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Use of graph theory for biomimetic microchannel network blood flow analysis

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Abstract— **This paper presents a novel application of graph theory to represent and analyze microcirculatory networks, specifically a biomimetic microfluidic chip designed to mimic the human retina. Utilizing experimental data obtained via high-speed video microscopy and Particle Image Velocimetry (PIV), the study develops a comprehensive graph-based framework. Key contributions include mapping experimental images onto a labeled retinal network, encoding fluid mechanical properties in graph nodes and edges, and storing experimental data in an organized structure. Results demonstrate the feasibility of the approach with a fully labeled network of 193 channels, offering insights into fluid dynamics and mass conservation in microcirculatory systems. The methodology facilitates future microfluidics research by providing a robust and scalable data storage and analysis tool, though further automation is needed to optimize workflow.**

Keywords— **microchannel networks, microfluids, graph theory, cell free layer.**

INTRODUCTION

Microcirculation in biological systems, such as the human retina, involves complex flow dynamics influenced by parameters that change over space and time [1]. Factors like viscosity, local density, and the cell-free layer (CFL) — a thin plasma layer near the vessel wall — are critical factors and are affected by shear-thinning behavior, hematocrit levels, vessel geometry, and blood velocity [2]. These interactions shape the flow characteristics in microcirculation, making it a challenging yet essential field for understanding vascular diseases.

Graph theory, a mathematical framework for modeling to model relationships between entities, offers a powerful tool for representing and analyzing such systems. In graph theory, nodes (circles) represent entities, while edges (lines) describe relationships between them [3]. By leveraging graph theory, this study introduces an innovative method to integrate flow characteristics, cell free layer information, velocity profiles and every other kind of data needed in the field of micro fluidics into a network model of the human retina.

METHODOLOGY

The application of graph theory aims to store and connect the behavior of each segment over time, enabling the overall network behavior to be analyzed without requiring specialized imaging devices. This project involved three main parts besides the data acquisition First, we created a graph representing the entire retina network. Second, we mapped the desired image to determine where each channel belongs. Finally, we developed a method to store the desired information in the different nodes. Each process is explained further in the next sections.

Experimental data acquisition

The network design was constructed based on medical imaging and established construction rules from the literature. The microfluidic chip was manufactured using backside lithography [4]. Blood flow was maintained at a low rate of 300 µL/h. High-speed video microscopy was employed to capture the movements of red blood cells (RBCs) within the chip. Subsequent image processing techniques [2] allowed us for the extraction of the cell-free layer (CFL) along the channels, while Particle Image Velocimetry (PIV) was used to estimate velocity data.

Graph creation

The vascular network, resembling a tree-like hierarchical structure, was modeled using a graph-theoretic approach. Nodes represented individual vessels, and edges captured their connections. The chosen graph type was a directed graph since the information will need to be access at different points of the analysis and the information of the descendants and ascendants node will be useful, for example, to perform a mass conservation analysis, or to update information within the nodes. In addition, as all the channels come from the same inlet and end to the same outlet, the graph is modeled as a fully connected graph, having the first and last nodes as the inlet and outlet respectively.

The process began by labeling channels on the original image (Figure 1, top) based on their bifurcation levels, enabling recognition of each channel across nine generations. To assign the channel number, a binary coordinate system was implemented, the inlet node was designated as 0. As the channels bifurcate, a 0 or 1 was added to the binary representation based on the branch taken. This binary sequence was then converted to a decimal number, resulting in a unique identifier for each channel. Finaly, the outlet was set at 1024 , the highest number in this system.

Image mapping

A binary mask of the retina network was created to facilitate data mapping. Experimental images were aligned with the network using correlation techniques, where the input image served as a kernel for convolutions through the entire network. The area with the highest correlation value was identified as the most likely network region. This approach ensures overall network behavior visualization and assignation, since it makes easer the recognition of the channel studied.

