Angiographic image analysis

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Chapter 5

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5.1   Introduction

The important rise of medical imaging during the 20th century, mainly induced by physics breakthroughs related to nuclear magnetic resonance and X-rays has led to the development of imaging modalities devoted to visualise vascular structures. The analysis of such *angiographic* images is of great interest for several clinical applications. Initially designed to generate 2D data, these imaging modalities progressively led to the acquisition of 3D images, enabling to visualise vascular volumes.

However, such 3D data are generally huge, being composed of several millions of voxels, while the useful –vascular– information generally represents less than 5% of the whole volume. In addition to this sparseness, the frequent low signal-to-noise ratio and the potential presence of artifacts make the analysis of such images quite a challenging task. In order to assist radiologists and clinicians, it is therefore necessary to design software tools enabling them to extract as well as possible the relevant information embedded in 3D angiographic data.

One of the main ways to perform such a task is to develop *segmentation* methods, *i.e.*, tools which (automatically or interactively) extract the vessels as 3D volumes from the angiographic images. A survey of such segmentation methods is proposed in Section 5.3. In particular, it sheds light on recent advances devoted to merge different

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image processing methodologies to improve the segmentation accuracy.

Another way to consider computer-aided analysis of 3D angiographic images is to provide human experts with a base of high-level anatomical knowledge which can possibly be involved in more specific analysis procedures such as vessel labelling. Such knowledge can in particular be embedded in *vascular atlases* which are devoted to model qualitative and/or quantitative information related to vessels. A survey of different existing vascular atlases, and ways they can be created is proposed in Section 5.4.

The purpose of this chapter is to provide some general background notions on 3D angiographic image analysis to the reader. Due to space limitations, it is impossible to propose an exhaustive overview on vessel segmentation and vascular knowledge modelling. Consequently, Sections 5.3 and 5.4 propose partial, but hopefully relevant, states of the art on these topics. They present some of the most classical and/or recent related works, and some pointers on more complete surveys linked to the main topics of this chapter (or to connected research fields, for the sake of completeness). They also present, in a more accurate fashion, some recent contributions of some of the authors, especially related to vessel segmentation.

5.2   Clinical context

Vascular pathologies are one of the main causes of morbidity and mortality in the Western world, and thus constitute an important issue in public health. The causes are manifold, from traumatic lesions (due to accidents) to genetic vascular diseases (such as some arteriovenous malformations), *via* those linked to obesity and stress (such as atheromatosis and diabetes).

An anomaly affecting vessels can provoke perturbations in organ circulation as well as in tissues supplied by the involved vascular network. If the lumen of the arteries is shrunk, such as in an atheromatosis disease, blood flow will be affected and the associated organ will be insufficiently supplied, leading, in the worst cases, to ischemia, and then tissue death. The breaking of a vessel, normal (as in a trauma) or pathological (as in an aneurysm rupture), can cause hemorrhages.

The various angiographic imaging techniques have to determine the nature of potential and actual vascular problems, and to accurately identify the affected vessels, in order to select the most effective treatment. Magnetic resonance angiography (MRA) was developed during the last decades, and presents the advantage to be non-invasive. X-ray angiography, and particularly computed tomography angiography (CTA) is invasive and irradiating, but remains, however, more performing one in terms of image accuracy.

5.3   Vessel segmentation

The segmentation of vascular structures from 3D images is a particularly challenging task. Here, the notion of segmentation is considered in a large sense. From an image processing point of view, segmentation consists of partitioning an image into an object, *i.e.*, a structure of interest, and a background, *i.e.*, the remainder of the image volume.

In the context of angiographic imaging, we consider that vessel segmentation embeds (*i*) methods that detect either whole vessels (*i.e.*, their lumen and/or walls) or their medial axes, and/or (*ii*) methods that perform low-level processing or high-level knowledge extraction (*e.g.*, vein/artery discrimination [100, 103] or vessel labelling [14, 42]). We also consider some methods which could be classified as filtering ones, since their purpose is to perform vessel enhancement, which consists mainly of denoising, but also of vessel reconnection (for example in case of stenosis, or of signal loss [27, 76]).

As discussed above, the difficulty to perform vessel segmentation is due to the sparseness of data, and the possible presence of irrelevant signal (other tissues, artifacts or noise). Moreover, anatomical properties of vessels are highly variable in size, appearance, geometry and topology, and even more so in pathological cases like aneurysms, stenoses, calcifications or arteriovenous malformations.

As stated in Section **??**, there exist several kinds of angiographic data, generally well-fitted for visualising specific vascular structures, and consequently for dealing with specific clinical issues. The choice of a segmentation method is often linked to the type of considered images, the vessel(s) to study and the clinical purpose. The next section discusses the different methodological segmentation strategies.

5.3.1 Survey of vessel segmentation methods

General overview

Several surveys devoted to 3D vascular segmentation have been proposed during the last ten years. The survey proposed in [94] focuses on vessel segmentation from MRA images[2], and divides them into skeleton methods (with an interest in medial axes) and non-skeleton ones (that aim at detecting whole vascular volumes). Another (globally similar) classification is proposed in [51] which deals more generally with vessel segmentation from any kind of data independently of their dimension or acquisition technique. Finally, the most recent survey [56] mainly refers to 3D vessel segmentation from MRA and CTA, and divides its description into (*i*) the *a priori* information which can be used for segmentation, (*ii*) the basic tools using this information for detecting vessels, and (*iii*) the methodological frameworks involving these tools, as well as a discussion on pre- and post-processing considerations.

In the next section, we introduce the segmentation methods divided into eight main families corresponding to the main image processing strategies on which they rely: region-growing, differential analysis, model-based filtering, deformable models, path finding, vessel tracking, statistical approaches, and mathematical morphology[3].

Region-growing methods

Region-growing has been one of the first strategies considered for image segmentation [117], and in particular medical/angiographic onesBasically, region-growing relies on

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[2]Part I of this survey [93] also describes MRA acquisition techniques, which can be read in complement to Section **??**.

[3]By lack of room, it has been chosen to omit those which led to few publications. Such methodological families, as neural network-based methods [52], for instance, may however deserve the reader's interest.

two elements: one (or several) seed(s) [1] assumed to belong to the structure of interest to be segmented, and a propagation criterion, enabling to segment the object from the seed, by iterative addition of adjacent voxels.

In the case of vessel segmentation, seeds are generally defined interactively inside vessels. The seeds can also be detected automatically, especially in the case where they constitute the root of a vascular tree [69]. The possible definition of several seeds can straightforwardly lead to an application of region-growing to vessel separation, and in particular, to vein/artery discrimination. In such a case, a set of seeds is defined for arteries and veins, respectively. A competitive region-growing is then performed, based on *ad hoc* propagation criteria (*e.g.*, a measure of grey-scale connectedness in [100])[4].

