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Reconstructing cerebrovascular networks under local physiological constraints by integer programming

Markus Rempfler[a,b,*], Matthias Schneider[b,c], Giovanna D. Ielacqua[d], Xianghui Xiao[e], Stuart R. Stock[f], Jan Klohs[d], Gábor Székely[b], Bjoern Andres[g], Bjoern H. Menze[a,h]

[a] Department of Computer Science, Technische Universität München, Germany
[b] Computer Vision Laboratory, ETH Zürich, Switzerland
[c] Institute of Pharmacology and Toxicology, University of Zürich, Switzerland
[d] Institute for Biomedical Engineering, University and ETH Zürich, Switzerland
[e] Advanced Photon Source, Argonne National Laboratory, Lemont, IL, USA
[f] Feinberg School of Medicine, Northwestern University, Chicago, IL, USA
[g] Max Planck Institute for Informatics, Saarbrücken, Germany
[h] Institute for Advanced Studies, Technische Universität München, Germany

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ABSTRACT

We introduce a probabilistic approach to vessel network extraction that enforces physiological constraints on the vessel structure. The method accounts for both image evidence and geometric relationships between vessels by solving an integer program, which is shown to yield the maximum a posteriori (MAP) estimate to a probabilistic model. Starting from an overconnected network, it is pruning vessel stumps and spurious connections by evaluating the local geometry and the global connectivity of the graph. We utilize a high-resolution micro computed tomography (μCT) dataset of a cerebrovascular corrosion cast to obtain a reference network and learn the prior distributions of our probabilistic model and we perform experiments on in-vivo magnetic resonance microangiography (μMRA) images of mouse brains. We finally discuss properties of the networks obtained under different tracking and pruning approaches.

1. Introduction

Many diseases affect general properties of the cerebrovascular network, examples are arteriosclerosis and dilative vascular malformations changing vessel shape and diameter, but also Alzheimer's and related neuro-degenerative diseases are suspected to affect the general vascularity and global network properties (Hunter et al., 2012; Klohs et al., 2012). Studies investigating such diseases frequently use mouse models for experiments and commonly acquire in-vivo cerebrovascular imagery by means of magnetic resonance microangiography (μMRA). While segmenting and tracing tubular structures is a longstanding field of interest in medical image computing (Aylward and Bullitt, 2002; Frangi et al., 1998; Kirbas and Quek, 2004; Lesage et al., 2009), we approach here the wider – and somewhat neglected (Jiang et al., 2010) – problem of extracting the full vascular network from image volumes under consideration of local geometric properties and global constraints of the vascular structure.

Most vessel segmentation techniques rely on tubularity measures or other vessel enhancement filters (Frangi et al., 1998), and then apply rule-based or learned decision algorithms to segment the vessels (Kirbas and Quek, 2004; Lesage et al., 2009; Schneider et al., 2015). The network graph – representing vessels by their centerline, complemented with additional information such as local radii – can be extracted from binary segmentations using morphological operators (Lee et al., 1994; Pudney, 1998), or by tracking vessels directly by minimal path techniques (Cohen and Kimmel, 1997), e.g. by applying a fast marching algorithm (Benmansour and Cohen, 2011) or a Dijkstra-like scheme (Gülsün and Tek, 2008). We point the interested reader to Kirbas and Quek (2004) and Lesage et al. (2009) for more extensive reviews. In most applications, however, the extracted graphs need further post-processing: Lu et al. (2009), for example, incorporated discriminative classifiers that examine local geometrical features of segments into a hierarchical approach for vessel-structure parsing. In order to deal with imperfections in vascular connectivity of extracted networks, Kaufhold et al. (2012) discussed a supervised learning approach to gap filling and network pruning, whereas Schneider et al. (2014) recently proposed a generative method for gap in-fill that is guided by a simplified angiogenesis model. While segmentation

* Corresponding author at: IMETUM, Boltzmannstr. 11, 85748 Garching, Germany. Tel.: +49 8928910840.
E-mail address: markurem@vision.ee.ethz.ch (M. Rempfler).

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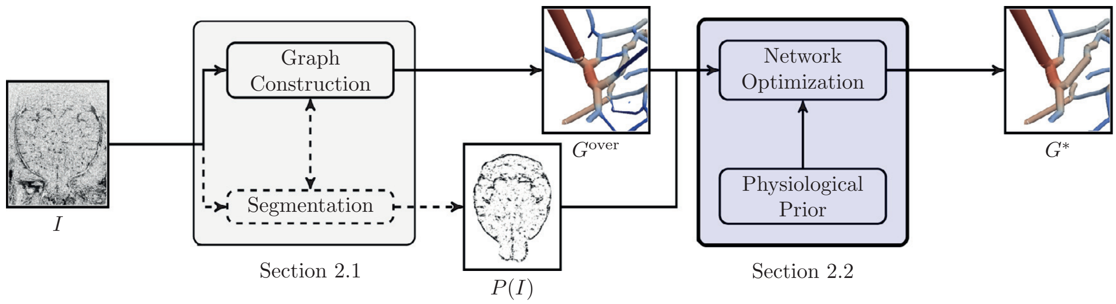

