image laplacian which allows handling structures with various sizes. However, these are curvature free evolutionary schemes, and rely on initial smoothing of data. The drawback is that it is not clear how much smoothing is required prior to segmentation. Geometric regularization is essential for obtaining smooth segmenting fronts without much altering initial data.

In order to reduce the risk of front leakage to the background, a number of methods use shape constraints. For example, topology constrained surface evolution has been proposed in [24], a method that uses 3-D skeletons of the front to refine the spurious branches for iterative bifurcation and vessel segmentation. Also, a soft prior has been introduced in [25] for minimizing the leakage from noisy edges using a ball-filter which penalizes the deviations from tubular structures. Obviously, any geometric regularization of the segmentation process, with the ability to minimize the leakage is important for vessel segmentation.

Fig. 1 illustrates another difficulty arising in most of vessel segmentation algorithms. The arrow in panel (a) indicates the pinching of a thin vessel caused by noise. However, in a higher magnetic field, the smooth intensity pattern from the same vessel clearly shows its extension. Such noise “speckles” may stop the front evolution towards the thinner part, and consequently multiple distinct vessel fragments may be obtained. Masutani et al. [26] addressed this issue, using a mathematical morphology region-growing method. However, the vessel structures remained un-interpolated between discontinuities.

In this paper, it is assumed that vessels are curvilinear structures, this is the basic assumption as in [2–8] for enhancing the vascular structures. Based on this general assumption, for effective geometrical regularization of tube-like structures, minimization of a shape functional is proposed. Our regularization method preserves cylindrical structures by imposing anisotropic front constraint in the level-set variational framework and has three important basic properties. 1) Unlike the previous curvature flows, the solution is not always a shrinking surface, but instead it can extend toward local “meaningful” surface features. 2) Since leakage develops isotropic structures, by applying anisotropic front constraint, the risk of leakage is minimized. 3) It is a curvature dependent flow with smoothing effect. Therefore, it can basically overcome some limitations encountered in previous methods. We also utilize the idea of the ball-filter to extract information about the local segmented structures, however, our methodology is basically different from [25] since it provides a robust image-independent estimation of the vessel direction for expansion. In fact, as the evolution may stop to extract the entire vessel, extracted structures show some elongations. One option is to utilize this “shape-induced” information to propagate the surface. This can be useful when the image information is not reliable due to noise or intensity ambiguities. In that case, our model enforces the surface to expand anisotropically in the main surface orientation so that it can pass over small noise speckles. The outlined framework can be combined with existing level-set-based vessel segmentation functionals. Our idea was first proposed in [27]. In this paper, two pioneer methods introduced in [20] and [22] are chosen for comparison purposes. These methods are especially preferred since they require a minimum set of parameters and simplify the comparison tasks.

The rest of the paper is organized as follows: illustration of the basic idea and the definition of the local anisotropy measure are included in II. Section III describes our shape functional energy minimization strategy. In Section IV, this shape functional is used to regularize the CURVES and flux maximizing flow functionals [20], [22] and Section V contains the result. Concluding remarks and discussion is included in Section VI.

II. DESCRIPTION OF THE ANISOTROPY CONSTRAINT

We assume that for a given open region \( D \) specified by its border \( \partial D \), the evolving surface \( S \) is represented as the zero level of the level-set function \( \phi(x) \) where \( \phi(x) < 0 \) for inside of the object, and \( \phi(x) > 0 \) for outside. \( H(x) \) is the Heaviside function such that \( H(x) = 1 \) if \( x \geq 0 \), otherwise \( H(x) = 0 \). Also, \( \delta(x) = (d/dx)H(x) \) is the Dirac delta function. Throughout this paper, the phrases such as: front, surface (3-D) or contour (2-D) are used interchangeably with implied dimensions.

A. Estimation of the Surface Local Structure

Robust estimation of local structure can be achieved using the correlation matrix of the image gradients (see Weickert et al. in [28]). Similarly, the local structure of the evolving contour \( C \) at point \( x \) can be expressed by the correlation matrix of its normal vectors \( \bar{N} \) inside a scale-selectable neighborhood. Since we are mainly interested in the orientation of underlying skeleton, the iso-level contours can be considered as “shape offsets” of the most internal iso-level and the orientation matrix is resolved only using inner contours. In fact, because the iso-levels tend to be spherical as they get farther from the surface, exclusion of outer region helps resolving the orientation ambiguity.

As illustrated in [29], in the level-set framework normal vectors to evolving surface can be computed as \( \bar{N} = (\nabla\phi/\|\nabla\phi\|) \). Therefore, assuming that level-set function holds the shape offset representation with \( \|\nabla\phi(x)\| = 1 \), we define the following matrix:

\[
M(x) = \int H(-\phi(x'))B(x,x')\nabla\phi(x')\nabla^t\phi(x')dx'
\] (1)
where \( \nabla^T \phi(x') \) is the transpose of the gradient vector \( \nabla \phi(x') \). \( B(x, x') \) is the neighborhood function with the general property of: \( B(x, x') = B(x', x) \). In this paper for the sake of simplicity we define: \( B(x, x') = 1 \) if \( x' \) lies inside the neighborhood of size \( R^3 \) pixels around \( x \). Therefore, \( M(x) \) corresponds to the correlation matrix of gradient vectors of the surface signed distance transform lying in the intersection area of the neighborhood of \( x \) and inside of the contour as shown in grey in Fig. 2.

We note that \( M(x) \) is a positive semi-definite matrix.

Application of anisotropy constraint is achieved by evaluating the availability of a major local orientation and propagating the surface at that direction. This is accomplished by analysing the eigenvalues and vectors of \( M(x) \). The following theorem standard in linear algebra will be illustrative.

**Theorem 1:** Let \( 0 \leq \lambda_1 < \lambda_2 \leq \lambda_3 \) to be the eigenvalues of the correlation matrix \( M(x) \) and \( e_1, e_2, e_3 \) to be their corresponding eigenvectors. Then

\[
\lambda_1 = \inf_{|e| = 1} \int H(-\phi(x'))B(x, x')(e \cdot \nabla \phi(x'))^2 dx'.
\]

**Proof:** It is easy to see that the right-hand side of the above equation is equal to \( e^\top M(x)e \). By taking its derivative with respect to \( e \), we have \( M(x)e = 0 \). Therefore, \( e \) should be an eigen vector of \( M(x) \), i.e., we should have \( e = e_1 \) and in that case the minimum value is the smallest eigenvalue: \( \lambda_1 \).

