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Vascular Tree Reconstruction by Minimizing A Physiological Functional Cost

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Abstract

The reconstruction of complete vascular trees from medical images has many important applications. Although vessel detection has been extensively investigated, little work has been done on how connect the results to reconstruct the full trees. In this paper, we propose a novel theoretical framework for automatic vessel connection, where the automation is achieved by leveraging constraints from the physiological properties of the vascular trees. In particular, a physiological functional cost for the whole vascular tree is derived and an efficient algorithm is developed to minimize it. The method is generic and can be applied to different vessel detection/segmentation results, *e.g.* the classic rigid detection method as adopted in this paper. We demonstrate the effectiveness of this method on both 2D and 3D data.

1. Introduction

Creating a complete 3D model of a vascular network is of key importance in many vascular imaging applications [12, 27]. Ideally, the vascular model would accurately quantify both 3D topology (connectivity) and morphology (radius, length, branching angles, etc) of the vascular systems. In this paper, a novel algorithm is proposed to automate this process, where the main emphasis is put on topology estimation.

1.1. Motivation

Complete vascular network models are essential in understanding the flow patterns in circulation, the possible design principles underlying the structural heterogeneity, and quantitative comparative analysis of vascular trees. Vascular network reconstruction is also widely applicable to modeling, autoregulation and metabolism studies. Despite the large number of publications in vascular image analysis, only a very limited number of attempts have been made to reconstruct a complete vascular network [25, 12, 2]. Commonly a two-stage approach is adopted, where the first step is vessel (or centerline) detection, and the second stage is vessel connection. While, much work has been published in the area of vessel detection and segmentation for vessel segments, so far relatively little work has been done on connecting the segments to reconstruct complicated vascular trees. A common weakness of much of the existing connection work is that numerous thresholds are required to be manually set. The thresholds might need to be adjusted for different part of the image, and some times manual correction of the connection is needed. For a large scale complicated vascular network, this is very tedious and error-prone. Their limited automation capability and the dependence on only local image context make the correctness of final vascular network highly dependent on the quality of the vessel detection used as an input.

From a methodological point of view, our motivation is to utilize the high-level prior-knowledge in vascular image analysis. Similarly to many tasks in image analysis, the use of appropriate prior-knowledge is desirable so as to reduce the uncertainty in estimation. Previous methods for this task largely depend on low-level prior-knowledge [10, 13], mostly the tubular geometry of the vessel segments [7], the distribution of image intensity [26], and some generic image prior of *smoothness* for both geometry and appearance. However a number of higher-level constraints largely remain unexplored, such as: (I.) The vascular tree has a (obviously) a tree topology; (II.) The statistical distribution of vessel location, orientation, intensity *etc.* for a specific vascular system [20]; (III.) Fractal properties of the vascular trees [28]; (IV.) Physiological principles, *e.g.* the minimum work principles from which the Murray's law was derived [17]. The flow and pressure within the vascular system has also been studied [19].

We hypothesize that the use of high-level prior-knowledge will achieve more reliable estimation. However, such constraints are often more difficult to quantify and thus implement. Among a few papers that employed high-level prior-knowledge, Passat *et al.* [20] learned from a group of segmented samples the distribution of vessel location, orientation, and other properties of the whole vascular network to facilitate the detection/segmentation for the new subject. This method requires substantial intra-subject similarity and a large pre-labeled training data set. Reconstructing the full vascular network was not discussed in [20] either. Bruynickx *et al.* [3] is, to our knowledge, among the first to integrate the physiology principle of minimum volume into vessel segmentation. However the geometry of vessel segments is extremely simplified in their work, and the outcome also heavily depends on the prior detection of the branching/bifurcation joints, which was found to be unreliable – large part of the vascular network was missing in the final results.

1.2. Our proposal

We also adopt a two-stage approach for vascular tree reconstruction [12, 2]. Compared with tracking approaches, *e.g.* using level set [15], particle filtering [6], or marked point process [11], *etc.*, a two-stage approach has less risk of missing whole part of sub vascular network. Our work focus on the second stage of model reconstruction (vessel connection), for which we propose to utilize a physiology principle, the *minimum flow resistance* with *minimum vascular volume* [23], as the high-level prior-knowledge, to guide the searching and connecting. The physiology principle is quantified by a cost function of vascular tree geometry, which is minimized by an efficient algorithm developed in this paper. For the vessel detection stage, we adopted the classic image ridge detection in the scale-space, but the proposed connection method is generic and applicable to different detection approaches.