Fig. 1. Workflow: In a first stage, the image volume I is processed so as to obtain an overconnected graph G^{over} as well as a confidence measure for vessels such as the confidence map $P(I)$. In the following step, the network $G*$ is extracted from G^{over} in an optimization scheme that considers both image evidence (according to $P(I)$) and geometric-physiological prior knowledge. In this paper, we focus on the network optimization step, where both image evidence and geometrical relationships of certain network motifs, namely continuing pairs and bifurcations are considered.

algorithms are likely to enforce expected local vessel shape and geometry, only few approaches consider both local properties and global network connectivity when extracting the full network: Jiang et al. (2011) incorporated assumptions about vessel diameters (Murray's hypothesis (Murray, 1926)) in a global optimization problem restricted to vascular trees. Tree shape priors have also been included into the segmentation of vasculature by Stühmer et al. (2013). In a different application, Türetken et al. (2015) introduced recently an integer programming approach that evaluates path coherence and connectivity of general curvilinear structures, such as streets in remote-sensing images or vessels in confocal image stacks. Starting from an overconnected graph, they are pruning edges that do not fulfill desired structural relationships of neighboring segment pairs using a path classifier that is trained from annotated 3-D networks.

All of these approaches enforce local coherence within the extracted network – a general property of the vascular network. More complex local properties of a structural network, however, can be described by network *motifs* (Alon, 2007; Milo et al., 2002). Network motifs are frequently recurring subgraphs, also called building blocks, that are characteristic for a type of network, such as bifurcations in vascular networks.

In this paper, we enforce local geometrical properties similar to Jiang et al. (2011), exploring the relevance of two basic motifs of vascular networks, i.e., the geometrical properties of continuing segment pairs and of vessel bifurcations and following the idea of pruning of Türetken et al. (2015). We present a probabilistic model which combines this geometric prior with local vessel evidence obtained from a segmentation algorithm (Schneider et al., 2015), and show that the maximum a posteriori (MAP) estimate can be computed by an integer linear program (ILP). We learn the global statistic of geometrical properties of the network motifs from a high resolution dataset. Finally, we identify a more efficient scheme to solve the ILP for large datasets and illustrate its application for reconstructing vascular networks from in-vivo μMRA images of the mouse brain.

2. Methods

In this section, we detail on the proposed vessel network extraction method that estimates the most probable network under consideration of image evidence and physiological prior knowledge. As depicted in the workflow (Fig. 1), this method starts from an overconnected network graph G^{over}. Hence, we briefly review the applied segmentation framework and skeletonization method as used in our experiments.

2.1. Vessel segmentation method and construction of the overconnected graph

As a first stage, we transform image intensities into confidence maps by using the framework of Schneider et al. (2013, 2015): In

$$I, G \longrightarrow X \longrightarrow \Omega$$

Fig. 2. Probabilistic model. I: Image; G: (overconnected) Graph; X: Set of binary variables denoting subgraphs of G; Ω: Set of feasible configurations of $\mathbf{x}$.

this approach, multiscale steerable filter templates (SFT) are used as efficient directional filters, offering features that are invariant with respect to the local vessel direction. An oblique random forest (RF) (Menze et al., 2011), which determines splits by solving a linear regression with elastic net penalty in each node, is used for a subsequent classification. The RF assigns each voxel v in an image volume I to a probability $p_v \in [0, 1]$, indicating the local presence of a vessel-like structure.

We apply a threshold θ to the probability volume $P(I)$ and skeletonize the resulting binary volume using distance-ordered homotopic thinning (DOHT) (Pudney, 1998), a method that iteratively removes voxels without altering the objects topology, to derive a network graph $G(\theta)$. We obtain an overconnected network by generating multiple binary segmentations from $P(I)$ with different thresholds $\{\theta_i\}$, skeletonizing each of them by DOHT to $G(\theta_i)$ and superposing them into one network $G^{over}(\{\theta_i\})$. The resulting network contains both segments with low confidence (contributed by graphs from low thresholds θ close to 0), but maintains the high spatial accuracy of a graph that is generated from conservative thresholds (i.e., with θ close to 1). Note, however, that any method which generates an overconnected graph G^{over} by proposing local vessel connections could be used instead.

2.2. Vessel network extraction

The goal of our method is to find the most plausible network $G*$ out of an overconnected network graph $G^{over} = (V, E)$ with edges $E = \{e_i\}$ and given image evidence $P(I)$. We encode subgraphs of G^{over} with a set of binary variables $X = \{x_i\}$ where each x_i indicates whether or not the corresponding segment $e_i \in E$ is active (i.e. $x_i = 1$). Therefore, we arrive at the equivalent problem of determining the MAP estimate of $\mathbf{x} \in \{0, 1\}^{|E|}$, for which we describe a probabilistic model (Section 2.2.1) that considers image evidence, local properties of specific network motifs as well as global connectivity, and derive an ILP that allows computing the MAP network (Section 2.2.2).

2.2.1. Probabilistic model

We formulate a probabilistic model $P(\mathbf{X} = \mathbf{x}, \Omega | I, G)$ according to Fig. 2, where I is the image evidence, G is the given (overconnected) graph and X is the set of binary variables denoting subgraphs of G. Ω is the set of all feasible solutions of $\mathbf{x}$:

$$\Omega = \{\mathbf{x} \in \{0, 1\}^{|E|} : \mathbf{Ax} \geq \mathbf{b}\}, \quad (1)$$

with $\mathbf{Ax} \geq \mathbf{b}$ being the short notation for all hard constraints that will be considered such as those enforcing connectivity. This introduces a