The propagation criterion is commonly based on intensity properties, related to the high-intensity vascular signal. However, more sophisticated properties can also be embedded in this segmentation strategy. In particular, it has been proposed to consider *a priori* knowledge related to the shape and size of the vessels to be segmented [68], or to their topology [78]. The correctness of the orientation of the vessels during the segmentation process has also been considered by proposing "wave propagation" strategies [115], which aim to constrain the segmentation front to remain normal to the vessel axis. It may be noticed that this kind of approaches has been further used for vessel tracking methods (discussed hereafter in the section). The concept of wave propagation has also further led to the development of methods related to both deformable models (level-sets) and path-finding approaches, namely, fast-marching methods [61].

Region-growing methods rely on a simple algorithmic framework, which makes their development and use quite easy and induces a low (generally linear) computational cost. In addition, they guarantee termination which is not systematically available for other non-monotonic strategies. However, the connectivity hypothesis intrinsically associated to this strategy constitutes a weakness, since the method may fail in segmenting vessels in case of vascular signal loss (due to partial volume effect, or flow artifacts, for instance). *A contrario*, the use of a criterion being too permissive may lead to leakage phenomena, and a final over-segmentation of vessels, requiring to anticipate this effect [66]. In this context, region-growing methods have often been preferentially devoted to the segmentation of large and/or well-contrasted vessels (for which intensity and connectivity hypotheses are generally reliable).

Differential analysis

Vessels are generally bright structures among a dark background. If an image is viewed as the discrete analogue of a function from $\mathbb{R}^3$ to $\mathbb{R}$, vessels then appear as the maxima of this function. Consequently, it may be possible to detect them by analysing the differential properties of the image.

In order to deal with the discrete/continuous issue involved by this strategy, the considered (discrete) image is convolved with a series of Gaussian derivatives with

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[4]Note that, by duality, region-growing also provides solutions to segment vessels by skeletonization. In such a case, the growing process starts from a seed being a subset of the background (which can then be automatically defined), and generally includes topological constraints in the propagation criterion [27, 76].

different standard deviations and in different directions, the obtained responses being combined into a matrix.

In the case of first derivatives analysis, this matrix, which is the covariance matrix of gradient vectors [2, 8], is called the *structure tensor*. Except for vessel segmentation, the first derivatives have also been involved in *diffusion filtering*, which consists in propagation of information in the orientations suggested by these derivatives [60].

In the case of second derivatives analysis, the resulting information is gathered in the *Hessian matrix*. The main idea behind eigen analysis of the Hessian matrix is to extract one or more principal directions of the local structure of the image. This gives the direction of the minimal curvature, the principal one in the tubular structure and a high curvature in the vessel cross-section plane, which makes the filter more efficient to the contrary to line filters.

Compared with the image gradient, the Hessian matrix can capture the shape characteristics of objects, such as tubes, planes, blob surfaces or noise. In particular, the eigenvalues of the Hessian matrix can be combined into a *vesselness* function in order to describe plate-, blob-like and tubular objects [34, 53, 84].

These methods can be performed in multi-scale frameworks in order to detect objects of different sizes. It has to be noticed that the choice and number of the considered scales is particularly important in such methods. If performed at a unique scale, they do not detect vessels of different sizes, and especially those out of the range of the considered scale. Conversely, if performed at numerous scales, they can potentially detect all the vessels but they become computationally quite expensive.

In addition, the robustness of such methods to noise is strongly related to the considered scale. For large scales, the blurring effect of Gaussian filtering tends to remove noise effects, and unfortunately, smaller objects. *A contrario*, for small scales, the noise is hardly corrected by this filtering, and may bias the derivative evaluation accuracy, thus requiring to incorporate assumptions related to noise in the method [113].

Despite some weaknesses, which require a specific care, derivative-based methods provide efficient solutions for detecting vessels, especially in a multi-scale framework, and have then often been considered for the design of segmentation methods based on model filtering (see next section) or for the guidance of deformable models, for instance.

Model-based filtering

In general, vessels appearance can be used as prior for segmentation. In this case, such prior can describe vessel specific characteristics: photometric (usually being brighter than the background) and/or geometric (curvilinear). The most simple ones are *intensity* and *geometry-based models*, which are often combined in deformable model methodologies (see next section). Further, we describe such models in the complexity increasing order.

Intensity models Intensity models, which are among the simplest ones, strongly depend on the considered imaging modality. They can integrate brightness, contrast and gradient prior, but also imaging properties, like intensity ranges or intensity vari-

ation based on location, or even noise distribution [2] (see also Section "Statistical approaches" for a discussion on noise modelling).

In [111] a cylindrical parametric intensity model is directly fit to the image intensities through an incremental process based on a Kalman filter for estimating the vessels radii. While in [79], local neighbourhood intensities are considered in a spherical polar coordinate system in order to capture the common properties for the different types of vascular points. A natural integration into this kind of models is background description [85, 102].

While being simple, intensity models are highly dependent on the nature of images. Therefore, they have to be tuned for all kinds of circumstances, like artifacts or other image distortions, as well as to compensate for image variability.

Geometry models   The assumption that vessels are elongated thin objects, globally similar to tubes has been used for the design of several geometric models, such as *generalised cylinders*, *superellipsoids*, *Gaussian lines*, or *bar-like* profiles [9, 53, 102].

Based on second-order derivatives (see previous section), several models incorporating geometrical properties have been developed. In [34], an ideal cylinder is proposed in order to enhance vessels within a measure called *vesselness*, while in [84] a more general model incorporates elliptical shapes.

The bifurcation issue has also been considered, for instance in [3] where a bifurcation models is proposed and optimised based on vessel centerline information.

Geometry models are powerful tools for describing vessels and aiding to their further extraction within tracking schemes or by deformation. However, these methods, assume image regularities that are present in high-quality images but not necessarily in noisier ones, nor in pathological cases. Furthermore, they often require careful parameter tuning, which may change from one data-set to the next. They can be used together with the intensity models often, combined in probabilistic and/or statistical approaches contributing to decision-making whether pixel belongs or not to a vascular structure.

Deformable models

Deformable models aim at fitting a geometric hypersurface (*e.g.*, a 2D surface in a 3D image), by moving it and modifying its shape from an initial model, under the guidance of several (generally antagonist) forces: *external* ("data-driven") ones, related to the image content, and *internal* ("model-driven") ones, devoted to preserve correct geometry properties (*e.g.*, regularity). Such models have been intensively used in the field of image analysis due to the following advantages: arbitrary shape representation, topological adaptivity, sub-pixel precision, etc.

Among the most classical methods, *snake* (often used in 2D in order to segment vessel cross-sections), have been considered, *e.g.*, in [64], or in [46], where two (1D and 2D) snakes are used for both segmentation and stenosis quantification.

Level-sets constitute another classical type of deformable models, and rely on an Eulerian version of contour evolution with partial derivative equations. The contour is integrated as the zero-level of a higher dimension function (level-set). In [59], an original level-set based scheme proposes to deform an initial boundary estimate toward the vascular structures in the image using a codimension-two regularisation force, based

on the vessel centerlines instead of the vessel surface. An other level-set based method [62] proposes to estimates the background and vessel intensity distributions based on the intensity histogram, to more efficiently steer the level-set onto the vessel boundaries.