According to this theorem, for a given point \( x \) placed on the evolving zero-level surface if \( \lambda_1 = 0 \), then one possibility is to have the \( e_1 \) normal to all the gradient vectors \( \nabla \phi \) in its neighborhood, i.e., \( e \cdot \nabla \phi(x') = 0 \). This happens when the gradient vectors are placed within a plane perpendicular to \( e_1 \) and the local structure has a cylindrical from.

Fig. 2 is a 2-D illustration of this idea using some sample points. We observe that for a point such as \( B \) where the local structure (shaded in grey) is rather ambiguous and isotropic, normal vectors to inner contours span every orientation, and, therefore, there is no preferred direction minimizing the right-hand side in Theorem 1. On the contrary, in the neighborhood of point \( A \) where the local structure is anisotropic, a large portion of normal vectors to inner iso-levels are in parallel and a minimizing local orientation can be identified by the medial of zero-level contour \( C \). Therefore, lower value of \( \lambda_3 \) is expected.

### B. Approximating the Local Anisotropy

From the discussion in the previous section, we realize that \( \lambda_1 = 0 \) and \( 0 < \lambda_2 \leq \lambda_3 \) implies a cylindrical local surface which should remain stable by further evolution. Therefore, such a condition must be considered as a contour-stopping criteria, resembling the behaviour of the edge in the geodesic active contour (GAC) model [30], [31]. In other words, we should devise a measure that selects large values for \( \lambda_1 = 0 \) and \( 0 < \lambda_2 \leq \lambda_3 \), similar to the gradient strength in GAC. Possible anisotropic measures similar to those suggested in [3]–[8] that are proportional to \( 1/\lambda_1, \lambda_2 \) and \( \lambda_3 \) are not good choices, since they are not analytically differentiable. Our solution is to “preserve” the cylindrical property all over the front by assuming that the initial structures are tube-like structures and \( R \) is sufficiently large so that \( 0 << \lambda_2 \leq \lambda_3 \). By this assumption, we only need to enforce \( \lambda_1 \) to be a very small value all over the surface. A differentiable form that takes large values for \( \lambda_1 = 0 \) is the trace of the inverse of the matrix \( M \)

\[
\text{Tr} M^{-1}(x) = \sum_{i=1}^{3} \frac{1}{\lambda_i}
\]

which is a good approximation to \( 1/\lambda_1 \) and, hence, the local anisotropy for elongated structures. It should be reminded that the proposed measure, can be infinite for noncylindrical structures as well. In general, it approaches infinity if: 1) \( \lambda_1 \) approaches zero, i.e., \( x \) is placed on a cylindrical surface locally; 2) \( \lambda_1 \) and \( \lambda_2 \) approaches zero, i.e., \( x \) is placed on a planar surface locally; 3) all \( \lambda \) values approach zero, i.e., a surface which is shrinking. As we will see in the next section, (2) is integrated within a shape functional to enforce large values on \( \text{Tr} M^{-1}(x) \).

This means that the final solution to our energy minimization scheme depends on the initial shape and will be either a tube like structure (planes are considered as tubes with infinite radius), or a shrinking surface. The later is also an interesting property which enables the method to remove small noise like structures.

We note that one may consider an alternative measure as

\[
det M^{-1} = 1/\lambda_1 \lambda_2 \lambda_3.
\]

Though this measure reduces complexity of derivation, but from computational point of view, it is not as sensitive as (2) in a sense that large values of \( \lambda_3 \) may moderate small values of \( \lambda_1 \).

### III. SHAPE-DEPENDENT FUNCTIONAL

Since our shape functional is based on the geometric [30] and geodesic active contours models [31], a brief review is provided.

#### A. Geodesic Active Contour Model

Geodesic active contour model proposed by Casselles et al. [31], is a curvature-dependent front propagation technique that has had outstanding applications for image segmentation. Given an image \( I \) and a non-negative decreasing function \( g(x) \), its minimization energy functional in the level-set framework can be described as

\[
E_g(\phi) = \int \delta(\phi(x))g(|\nabla I(x)|)|\nabla \phi(x)| dx.
\]

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\]
According to (3), the minimum occurs when the evolving contour \( C \) identified by \( \phi(x) = 0 \), lies on the minimum cost path specified by \( g(\nabla I(x)) \). Since \( g \) is a decreasing function of gradient magnitude, the method can detect the object border if the initial contour is placed close enough to the edge. Minimization is achieved using gradient-descent method and it can be shown that the corresponding Euler–Lagrange (EL) equation of (3) is

\[
\frac{\partial \phi}{\partial t} = \delta(\phi) \nabla \cdot \left( g(I) \nabla \phi \right). \tag{4}
\]

Similar to [32], since we are interested in steady state solution of (4), the \( \delta(\phi) \) can be replaced with \( |\nabla \phi| \). Therefore, (4) can be written as

\[
\frac{\partial \phi}{\partial t} = |\nabla \phi| \left\{ g(I) \nabla \cdot \left( \frac{\nabla \phi}{|\nabla \phi|} \right) + \nabla g(I) \cdot \frac{\nabla \phi}{|\nabla \phi|} \right\} \tag{5}
\]

where \( \phi \) is the embedding level-set function. This later formulation tends to keep the level-set representation as a signed distance function since evolution is applied on every level. The term \( \nabla \cdot (\nabla \phi / |\nabla \phi|) \) is the mean curvature \( \kappa \) of the evolving front computed directly from level-set function and provides smoothness. \( \nabla g(I) \cdot \nabla \phi \) is the advection term that pulls the curve into areas with lower values of \( g \), i.e., object’s borders.

### B. Definition of the Shape Functional

In definition of our shape functional, we are inspired by GAC. The main idea is to replace the edge indicator with our previously defined anisotropy approximation. In this way, the geodesic minimal path is affected by contour evolution. Let \( \phi(x) \), be the level-set function, and \( f(x) : R^+ \rightarrow R^+ \) be a non-negative decreasing function. Consider the following functional:

\[
E_a(\phi) = \int \delta(\phi(x)) f(\text{Tr} \, M^{-1}(x)) |\nabla \phi(x)| dx. \tag{6}
\]

The important point is that since estimation of local structure in (1) is based on the fact that the underlying level-set function is a shape offset representation, minimization should be performed in the constraint space of signed distance functions. In other words, our constrained minimization problem is

\[
\inf_{|\nabla \phi| \equiv 1} E_a(\phi). \tag{7}
\]

### C. Minimization

As explained in [32], the constraint in (7) can be fulfilled by different methodologies. One approach is to specify the speed function values exactly on the zero level contour, and then extend it over other levels. In this method, off-the-border speed values are replaced by the values from the closest points on the border. But in our application since we deal with sharp corners, finding the closest point on the border around theses corners can introduce inaccuracy. As we will see, a more natural extension of speed values over off-front area can be achieved by using the smeared out version of delta function, i.e., \( \delta_r(x) \), obtained directly from derivation of minimization equation. This is followed by reinitialization of the level-set function into signed distance function to ensure a true shape offset representation of the evolving contour.