Information storage

Nodes supported diverse data types, including images, CSV files, and metadata, offering flexibility for future analysis. Data from all channels and experiments were systematically stored in graph nodes. This information includes but is not limited to velocity profiles, CFL information, filenames for the images where the channel is, geometric information of the channel (like diameter and length), images of the channel, etc. The versatility of graphs allows performing experiments focusing on different properties within each channel without restricting researchers to a specific data type.

RESULTS

The resulting network comprises 193 channels. The network's structure reflects the branching hierarchy of the human retinal microcirculation, with distinct generations of bifurcations represented by a color-coded scheme (Figure 1, bottom).

The resulting graph, depicted in Figure 2, offers an advantage for storing and managing large datasets from experimental studies without restricting the need for specialized high-cost imaging equipment with an extended field of view and high pixel depth. To enhance visualization, a color overlay was applied to match the labeling scheme previously introduced. As illustrated, all nodes are interconnected, ultimately converging at the end on node 1024

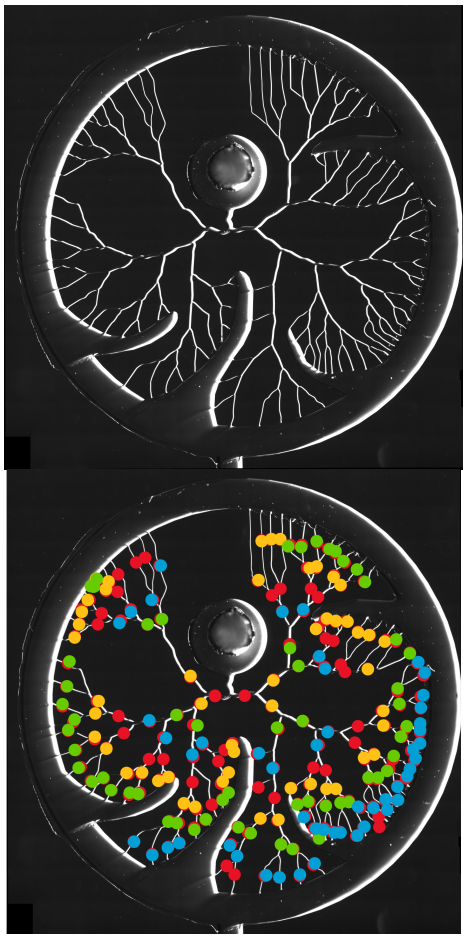

Figure 1: Original Retina chip (top) and labelled (bottom). A color-coded scheme was applied for clarity with red for the first bifurcation (generation), orange for the second, green for the third, blue for the fourth, and repeating the sequence again

Using data obtained in [1], some parameters were tested on a subgraph (a smaller section derived from the main graph). This subgraph corresponds to the lower-left portion of the chip and contains averaged measurements of velocity, flow rate, hematocrit levels and the CFL thickness for individual vessel analysis. These values were entered on an Excel document to be added to the nodes through an algorithm. Although these values have an inherent error due to the nature of the channel's geometry and the high-speed camera acquisition protocol, they can offer a very good glimpse of the versatility or graph-based analysis.

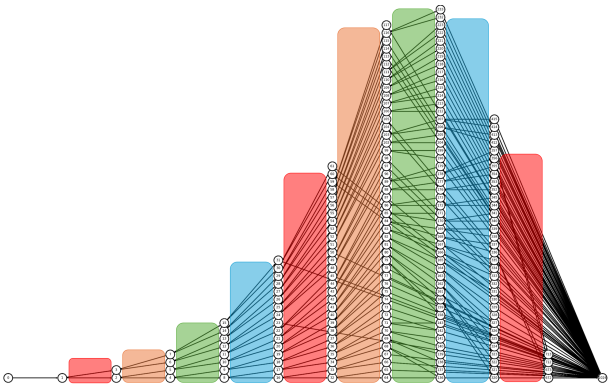

Figure 2: Retina chip representation using graphs and the corresponding colour showcasing the original label.

Figure 3 presents the previously mentioned subgraph, which retains the initial structure but focuses on a smaller section of the network, resulting in a subgraph with only 35 of the original 193 nodes. Additionally, it visually represents the blood flow values calculated using speed data from micro-PIV analysis and Poiseuille's law.