2. Method

As mentioned above, here we mainly discuss the vessel connection process. Vessel detection will be briefly discussed in Section 2.4.1. Note that there is certain duality between these two problems: if the detection is perfect, the solution for connection is trivial. Conversely, if the connection strategy is perfect, it is only necessary for detection to provide very sparse set of points, where in an extreme case only vascular tree root is needed, given that the perfusion volume is known. In practice, only imperfect solutions could be found for either of them, such as the case in this paper. As a future work, iterations between both solutions hopefully would lead to better results.

2.1. A functional cost of vascular tree

A fundamental hypothesis in theoretical science is that nature pursues optimality in all her workings [23]. For the vascular system [17], the functional optimality implies that a vascular

tree fulfills the perfusion task with the minimum effort for maintaining of its anatomical structure. A corresponding functional cost can be written as

$$f^c = \sum_{p_k \in V^p} R_k^p(\mathcal{T}) + \lambda \cdot M(\mathcal{T}), \quad (1)$$

where $\mathcal{T}$ represents the vascular tree model, $R_k(\mathcal{T})$ denotes the perfusion resistance from the tree root to a cell group in the target volume V^p – lower flow resistance results in greater perfusing capability, $M(\mathcal{T})$ stands for the cost of structure maintenance the the vascular tree and blood, which is assumed to be proportional to its volume, and finally λ is a weight to balance the two costs. Note that R_k^p consists of both the flow resistance in the vessel tubes and the diffusion resistance from the capillary to the cell groups.

In the context of image analysis, the vascular tree can be described by a directed tree graph $\mathcal{T} = (\mathcal{V}, \mathcal{E}, \mathbf{R})$, where vertices $\mathcal{V}$ denote all the vessel centerline points, edges $\mathcal{E}$ refer to the connections (vessel segments), and $\mathbf{R}$ indicates the radius of each vessel segment. For each vascular tree, there is one root vertex v^r and a set of branch end vertices $\mathcal{V}^e = \{v_j^e\}$. Each vessel segment e_i is described by (l_i, r_i, α_i) , where l_i is its length, r_i as the radius, and α_i is its orientation change from the preceding segment ($\alpha_i = 0$ if there is no preceding segment). For each branch end v_j^e , we assume that it is perfusing N_j^p closest unit volume of tissue $\{p_k, k=1 \dots N_j^p\}$. Each p_k is only perfused by one v_j^e . Both $v_i \in \mathcal{V}$ and $p_k \in V^p$ have a resolution of image voxel due to the limitation of imaging capability. Then, regardless of the complexity of the vascular tree, its functional cost can be simply written as in (2), where $R^f(\cdot)$ denotes the flow resistance within vessel tubes, $P(\mathcal{T}, v_j^e)$ denotes the shortest path from v^r to v_j^e and η represents blood viscosity:

$$R^f(l_i, r_i, \alpha_i, \eta) = \frac{8\eta(l_i + L^{eq}(\alpha_i, r_i))}{\pi r_i^4}, \quad (3)$$

where $L^{eq}(\alpha_i, r_i)$ represents the equivalent length of vessel segment caused by the change of flow orientation. $R_j^d(\cdot)$ in (2) is the flow resistance from a vessel end to a unit of tissue volume. This is a function of the flow resistance within the small vessels beyond the image resolution, in the capillary, and the diffusion resistance between p_k and its closest capillary. $S(l, r) = \pi l r^2$ is the volume of the vascular tree.

Note that Eq. (2) can be easily re-arranged as in (4), so that a “local” cost f_i^{cl} for each l_i can be obtained individually, so is for each $v_n \in \mathcal{V}$. If $v_n \notin \mathcal{V}^e$, the local cost, f_n^{cv} , can be set to the average of all the f_i^{cl} that are connected to it. If $v_n = v_j^e \in \mathcal{V}^e$, then it is f_j^{ce} . This local cost can be used to evaluate how good the local connection is, *i.e.*, the reducing of f_n^{cv} indicates the improvement of the connections around v_n . However, it is not able to compare the goodness of connections at different v_n . So we further

