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Supporting reconstruction of the blood vessel network using graph theory: an abstraction method

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Abstract— **The blood vessel network (BVN) has a complex structure. As this structure is unique for each individual, it is not possible to establish a general model for the BVN. However, many medical applications do rely on this structure. For example, a drug delivery system would be greatly improved if it could control the drug flow towards destination. To address this BVN structure issue, several reconstruction methods have been introduced. In this paper, we describe an abstraction method supporting BVN reconstruction by using graph theory. Starting from an original BVN reconstruction, we define the so-called induced graph of that reconstruction, allowing for an efficient analysis. By applying this method, we were able to improve an original BVN reconstruction of a human kidney by pointing out probable errors inside that original reconstruction.**

I. INTRODUCTION

The blood vessel network (BVN) of the human body has a complex structure and its spatial configuration significantly varies from one individual to another. Hence, one can not establish a general model of the BVN that would be applicable to any subject; anticipating the structure and position of the BVN is simply not feasible. However, many applications would benefit from a reconstruction, even partial, of the BVN. One can cite as example thermal therapy and drug delivery using microbubbles. Effectively, thanks to several properties of microbubbles, like heat and shock waves generated from oscillation, microbubbles are suitable for these types of therapy [1], [2]. Also, it has been shown that by using acoustic radiation force, one can alter the flow of these microbubbles [3]. Expanding on this topic, Masuda et al. have developed a method to realize active path selection of a flow of microbubbles inside the BVN [4], [5].

Thus, we understand that for such a path selection to be applied *in vivo*, a precise reconstruction of the BVN is needed beforehand. Reconstructing the BVN in this context refers to the creation of a human-visible object faithfully representing the underlying structure of the network of the blood vessels, so that this object can act as a map of the BVN.

BVN reconstruction is an active research topic, and several methods have been introduced [6], [7], [8], [9]. A reconstruction can be either two or three-dimensional. It can include different information, like blood flow directions or vessels diameters.

Wahl et al. performed the analysis of renal microvascular networks [10] from already constructed graphs. We propose in this paper a systematic method for the construction of induced grahs corresponding to an original BVN reconstruction. Another work, by Paradowski et al. aiming at measuring vessels tortuosity, is using graph analysis [11], but in a completely different way: each pixel of a blood vessel is considered as a vertex of the graph.

In this paper, we first describe an abstraction method of an original BVN reconstruction; this is the induced graph. Such an abstraction is a convenient way to perform an efficient analysis of the corresponding original BVN reconstruction. Effectively, an original BVN reconstruction as that of [6] is pixel-based, and can thus not be efficiently analysed as per-pixel processes are time and power consuming. Then we present several techniques using the aforementioned abstraction to perform several kinds of analyses of the corresponding BVN reconstruction.

II. PRELIMINARIES

In this section, we recall several general definitions of graph theory, following [12]. First and foremost, let us recall the definition of a graph. A graph $G = (V, E)$ is a pair of a set V of vertices and a set E of edges (also called links) such that $E \subseteq V \times V$. For any vertex $u \in V$, let $N(u) \subseteq V$ be the set of the neighbours of u, that is $N(u) = \{v \mid v \in V, uv \in E\}$. The degree of a vertex $u \in V$, denoted by $d(u)$, is the number of edges incident to u. Formally, $d(u) = |\{e \mid e \in E, u \in e\}|$. A graph is directed if for any edge, there is an initial and a final vertex. Simply said, a graph is undirected if the elements $uv \in E$ and $vu \in E$ represents the same edge, and directed otherwise. A path is an alternate sequence of distinct vertices and edges. A cycle is a path with one additional edge linking its two extremities. The length of a cycle is its number of edges. The cycle of length k is denoted by C^k. A graph including C^3 is represented in Figure 1.

A graph $G = (V, E)$ is connected if for any two vertices u, v, there exists a path between u and v. A graph $H = (V', E')$ is a subgraph of G if $V' \subseteq V$ and $E' \subseteq E$. A maximal connected subgraph of G is a component of G.

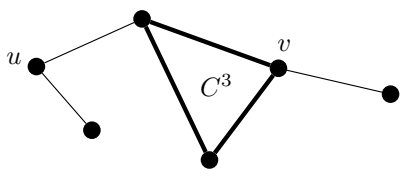

Fig. 1. A graph of five vertices, containing a cycle of length three (thick lines). The vertex u has degree $d(u) = 2$ and v has degree $d(v) = 3$.