Several efforts have been conducted to improve deformable models in the quite specific case of elongated structures. In this context, [104] proposes to use flux maximisation as an alternative curvature-based regularisation which make surface normals evolve according to gradient vector field. The key idea was to evolve a curve or a surface under constraints by incorporating not only the magnitude but also the direction of an appropriate vector field.

In [54], local variances are measured with first-order derivatives and are propagated according to their strengths and directions with an optimally oriented flux reporting more accurate and stable responses and higher robustness to disturbances from adjacent structures in comparison with Hessian-based measures.

The major advantage of deformable models methods is that they are sensitive to weak edges and robust to noisy structures. However, the intensity variation inside vascular structures can generate significant intensity gradient with this undesired discontinuity stopping the contour evolution at these regions. Due to this local minima, the initial forces should be described with such precision that the final object borders are not far from the initial ones. While the evolution of the deformation can be a costly process. But, by integrating vessel features and forces in powerful optimisation schemes help overcoming these problems.

Statistical approaches

Vessel segmentation based on statistical approaches generally relies on specific assumptions related to the intensity distribution of the vascular/non-vascular signals in MRA data (only very few statistical methods have been devoted to CTA, see, *e.g.*, [32], which proposes a particle-filtering strategy for coronary arteries segmentation), and especially physical models of blood flow. If the number and the nature of these distributions is supposed to be known correctly, it is then possible to determine their respective parameters (and in particular the mean intensity characterising the associated structures), *via* a standard Expectation-Maximisation (EM) technique [23].

In MRA, two or three distributions are generally considered, for the blood, and the other anatomical structures and the background, respectively. They led, in particular to the definition of Gaussian-Gaussian-uniform [107] and normal-Rayleigh–2×normal [80] mixtures for time-of-flight (TOF) MRA, and Maxwell-Gaussian [19], Maxwell-Gaussian-uniform [17] mixtures for phase-contrast (PC) MRA. In [18], a hybrid model, enables to choose between these two kinds of mixtures. Alternatively, to these "constrained" mixture choices, it has been proposed in [29] to consider a linear combination of discrete Gaussians with alternate signs, involved in a modified EM, which enables to adaptively deal with both laminar and turbulent (pathological) blood flow [28].

In the primarily considered strategies, the determination of the vascular intensity led to a straightforward segmentation by thresholding of the image (sometimes enriched by a hierarchical analysis of the image by octree decomposition [107]). From an algorithmic point of view, segmentation improvements were also performed in con-

sidering of spatial information (*i.e.*, statistical dependence) between neighbour voxels, by integrating Markov random fields (MRF) [38] in a post-classification correction step [80]. In other works, speed and phase information provided by PC-MRA were fused and involved in a maximum *a posteriori*-MRF framework to enhance vessel segmentation [17, 18].

Statistical methods globally inherit from the strengths and weaknesses of the EM algorithm. First, they generally require to establish hypotheses on the signal distribution. Moreover, they involve several parameters, for instance, weight, mean and standard deviation, of the distributions. The initialisation of the segmentation process then requires a special attention. Indeed, the convergence may possibly depend on the quality of the initial distribution settings (sometimes automatically determined based on heuristic rules [17, 107]). As for any optimisation strategy, the termination also requires to decide whether the process has correctly converged or not (which is sometimes empirically determined, for instance by a maximal number of iterations [107]). Finally, since the segmentation process is strongly based on photometric properties (the results often consist of global or local thresholdings), higher-level knowledge such as geometric assumptions are hardly considered, and require post-processing steps based on a statistical framework [80], or, more efficiently the collaboration of alternative image processing techniques (see examples in Section 5.3.1).

Path finding

Based on extremal intensity and connectedness criteria, the detection of a vessel segment (or more precisely of its medial axis) can be expressed as the determination of a minimal cost path in a weighted graph modelling voxels, their neighbourhood relations and their intensity.

Vessel segmentation based on such strategies can rely on standard minimal path finding techniques [25] (*i.e.*, on "global" minimisation strategies, while methods categorised in the next *Vessel tracking* section will rely on "local" (step by step) minimisation strategies). This is, for instance, the case in [75].

Alternatively to classic path-finding methods, fast-marching strategies [101] have been considered. They are both related to the level-sets methodology (see Section "Deformable models") and minimal path-finding ones (they remain, in particular, consistent with the continuous formulation of the minimal-path research). By opposition to fully discrete path-finding, they enable in particular to determine paths with a sub-voxel accuracy [4].

The methods based on path-finding are globally well-fitted for the detection of vessel medial axes, especially in the case of small vessels which justifies in particular their frequent use in coronary detection. (For larger vessels, the optimal path may diverge from the medial axis, leading to eccentric results, this issue then requiring a specific care [57].) However, it has to be noticed that efforts have also been conducted to develop segmentation methods enabling to extract both vessel axes and vessel walls [7, 57], which express the whole vascular volume segmentation as the minimisation of a path in a space enriched with a supplementary "scale" dimension corresponding to the vessel radius.

Despite attempts for segmenting whole vascular trees [114], such methods generally remain devoted to the segmentation of vessel segments, thus requiring to interactively provide at least an initial point, and also a final one [75, 108]. In this case, they may be robust to noise, and signal decrease (or short signal loss) along the vessel, especially in case of stenoses. These methods being based on monotonic and/or finite algorithmic processes, their termination is guaranteed, and their theoretical algorithmic cost is generally low. Practically, the computational cost may however be high, and in this context, the proposal of initial and final points can potentially enable its reduction by computing paths from both points simultaneously [75].

Tracking methods

By opposition to path-finding methods, tracking ones consist in finding a vessel in a local fashion, by progressively determining successive segments composing it. Such an approach requires to interactively propose a seed, namely the starting point of the tracking process, located in the vessel, and (in most cases) the direction in which the vessel has to be tracked.

This strategy has to be applied step by step, a small segment of the vessel being detected at each step. The principal issues to consider in such methods are the determination of a correct geometry of the detected segment (namely the determination of its cross section), the determination of the vessel axis, and the evaluation of the direction of the next segment to be found (*i.e.*, the trajectory modification), or equivalently, the next point in the vessel. Less frequently, vessel tracking methods, such as the one proposed in [63], directly perform a more global iterative vascular volume detection, corrected, at each step, by the analysis of the induced vessel axis, which can in particular be constrained by *ad hoc* topological hypotheses.

The determination of the vessel cross-section at the current point (which enables in particular its correct repositioning on the vessel axis) can be performed according to several strategies. The use of a gradient-based measure is considered in [109] (a centerline measure based on the vessel profile then enables to approximate the vessel centerline, even in case of non-circularity). The explicit determination of vessel cross-sections to estimate the vessel axis may however be avoided. In particular, it can be done by considering that the medial axis is necessarily located on a ridge point [5], which may be detected thanks to second-derivatives criteria. Such an approach requires *a minima* the use of cross section information related to the size of the vessel (in order to determine the correct scale factor), and circularity hypotheses. It can also be performed based on a local optimisation of 3D models [102, 112], which may also lead to the determination of the vessel axis orientation. More classically, the next tracking point may be determined according to the best fit of a sphere modelling the vessel into the image [12, 47, 69].