$$f^c = \sum_j \sum_k^{N_j^p} \left[\sum_{i \in P(T, v_j^e)} R^f(l_i, r_i, \alpha_i, \eta) + R_j^d(v_j^e, p_k, \eta) \right] + \lambda \cdot \sum_i S(l_i, r_i), \quad (2)$$

$$f^c = \sum_i \underbrace{\left[\sum_{j \in \{j: i \in P(T, v_j^e)\}} \sum_k^{N_j^p} R^f(l_i, r_i, \alpha_i, \eta) + \lambda \cdot \sum_i S(l_i, r_i) \right]}_{f_i^{cl}: \text{cost for each } l_i} + \sum_j \underbrace{\sum_k^{N_j^p} R_j^d(v_j^e, p_k, \eta)}_{f_j^{ce}: \text{cost for each } v_j^e}, \quad (4)$$

define a new measure g_n^c as:

$$g_n^c = \begin{cases} L^{eq}(\alpha, r) & \text{if } d(v_n)=2 \\ (\alpha - \theta(r_0, r_1, r_2, \dots))^2 & \text{if } d(v_n) \geq 3 \\ f_j^{ce} & \text{o/w } (v_n \in V^e) \end{cases} \quad (5)$$

where $d(v_n)$ is the degree of v_n , and $\theta(r_0, r_1, r_2) = \arccos\left(\frac{r_0^4 - r_1^4 - r_2^4}{2r_1^2 r_2^2}\right)$ is the optimal branching angle derived by Murray [16]. In this case, we have a measurement that comparable for v_n within each of the three categories.

2.1.1 Vascular tree reconstruction—Based on the above functional cost f^c , the full problem of vascular model reconstruction could be considered as: **given** tree root v^r and the perfusion volume V^p , **find** a vascular tree T that satisfies

$$T = \arg \min_T f^c(T, v^r, V^p). \quad (6)$$

This is a very difficult problem where all $\mathcal{V}$ and $\mathbf{R}$ need to be estimated. In nature it is solved by the vascular growth process, for which simple simulation models were proposed [24]. The vessel connection problem can be considered as a sub-problem, where ideally both $\mathcal{V}$ and $\mathbf{R}$ are given and it is only $\mathcal{E}$ that needs to be estimated:

$$\mathcal{E} = \arg \min_{\mathcal{E}} f^c(\mathcal{E}, \mathbf{V}, \mathbf{R}, v^r, V^p). \quad (7)$$

2.1.2 A simplified cost—A simplification of f^c can be made when all v_j^e are perfusing the same volume of tissue (so $N_i^p = N_j^p, \forall i, j$), and the distribution of both the vascular network beyond v_j^e and the tissue under perfusion are the same (so $R_i^d = R_j^d, \forall i, j$). In this case, we have (8), where λ is updated to be λ' to incorporate the terms N^p, R^d , and other constants. The simplified cost function, $f^{sc} = f^{SPT} + \lambda' f^{MST}$, is a weighted sum of the cost for a **shortest path tree (SPT)**, f^{SPT} , and a **minimum spanning tree (MST)**, f^{MST} .

Using f^c , given the full set of $\mathcal{V}$ and $\mathbf{R}$, the vessel connection problem presented in (7), can be solved by an efficient greedy algorithm introduced in Section 2.3. We denote such a spanning tree a **rooted minimum spanning tree** (RMST). However, for the original cost f^c (2), it is impossible to find an efficient algorithm for tree connection, because there is no way to know N_j^p and R_j^d before reaching the branch ends v_j^e .

2.2. Our problem and its formulation

After defining the basic formulation based on the functional cost of a vascular tree, we come to the vessel connection problem in the scenario of a two-stage vascular tree reconstruction approach: **Given** the detected vessel centerline points $\mathcal{V}^*$ with estimated vessel radii $\mathbf{R}^*$, vascular tree root v^r , and perfusion volume V^p , to **find** a vascular tree $\mathcal{T}^\wedge$ that is as similar as possible to the true vascular tree $\mathcal{T}$ in terms of topology. No vessel detection methods can produce the ideal data set $(\mathcal{V}, \mathbf{R})$, so there always exist a set of outlier points $\mathcal{V}^o = \mathcal{V}^* \setminus \mathcal{V}$ (false positive) along with a set of missing points $\mathcal{V}^m = \mathcal{V} \setminus \mathcal{V}^*$ (false negative), due to spatially-variant detection performance.