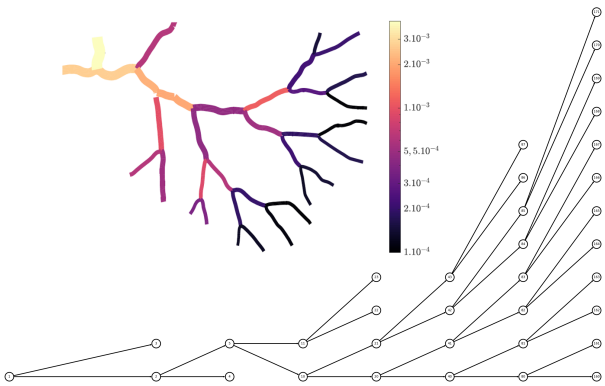

Figure 3. Retina blood flow in channels µl/min [1] along with the subgraph representing all the channels depicted.

Various data types were stored on each node for subsequent analysis. To illustrate this, Figure 4 provides a breakdown of the stored information and potential data (like the images) to be included. Data storage was implemented using a loop, ensuring each node received its value from the experiment's output file.

After creating the subgraph, mass conservation analysis for blood flow was performed considering the third bifurcation as the start point and subsequent connections depicted on Figure 3 as the endpoints. While the calculated output did not exactly match the input, the relative error was 8.6% when compared with the input flow, indicating a reasonable level of accuracy given some experimental constraints such as the calculation of the flow rate using the geometry of the channel and the PIV acquisition protocol tracking down the red blood cells to calculate the velocity.

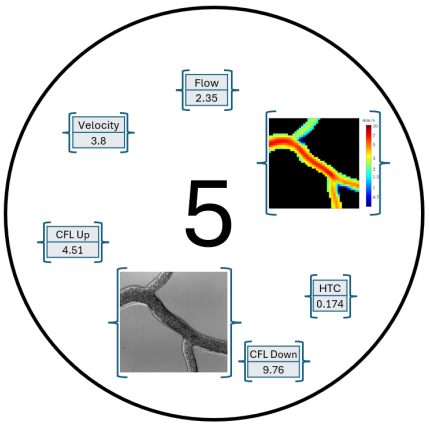

Figure 4. Graphic representation of information contained on node 5.

CONCLUSION

By applying graph theory, a comprehensive network model of 193 nodes was successfully created to represent a biomimetic chip resembling the human retina. This study demonstrates that graph-based methods offer significant potential for advancing the analysis of microfluidic networks, facilitating data integration and visualization in a manner that traditional imaging methods alone cannot achieve. The use of a number-based labeling system significantly simplified the graph creation and storage process, making it more efficient and enabling a semi-automated workflow.

The ability to encode large datasets within the graph structure enhances the scalability of the methodology, making it applicable to larger or more intricate networks with relatively good accuracy.

As per future integration we could calculate other parameters like, study the pressure gradients and distribution throughout the network, assess the efficiency of oxygen and nutrient delivery, model the effects of pathological conditions and treatments, we could assess its robustness to various perturbations, such as vessel blockages, and a broad selection of phenomena that need to be studied within networks.

This study also highlights areas requiring improvement. For example the manual labeling, mask creation and averaging processes were time-intensive and prone to human error. Therefore, future work should focus on automated network labeling as automating these steps would not only streamline the workflow but also increase the reproducibility and scalability of the methodology.

. Additionally, some caution must be taken when performing this type of analysis, as the reproducibility of experimental conditions is crucial for ensuring consistency across the network. Any discrepancies can introduce errors that propagate through the analysis, making it difficult to trace inaccuracies and compromising the reliability of the results. Potential improvements include refining the PIV acquisition protocol, enhancing CFL calculation methods, and accounting for the complex geometry of individual vessels.

Ultimately, the combination of graph theory and experimental data opens the door to a new paradigm in microfluidics research, bridging the gap between complex biological systems and scalable, data-driven analytical tools. This framework has the potential to enhance our understanding of microcirculatory networks and support the development of innovative solutions for vascular diseases and biomedical applications.

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