Despite a few attempts to deal with the case of bifurcations, which can enable the recursive processing of a whole vascular tree [9, 13, 31], vessel tracking is especially well-fit for the segmentation of single vessels. In this case, the termination has to be considered. Some methods require, in particular, to provide both a starting and an ending point [109].

It has to be noticed that, similarly to the other local approaches (which aim at

detecting a part of the vessels, and/or are guided by providing a seed), such methods present a generally low algorithmic/computational cost.

They however present some drawbacks related to the determination of multiple parameters and to possible error propagation (which characterise such local methods), potentially leading to incorrect segmentation if vessel orientation and/or axis is miscalculated at a given step, for instance due to a bifurcation, non circular section, or a strong axis curvature.

Mathematical morphology methods

Mathematical morphology (MM) is a well-established theory of non-linear, order-based image analysis. Fundamental texts on morphology include the books by Serra [86, 87], but more recent and more synthetic texts are also available, including the works by Soille [89] and by Najman and Talbot [72].

Filtering thin objects with morphology can be achieved using appropriate structuring elements. Typically, thin structuring elements include segments and paths, combined over families. To account for arbitrary orientation, one can use families of oriented segments and compute a supremum of openings or an infimum of closings as described in [90].

To account for noise or disconnection, families of incomplete segments can be used instead, yielding so-called *rank-max openings*, which are just as efficient and also described in the same reference.

Paths are elongated structuring elements, but that are not necessarily locally straight. Even though the size of families of paths grow exponentially with their length, there exists a recursive decomposition that makes the use of such families tractable [43]. As with segments, it is useful to account for some discontinuities using so-called *incomplete paths*. As with segments, there exists an efficient implementation [95]. *In fine*, path and segment operations are comparable in speed.

In [96], it is shown that path and segment morphological operators significantly outperform linear and steerable filters for the segmentation of thin (2D) structures, even in the presence of heavy noise. Paths operators have been extended to 3D in [44], and show to outperform all other morphological filters for thin object segmentation in 3D, both for efficiency and performance.

Connected operators are also supremum of openings or infimum of closings, but use families of structuring elements that are so large that it makes little sense to present them in this way. Instead, the concept of connectivity is used [83, 105]. The simplest of those is the area opening or closing. Informally, the area opening suppresses objects that are smaller in area than a given size λ. It extends readily to arbitrary lattices, and corresponds to a supremum of openings with a very large family of structuring elements: all the connected sets that have an area smaller than λ. In the continuum, this family is not countable, but in the discrete case it is still very large. Fortunately it is not implemented in this way. A very efficient way to implement this operator is via the *component tree* [65, 71, 82].

In [106], a scale-independent elongation criterion was introduced to find vascular structures, while in [11], component tree was mixed with classification strategies to segment 3D vessels in an automated fashion.

Other useful connected operators are thinnings rather than openings, as they make it possible to use more complex criteria for object selection, for instance using elongation measures, that are not necessarily increasing.

Hit-or-miss transforms repeatedly use pairs of structuring elements (SEs) to select objects of interest, rather than single SEs. In [10, 68], authors used such operators for 3D vessel segmentation, including brain, liver and heart vessels.
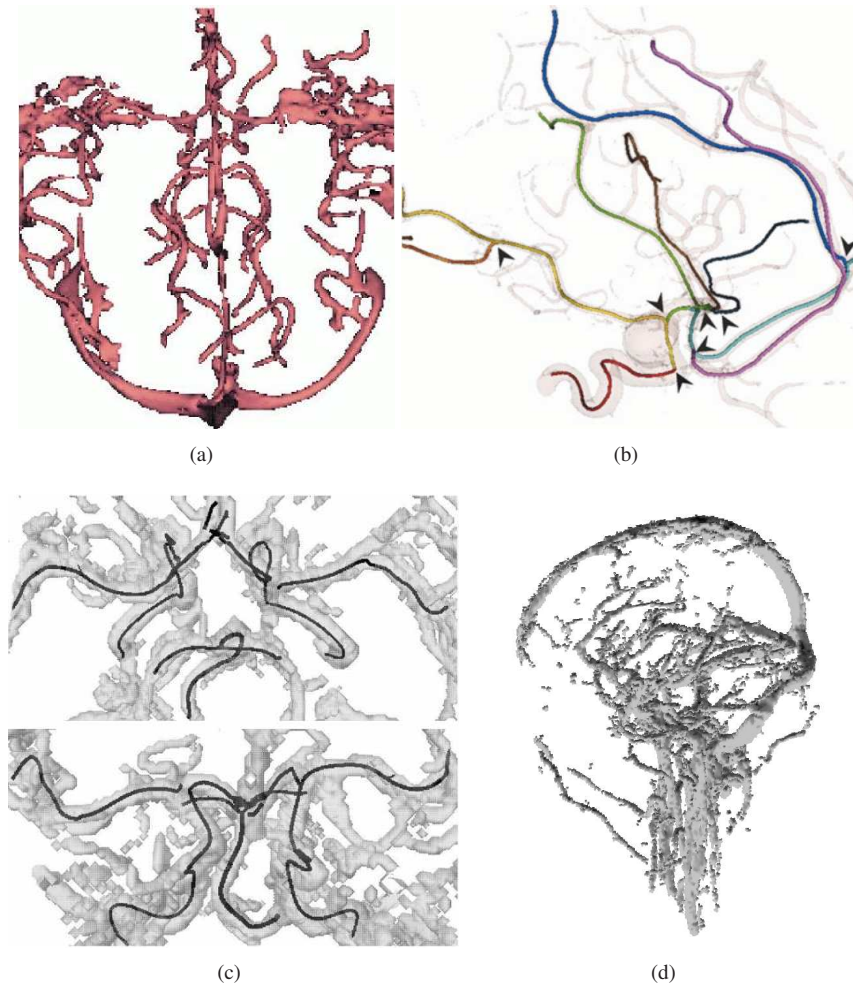

Figure 5.1: Vessel segmentation examples. (a) Brain vessels segmentation based on deformable models. (b) Brain arteries segmentation based on path-finding and statistical approaches. (c) Brain arteries segmentation based on vessel tracking. (d) Brain vessels segmentation based on grey-level hit-or-miss transform. Illustrations from (a) [59], (b) [110], (c) [31], (d) [68].

Hybrid methods

Despite the huge amount of methodological contributions dedicated to 3D vessel segmentation, proposed during the last twenty years, the results provided by such segmentation methods generally remain perfectible.