Following the principle of optimality described in Section 2.1, the formulation of the current vessel connection problem directly extends Equation (7) to yield:

$$\begin{aligned} (\mathcal{E}, \mathcal{V}^m, \mathcal{V}^o) &= \arg \min_{(\mathcal{E}, \mathcal{V}^m, \mathcal{V}^o)} f^c(\mathcal{E}, \mathcal{V}^* \setminus \mathcal{V}^o \cup \mathcal{V}^m, \mathbf{R}^* \setminus \mathbf{R}^o \cup \mathbf{R}^m, v^r, V^p), \\ &= \arg \min_{(\mathcal{E}, \mathcal{V}^m, \mathcal{V}^o)} f^{sc}(\mathcal{E}, \mathcal{V}^* \setminus \mathcal{V}^o \cup \mathcal{V}^m, \mathbf{R}^* \setminus \mathbf{R}^o \cup \mathbf{R}^m, v^r), \end{aligned} \quad (9)$$

where f^c can be simplified to be f^{sc} because $\mathcal{V}^* \setminus \mathcal{V}^o \cup \mathcal{V}^m = \mathcal{V}$. However, due to the missing point $\mathcal{V}^m$ it is a **Steiner tree problem** for which no efficient solution exists.

Alternatively, when $\mathcal{V}^*$ is dense enough, we can still find a $\mathcal{T}^\wedge$ that is similar to $\mathcal{T}$ without estimating $\mathcal{V}^m$:

$$(\mathcal{E}, \mathcal{V}^o) = \arg \min_{\mathcal{E}, \mathcal{V}^o} f^c(\mathcal{E}, \mathcal{V}^* \setminus \mathcal{V}^o, \mathbf{R}^* \setminus \mathbf{R}^o, v^r, V^p). \quad (10)$$

But in this case, the possible missing of the points at the true branching ends v_j^e make the simplification from f^c to f^{sc} invalid, and thus no efficient solution exists either.

Both (9) and (10) are difficult to solve, however, it is not difficult to notice that if the ideal centerline point set $\mathcal{V}$ is given (back to our previous formulation (7)), the right vascular tree $\mathcal{T}$ can also be easily found by minimum spanning tree (MST). This would provide hints for an efficient solution for either (9) or (10). Consider the ideal vessel centerline point set $\mathcal{V}$. Given a vascular image, we define $\mathcal{V}$ to be

$$\begin{aligned} \mathcal{T} &= \arg \min_{\mathcal{T}} N^p \sum_j \left[\sum_{i \in P(\mathcal{T}, v_j^e)} \frac{l_i + L^{eq}(\alpha_i, r_i)}{r_i^4} \frac{8\eta}{\pi} + R^d \right] + \lambda \cdot \sum_i \pi l_i r_i^2 \\ &= \arg \min_{\mathcal{T}} \underbrace{\sum_j \sum_{i \in P(\mathcal{T}, v_j^e)} \frac{l_i + L^{eq}(\alpha_i, r_i)}{r_i^4}}_{\text{shortest path tree}} + \lambda' \cdot \underbrace{\sum_i l_i r_i^2}_{\text{minimum spanning tree}}, \end{aligned} \quad (8)$$

the densest point set that the image grids can ever sample the true vessel centerlines $\mathcal{S}$, which are continuous curves. It can be safely assumed that, at a resolution level of voxel size, that vessel centerline points from different vessel segments are not adjacent to each other in the image. In this case, and assuming cubic image voxels with diagonal length d , for any point at the end of a vessel branch, v_j^e , there is one and only one point that can be found in $\mathcal{V}$, whose distance from v_j^e is less than or equal to d . For any vessel centerline point at a branching or bifurcation spot, it has three and only three such points. For the rest points, there are two and only two such points. Following this definition, it is obvious that the right connection between $\mathcal{V}$ can be simply established by MST, $\mathcal{T} = MST(\mathcal{V})$. This simplicity reflects the duality between vessel detection and connection as mentioned earlier. Here we need to further assume that the true vascular tree indeed conforms to the functional cost of a vascular tree f^c (2), and the image resolution is fine enough that $MST(\mathcal{V})$ is equal to the $\mathcal{T}$ estimated by Eq. (7) (in practice, a smoothing process is necessary to eliminate the zig-zag effect of discretization due to the term $L^{eq}(\alpha_i, r_i)$ in f^c).

