NETWORK-BASED APPROACH FOR MODELING AND ANALYZING CORONARY ANGIOGRAPHY

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ABSTRACT

Significant intra-observer and inter-observer variability in the interpretation of coronary angiograms are reported. This variability is in part due to the common practices that rely on performing visual inspections by specialists (e.g., the thickness of coronaries). Quantitative Coronary Angiography (QCA) approaches are emerging to minimize observer’s error and furthermore perform predictions and analysis on angiography images. However, QCA approaches suffer from the same problem as they mainly rely on performing visual inspections by utilizing image processing techniques.

In this work, we propose an approach to model and analyze the entire cardiovascular tree as a complex network derived from coronary angiography images. This approach enables to analyze the graph structure of coronary arteries. We conduct the assessments of network integration, degree distribution, and controllability on a healthy and a diseased coronary angiogram. Through our discussion and assessments, we propose modeling the cardiovascular system as a complex network is an essential phase to fully automate the interpretation of coronary angiographic images. We show how network science can provide a new perspective to look at coronary angiograms.

1 Introduction

Coronary Heart Disease (CHD) is a major cause of disability and death in developed countries. Although over the past four decades CHD mortality rates have declined worldwide, CHD remains responsible for one-third of all deaths in people over age of 35 [1]. Invasive coronary angiography is the current gold standard to determine the presence, location, and stage of coronary artery disease as well as to follow-up with the patients after therapeutic procedures [2]. However, potential observer error from performing visual analysis of Coronary Angiograms (CAs) has been estimated to be over 35% [3]. Quantitative Coronary Angiography (QCA) approaches are emerging to minimize the observer error and further perform predictions and analysis on angiography images [4]. Feyter et al. [5] classified the limitations of QCA approaches to three categories: patient related, technique related, and methodology related. Subsequently, immense technical improvements in the medical imaging techniques and advances in machine learning have been achieved [6] [7] [8]; notably, 3D Reconstruction of coronary angiography from 2D images [9] [10]. However, the main limitation of QCA approaches remains on capturing physiological characteristics such as side branches and bifurcations, hemodynamic assessment, and vasomotion that are technically difficult to measure [11] [12] [13]. Hence, several angiography phenomena can lead QCA approaches toward over or underestimation of parameters such as extensive calcium deposits, acute or chronic thrombus, and slow flow [14]. Due to these limitations, QCA approaches lack sufficient accuracy to be employed for clinical purposes [4]. We believe the missing key is dynamization of QCA; that can be achieved by utilizing the structural characteristics of the cardiovascular coronary tree as a complex network.

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The advantage of utilizing networks naturally arises from the way of thinking behind it, that is focusing on the relations among the entities rather than the entities themselves. For instance, consider the fact that humans and some plants have about 25,000 genes [15]. Having around the same number of genes does not reflect the biological complexity of humans compared to such plants. Many biologists believe the complexity of an organism arises from the complexity of the interactions between its genes. The great genome project provided us with the book of life containing the description of all genes, and networks are providing the map of life that describes the dynamics in which genes interact with each other [16] [17].

1.1 Innovation

Heart is a complex system consist of an interconnected network of coronary arteries as the heart’s blood supplier. The innovation of the proposed approach is its ability to create a collective view of the heart’s coronary circulation system by capturing the structure of coronary tree. Our approach enables analyzing network structure-functions relationships, through which, we can identify hidden patterns in coronary networks. Such patterns relate to the formation or existence of conditions such as stenosis. The following summarizes contributions of this work:

- We propose a new perspective to analyze and understand coronary angiography images based on capturing the network structure of coronary tree.
- We treat the cardiovascular system as a complex system and present a showcase of three network assessments on a healthy and a diseased coronary angiogram.
- We discuss how network science can provide insights from the graph structure of coronary arteries, and ultimately paves the way to fully automate the interpretation of coronary angiography images.

This article is organized as follows: Section 2 provides a brief overview of employing network science in modeling and understanding biological systems. In Section 3, we introduce our modeling approach by conducting three network-based assessments on two CA. Lastly, we discuss our vision in Section 4.