The handling of under-segmentation (especially in the case of small vessels, whose size is close to the image resolution, of signal decrease, or of partial volume effect) and over-segmentation (especially in the case of neighbouring with other anatomical structures, or of high intensity artifacts), the robustness to image degradations (low signal-to-noise ratio), the ergonomy (automation, or easy interaction), the low computational cost, the guarantee of termination and convergence, accuracy of the result (for instance, the ability to provide results at a higher resolution than the image one) are desirable properties for such methods. Unfortunately, none is generally exempt from drawbacks, even in the frequent (and justified) case where the method is devoted to a quite specific task, vascular structure, and/or image modality.

As nearly all the main strategies of image processing have been –not fully satisfactorily– investigated to propose solutions to this issue, a reasonable trend during the last years has consisted in designing hybrid segmentation methods obtained by crossing methodologies. An alternative way to overcome this issue is to inject more guiding knowledge in the segmentation processes, which justifies –among other reasons– the generation of anatomical vascular models, as discussed in Section 5.4. These strategies aim, in particular, at taking advantage of (distinct and complementary) advantages of different segmentation techniques.

A synthetic overview of such hybrid methods is proposed hereafter.

Principal strategies Hybrid vessel segmentation methods present a range of possible solutions for overcoming certain weaknesses of each method and combining their advantages.

One of the most popular hybrid methods is combination of multi-scale differential analysis within vessel detection schemes as in [34, 84] with deformable models, such as level-sets [15], B-spline snakes [33] and maximum geometric flow [24, 103].

The deformable method with energy minimising functionals has also been combined with statistical region-based information in a multi-scale feature space for automatic cerebral vessel segmentation [45].

The tracking strategies have been as well reinforced by gradient flux of circular cross-sections as in [55], while in [35] a multiple hypothesis tracking was used with Gaussian vessel profile and a statistical model fitting.

In [110] a probabilistic method for axis finding is used within a tracking with minimal path finding strategy together with a possible used guidance. This method is especially well-fitted for pathological cases.

Multi-scale morphology has been used with Gabor wavelets (providing vessel size and direction) filters in [92]. Advantage of the Gabor wavelet that it is capable of tuning to specific frequencies allowing estimation of the vessel dimension while the morphological top-hat filter enhances the contrast between vessel structures and background.

5.4 Vessel modelling

5.4.1 Motivation

Context

The availability of accurate knowledge related to anatomical structures is of precious use in nearly all the fields related to medical image analysis, and more generally to medical applications. Being able to know where an organ is located, what its shape, dimensions, functions, cellular or chemical composition, and its spatial relations or collaborations with other organs are, constitutes the basics of anatomy and medicine.

In the case of vessels, and more generally of vascular trees[5], the anatomical knowledge can be classified into three categories:

- *morphological* properties: what is the shape of a vessel (cross-section, trajectory), its size (diameter, cross-section area), its orientation, etc.?

- *structural* properties: what is the topology of a vascular network (number of branches, bifurcations, presence of cycles/anastomoses), its position, its spatial relations with other organs, etc.?

- *functional* properties: what are the vascular territories of an organ (*i.e.*, what parts of an organ are supplied by a given branch of a vascular network)?

In the field of angiographic image analysis, the question of functional properties, and more specifically the partition of an organ into vascular territories has not been intensively considered. In the case of coronaries, the vascular territories are generally implicitly provided by the different branches of the coronary tree (the knowledge of such regions is of actual importance for determining the parts of the heart being affected by vessel stenoses, and possible subsequent heart attack). It will be observed in the sequel of this chapter that the computational modelling of these branches has been carefully studied for several years. In the case of cerebral vasculature, the different areas of the brain supplied by the main branches originated from the Willis polygon have been described since long ago in the medical literature (see, *e.g.*, [70, 97, 98] for recent contributions)[6]. But these areas have not yet played a crucial role in angiographic/medical image analysis, despite their potential helpfulness. Similar considerations can be made for the liver vascular networks, and in particular the portal network, the branches of which define the main hepatic anatomical segments [21].

Usefulness

The other two kinds of anatomical knowledge, namely, morphological and structural ones, have been the object of a few works related to medical image analysis since the

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[5]From a structural (and more especially from a topological) point of view, the terminology of "tree" is generally incorrect for most of vascular networks, despite its frequent use in the literature devoted to angiographic imaging. In the sequel of the chapter we will generally distinguish vascular *trees* from vascular *networks*. This distinction will be clarified in the next sections.

[6]A notion of "vascular areas", which actually does not match the anatomical notion of vascular territories has been introduced in [78] in order to propose a partition of the cerebral volume enabling to facilitate the segmentation of vessels from PC-MRA data.

end of the 80's. In particular, the coronary tree and the (arterial and venous) networks of the brain have been considered.

The first studies, related to the heart, have essentially been devoted to gather and model structural information related to the coronary arteries in order to assist the radiologists in their analysis of vessels from CT data, especially for the diagnosis and follow-up of stenoses and their consequences on heart blood supply. The globally simple structure of the coronary tree and its (relative) invariance has led to the design of the first vascular models. Such vascular models will be referred to as *atlases*[7] in the sequel of the chapter. A survey of this first family of (deterministic) atlases is proposed in Section 5.4.2.

More recent studies, essentially devoted to the cerebrovasculature, have intended to gather and model morphological information related to potentially complex vascular networks. It has to be noticed that, by opposition to vascular structures such as coronary arteries or hepatic vessels, vascular networks as the cerebral ones are not actually tree structures. A *vascular tree* originates from a single vessel, which progressively divides itself (by bifurcations) into branches, leading to an arborescent hierarchy (which, in particular, does not present any cycle). Vascular networks, such as the cerebral ones, present a more complex organisation. They can originate from several vessels, which divide themselves to refine into smaller branches, but which can also join together to give birth to new vessels, or present cyclic structures, as anastomoses. To the complexity induced by the structure of such vascular networks, one must add the complexity induced by the nature of the vessels visualised in the considered images (both veins and arteries, large and small vessels), from the image modalities (generally non-injected data, especially in MRA, in the case of brain vessels), but also from the anatomical variability of the vessels (from both morphological and structural points of view). In this context, the design of no longer deterministic, but *statistical* atlases had to be considered. A survey of this second family of atlases is proposed in Section 5.4.3. One of the main uses of such statistical atlases is the guidance of automated vessel segmentation procedures [68], which is a crucial step for several medical image analysis applications.

5.4.2 Deterministic atlases

The first works on vascular atlases have consisted in developing *deterministic* models of the vessels. By deterministic, we mean that a model is a (representative) example of what can be a vascular network. Although being a good (and actually useful) representation of the anatomical truth, such a deterministic atlas is however not necessarily able to take in consideration in an accurate way the interindividual variability. Broadly speaking, these atlases can be seen as a direct transcription of the models described (both textually and visually) in the anatomy literature. The pioneering works related to this topic were actually based on this approach.

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[7]The notion of atlas has been the subject of a quite intensive research activity during the last fifteen years, especially in the field of brain imaging. The emergence of *computational anatomy* [39, 50, 99] is, in particular, a direct expression of such research activities.