We note that some previous publications have simply formulated the vessel connection as a MST problem with various distance metrics, *e.g.* Euclidean distance [4], Mahalanobis distance [8], and a mixture of Euclidean distance and vessel orientation difference [25]. However, it is hard to justify the correctness of those metrics when $\mathcal{V}^*$ and $\mathcal{V}$ are considerably different. Furthermore, using a consistent distance metric leads MST to incorrect connections with spatially variant missing point situations.

2.3. An efficient solution

We propose an efficient solution by first introducing of a pseudo-distance matrix $\mathbf{D}(\mathcal{V}^*)$. Let $N = |\mathcal{V}^*|$ and then $\mathbf{D}$ is a $N \times N$ matrix where each element $d_{i,j}$ records a positive variable value as a pseudo-distance between $v_i^*, v_j^* \in \mathcal{V}^*$. We reformulate the optimization problem (10) to be

$$\widehat{\mathbf{D}} = \arg \min_{\mathbf{D}} f^c(\mathbf{T}(\mathbf{D}), \mathbf{R}^*, \mathbf{v}^r, \mathbf{V}^p), \text{ s.t. } \mathbf{D} > 0 \quad (11)$$

where $\mathbf{T}(\cdot)$ is a function (algorithm) that finds a tree $\mathcal{T}^*$ given an arbitrary distance matrix $\mathbf{D}$, and it is able to traverse all possible trees spanning $\mathcal{V}^*$ by varying $\mathbf{D}$. $v_i^* \in \mathcal{V}^o$ can be implied by setting $d_{i,j} = \infty$, $\forall j$, so both $(\mathcal{E}, \mathcal{V}^o)$ in (10) are embedded in $\mathbf{D}$. Note that each time $\mathbf{T}(\mathbf{D})$ establishes a complete tree with all $\{v_j^e\}$ known so the full functional cost f^c can be calculated.

Eq. (11) can be efficiently optimized if (I.) $\mathbf{T}(\cdot)$ has a very efficient implementation, (II.) given an appropriate distance metric for $\mathbf{D}$, $\mathbf{T}(\mathbf{D}(\mathcal{V}^*))$ can yield a tree that is very close to the one that minimizes f^c thus provides a good initial condition for optimization, (III.) the optimization is only conducted at the sites where $\mathbf{T}(\mathbf{D}(\mathcal{V}^*))$ is most different from the real tree. For the first two conditions, we already know that when $\mathcal{V}^*$ is very close to the ideal $\mathcal{V}$, MST, with an Euclidean metric for $\mathbf{D}$, can reconstruct a tree that similar to $\mathcal{T}^*$, but in more general case, the rooted minimum spanning tree (RMST) defined in (8), which is more close to the real functional cost, can perform significant better than MST. This will be clearly illustrated in the experiments later. So in this work, we set $\mathbf{T}(\cdot) = RMST(\cdot)$. A Prim's-like algorithm for RMST is proposed in Alg. 1.

The last condition requires to evaluate the goodness of local connections at each v_n , this is achieved in Eq. (5). Let $\mathcal{V}^{opt}$ be the set of vertices with worst local cost, the number of

parameter of the optimization problem is reduced from $N \times N$ to $|\mathcal{V}^{opt}| \times N$. We further assume that at least one of the current connections of v_i^{opt} is correct – let the corresponding vertex as v_{j^*} . v_{j^*} can be selected by comparing the local costs g_n^c of all the adjacent vertices. Then we fix the distance between v_i^{opt} , v_{j^*} , and adjust the distance from v_i^{opt} to all the rest points, $d_{i,j}$, $\forall j \neq j^*$, by move v_i^{opt} along the direction of $\vec{v} = (v_i^{opt} - v_{j^*}) / \|v_i^{opt} - v_{j^*}\|$, or if provided, using the vessel tangent orientation at this point calculated from the vessel centerline detection stage. In this case, for each v_i^{opt} , the N parameters can be modeled by three, the length l that v_i^{opt} moved, and two angles (θ_x, θ_y) that indicate the deviation from $\vec{v}$. The new position of v_i^{opt} is

$$v_i' = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta_x & \sin\theta_x \\ 0 & -\sin\theta_x & \cos\theta_x \end{bmatrix} \begin{bmatrix} \cos\theta_y & 0 & \sin\theta_y \\ 0 & 1 & 0 \\ -\sin\theta_y & 0 & \cos\theta_y \end{bmatrix} \vec{v} \cdot l.$$