Therefore, the solution of the constrained problem in (7) is obtained by first considering the unconstrained problem and deriving the corresponding EL equation. We have used the Fréchet derivative [33] in a similar variational level-set framework outlined in [32]. For the sake of completeness of this paper, the definition of Fréchet derivative and its basic properties are covered in Appendix A. The following theorem holds.

**Theorem 2:** The level-set solution of (7) can be achieved by the following gradient-descent evolutionary equation:

\[
\frac{\partial \phi}{\partial t} = \delta(\phi) \left\{ f(\text{Tr} \, M^{-1}) \nabla \cdot \left( \frac{\nabla \phi}{|\nabla \phi|} \right) + \nabla f(\text{Tr} \, M^{-1}) \cdot \frac{\nabla \phi}{|\nabla \phi|} + \nabla f \cdot L \nabla \phi \right\} \tag{8}
\]

where the dependency on \( x \) is implied and the matrix \( L(x) \) is defined as follows:

\[
L(x) = \int B(x, x') \delta(\phi(x')) |\nabla \phi(x')| f(x') M^{-2}(x') dx'. \tag{9}
\]

in which \( f' \) denotes the derivative of \( f \).

**Proof:** See Appendix B.

- It is interesting to look at the properties of (8) in further detail. The right-hand side of evolution consists of three different terms:
  - **Smoothing:** \( f(\text{Tr} \, M^{-1}) \nabla \cdot (\nabla \phi / |\nabla \phi|) \) is a mean curvature dependent smoothing term. Note that by multiplication of \( f(\cdot) \), the curvature remains effective if the local structure is isotropic; therefore, annihilation of narrow structures with lower values of \( f(\cdot) \) is limited.
  - **Advection:** The second term is an advection term that attracts the object’s border toward lower values of \( f \). It reduces the orientation ambiguity and also minimizes the leakage from spurious noisy edges.

- **Propagation:** To analyze this term, we note that for a given point \( x \), the matrix \( L(x) \) is the weighted average of positive semi-definite matrices \( M^{-2}(x') \) of its neighborhood determined by \( B(x, x') \). Hence, \( L(x) \) is a robust estimation of a bigger local structure. Since \( f < 0 \), we have \( \nabla f(x') L(x) \nabla \phi(x') < 0 \), i.e., this term propagates the surface outward. The important point is that depending on the orientations of \( \nabla \phi(x) \) and eigenvectors of \( L(x) \) the expansion is anisotropic. For segmentation of tubular structures, provided that the size of neighborhood \( R \) in Fig. 5 is large enough, \( L(x) \) maintains its main component in the axial orientation. As a result, propagation may only appear at the endpoints of those structures.

### D. Implementation

The central-differencing scheme was used for computing \( M \) and \( L \) defined in (1) and (9), respectively. Having the values of cost function \( f \), advection term: \( \nabla^r \phi \nabla f \) is calculated by simple
up-winding scheme. The first order forward-Euler method is used for digitization over time and Heaviside and delta functions are evaluated using their smeared-out versions $\delta_\epsilon(\phi)$ and $H_\epsilon(\phi)$ with $\epsilon = 1.5$ pixel, as explained in [34]

$$H_\epsilon(\phi) = \frac{1}{2} \left( 1 + \frac{\phi}{\delta_\epsilon(\phi)} \right),$$

$$\delta_\epsilon(\phi) = \frac{\epsilon}{\pi(\epsilon^2 + \phi^2)}.$$  \hspace{1cm} (10)

In this paper, we have set $f(x) = (1/\varepsilon + \varepsilon)$ where $\varepsilon$ is a small positive number ($\varepsilon = 10^{-3}$) to prevent singularity of division by zero. This setting is optional but, practically we obtained better results using this definition. The algorithm is implemented using a fast narrow band level-set method [35]. We note that, in (9), computation of matrix $L(x)$ is expensive in terms of CPU cycles. As an optimization, at each iteration the evolving front is compared to its status in previous iteration and $L(x)$ is computed at places where the front has displacements. By this means, a large portion of the surface that remains intact does not require updating of structural matrix and the program executes much faster.

As described in Section III-B, in our algorithm, reinitialization is crucial. For that purpose, we follow the method described in [36] by solving the following equation:

$$\varphi_4 = \text{sign}(\phi)(1 - |\nabla \phi|)$$

(11)

where $\varphi(0, x) = \phi(x)$. To minimize numerical errors in our simulated examples, discretization over spatial coordinates is achieved using Hamilton–Jacobi WENO scheme [29].

**IV. VASCULAR SEGMENTATION**

In this section, the proposed energy functional is used for geometrical regularization of level-set-based vessel segmentation techniques such as [22] and [20]. Though these state-of-the-art
methods are well proved, here the main emphasis is given to the improvement of the performance upon using our proposed regularization method. We briefly review the concept of both algorithms. To keep consistency with the original works, the same function definitions and implementation issues have been followed and the common factor $\delta(\phi)$ arising from minimization of energy functionals, similar to [32], is replaced by $|\nabla \phi|$ whenever required.