Pioneering works

To the best of our knowledge, the first vascular atlas generated from angiographic data has been developed for the modelling of coronary arteries [26]. This "hand-made" atlas consists of a (piecewise linear) skeleton modelling the main coronary artery segments and branches, and then provides information on topology (*e.g.*, position of the bifurcations), position and trajectory of vessels. Starting from 2D arteriographies of 37 patients, vessels were manually segmented from two orthogonal views, from the origin of the coronaries to the most distal visible point on each considered branch. A total set of approximately 100 points was then regularly sampled on each segmented tree, leading to a 3D mean positioning of each point. An interactive choice of the structures to be visualised, and the visualisation angle could then permit to automatically generate 2D projections of the atlas. At the same period, a second approach has been proposed in [36], relying on a model composed of two orthogonal planes embedding a structural and spatial representation of each one of the left and right coronary trees. Based on this pseudo-3D reference, a symbolic description of the arteries is proposed, providing in particular information on branch names and hierarchy, position, (qualitative) orientation, or vascular territories. This description was made by use of declarative programming with each predicate formalising a given information related to a vessel, while some more general rules modelled heuristic information, such as continuity or angular limits at bifurcations.

By opposition to methods such as [36], which rely on bases of semantic knowledge, those which took advantage of the emerging technologies offered by computer graphics at the end of the 80's (as [26]), gave rise to related strategies, essentially based on graph modelling and geometric information.

Graph-based and geometric atlases

Among the methods aiming at generating deterministic atlases, one can distinguish those based on graphs, and those based on geometry. The first ones essentially focus on a symbolic description of the vascular structures (independently from their embedding in the 3D space, *i.e.*, from their anatomical reality), while the second ones especially aim at defining such models as objects which "match at best" a spatial reality.

One of the main uses of such atlases, is the labelling of coronary branches, *i.e.*, the automatic naming of vessels, in order to assist radiological analysis. The extraction of reliable vascular information from cardiovascular data (generally 2D or 3D CT angiography) is of precious use for coronary disease assessment. In this context, it is not only required to segment these vessels (which is a non-trivial task, subject to strong research efforts by the medical image analysis community [67]), but also to be able to name each branch of the coronary tree, in order to facilitate the radiological analysis. Such a highly semantic task can not, of course, be carried out without using high-level *a priori* anatomical knowledge. Based on these considerations, several vascular atlases have been involved in –and sometimes specifically designed for– this labelling task [14, 30, 36, 41, 42].

Graph-based atlases   The extraction of a graph modelling the structure of a vascular network (*i.e.*, assigning an edge to each vessel branch, and a node to each junction/bifurcation) has been a purpose frequently considered by the first vessel segmentation methods devoted to 3D angiographic data [37, 115]. Note that the main weakness of these first approaches was propagation of segmentation errors in the obtained model.

A solution proposed in [30] relies on the data collected, and validated, in [26]. It is proposed to define both a symbolic graph-based atlas, which models the tree structure of the coronary arteries, and to couple it with a geometric 3D atlas which models spatial and geometric relationships. Unclassically, the nodes of the graph represent vessel segments while the edges model their bifurcations. Each node of the graph is then associated with a vessel name, a width, but also a list of points located on the vessel medial axis. This information then intrinsically provides a geometric model of the vessels.

In order to automatically build a graph-model of a vascular tree without depending on possible errors inherited from the segmentation process of real images, an alternative consists in generating such a graph from a realistic anatomical phantom. This is the approach proposed in [14] for generating a graph-based atlas of the coronary arteries. The use of a phantom enables to easily obtain a segmentation (which can be validated *a posteriori*) and to derive, by a topological post-processing, curvilinear structures enabling to define a graph structure. In [14], such an atlas can be achieved by storing at each edge/vessel segment information attributes such as its name, length, orientation and diameter.

Geometry-based atlases   The works described above have focused on vascular structures presenting simple properties, namely the coronary arteries, out of their anatomical neighbouring context. In recent works, efforts have been conducted to design vascular atlases related to more complex structures. These contributions rely, in particular, on the use of geometric models, and specifically surfacic meshes.

In [74], a geometric atlas of the whole cerebral vascular network is proposed (see Figure 5.2(a)). This network is quite complex, being composed of veins and arteries of varying sizes (at the resolutions available in 3D CT and MR angiographic data, namely 0.5 mm), organised in a non-arborescent fashion. The generation process, based on the TOF MRA of a healthy patient, is composed of several iterative steps, the most crucial of which is segmentation (performed manually, for the sake of correctness), medial axes determination and topology correction (also performed interactively), vessel surface generation, quantitative knowledge extraction and vessel labelling. It leads to a quite accurate vascular atlas providing information on the type of vessels (arteries or veins), their position in the intracranial volume, their name, size and topology. Such an atlas, essentially designed with high-level image processing tools, but in a basically manual fashion, however, remains strongly related to the only patient involved in the image acquisition process.

In [58], a geometric atlas of the whole heart, made of surfacic meshes corresponding to different anatomical structures, is proposed (see Figure 5.2(b)). In addition to the coronary arteries, it also models several anatomical structures such as the heart chambers and the trunks of the connected vasculature (the model generation of which

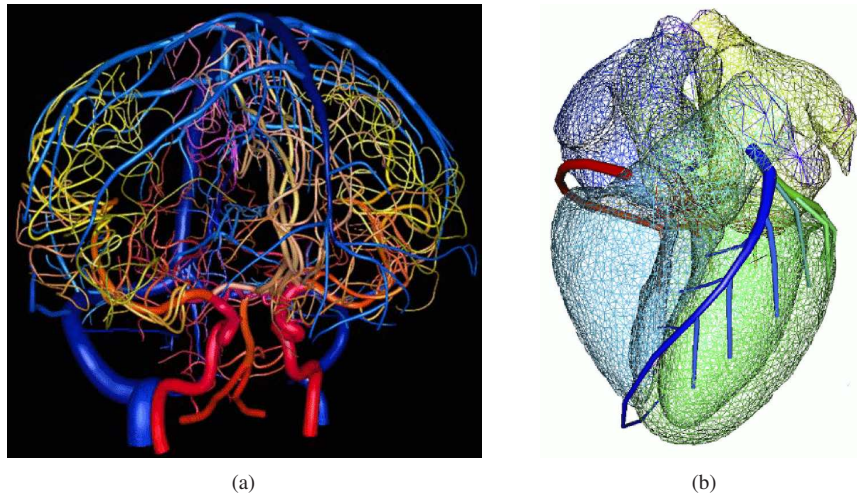(a)   (b)

Figure 5.2: Geometry-based atlases. (a) Atlas of the cerebral vascular (arterial and venous) networks. (b) Atlas of the whole heart and of the coronary arteries. Illustrations from (a) [74] and (b) [58].

is beyond the scope of this chapter). The information used for generating this vascular atlas consists of measurements from [26], which helped to create a first vascular model. In order to correctly fit this model on its neighbouring cardiac structures, a registration step is carried out[8]. The registration process is driven by the medial axes of the main artery segments, interactively delineated from 27 3D CT data (which had previously been involved in the mesh generation of the other anatomical structures). It is based on an incremental relaxation of the authorised degrees of freedom, first accepting rigid (translation, rotation) transformation, then scaling, and finally, affine transformation. By opposition to the vascular atlas proposed in [74] for the cerebrovasculature, the one presented here, despite the relative simplicity of the modelled vascular tree, presents the specificity to model spatial relationships with neighbouring –non vascular– structures. This is the first (and to our knowledge, the only) vascular atlas presenting such a property. Still, by opposition to the previous atlas, this one has been created (at least partially) thanks to the vascular information provided by 3D CT data of several patients. As stated in the synthetic description of the generation protocol, this required to be able to process heterogeneous anatomical knowledge, possibly presenting variability. In particular, this implies to consider tools enabling to fuse the information related to several patients in a unified result. In the present case, this was done by considering registration. In Section 5.4.3 it will be shown that based on similar registration-based strategies, it is possible to obtain results which are no longer deterministic, but statistical, enabling in particular to model the interindividual variability.