Given $\mathcal{V}^{opt}$, the optimization problem (11) becomes

$$\hat{\Theta} = \arg \min_{\Theta} f^c(T(D(\Theta)), R^*, v^r, V^p), \quad (12)$$

Algorithm 1: Rooted Minimum Spanning Tree

input : $\mathcal{V} = v[N]$, λ' , $\mathbf{D} = d[N][N]$, n^r //index of root

output : Pre $[N]$ /*The index of the parent node of $v[n]$, equivalent to $\mathcal{E}$ */

begin

/*For simplicity, set $r_i = 1$ in (8) */

/*Vertex in tree */

$\mathcal{S} = \{v[n^r]\};$

for $v[n] \in \mathcal{V} - \mathcal{S}$ **do**

/*distance from the tree */

$d_{tree}[n] = d[n^r][n];$

/*distance from the root */

$d_{root}[n] = \frac{1}{\lambda'} d[n^r][n];$

Pre $[n] = n^r;$

while $\mathcal{S} \neq \mathcal{V}$ **do**

$m = \min_{v[n] \in \mathcal{V} - \mathcal{S}} d_{root}[n];$

$\mathcal{S} = \mathcal{S} \cup v[m];$

$d_{root}[m] = d_{root}[Pre[m]] + \frac{1}{\lambda'} d_{tree}[m];$

for $v[n] \in \mathcal{V} - \mathcal{S}$ **do**

if $d_{root}[n] > d[m][n] + d_{root}[m]$ **then**

$d_{tree}[n] = d[m][n];$

$d_{root}[n] = d[m][n] + d_{root}[m];$

Pre[n] = m;

end

where $\Theta = \{(l_i, \theta_{xi}, \theta_{yi}) : v_i \in \mathcal{V}^{opt}\}$. Steepest descent method is found to be good enough for this optimization. The optimization for the outlier vertices $\mathcal{V}^o$ (Which needs to set certain d_{ij} to be ∞) is not conducted together with $\mathcal{V}^{opt}$ right now. They are handled in a trimming process after the optimization with respect to $\mathcal{V}^{opt}$ is completed. In this paper, we propose to use an iteration algorithm for the whole vascular tree reconstruction based on (12). This is described in Alg. 2.

Algorithm 2: Vascular tree reconstruction

begin

 Initialize $\mathbf{D}^{(0)}$ by the Euclidean distance between any pair of vertices in $\mathcal{V}^*$;

 while $f^c(\mathbf{D}^{(k)}) - f^c(\mathbf{D}^{(k+1)}) > \varepsilon$ do

 /*Optimize connections at vertices in each category, refer (5) */

 for Category = 1 to 3 do

 Update the tree by $RMST(\mathbf{D}^{(k)})$;

 Calculate $\{\mathcal{G}_n^C\}$ for the current category;

 Sort $\mathcal{G}_n^C$ to select $\mathcal{V}^{opt}$ with first N^g greatest $\mathcal{G}_n^C$ in the current category;

 Update $\mathbf{D}^{(k)} \rightarrow \mathbf{D}^{(k+1)}$ by (12);

$\mathcal{T}^\wedge = RMST(\mathbf{D}^{(final)})$;

end

2.4. Implementation

2.4.1 Vessel detection—Vessel centerline can be detected directly, or skeletonized from the vessel contours segmented from images. Further, many methods [1, 12, 2] alternate between these steps to improve reliability. The result of centerline detection is expected to include the location $\{x_i\}$ of a set of points on vessel centerlines, hopefully also include the tangent vessel orientation $\{\theta_i\}$ and radius $\{r_i\}$ for each point.

There are a number of ways to estimate vessel centerline directly, *e.g.* using Hessian-based estimation, moments of inertia, and gradient vector distribution. Local image maxima have also been adopted as the initial candidates for centerline points [25, 12]. In this paper, we adopt the classical scale-space ridge detection [14] due to its simplicity. We describe this briefly next.