A. Regularization of the CURVES Algorithm

Lorigo et al. in [20] proposed the CURVES, a vessel segmentation method based on GAC model. To prevent annihilation of narrow structures, mean curvature in (5) was replaced with surface minimal curvature, $\kappa_2$ that was an approximation to the curvature of underlying 1-D curve. Ambrosio and Soner in [21] proved that such curvature can be directly computed using level-set function $\phi$, if we consider the minimum magnitude eigenvalue of projection of Hessian matrix $\nabla^2 \phi$ into the tangential direction of the underlying curve, i.e.,

$$J = \frac{1}{|\nabla \phi|} P_{\nabla \phi} \nabla^2 \phi P_{\nabla \phi}$$  \hspace{1cm} (12)

where the projection operator is defined as follows:

$$P_{\nabla \phi} = I - \frac{\nabla \phi \nabla^t \phi}{|\nabla \phi|^2}.$$  \hspace{1cm} (13)

Therefore, the level-set update equation of CURVES becomes

$$\frac{\partial \phi}{\partial t} = \kappa_2 + \rho (\nabla^t \phi \cdot \nabla I) \frac{\nabla \phi}{g} \cdot \nabla \phi$$  \hspace{1cm} (14)

where $g(\nabla I)$ is the edge detector function described in Section III-A and, as in the original work, is set to $e^{-\kappa}.$

Incorporation of $\rho (\nabla^t \phi \cdot \nabla I)$ is heuristic and required for vessel segmentation. This term encourages the alignment of $\nabla I$ and $\nabla \phi$ vectors by maximizing their inner product, a notion which was also further considered in [22] as the basic flux term. To enforce anisotropy using CURVES algorithm, a general combinatorial energy functional is proposed

$$E = E_g + \beta E_{\delta}$$  \hspace{1cm} (15)

where $\beta \geq 0$ is a user defined constant. The final level-set equation with implied dependency on $x$ is given by

$$\frac{\partial \phi}{\partial t} = \left(1 + \beta \frac{f}{g}\right) \kappa_2 + \left[\beta \nabla^t f + \rho (\nabla^t \phi \cdot \nabla I) \nabla g\right] \frac{\nabla \phi}{g} + \beta \frac{\nabla^t \phi \mathbf{L} \nabla \phi}{g} |\nabla \phi|$$  \hspace{1cm} (16)

where the $f(x)$ has the same definition as in Section III. Note that, in order to yield a consistent formulation with CURVES, the total minimizing equation has been divided by $g(x)$, so that by $\beta = 0$, (16) reduces to the standard CURVES equation.

B. Regularization of the Flux Maximizing Flow

Vasilevskiy and Siddiqi in [22] proposed the flux maximizing geometric flow (FLUX) for low contrast blood vessel segmentation. This is an edge integration method which finds the locations where $|\nabla I \cdot \nabla \phi|$ is maximized. The flux functional to be minimized (maximized in norm) can be written as

$$E_{\phi}(\phi) = \int \delta(\phi(x))|\nabla \phi(x)| \cdot \nabla I \cdot dx.$$  \hspace{1cm} (17)

This integration is an estimation of the inward flux, and, similar to the outlined proof in the Appendix B, the EL equation can be easily shown to be

$$\frac{\partial \phi}{\partial t} = |\nabla \phi| \Delta I.$$  \hspace{1cm} (18)

The relevant point to our paper is that, using FLUX in order to obtain a smooth segmenting surface, the data should be initially smoothed. This filtering damages the available edge information and introduces size complexity. Introduction of geometrical regularization term can prevent leakage from noisy edges and is also essential for obtaining a smooth surface without much altering the original data. Hence, in this paper, the FLUX energy functional in (17) is integrated with the proposed geometric regularization functional. For comparison purposes, we suggest to minimize a more general from

$$E = E_{\phi} + \alpha \Delta I + \beta \left(\nabla^t \phi \mathbf{L} \nabla \phi + \nabla \cdot \phi \frac{\nabla \phi}{|\nabla \phi|}\right)$$  \hspace{1cm} (19)

Replacing the mean curvature with the minimum principal curvature, this corresponds to the following minimizer equation:

$$\frac{\partial \phi}{\partial t} = |\nabla \phi| \left\{ \Delta I + \beta \left[ \nabla^t \phi \mathbf{L} \nabla \phi + \nabla \cdot \left(\phi \frac{\nabla \phi}{|\nabla \phi|}\right)\right] \right\}$$  \hspace{1cm} (20)

where $\alpha \geq 0$ and $\beta \geq 0$ control the smoothness and anisotropy constraints respectively.

As in the original version of the FLUX, to handle the various sizes of the vessels, we compute the Laplacian operator using a multiscale method, i.e., the inward flux is computed on the periphery of 2-D discs or 3-D spheres with various scales, then the result is divided by the number of the points on the periphery [22] and the largest magnitude over the scales is chosen. Depending on the application, the scales are linearly varied from the minimum (1 pixel or voxel) to the maximum radius of the available vessels (up to 6 pixels or voxels).

V. RESULTS AND EXPERIMENTS

In this section, the effect of anisotropy constraint on the segmentations of synthetic image volumes as well as actual 2-D retinal angiography and 3-D MRA data sets is evaluated. We approximate: $\mathbf{L}(\mathbf{x}) = \sum_{i=1}^{3} \lambda_i e_i e_i^t \simeq \lambda_1 e_1 e_1^t$, where $\lambda_1 \leq \lambda_2 \leq \lambda_3 \leq 0$ and $e_1, e_2, e_3$ are the eigenvectors of $\mathbf{L}(\mathbf{x})$, so that the propagation is only applied in the main orientation of the local surface structure.

A. Selection of Parameters

The size of the neighborhood, i.e., $R$ can be decided based on the scale of the target vessels, as it is the case with our 2-D experiments. Nevertheless, since usually thinner vessels are more
challenging, in our 3-D experiments, we set $R = 2$. This suffices to produce reliable orientations. Also, since our volumetric MRA data sets had different dynamic ranges and setting an appropriate value for $\beta$ was difficult, the data sets were normalized to the range of $[0, 65535]$ prior to segmentation. Upon this normalization, better results were obtained using $1000 < \beta < 3000$ for the regularization of CURVES, and $500 < \beta < 3000$ for FLUX. Nevertheless, these settings can be further refined by the user.

B. Synthetic Image Volumes

In this study, a synthetic image as shown in Fig. 5 with the resolution of $101 \times 101 \times 101$ voxels is used to evaluate the performance of the proposed combinational segmentation schemes. The helix tube is chosen to resemble an actual vessel pattern by decreasing in thickness from 4 voxels in the bottom up to the pixelation level in the top as shown in panel (a). The curvature is increasing in the same bottom-to-top direction as it can be seen from the MIP images. The original binary volume was convolved with a low pass averaging filter. We observed that maximum intensity value in the original data set was 1280. This was corrupted by different Gaussian noise levels having zero means and standard deviations $\sigma$ of 50, 100, 200, 300 as shown in Fig. 5(b)–(d), respectively. Fig. 6 shows the middle slice of the sample noisy volumes, indicating the relative strength of the random noise in the corresponding slice. As shown, the higher noise levels effectively destroy the thinner parts.