2 Complex Networks and Biological Systems

In recent years, there has been growing interest in complex, self-organizing networks often employed to model the dynamics and structure of complex systems [18]. These are dynamical networks of diffusely interconnected components. Their behavior is a manifestation of the behavior of the individual components and a reflection of the structural connections between these components. Examples of complex dynamic graphs abound in nature, from the microscopic cellular level where cells synchronize to perform their functions (heart beating [19] and neural graphs [20]) to large ecological graphs that respond to perturbations through very slow evolutionary behaviors [21].

Lusis and Weiss [22] provided a comprehensive review of the advances achieved by employing network science to investigate the cardiovascular system and diseases from the molecular level (genes and proteins). They showed system-based approaches are likely to play an important role in understanding the higher-order interactions that lead to formation of diseases such as heart failure, atherosclerosis, cardiac hypertrophy, and arrhythmias. Moreover, Dashtbozorg et al. [6] proposed an automated graph-based approach to classify the retinal blood vessels. Their study was able to label retinal blood vessels with up to 89% accuracy. In another study, Estrada et al. [23] proposed a graph-theoretic framework to classify the retinal blood vessels. Their approach obtained an accuracy level up to 93.5%. Furthermore, West et al. [24] introduced a general model of the circulatory systems as space-filling fractal networks. Their model derives the well-known biological scaling relationship (i.e., \( \text{metabolic-rate} \propto \text{body-mass}^{3/4} \)) shedding light on the evolution of biological systems. The above studies demonstrate the practicality and advantages of modeling blood vessels as a complex network and utilizing network sciences to analyze the graph structure of the circulatory system.

3 Proposed Approach and Case Study

In this section, we propose our model by presenting a case study for both healthy and diseased CAs. The case study concentrates only on the Left Coronary Arteries (LCA). We label an angiogram as diseased if a stenosis exists in the LCA. However, without loss of generality, the proposed model is naturally extendable to integrate all cardiac vessels and provide a complete map of heart coronary arteries. Figure 1 illustrates a CA and the process to derive a network of coronary vessels. A network consists of a set of nodes (representing a system entities) and a set of edges (capturing a relationship between those entities). In the proposed model, a node represents an intersection between vessels, and a weighted edge represents a vessel. The weight of an edge is calculated by multiplying the diameter of a vessel by its length. Two steps were taken to create the coronary networks in this work: 1) identify the intersections of vessels
Figure 1: An example of network creation process

(i.e., nodes), and 2) measure the length and diameter of each sub-vessel between the identified nodes and calculate the weights of edges. We employed graphical filters to magnify the vessels as presented in Fig. 1(b) and manually conducted these steps. However, without loss of generality, one can fully automate the network creation process by employing the variety of tools developed for performing visual inspections on angiography images [25, 9, 26, 11]. Figure 1(c) presents the created weighted coronary network.

3.1 Healthy and Diseased Coronary Networks

Figure 2 presents angiograms for both a healthy and a diseased heart alongside their corresponding coronary networks. The healthy angiogram is collected from [27] and the source of diseased angiogram is in [28]. In the diseased angiogram, a stenosis is marked by the green arrow. The healthy-case and disease-case angiograms in Fig. 2 are not related to each other. Our goal is to utilize the CAs in Fig. 2 to introduce our modeling approach. The global network characteristics [18] of healthy-case and disease-case networks are summarized in Table 1 in the following five columns: 1) number of nodes represents the number of intersections between the vessels, 2) number of edges represents the number of vessels, 3) average degree presents the average number of connections of the nodes, 4) average clustering coefficient captures the degree of connectedness among neighbors of nodes, and 5) diameter length of a network presents the length of the longest shortest path between all combinations of nodes. At the first glance, the average clustering coefficient of the disease-case network is relatively smaller than the healthy-case by 36%.