Given a image $\mathbb{R}^3 \times \rightarrow \mathbb{R}$, its scale-space representation is defined by $L(\cdot; t) = g(\cdot; t) * f$, where g denotes the Gaussian kernel, and t is the scale parameter. At any image point (x_0, y_0, z_0) , a local (o, p, q) -system is defined to be aligned to the principal curvature directions of the brightness function, which is corresponding to the eigenvectors of the Hessian matrix. Naturally a ridge point should satisfy

$$\begin{cases} L_p=0, & L_q=0, \\ L_{pp}<0, & L_{qq}<0, \\ |L_{pp}| \geq |L_{qq}| > |L_{oo}|, \end{cases} \quad (13)$$

Then a key concept in scale-space theory, γ -*normalized derivatives*, $\partial_{x,\gamma\text{-norm}} = t^{\gamma/2}\partial_x$, was proposed to serve as indicators reflecting the spatial extent of corresponding image structures. Based on $\partial_{x,\gamma\text{-norm}}$ a normalized measure of ridge strength is associated to each point in scale-space,

$$\mathcal{M}_{\gamma\text{-norm}}L = |L_{pp,\gamma\text{-norm}}|. \quad (14)$$

It can be proved that for a cylindrical Gaussian ridge whose variance is t_0 , we get maximum $\mathcal{M}_{\gamma\text{-norm}}L$ at scale of

$$t_{\mathcal{M}_{\gamma\text{-norm}}} = \frac{2\gamma}{3-2\gamma}t_0. \quad (15)$$

Clearly, $0 < \gamma < \frac{3}{2}$ is a necessary condition to give a local maximum over scales. We set $\gamma = \frac{3}{4}$ which makes $t_{\mathcal{M}_{\gamma\text{-norm}}} = t_0$.

During implementation, ridge missing often arises because of the discretization effects (e.g. $L_p = 0$, $L_q = 0$ are difficult to satisfy simultaneously), and also occurs at vessel junctions. In this paper, we simply leave the missing part as gaps that are expected to be dealt with the vessel connection process.

2.4.2 Vessel connection—The main issue during implementation is on the calculation of the cost functions (2), due to the lack of information on details of blood flow and tissue distribution. This forces us to make the following simplifications:

(I.) For computing $L^{eq}(\alpha, r)$, there are experimental results in engineering of pumping systems [18] (to calculate the equivalent length for fittings) but not in analytic form. If we let $L^{eq} = K \cdot r$, generally K adopts a very large number, e.g. for a 45° elbow fitting, $K \approx 12$, and for a 90° elbow fitting, $K \approx 30$. In this paper we approximate $L^{eq}(\alpha, r) = 60\alpha/\pi \cdot r$. (II.) If both branch ends $\mathcal{V}^e$ and perfusion volume $\mathcal{V}^p$ are given, it is straightforward to calculate N^p , the number of closest voxels to each branch end. However, in the context of image analysis, finding $\mathcal{V}^p$ is often a difficult segmentation problem itself. Further, $R_j^d(\mathcal{V}^e, p)$ is concerned with the distribution of tissue which is often unknown. In this paper, we circumvent this issue by assuming $R_j^d(\mathcal{V}^e, p)$ to be constant, $R_j^d(\mathcal{V}^e, p) = 1$, and N_j^p be proportional to the vessel radius at $\mathcal{V}_j^e$, $N_j^p = \lceil K \cdot r_j^e \rceil$ where we set $K = 3$. This is the probably the most simplistic approximation made in this paper, and it largely cancels the intrinsic discrimination ability of the proposed cost function for the outlier $\mathcal{V}^o$. Nevertheless, the resulting algorithm is still found very effective, and we leave this issue to further investigation. Note that this assumption also affect the definition of local cost g_n^c for $\mathcal{V}^e$ in (5). (III.) W.r.t. to setting λ in (2) and λ' in (8), due to all the assumptions made in this paper, and also the lack of information as to the flow velocity, we are not able to use a theoretical result [17], so we set these experimentally. In the current implementation, we set $\lambda = 15$ and $\lambda' = 10$. A initial guess of λ' was found by minimizing the sum of first category of local cost $\sum_n g_n^{c(1)}$ (without adjust $\mathbf{D}$). $\sum_n g_n^{c(1)}$ is also used to find the tree root $\mathcal{V}^r$, from a set of $\mathcal{V}^*$ with large r^* before the optimization.