In these experiments, in order to have the maximum gain on the elongations, all curvature smoothing terms are ignored, i.e., we set $\alpha = 0$ in (20) and ignore the constant $k_2$ in (16). The front evolution starts from seeding in the thicker parts and approaches the thinner and curly parts. This process ends upon the convergence of the segmentation algorithm. This is repeated for three times for each of $\sigma$ levels. The segmentation errors are calculated using the Dice similarity coefficient [37]

$$\text{Segmentation error} = \left(1 - 2 \times \frac{n\{A \cap B\}}{n\{A\} + n\{B\}}\right) \times 100 \quad (21)$$

where $A$ and $B$ are the target and obtained segmentation sets. The regularized CURVES and FLUX schemes are obtained by setting $\beta = 1000$ and $\beta = 500$ in (16) and (20) respectively. Fig. 7 shows the sample segmentation results obtained from noisy data sets with $\sigma = 100$. By comparing the CURVES

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1Through our experiments, we observed that convergence for the higher noise level of $\sigma = 300, 200, 100$ in FLUX segmentation was not possible since the segmentation was adapting itself toward the background. So, in that case, we used a fixed number of iterations to evaluate the efficiency.
segments in panels (a) and (b), a significant elongation improvement using our method is observable. This corresponds to the improvement of the segmentation errors from 68.9% to 43.41% as indicated in the Table I. Also by comparing the segmentations of FLUX in Fig. 7(c) and (d), we can notice the start of some leakage in (c) which is not present in (d). It shows that while preserving a better tubular shape, elongation improvement in the main orientation is achievable using our regularization method. The last column of the Table I indicates the elapsed CPU time for different segmentation methods. These are for a C++ code running on a 3.0 GHz PC under Linux. As shown, the inclusion of our regularization terms increases the execution time by a maximum factor of two, but improvements of segmentation is noticeable in most cases.

We further segmented our model volume using values of 0 < $\beta < 3000$ and 0 < $\beta < 4000$ for CURVES and FLUX respectively. As shown in Table II, the performance of regularized CURVES method degrades beyond an optimal value of $\beta$. The reason is that by too much enforcing the anisotropic constraint, the segmented tubes do not follow the actual paths in the higher curvature parts. On the other hand, as shown in the Table III, segmentation error of the anisotropic regularized FLUX, does not significantly change by varying $\beta$. The reason can be explained as follows: for lower noise levels, the FLUX propagates through lower contrast regions without significant leakage. Therefore, in that case, anisotropic constraint is not much effective. The efficiency of the FLUX is more improved in higher noise levels, where the leakage happens using the original method. We also note that over enforcing the shape constraint by higher values of $\beta$ deteriorates the segmentation performance.

C. Two-Dimensional Examples

Fig. 8 shows example retinal angiogram image segmentations using the regularized and relax FLUX schemes. The multiscale outward flux of the image gradient field is obtained as indicated in Fig. 8(b). This is in fact a bi-directional speed image that controls the front expansion and contraction. Initial seeds are indicated in Fig. 8(c). Fig. 8(d) is the segmentation from the relax flux maximizing scheme obtained by $\alpha = 0$ and $\beta = 0$ in (20). Note that significant adaption to background has occurred, because the flux image is expansive (negative) at those regions. Fig. 8(e) is the segmentation obtained from applying our defined anisotropic constraint by $\alpha = 0$ and $\beta = 4$. The neighborhood radius $R = 4$ is selected for this experiment only by visual assessment of the approximate vessels width. Note that the leakage has been controlled and the main structure of the dim vessel is extracted successfully.

Fig. 9 is another selected region from the same retinal angiogram. The data was initially smoothed by application of a Gaussian filter and the multiscale-flux image was computed. Fig. 9(d) is the segmentation achieved by the original FLUX. Note that, although the main vessels are captured, leakage has occurred into the background region. Inclusion of curvature in evolution by setting $\alpha = 5$ and $\beta = 0$, has resulted a better regularized segmentation in Fig. 9(e), but at the same time it has been a constraint to allow enough elongations. Fig. 9(f) is the segmentation obtained from applying both smoothness and anisotropy constraints by $\alpha = 5$ and $\beta = 10$. The neighborhood radius $R = 2$ is selected for this experiment based on approximate visual assessment of the vessel widths. Note that while the main vascular region has been extracted, leakage to background has been significantly limited compared to Fig. 9(f).

D. Three-Dimensional Examples

Volumetric segmentations were achieved using ten phase contrast (PC) and time-of-flight (TOF) MRA data sets obtained from different scanners of variable magnetic strengths. Some typical examples are given here for illustration purposes. Qualitative comparisons are mainly presented since obtaining the ground-truth segmentation of these low-contrast complex vascular structures was difficult. Maximum intensity projection (MIP) images are included for visual evaluation, though we believe that MIP partially indicates the low-contrast vessels.

Fig. 10 is the first example using a 3T TOF-MRA data set. One important objective is to illustrate the intrinsic difference

---

### TABLE I

<table>
<thead>
<tr>
<th>Methods</th>
<th>$\sigma = 50$</th>
<th>$\sigma = 100$</th>
<th>$\sigma = 200$</th>
<th>$\sigma = 300$</th>
<th>CPU time (min.)</th>
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</thead>
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<tr>
<td>CURVES</td>
<td>62.29±0.84%</td>
<td>68.90±0.03%</td>
<td>73.28±1.09%</td>
<td>80.18±1.39%</td>
<td>21</td>
</tr>
<tr>
<td>Regularized CURVES</td>
<td>27.43±0.07%</td>
<td>43.41±0.01%</td>
<td>64.54±0.03%</td>
<td>73.42±1.02%</td>
<td>40</td>
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<tr>
<td>FLUX</td>
<td>25.06±0.1%</td>
<td>26.78±0.55%</td>
<td>46.55±1.55%</td>
<td>62.1±1.8%</td>
<td>28</td>
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<tr>
<td>Regularized FLUX</td>
<td>24.40±0.03%</td>
<td>25.74±0.38%</td>
<td>36.82±1.03%</td>
<td>46.23±1.93%</td>
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### TABLE II

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<th>$\sigma = 200$</th>
<th>$\sigma = 300$</th>
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<td>58.49%</td>
<td>62.29%</td>
<td>26.36%</td>
<td>29.38%</td>
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<tr>
<td>1000</td>
<td>26.36%</td>
<td>27.43%</td>
<td>38.58%</td>
<td>40.62%</td>
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<tr>
<td>5000</td>
<td>25.06%</td>
<td>26.78%</td>
<td>24.40%</td>
<td>25.74%</td>
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</table>