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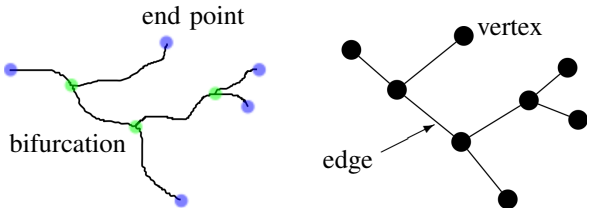

Fig. 2. The induced graph (right) of an original BVN reconstruction (left).

III. METHOD

A. The induced graph: an abstraction of the BVN

Depending on the type of data present in the original BVN reconstruction, we can induce different kinds of graphs. However, some core data is required to construct a most basic graph representation of an original BVN reconstruction. Indeed, so as to obtain the induced graph of an original BVN reconstruction, that reconstruction must include information locating blood vessels bifurcations and end points. From there, we perform a mapping of the set of all vessels bifurcations and end points to a set V of vertices. Then, the set E of edges connecting vertices each other is obtained by performing a simple pixel analysis (e.g. pixel-neighbourhood analysis) between the vessels bifurcations and end points. Typically, the information needed to create the sets V, E can be obtained from a basic blood vessel segmentation process. In the case no other information is provided by the original BVN reconstruction, the induced graph obtained is a simple, undirected, graph, as defined in Section II. As an example, the induced graph of an original BVN reconstruction is represented in Figure 2.

Now, if the BVN reconstruction includes additional information, like blood flow directions, the induced graph of that reconstruction can be enhanced. In the case blood flow directions are known (e.g. by using a colour Doppler echography as in [8]), we can set a direction for each edge. Furthermore, a colour Doppler echography enables the colouring of the induced graph: vessels whose blood flows towards the ultrasound probe are coloured in red, others in blue. This can be represented in the induced graph by colouring each vertex accordingly. The induced graph in this case is thus a vertex-coloured directed graph. See Figure 3.

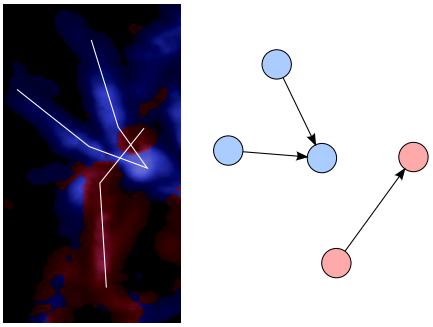

Fig. 3. Deducing a vertex-coloured directed graph (right) from an original BVN reconstruction (left) including blood flow directions (colour Doppler echography).

Also, providing the original BVN reconstruction includes blood vessels diameter, or even flow quantity, we can set the corresponding value for each edge. Makita et al. obtained the diameter of retinal blood vessels as well as blood flow information using Doppler optical coherence angiography [7]. Image processing can be subsequently applied to compute an average value of the vessel diameter (or flow quantity). The induced graph in this case is thus an edge-valued graph.

We can think of several other kinds of information than can be used to enhanced the induced graph. For example, by using a blood vessel segmentation process as described by Rokicki et al. in [13], we can obtain an edge-coloured graph.

B. Supporting BVN reconstruction by graph analysis

Let us first recall a simple graph traversal algorithm: Depth First Search (DFS) [14]. Initially, all vertices are unmarked. Pseudocode is given in Algorithms 1 and 2. An example of a graph traversal by a DFS algorithm is illustrated in Figure 4.

Algorithm 1 DFS_init(G)

Input: A graph $G = (V, E)$.
  for all $u \in V$ **do**
    if u unmarked **then** DFS(G, u) **end if**
  end for

Algorithm 2 DFS(G, u)

Input: A graph $G = (V, E)$ and a vertex $u \in V$.
  mark u;
  for all $v \in N(u)$ **do**
    if v unmarked **then** DFS(G, v) **end if**
  end for

Now, by using such a graph traversal algorithm, one can very easily check several properties of an induced graph, that is indirectly checking the original BVN reconstruction.