Figure 2: Healthy and disease-case coronary angiograms and their networks.
### Table 1: Coronary network characteristics

| Network      | Number of nodes | Number of edges | Average degree | Average clustering coefficient | Diameter length |
|--------------|-----------------|-----------------|----------------|-------------------------------|-----------------|
| Healthy-Case | 115             | 140             | 2.4348         | 0.099                         | 23              |
| Disease-Case | 109             | 138             | 2.5321         | 0.063                         | 24              |

### 3.2 Network Visualization

Visualizations of networks may provide insights on their structure and patterns of connections. Figure 3 illustrates the derived coronary networks in a circular layout. The thickness of edges (i.e., weights) represents the diameter of vessels multiplied by their length (the unit of measurements is pixel). Also, the green boxes in Fig. 3 mark Λ-branches as illustrated by Fig. 4. A Λ-branch consists of a single parent node that only has two children (i.e., the coronary tree leaves) who are not connected to any other nodes. Also, the parent node must only have a single additional connection other than its children.

The disease-case network has several more Λ-branches compared to the healthy-case network. This indicates blood is not being properly supplied to the diseased heart. The abundance of Λ-branches could reflect the Neovascularization phenomenon [29], which happens when the blood is not being properly supplied and the heart starts creating new vessels. These vessels can be observed in Fig. 2(b) where many small vessels are emerged from the main arteries. In the next section, we show how to systematically capture this behavior by analyzing the degree distribution of coronary networks.

![Healthy-Case Network](image1)

![Disease-Case Network](image2)

**Figure 3:** Coronary networks visualizations. Thickness of edges indicate the vessel’s diameter times their length and the green boxes mark Λ-branches.

![Λ-branch structure](image3)

**Figure 4:** Λ-branch structure.
3.3 Assessment of Degree Distribution

The degree distribution of a network represents the distribution of connections among nodes. In the coronary networks, the degree distribution presents the extent, in which, vessels are connected to each other. Blood flows in a fixed direction in human’s cardiovascular system. Hence, we employ directed edges to capture the direction of blood flow. Figure 5 illustrates a directed Λ-branch with the degrees of its nodes. For a given node, the total-degree indicates its number of connections, the in-degree indicates the number of connections to the node, and the out-degree indicates the number of connections from the node.

Figure 6 presents the in-degree, out-degree, and total-degree distributions of the healthy-case and disease-case networks. At the first glance, there is no significant difference between the degree distributions of the coronary networks. However, a significant difference is observed by comparing the quartile-degree distributions of the healthy-case and disease-case networks, which is presented in Fig. 7. In the healthy-case network, most nodes are concentrated in the fourth quartile for all three degree distributions. However, in the disease-case network, the concentration of in-degree distribution is shifted to the third quartile. This shift is due to the abundance of directed Λ-branches in the disease-case network. To conclude, the patterns of connections in coronary networks could provide insights on the condition of the cardiovascular system. For example, the analysis of degree-distribution could be used to determine the extent, in which, a heart is trying to create new vessels to overcome inefficient blood circulation.
3.4 Assessment of Network Integration

The efficiency of a network is the measurement of how efficiently it exchanges information. In transportation networks, this measurement corresponds to the efficiency of patrons commuting in terms of time and distance. We can utilize the patterns of connections in structure of systems to infer their functional efficiency \[30\]. The assessment of integration in the coronary networks corresponds to quantifying the efficiency of blood circulation in the cardiovascular system.

Figure 8 provides three measures of network integration: shortest-paths length, routing-efficiency, and search-information. The shortest-paths length provides the least number of hops (i.e., edges) that needs to be taken to navigate from any source node to any destination node \[18\]. Figure 8(a) and (d) present the lengths of shortest-paths between all pairs of nodes.

The routing efficiency, also known as global efficiency enables to quantify how cost-efficient a particular network is, where the cost depends on the weight of edges \[31\]. Hence, this assessment enables to include the vessel’s diameter and length (i.e., weight of edges) in quantifying the efficiency of blood circulation. For all pairs of nodes, we present this measurement in Fig. 8(b) and (e).