### TABLE III

<table>
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<tr>
<th>$\beta$</th>
<th>$\sigma = 50$</th>
<th>$\sigma = 100$</th>
<th>$\sigma = 200$</th>
<th>$\sigma = 300$</th>
<th>$\sigma = 4000$</th>
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<td>25.06%</td>
<td>26.78%</td>
<td>23.7%</td>
<td>24.57%</td>
<td>28.2%</td>
</tr>
<tr>
<td>500</td>
<td>26.36%</td>
<td>27.43%</td>
<td>29.38%</td>
<td>40.62%</td>
<td></td>
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<tr>
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<td>26.78%</td>
<td>24.40%</td>
<td>25.74%</td>
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</tr>
</tbody>
</table>
between our proposed “anisotropic constraint regularization” and “minimum surface curvature” methods. The latter has been employed in CURVES for smoothing. To that end, anisotropically regularized GAC was compared to the CURVES. For a fair comparison image driven terms were kept the same, this was necessary since without the heuristic term of the CURVES, segmentation was not possible. We can observe that because of minimum curvature smoothing in Fig. 10(b), thin vessels in the CURVES segmentation appear to be contracted and obscured. While using anisotropic constraint regularization in panel (d), the surface is equivalently smooth and the shape information has introduced significant extensions of thinner vessels. Anisotropic constraint regularization was also applied on FLUX segmentation. The multiscale FLUX image was computed for the discrete scales ranging from 1 to 6 voxels using the principle described in [22]. As shown the extracted vessels in the original FLUX segmentation appear to be irregularly shaped, while a few low-contrast segments have been missed Fig. 10(c). Irregularity was even increasing by further iterations making the visualization difficult. Whereas, using our regularization method, the extracted vessels appear more tubular and smooth Fig. 10(e). Most importantly, this smoothness has not compromised thin vessels segmentation. In fact, those structures show better segmentation (indicated by arrows).

Fig. 11 is our second example using another 3T TOF-MRA data set. By comparing the results of CURVES and anisotropic constraint regularized GAC in panels (b) and (d), respectively, we similarly find out that minimum surface curvature can obscure the extension of the segmentation toward thinner vessels, but using our method obtaining both smooth and extended structures is possible. Also by comparing the results of the multiscale FLUX and anisotropic constraint regularized FLUX in panels (c) and (e), respectively, we realize enhanced tubularity and smoothness of the surface in (e), as well as extension of a few low-contrast vessels, that is achieved by introduction of the anisotropic constraint.

Since the minimum curvature smoothing term discourages expansion, a question may arise is that if the smoothing term is excluded from CURVES, how would it compare to our anisotropic regularization method? Fig. 12 shows the result of such study. The surface curvature term is ignored in CURVES, and, therefore, Fig. 12(b) is the maximum gain out of unregularized GAC segmentation. We observe that even though the smoothing term is excluded from evolution there are still some missing faint vessels, which are segmented using anisotropic constraint as shown by arrows in (d). Also, by comparing the results of the multiscale FLUX and anisotropic constraint regularized FLUX in panels (c) and (e), respectively, we find out that although the difference is not so significant (partly because of smaller $\beta = 1000$ compared to Figs. 10 and 11), there are still a few gaps between some vessel segments which are merged in (e). It should be noted that the FLUX can detect
the missing gaps by further iterations, however, vessels lose their tubular shape.

Finally, similar results have been obtained using low-Tesla MRA data sets. These experiments can be regarded as the benchmark studies with lower SNR. Figs. 13 and 14 are segmentations of sample intraoperative 0.4T PC-MRA and 0.3T TOF-MRA data sets by CURVES and FLUX alternatives. In these implementation the curvature term is included in CURVES to obtain a smooth surface. This has partly contributed to occlude the segmenting front in some thinner vessels as shown in (b), whereas anisotropic regularization of CURVES has resulted a better segmentation in (d). Note that how several distinct segments have merged together and over all the continuity seems much better. Similarly, the smoothness and tubularity of the segmentation surface of anisotropically regularized FLUX in Fig. 14(e) compared to the original FLUX in Fig. 14(c) is noticeable.

A quantitative validation experiment is shown in Fig. 15. For this case we had the possibility to scan a volunteer with two different magnetic strengths; the lower field was used for segmentation and higher field for validation. The first data, a TOF-MRA 256 × 256 × 153 matrix used for validation purpose only, was obtained from a higher 3 Tesla MR scanner. A noise clean region of interest was separated as shown in panel (a). The second data was obtained from a 1.5 Tesla scanner and registered to the first volume. The corresponding ROI is shown in (b). Clarity of the vessels in high Tesla field, allowed us to make a reference segmentation volume using an appropriate thresholding value as shown in panel (c). Fig. 16 shows the segmentation results. No curvature was employed in this segmentation to obtain the maximum gain from CURVES. By visual comparison of (a) to (b) and (c) to (d), we see that most of extensions achieved in (b) and (d) are in accordance with the reference volume in Fig. 15(c), showing the advantageous of our method to improve the elongations of low contrast vessels. Moreover, by comparing the panels (c) and (d), we may observe that using our regularization method, extracted structures appear to preserve better tubular shapes. The segmentation errors were obtained using (21) and
indicated in Table IV. Note the lower segmentation errors of the regularized methods versus original methods, i.e., 49.55% and 43.89% versus 52.88% and 46.64%, respectively.

VI. DISCUSSION AND CONCLUSION

A new geometric regularization method is proposed for segmenting human blood vessels. This regularization enforces structural anisotropy and has the ability to detect the major front orientation to enforce the elongation in that orientation. The method takes the advantage of shape induced information, and, therefore, the anisotropic expansion at the ending of narrow vessels is independent from the image content. The advantage is that these straight extensions encourage thin vessel extensions if no image gradient data is available, so a few closely apart vessel segments can merge without losing the tubular shape. However, as it has been notified by one of our anonymous reviewers, leakage in the form of over-extension may arise, particularly when the anisotropic constraint or the value of $\beta$ is rather high. Unfortunately given a 2-D/3-D image, setting an appropriate value for $\beta$ is not straightforward in general, but for a typical PC and TOF MRA data set, as discussed in the Section V-A upon normalizing the image dynamic range, an optimum value can be selected from a conservative range of $\beta < 3000$. Within this range, improvement of segmentation from visual and quantitative aspects was achievable without significant leakage. One research direction to control the over-segmentation at the vessel endings, is to select a different definition $f(x)$, e.g., $f(x) = 1/x^n, 0 < n < 1$ so that it can tolerate higher values of isotropy in the vessel endings.