We address separately each type of graph depending on its characteristics: directed or not, valued or not, coloured or not. In the case of a most simple induced graph (undirected, not valued and not coloured), we can first check the degree of each vertex. Effectively, the probability there is a vertex u with $d(u) \geq 4$ in the BVN is very low. Also, $d(u) = 2$ wrongly situates a bifurcation. Hence the presence of such a vertex in an induced graph is likely to point out an error

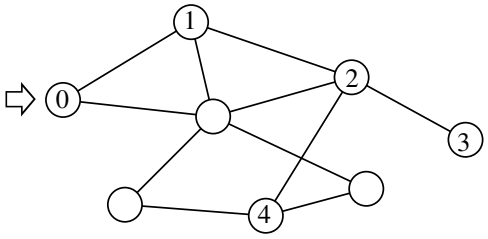

Fig. 4. Intermediary state of a graph traversal by DFS. Numbered vertices have been already visited according to the order indicated inside each vertex.

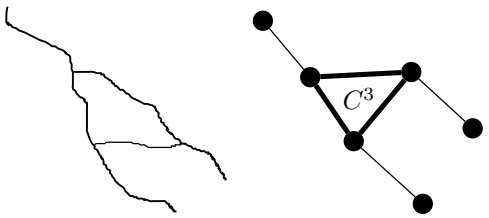

Fig. 5. The presence of C^3 in the induced graph (right) indicates a probable error in the original BVN reconstruction (left).

in the original BVN reconstruction. Then, depending on the context (organ, scale), of the original BVN reconstruction, the presence of a cycle in the induced graph, and especially C^3, may also indicate an error in the original BVN reconstruction. Effectively, it is more likely that a reconstruction of the BVN wrongly indicates a crossing of two vessels. See Figure 5.

We can slightly modify Algorithm 2 to detect a cycle of any length in the induced graph. Initially all vertices and edges are unmarked. Pseudocode is given in Algorithm 3. Once an edge uv has been found to be part of a cycle, one can easily check for the inclusion of uv into C^3 as it is implied by $N(u) \cap N(v) \neq \emptyset$.

Algorithm 3 DFS2(G, u)

Input: A graph $G = (V, E)$ and a vertex $u \in V$.
  mark u;
  for all $v \in N(u)$ **do**
    if v unmarked **then**
      DFS(G, v)
    else
      / uv is part of a cycle */*
    end if
  end for

Now, in the case the induced graph is directed, we can first check at each vessel bifurcation (i.e. each vertex u of the induced graph with $d(u) \geq 2$) the coherence of the directions. At a vessel bifurcation, the presence of a sink, that is a vertex with only incoming edges, is very likely to indicate an error in the original BVN reconstruction. The same conclusion can be deduced from the presence of a source, that is a vertex with only outgoing edges. See Figure 6.

We note that blood flow directions are usually obtained by colour Doppler echography. However, this method does not always provide reliable results. Hence, such a flow analysis in the induced graph is an efficient way for improving colour Doppler echography results.

In the case the induced graph is directed with valued edges

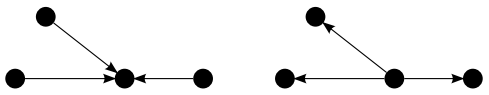

Fig. 6. A sink (left) or a source (right) in the induced graph indicate a probable error in the original BVN reconstruction.

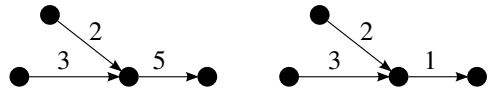

Fig. 7. A coherent flow (left) and an incoherent one (right).

(e.g. vessel diameter or blood flow quantity), we can perform at each bifurcation a flow integrity check: the sum of the incoming edges values must equal the sum of the outgoing edges values. See Figure 7. In a real situation, it is difficult to obtain exact values for vessels diameters of blood flow quantities. So, such verification should be performed with an error tolerance. But even if the precision of obtained data is medium, we can detect erroneous configurations like a large vessel connected to a very thin one. If the induced graph is undirected with valued edges, the blood flow direction at each edge incident to a bifurcation can be deduced by simple computation on the edge values, looking for a coherent flow. Note that the reliability of computed directions depends on the error tolerance of the original edges values.

In the case the induced graph is vertex-coloured, as obviously the arterial and venous networks are not connected, each component of the induced graph must be monochrome. As DFS traverses one component of the induced graph, we can use this algorithm to check the monochromicity of each component. Also, if the induced graph is directed, we can combine colours and directions to check for coherence with the venous and arterial system: at a vein bifurcation, there are always more incoming than outgoing edges. The contrary holds for artery bifurcations.