In the whole procedure of vascular tree reconstruction, a few extra steps would improve the performance, as in Fig. 1. A vascular image enhancement module [7, 21] could be used to improve the ridge detection by reducing the number of outliers; data smoothing and outlier trimming would also be helpful to both ridge detection and vascular tree reconstruction. To smooth the ridge detection results, the detected points are clustered into short segments which are fitted by smoothing splines. So far the outlier detection has not yet been implemented in the optimization framework, and they are largely trimmed within the post-processing modules. Basically connections that still have large local cost after optimization would be considered as candidate outlier points.

3. Experimental results

In this paper, we present initial results to demonstrate the efficiency of the proposed methods on both 2D and 3D vascular images. We first present a 2D case in Fig. 2 as it provides a much easier illustration than 3D cases. The 2D image under test is chosen not to include overlapping vessels since the proposed algorithm has no mechanism to handle occlusion right now. A 3D case is illustrated in Fig. 3. The proposed algorithm is used to reconstruct the coronary vascular tree from a 3D mouse CT image. We label each vessel segment with a color associated with its branch level, ranging from blue (the root, level=0) to red (branch ends with deepest levels), to visualize the pattern of branch levels. This pattern also indicates the flow direction of a vascular tree. It is obvious that the result by the proposed algorithm shows a much more realistic pattern than the result from MST, where the branch ends mostly cluster at the bottom, instead of randomly scattered in the space. In this case, the image size is $183 \times 215 \times 240$, the number of resulting vessel segments is 1136, and the computation time for vessel connection is less than one hour on a state-of-the-art PC with our current implementation of Alg. 1 and 2 in Matlab.

4. Discussion and future work

In this mostly theoretical paper, we propose a new formulation for an automatic vessel connection method for reconstructing a complete vascular tree from images. Our method leverages high-level prior-knowledge based on principles derived from vascular physiology. A physiological functional cost for the whole vascular tree is derived and an efficient optimization is also developed. The proposed method was inspired by the shape registration work based on Minimum Description Length (MDL) principle [5], where the problem is to find the correspondence between shapes. Shape correspondence is often optimized according to some local criteria, but in [5] a global criterion that evaluates the goodness of statistical shape model is found to be very effective to guide the optimization.

The most similar previous work to ours is that of Bruyninckx *et al.* [3], as briefly mentioned in Section 1.1, where a two-stage approach and basic physiology principles are also adopted. For the first stage, a set of branching/bifurcation joint points instead of vessel centerlines are detected, and during the second stage, the connection problem is formulated to be a Steiner minimal tree problem, where the weight (cost) is obtained from both image intensity and a couple of physiology principles: Murray's law and the minimum volume principle. The problem is nicely formulated, but since a Steiner tree is a much more difficult problem to solve, they need to adopt a global optimization approach (ant colony optimization). Their overall approach is also much more sensitive to the detection stage, because missing one branching/bifurcation points would very likely cause at least one whole segment missing in the final tree, as observed in their results. Using Murray's law, only the perfusion capability at branching/bifurcation joints is considered in their cost function.

As to other closely related work, it has been briefly mentioned in Section 2.2 that MST was directly adopted by a number of vascular modeling work, *e.g.* [4, 8, 25]. There also exist a few publications focusing on the “gap filling” for vessel connection, *e.g.* distance based on vessel tangent orientation [25], adaptive thresholding [9], tensor voting [22]. In all of these papers, the goodness of connection was evaluated in a local range of image or vascular network, instead of the whole vascular tree.

Future work will include further investigation on the approximation for the proposed cost function and an extensive validation for the proposed method. We will also investigate the issue of existence of multiple-trees (forest), and develop a probably hierarchical approach to speed the optimization process for the large scale vascular systems. The interaction between the first (bottom-up) and second (top-down) stage in our approach hopefully can also improve the results.

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Figure 1.
Extra modules for vascular tree reconstruction.

Figure 2.

A 2D result of the proposed algorithm. (1) the original image; (2) Scale-space ridge detection results, where each ridge point are shown as red dot followed by a green tail indicating its orientation; (3) smoothed ridges by splines. (4) vascular tree reconstructed by Minimum Spanning Tree; (5) vascular tree reconstructed by the proposed Rooted Minimum Spanning Tree; (6) vascular tree reconstructed by the proposed optimization process. On (4-6) red circles are used to mark the spots where the connection is obviously wrong.

Figure 3.

A coronary tree reconstructed from a 3D mouse CT image. The root branch is shown in blue, and branches with deepest levels are shown in red. The result of the proposed algorithm has much a more realistic branch level pattern than the one of MST.