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[8]The reader interested in registration –which is an issue strongly linked to (vascular) atlas generation– may complete the study of this chapter by reading the following surveys [48, 116].

5.4.3 Statistical atlases

In the above section, we have considered the vascular atlases which can be qualified as *deterministic*, in the sense that they present a model of vasculature which could be seen as the vascular network of a representative patient among the population. In this section, we now focus on non deterministic vascular atlases, and more especially on *statistical* ones, which are intuitively less similar to a hard anatomical model, but which aim at gathering and modelling more completely and efficiently the characteristics of a whole population of patients.

Anatomical variability handling

When designing an anatomical model (in the present case, a vascular atlas), two questions have to be considered carefully:

1. How to model the invariant information, *i.e.*, the set of characteristics shared by the whole population?

2. How to model the interindividual variability, *i.e.*, the set of varying characteristics among this population, in a unified framework?

The deterministic atlases described in Section 5.4.2 actually provide efficient answers to the first question. However, since they are based on a hard (graph or geometric) model, their ability to handle interindividual variability is not obvious[9].

Most of the contributions devoted to deterministic vascular atlas generation propose various (partial) solutions to this issue. In the preliminary works on coronary modelling [26], it is mentioned that there exist three variants in the coronary trees structure: right dominant (10%), balanced anatomic distribution (80%), and left dominant (10%)[10]. In [36], such variations are considered by exhaustively modelling each induced branch distribution (in this case by integrating them into the symbolic base of knowledge).

In the case of cerebral vessels, there also exists a strong interindividual variability from both topological and geometrical points of view [81]. In order to cope with this issue in the case of the vascular atlas proposed in [74] (and obtained from a single patient), a straightforward solution is an exhaustive list of each topological variation described in the anatomy literature [73]. In [41], a more unified solution is proposed for the modelling and storing of such interindividual topological variations. This is done by initially considering a classical graph-based modelling (see Section 5.4.2) enriched by fusing of several anatomical models/graphs into a "vascular catalogue", composed of a graph of all variations, and a discrimination matrix. This matrix helps to extract these variations as graphs similar to those of [14, 30]. (See also [40] for a more theoretical/methodological contribution related to the same concepts.)

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[9]However, this fact does not represent a crippling drawback, since the relevance of interindividual variability handling is essentially modulated by the applications requiring the designed atlas. In particular, deterministic atlases must not be considered as less (or more) relevant than statistical ones.

[10]Note that the information on coronary arteries gathered in [26] corresponds to a sample of patients with "normal-sized hearts". This example illustrates the general necessity to constraint some anatomical hypotheses if we may hope to finally obtain a useful model from a finite (and generally restricted) set of patients. Such a consideration remains valid when considering statistical models: a classical example is the restriction to either healthy or non-healthy people in the considered pool of patients.

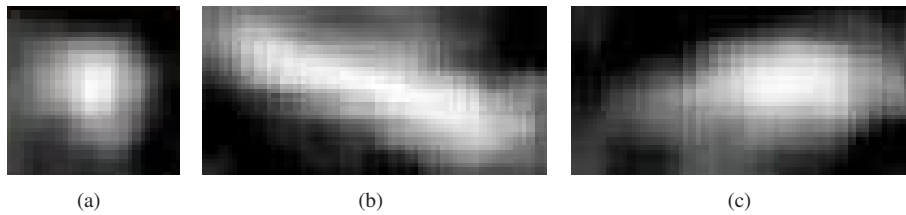(a)   (b)   (c)

Figure 5.3: Atlas for the portal vein entry, in the liver. (a) Sagittal, (b) coronal and (c) axial slices. Illustration from [68].

The handling of variability proposed in these contributions is essentially based on characteristics related to the structure of the vascular networks. This is a straightforward consequence of the modelling strategies which are primarily based on topological data-structures. In particular, the quantitative variations are generally omitted from these atlases, and the answer of these methods to the second question actually remains partial.

Some recent contributions try to propose complementary answers to this second question. They are specifically devoted to cope with the issue of modelling the variability of anatomical characteristics which can be quantified, for instance the size, orientation, position, or even the shape of the vessels. To this end, they propose to generate non-deterministic (namely *statistical*) atlases.

Recent works

The methods described hereafter are mainly devoted to design vascular atlases of vessels or vascular trees/networks from a set of patients/images presenting possible anatomical variations. In all these contributions, the input data consist of vascular volumes extracted from angiographic images. Similarly to most of the methods for deterministic atlas generation, the ones for statistical atlas generation then strongly rely on vessel segmentation. The following methods have been classified according to the degree of complexity of the modelled anatomical information.

Shape model When the vascular structures of interest are sufficiently simple, for instance when only a vessel, or a vessel segment has to be modelled, a first (and straightforward) approach for generating vascular atlases can consist in creating shape models. Such models can be defined by computing the mean image of data obtained from the segmentation of a (learning) image database. This mean image of binary functions can be seen as a fuzzy function with values in the interval $[0, 1]$.

In [69], such a model (which can in particular be involved in subsequent segmentation procedures [68]) has been proposed for a vessel segment, namely the entrance of the portal vein, in the liver. The atlas, built from a database of 15 segmented images of the portal vein entry, is illustrated in Figure 5.3.
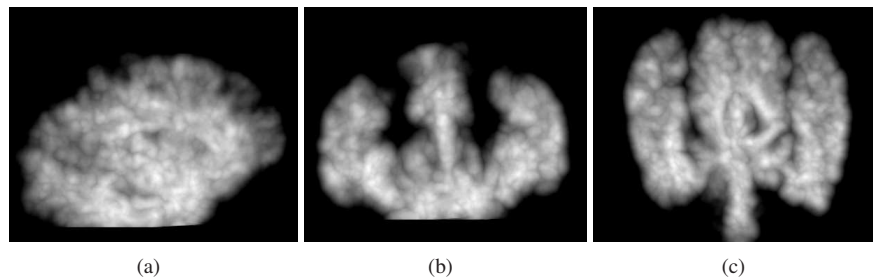
(a)　　　　　　　　(b)　　　　　　　　(c)

Figure 5.4: Atlas of the cerebral arteries. (a) Sagittal, (b) coronal and (c) axial maximum intensity projections. Illustration from [20] (with kind permission from Springer Science+Business Media: MICCAI 2003, Tissue-based affine registration of brain images to form a vascular density atlas, volume 2879 of LNCS, 2003, p. 12, D. Cool *et al.*, Figure 1).