IV. RESULTS

A. A real-world example: analysing an original BVN reconstruction of a human kidney

In this section, we perform the analysis of an original BVN reconstruction of a human kidney. This reconstruction is a most basic one: it includes only blood vessels and their bifurcations, no other information like blood flow directions or vessels diameters is included. Hence we traverse the induced graph to check vertices degrees and for the presence of cycles. A sample of the results of this analysis is given in Figure 8.

We have given two particular portions of the induced graph for that original BVN reconstruction. First, we observe that the induced graph includes a cycle of length three (C^3), indicating a probable original BVN reconstruction error. Then, on the second portion of the induced graph, we have explicitly given the noticeable degrees, that is the degrees indicating probable reconstruction errors. One vertex of degree 4 and four vertices of degrees 2 have been identified, thus also indicating probable reconstruction errors. By definition of the induced graph, we can also note that vertices of degree 1 correspond to end points as identified in the original BVN reconstruction.

B. Discussion of the graph analysis results

For the sake of simplicity, we have analysed the original BVN reconstruction of Figure 8 assuming it is two-

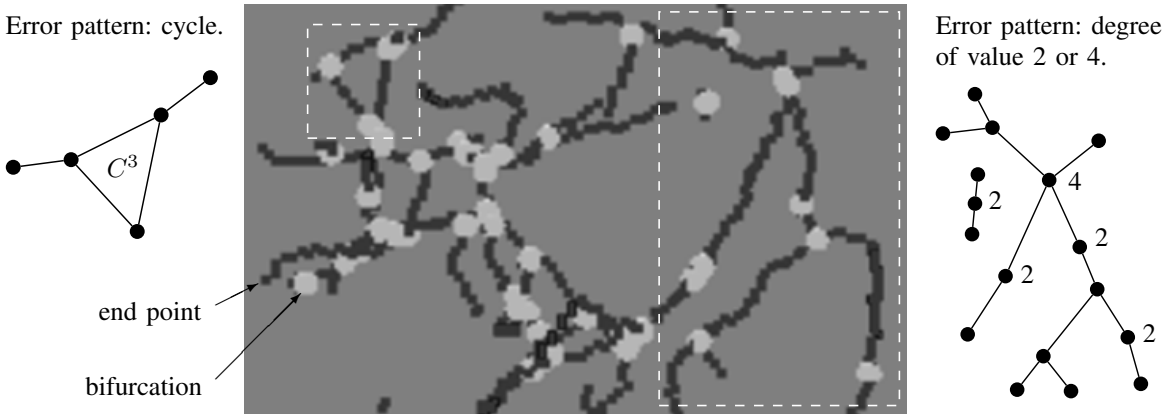

Fig. 8. Analysis of an original BVN reconstruction of a human kidney (center). Vessels bifurcations are materialised by light gray dots; end points are implicit. Several error patterns are identified inside the induced graph (two parts of the induced graph are represented aside).

dimensional. Nevertheless, a three-dimensional reconstruction could be similarly analysed as the definition of the induced graph is completely independent from dimension considerations. This may be the reason why several vertices of degree 2 are identified: since Figure 8 is a two-dimensional projection of a three-dimensional original BVN reconstruction, several vertices look like they have degree two, but in fact they may have degree three.

The merit of the construction of the induced graph for an original BVN reconstruction is obvious. For example, a cycle detection would be very difficult if performed directly on the original, pixel-based, BVN reconstruction. By using our abstraction method, this task is tremendously simplified, that is, concretely, much faster and easy to implement (see Algorithms 1–3).

V. CONCLUSIONS

We have described in this paper a formal method to obtain a graph induced by an original BVN reconstruction. Several kinds of graphs could thus be deduced: undirected graphs, directed graphs and valued-edge graphs are some examples. After briefly recalling how to automate a graph analysis, we have detailed basic analyses that can be performed to concretely support BVN reconstruction. Finally, we have applied our approach to a real-world example by analyzing an original BVN reconstruction of a human kidney. We were able to identify several probable error patterns that could be used as feedback to improve the original reconstruction or to estimate the correctness probability of an original reconstruction.

As for future works, one could think of the description of an evaluation method for BVN reconstructions. Effectively, measuring the correctness of a BVN reconstruction is a difficult problem as there does not exist any reference object to perform a comparison with. Hence, as described in this paper, we could check for several properties of the induced graph and, subsequently, tentatively compute a correctness rating for the corresponding original BVN reconstruction.

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