The size of neighborhood $R$ used for computation of local surface structures, is a feature which should be assigned to the scale of target vessels. Small neighborhood size fails to provide robust orientation estimation and large sizes will include other surrounding structures and consequently may produce erroneous results. Fortunately, for our 3-D MRA data sets, in which the most challenging part is to detect thin vessels, selecting $R = 2$ suffices. We emphasize that this selection does not affect the final segmented vessel thickness, but is a feature to encourage segmenting vessels thinner or equal to that size. This can be realized if we note that with a same $R$ in both CURVES and FLUX algorithms, segmented vessels using CURVES appear thinner than actual MIP images.

The proposed regularization method has various improvements over original FLUX and CURVES methods. Elongation of thin vessels is significantly improved when our anisotropic constraint is applied on CURVES. On the other hand, although the FLUX is capable to detect the low contrast vessels, the method is basically weak in preventing leakage and by further iterations the segmented structures may lose their tubular patterns. This is shown in most of our experiments as well as in a recent publication [38]. Anisotropic constraint when applied on the FLUX improves the tubularity of the extracted vessels, inhibits the leakage, and enhances the elongations in the main orientations.

Compared to the minimal surface curvature smoothing method, the proposed method is computationally expensive but it can provide smoothness and anisotropic elongation which is particularly important for thin structure segmentation. Since our regularization method enforces an implicit tubular shape
prior, vessel bifurcation is inhibited because such structures contribute to orientation ambiguity (or isotropy) at bifurcations. One possible interesting direction for research is the development of a mechanism to suppress our regularization model at vessel branchings. Whether this can be achieved using geometrical features or image content features remains as our future research activities. Finally, it should be noted that though we applied our method for segmentation of vessels in medical images, the proposed method is quite general and it can be used for segmenting other elongated patterns in nonmedical images, e.g., road detection in synthetic aperture radar images.

**APPENDIX A**

**Fréchet Derivative and Its Properties**

The following review of basic derivation concepts and supplementary propositions is adapted from [33].

**Definition A1 Fréchet Derivative:** Let $V$ and $W$ be linear normed vector spaces, and $U \subset V$ be an open subset of function $f : U \rightarrow W$ is called Fréchet differentiable at $x \in U$ if there exists a bounded linear operator $A : V \rightarrow W$ such that

$$f(x + h) = f(x) + Ah + o(||h||), \quad h \rightarrow 0 \quad (A1)$$

where $||\cdot||$ denotes the space metric. We write $Df(x) = A$ and call it the Fréchet derivative of $f$ at $x$. $Ah$ is called the Fréchet differential of $f$ at $x$.

The basic differentiation properties for Fréchet derivative are as follows.

**Proposition A1 (Linearity):** If $f$ and $g$ are two maps from $V \rightarrow W$ which are differentiable at $x$, and $r$ and $s$ are scalars (two real or complex numbers), then $rf + sg$ is differentiable at $x$ with $D(rf + sg)(x) = rDf(x) + sDg(x)$.

**Proposition A2 (Product Rule):** Let $V, V_1, V_2$ and $W$ be normed spaces. If $f_1 : K \subset V \rightarrow V_1$ and $f_2 : K \subset V \rightarrow V_2$ are differentiable at $u_0$, and $b : V_1 \times V_2 \rightarrow W$ is a bounded
bilinear form, then the operator $B(u) = b(f_1(u), f_2(u))$ is differentiable at $u_0$, and for $h \in V$

$$DB(u_0) = b(Df_1(u)h_1, f_2(u)) + b(f_1(u), Dh_2(u)), \quad (A2)$$

**Proposition A3 (Chain Rule):** If $f : U \to Y$ is differentiable at $x$ in $U$, and $g : Y \to W$ is differentiable at $y = f(x)$, then the composition $g \circ f$ is differentiable in $x$ and the derivative is the composition of the derivatives: $D(g \circ f)(x) = D(g)(f(x)) \circ D(f)(x)$.

We are interested in minimizing our shape-dependent functional defined in (6); therefore, the Fréchet derivative should be applied for $E_\kappa(\phi) : \Phi \to R^+$, where $\Phi$ is the set of continuous level-set functions defined over the region $D$ and $R^+$ is the set of non-negative real numbers.

The necessary condition for $E_\kappa$ to have an extrema on $\phi_0 \in \Phi$ can be stated using Fréchet derivative as

$$DE_\kappa(\phi_0)\psi = 0 \quad \text{for all} \quad \psi \in \Phi, \quad (A3)$$

To keep the consistency with notations on [32] and [27], we denote: $DE_\kappa(\phi)\psi \equiv \langle \partial E_\kappa(\phi), \psi \rangle$ as the Fréchet differential of $E_\kappa$ at $\phi$ in $\psi$ direction.

**APPENDIX B PROOF OF THEOREM 2**

In order to derive the EL equation of (7), we follow the variational framework outlined in [32]. For abbreviation purposes, we denote $q(x) = f(\text{Tr}\mathbf{M}^{-1}(x))$, where the matrix $\mathbf{M}$ has
been defined in (1). According to definition in (A1), derivative can be written as

\[
\langle \partial E_s, \psi \rangle = E_a(\phi + \psi) - E_a(\phi), \quad \|\psi\| \to 0
\]

\[
= \int \langle \partial(q(x)\delta(\phi(x)))|\nabla \phi(x)|, \psi(\cdot) \rangle dx
\]

\[
P_1 + P_2
\]

(B1)

where \(P_1\) and \(P_2\), using the product rule (A2) and setting \(b(f_1, f_2) = f_1 f_2\), i.e., normal scalar product, (B1) can be written as

\[
P_1 = \int q(x) \partial [\delta(\phi(x))]|\nabla \phi(x)|, \psi(\cdot) dx
\]

\[
P_2 = \int \partial q(x), \psi(\cdot) \delta(\phi(x))|\nabla \phi(x)| dx
\]

(B2)

The term \(\langle \partial E_s(\phi), \psi \|\psi\||\nabla \phi(x)\|, \psi(\cdot) \rangle \) in (B2) is in fact the scalar differential and with implied dependency on \(x\), can be written as

\[
\delta(\phi + \psi)|\nabla (\phi + \psi)| - \delta(\phi)|\nabla \phi| = \psi \delta(\phi)|\nabla \phi| + \delta(\phi) \frac{\nabla^t \phi \cdot \nabla \psi}{|\nabla \phi|} + \alpha(\|\psi\|)
\]