Density atlas   When the vascular structures become more complex, in particular in the case where a whole vascular tree/network is considered, a straightforward mean image gathering each patient vascular information is no longer sufficient to accurately generate a satisfactory vascular atlas. In this more difficult context, it becomes necessary to develop adequate strategies for fusing several vascular images onto a coherent anatomical reference. Such strategies thus require the use of a registration procedure.

Intuitively, a first and natural way to proceed consists in attempting to register all the (segmented) vascular networks onto a chosen one, considered as the reference. Such an approach has been developed in [16], where the reference network is first skeletonized and then processed to provide a distance map (providing the distance to the closest vessel). The other segmented vascular networks are then registered (by affine transformation) on this template. The mean and variance images obtained from the distance maps of all the registered images finally provide a kind of probabilistic vascular atlas.

If such an approach enables the discrimination between healthy and non-healthy patients (especially in the case of arterio-venous malformations), it is actually not sufficient to accurately model the vessels. This is due, in particular, to the lack of a morphological reference. In order to correct this drawback, it is possible to perform registration no longer to angiographic data, but to associated morphological images. This alternative approach is proposed in [20], where each angiographic data (in this case, cerebral MRA) is associated with a T2-weighted MRI of the same patient. An affine registration procedure is then applied between these T2 data, leading to morphology-based deformation fields which are then applied on distance maps similar to the ones previously described, leading to an atlas consisting of a vascular density map. A result for cerebral arteries, obtained from 9 patients is depicted in Figure 5.4. Nonetheless, for creating vascular atlases as density fields, a recent strategy has been proposed in [88], for cardiovascular CT data. By opposition to the case of cerebral MRA data, which requires the simultaneous use of MRI data, here, the considered CTA images contained
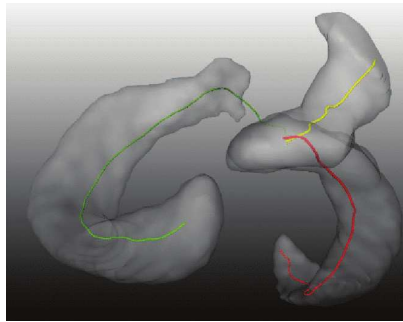
Figure 5.5: 3D visualisation of the vascular atlas (here, thresholded density field) for the three main coronary arteries (centerlines of which, for a given CTA, are depicted in green, red and yellow). Illustration from [88], (©2010 IEEE).

both morphological (cardiac) structures and angiographic ones. It is then possible to directly perform registration on such data. In this context, after (non-rigid) registration of the main vessel centerlines of each image with the chosen reference image and estimation of the closest centerline for each point of the image, a mean-shift clustering is performed in order to assign each point to one of the three main vessel clusters. An artery-specific density at each point can then be computed from a covariance analysis. A result obtained from 85 CTA is depicted in Figure 5.5.

Enriched atlas　The statistical atlas generation protocols presented above are essentially devoted to a density field generation. This density field models information related to a "vascular presence probability" and possibly a shape, when the interindividual variability is sufficiently low.

It may however be useful to be able to model more accurate information, related for instance to size and orientation. An approach described in [77] proposes such a method. It requires as input more information than a simple segmentation, namely a segmented volume (as in [69]), the associated medial axes (as in [16, 20, 88]), but also information on the vessel orientation (it has to be noticed that all these information elements may be obtained from a segmented volume, by using adequate methods[11]). It also requires correct deformation fields in order to register these different data with an anatomical reference. In order to do so, each angiographic image (in the current case, cerebral PC-MRA phase image) is associated with a morphological image (namely the associate PC-MRA magnitude image), following a strategy similar to the one proposed in [20]. Non-rigid registration of these morphological images then provides the deformation fields enabling to match the segmentation, medial axes and orientation maps associated to each image onto the anatomical reference. The mean and variance values for each one of these scalar and vectorial attributes finally lead to a vascular density field (as in [16, 20, 88]), but also to size and orientation intervals at each vascular point of the

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[11]See, *e.g.*, [22] for a robust medial axis computation method.
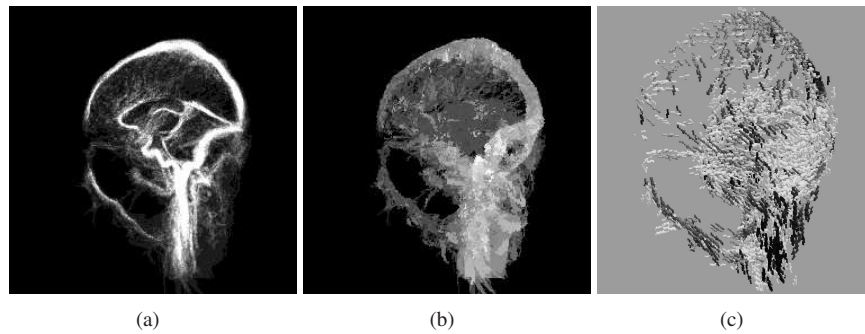
(a)   (b)   (c)

Figure 5.6: Atlas of the cerebral vascular network. (a) Vascular density, visualised as a maximum intensity projection (sagittal view). (b) Mean vessel diameters, visualised as a maximum intensity projection (sagittal view). (c) 3D visualisation of a part of the orientation image. Illustration from [77].

atlas. Such an atlas, modelling both cerebral veins and arteries, built from 16 patients is partially illustrated in Figure 5.6.

Remaining challenges   The vascular atlas generation protocols discussed in the previous section provide, by opposition to most of the ones devoted to deterministic atlases, the way to pull together and fuse information from a potentially large set of data, in a globally automated fashion. Such automation requirements however induce several conditions related to vessel segmentation which can be performed automatically as already discussed in Section 5.3.1, but which (at least in the case of vessels) still does not propose perfect results. However, it has to be noticed that in the context of atlas generation, a sufficient condition for a correct use of automatically segmented data would be the guarantee that they do not present any false positives (the presence of false negatives being possibly compensated by the possibly high number of segmented data).

Another crucial issue related to non-deterministic atlas generation is the availability of efficient registration methods. The most recent methods [77, 88] are based on non-rigid registration techniques, the accuracy of which (by opposition to rigid or even affine registration) is probably a *sine qua non* condition to obtain satisfactory results. Since such non-rigid registration algorithms have probably reached a correct degree of efficiency for the processing of dense images (such as morphological cerebral data, for instance), the development of efficient registration procedures in the case of sparse –and more especially of angiographic– data seems to remain, despite few recent works [6, 16, 49, 91], a globally open question.

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