Lastly, the search-information quantifies the amount of information needed for a walker to perform an efficient routing (i.e., quantify accessibility or hiddenness). That is, how much information is needed for a walker to walk on a shortest path when the walker randomly travels between the nodes \[32, 33\]. Figure 8(c) and (f) present this measurement between all pairs of nodes in the healthy-case and disease-case coronary networks.

Through the assessment of network integration, we observe that the healthy-case network requires less information to find efficient routes. In other words, shortest paths are less hidden in the healthy-case network compared to the disease-case (i.e., smaller search-information). This observation indicates the measurement of search-information could be used as a feature to classify healthy and diseased coronary networks.

\[
\begin{align*}
\text{(a) Healthy-Case – Shortest Paths Length } & \quad \text{AvgTop10\% = 18.29} \\
\text{(b) Healthy-Case – Routing Efficiency } & \quad \text{AvgTop10\% = 0.34} \\
\text{(c) Healthy-Case – Search Information } & \quad \text{AvgTop10\% = 18.98} \\
\text{(d) Disease-Case – Shortest Paths Length } & \quad \text{AvgTop10\% = 16.74} \\
\text{(e) Disease-Case – Routing Efficiency } & \quad \text{AvgTop10\% = 0.3} \\
\text{(f) Disease-Case – Search Information } & \quad \text{AvgTop10\% = 21.48}
\end{align*}
\]

Figure 8: Analysis of network integration between all pairs of nodes.
3.5 Assessment of Controllability

The controllability of complex networks is the study of controlling the state of networks from any initial value to a desired value in finite time via stimulating a set of key nodes called driver nodes. Efficient algorithms are developed to identify driver nodes in complex networks [34, 35]. Most control scenarios are interested in identifying a minimum number of driver nodes needed to control a system. In coronary networks, this is analogous with controlling the flow of blood by modifying the flow that can pass through each node (arteries’ intersections). Figure 9 presents the driver nodes (marked red) for both coronary networks.

Intuitively, being easy to control (for cardiovascular systems) might be taken as a sign for healthiness. However, having a small percentage of driver nodes in a coronary network indicates a small number of malfunctions can perturb the whole system. Hence, a healthy network with a high percentage of driver nodes is more resilient to malfunctions. Figure 9 shows the disease-case network has less driver nodes (37%) compared to the healthy-case network (42%).

4 Discussion and Conclusion

The predominant methods to identify cardiovascular conditions primarily focus on analyzing the visual properties of coronary arteries (e.g., the diameter of arteries). For instance, Soroushmehr et al. [26] proposed a QCA approach to assist the diagnosis of CAs. Their approach is primarily based on the visual properties of coronary arteries (e.g., thickness of the arteries) and it can be extended by employing network science. In addition to employing the visual properties of CAs, our proposed approach enables to analyze the dynamics of cardiovascular system. Moreover, Andrikos et al. [9] introduced a novel approach for 3D reconstruction of CAs as illustrated in Fig. 10. Their approach can be naturally utilized to automate the process of network construction from CAs.

The proposed modeling approach provides the basis for development of a new systematic methodology to study the cardiovascular system and automate the diagnosis of coronary network pathology. An advantage of such a methodology is introducing new features based on network measurements such as the routing efficiency and controllability. For instance, these features could be used for the early detection of cardiovascular pathology by training machine learning classifiers and developing network-based diagnostic methods. Similarly, the proposed approach can improve the accuracy of procedure follow-ups such as the early detection of revascularization after stent implantation. Another important advantage of developing a systematic methodology is minimizing human error that accounts for a significant observer error [3].
Furthermore, non-invasive coronary angiography such as Computed Tomography Angiography (CTA) are already of significant value in the diagnostic procedure of patients. Our modeling approach can enhance the current literature on computer-based approaches for the interpretation of CTA images [8, 7].

The proposed network-based approach paves the way to apply the whole arsenal of network science tools on analyzing and classifying the CAs. However, the authors acknowledge that a rigorous study with more than two CAs should be done to further formalize and validate this approach.

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