(B4)

where \(\alpha(\|\psi\|) \to 0\) as \(\|\psi\| \to 0\). After replacing (B4) in (B2), \(P_1\) can be obtained as

\[
P_1 = \int q(x) \psi(\phi(x))|\nabla \phi(x)| dx
\]

\[
+ \int q(x) \delta(\phi(x)) \frac{\nabla^t \phi(x) \cdot \nabla \psi(x)}{|\nabla \phi(x)|} dx.
\]

(B5)
By using Green (divergence) theorem, (B5) is equal to

\[ P_1 = \int q(x)\psi(x)\delta'(\phi(x))|\nabla \phi(x)| \, dx \]
- \[ \int \psi(x)\nabla \cdot (q(x)\delta'(\phi(x))\frac{\nabla \phi(x)}{|\nabla \phi(x)|}) \, dx \]
= \[ \int -\psi(x)\delta'(\phi(x))\nabla \cdot (q(x)\frac{\nabla \phi(x)}{|\nabla \phi(x)|}) \, dx. \]  \hspace{1cm} (B6)

Simplification of \( P_2 \) in (B3) is also straightforward but requires further manipulation. Using the chain rule introduced in proposition (A3) and according to derivative of matrix trace and inverse operator properties

\[ \langle \partial f(x), \psi(\cdot) \rangle = \langle \partial f(\text{Tr} \ M^{-1}), \psi(\cdot) \rangle \]
= \[ f(x)(\partial \text{Tr} \ M^{-1}, \psi(\cdot)) \]
= \[ f(x)(\text{Tr}(\partial M^{-1}, \psi(\cdot)) \]
= \[ f(x)(\text{Tr}(\partial M, \psi(\cdot))M^{-1}) \]  \hspace{1cm} (B7)

where the dependency of \( M^{-1} \) and \( M \) on \( x \) is implied. The term \( \langle \partial M(x), \psi(\cdot) \rangle \) using definition of \( M \) in (1) can be expressed as

\[ \langle \partial M(x), \psi(\cdot) \rangle \]
= \[ \int B(x,x')[-\delta(\phi(x'))\psi(x')|\nabla \phi(x')|\nabla \phi(x')] \]
+ \[ H(-\phi(x'))|\nabla \psi(x')|\nabla \phi(x')] \]
+ \[ |\nabla \phi(x')|\nabla \psi(x')) \]  \hspace{1cm} (B8)

Fig. 15. TOF-MRA 256 \times 256 \times 153 data sets with two different magnetic strengths used for our validation experiment. (a) MIP from a portion of a 1.5 Tesla data, used for segmentation. (b) MIP of a the 3 Tesla data of the same volunteer used for validation. (c) The reference volume obtained from 3T data.

Fig. 16. Segmentations of the 1.5T TOF data set. (a) Original CURVES, (b) regularized CURVES with anisotropy constraint, (c) original FLUX, (d) FLUX with anisotropy constraint. Arrows indicate a few merging vessels using our method. Note that the most of extensions and merging obtained in (b) and (d) are in accordance with the reference segmentation in Fig. 15(c).

| TABLE IV |

| Segmentation Errors of Original and Regularized FLUX and CURVES Schemes on a 1.5T TOF-MRA Data Set |

| Error | 52.88\% | 49.55\% | 46.64\% | 43.89\% |

Replacing (B8) in (B7), and changing the order of trace and integral operators, i.e., \( \text{Tr} f(\cdot) = f(\text{Tr}(\cdot)) \), we get

\[ \langle \partial f(x), \psi(\cdot) \rangle = I_1 - I_2 - I_3 \]  \hspace{1cm} (B9)

where

\[ I_1 = \int B(x,x')\delta(\phi(x'))\psi(x')f'(x) \]
\[ \times \text{Tr}(M^{-1}(x)|\nabla \phi(x')|\nabla \phi(x')M^{-1}(x)) \, dx' \]  \hspace{1cm} (B10)

\[ I_2 = \int B(x,x')H(-\phi(x'))f'(x) \]
\[ \times \text{Tr}(M^{-1}(x)|\nabla \psi(x')|\nabla \phi(x')M^{-1}(x)) \, dx' \]  \hspace{1cm} (B11)

\[ I_3 = \int B(x,x')H(-\phi(x'))f'(x) \]
\[ \times \text{Tr}(M^{-1}(x)|\nabla \phi(x')|\nabla \psi(x')M^{-1}(x)) \, dx'. \]  \hspace{1cm} (B12)
We note that $M^{-1}$ is a positive symmetric matrix; hence, further simplifications can be achieved by noticing that

$$
\text{Tr}[M^{-1}(x) \nabla \phi(x) \nabla \psi(x) M^{-1}(x)] = \nabla \psi(x)^T M^{-2}(x) \nabla \phi(x).
$$

(B13)

Other terms can be written in the same way and therefore

$$
I_1 = \int B(x, x') \delta(\phi(x')) \psi(x') f'(x) \times \nabla \phi(x') M^{-2}(x) \nabla \phi(x') dx'.
$$

(B14)

$$
I_2 = I_3 = \int B(x, x') H(-\phi(x')) \hat{f}(x) \times \nabla \psi(x') M^{-2}(x) \nabla \phi(x') dx'.
$$

(B15)

Equation (B20) is the level-set EL equation for unconstrained minimization of $E_\alpha$. The constrained optimization in (7) can be achieved by replacing the regional update values with values extended from zero level set [32]. We note that $2 H(-\phi(x)) \nabla \phi$ is a nonsymmetric regional “source” term that clearly violates our constraint. This must be replaced by values from border. However, since we are dealing with sharp corners in which finding the closest points on the border is inaccurate, the second methodology is to ignore this regional source term and use reinitialization. This has been shown to be equal to the extension method in the steady state solution [32]. Therefore, the EL equation of constraint minimization problem introduced in (7) can be written as

$$
\frac{\partial \phi(x)}{\partial t} = \delta_\epsilon(\phi(x)) \left[ \nabla \psi(x) \nabla \phi(x) + \nabla \cdot \left( f(x) \frac{\nabla \phi(x)}{|\nabla \phi(x)|} \right) \right].
$$

(B16)

Starting from an initial signed distance function, every after a few iterations $\phi$ is explicitly reinitialized to the signed distance function.

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REFERENCES


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