Quantifying Growth Modelling of Computational Models of Angiogenesis

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1 Background

The vascular network is the network of different types of blood vessels such as arteries, capillaries and veins through which blood flows through our bodies. How these blood vessels grow plays an important role in processes such as embryonal as well as tumour development as blood needs to reach every part of the tissue to deliver oxygen and discard waste products.

Specifically for tumour development, angiogenesis describes the formation of new blood vessels from already existing ones. Once these new blood vessels reach the tumour, this starts a critical new phase of tumour development which we want to understand better. To promote this understanding, different mathematical and computational models exist that simulate the angiogenic process, however, it is difficult to quantify how well the vascular networks generated by those models function compared to the networks found in vivo or in vitro experiments.

Therefore, we are motiviated to develop a technique or process to compare such models. To do so we will need to initially have a way to represent the networks as graphs. Given the graph representations of two networks and a characterisitc of a graph, we can measure how similar the two graphs are with respect to that measure. In this sense, we will define a characterisitic of a graph to be some quantifiable metric of the network structure. An example of such a characteristic would be the weighted network efficiency of a network [1]. Furthermore, if we have a sample set of real networks that are the result of the angiogenic process, then we have a way to evaluate how similar the computational models are to these real samples with respect to a characterisitic. Hence, the primary focus of the thesis is to determine and present various characteristics that are the most prevalent to determining the behaviour of branching as networks that are a result of the angiogenic process. With such a result, we would be able to provide a process that will allow the comparision of two networks and how similar they are, as well as, providing a way to evaluate if current computational models of angiogenesis are generating networks that are similar to these characteristics, [2].

2 Description of the Task

We can breakdown the task into smaller and concrete components:

1. Construct an image analysis pipeline to convert simulated and real images of vascular networks into a graph representation. This will be done as part of the preliminary work to the thesis.

2. Given that we want to 'evaluate' these networks it is important to have a sample set of graphs and images of vascular networks that are and are not a result of the angiogenic process. As such, we are required to collect a sample of images that we can use.

3. We then start by evaluating the weighted-network efficiency of graphs. To evaluate such a characteristic we want to provide both a mathematical and statistical reasoning for the strengths and weaknesses of its ability to discern between networks that do or do not exhibit the branching tendencies as described before.

4. Based on the results and the reasonings of this evaluation, we are then able to consider and explore other potential combinations of characteristics. Thus, the thesis can follow this iterative workflow of trying and testing new characteristics to create a combination or set of them.

5. Throughout this process, we will develop code that allows the user to input two images of vascular networks and compare them with respect to a particular characteristic.

6. With the set of characteristics, we then can analyze the various models used to generate such networks and if they are 'realistic'.

Given the iterative nature of the development process we are able to do these tasks a flexible number of times depending on the time required to do each iteration. Furthermore, the various mathematical and statisical reasoning that is used will accumulate as various techniques will be required and allow us to further evaluate the previous characterisitcs with the accumulated knowledge. With this in mind, we will want to set the definitive goal of documenting the findings of 3 different characteristics to allow for a set pacing when working on the thesis.

3 Methods

The thesis will be conducted as a combination of empirical reasearch, as well as, literature review. Empirically, the task will be to evaluate and find various characteristics that describe the branching behaviour of a network. Literature review will be a neccesity with regards to the graph theory aspects of formulating and evaluating these quantifications. This research will be a guiding factor when defining exploring various options.

4 Relevant Courses

1. **Introduction to Combinatorics**

   Introductory concepts of graph theory that will allow for a lower barrier of entry into graph theory literature

2. **Computational Modelling of Cellular Systems**

   Overview of a wide range of mathematical modelling concepts within biology to provide many perspectives of the problem

3. **Computational Neuroscience & Image Analysis**

   Experience in developing image analysis pipelines, in particular projects were used in a scientific setting

4. **Modelling of Complex Systems**

   General knowledge in the modelling of various systems and gained practical experience in developing modles

5 Delimitations

We would like to primarily focus on developing a good process of evaluting how a characteristics can encapsulate the branching behaviour of a network. As such, the steps of creating an image analysis pipeline and the usability of the code are areas that could be compressed or expanded on the basis of available time. For example, tasks such as creating a visualization of a gprah representation and/or usability of the end code are tasks that can be done with this in mind. If a loop in the iterative process takes more/less time than expected we can also change the project to consider more/less characteristics. However, this wouldn't be ideal.

6 Time Plan

We consider the time plan to be done full-time over the fall term of 2023 (week 35-52). However, I will 'begin' during the summer leading up to the thesis period with preliminary self-study within graph theory and angiogenesis. Additionally, the implementation of the image analysis portion will be done in advance.

- **Week 35-36**

  Before we want to evaluate or find possible characterisitcs, then it is important to conduct some readings on the computational models that are used to generate our networks to gain an understanding of the mathematical and statistical reasoning behind their methods. We also want to do readings within statistical analysis of networks and graph theory in general to get a broader scope of the types of measurements or techniques of

quantifying behaviours in graphs. Collecting sample images of real and generated networks.

- **Week 37-38**

  Continue the readings from before. Begin to evaluate the weighted-network efficiency by comparing the difference of measurements between graphs of the different behaviours. Formulate arguments for why it is and isn't a good measure of the branching behaviour. Important to motivate and record how we evaluated the weighted-network efficiency characteristics to extend and use in later weeks.

- **Week 39-41**

  From the readings we will have the knowledge and can try out various characteristics. We want to do the same evaluation process as week 37-38 for 1 new characteristic.

- **Week 41-44**

  Begin work on writing draft thesis, laying out the thoughts and methods behind the methods used to evaluate our characteristics so far. We also want to repeat the process of finding and determining a new charactersitic.

- **Week 45-46**

  We now have 3 characteristics that have the reasoning as to why they are or aren't a good measure of the branching behaviour. We want to formulate the specific reasonings into our draft thesis. Use these charactersitics to investigate how similar the generated computational models are to the real networks. Document the findings into the draft thesis.

- **Week 47-50**

  Finalize the thesis report and accompanying code, as well as prepare for presentation and we will allow a buffer period here.

References

[1] Vilanova, G., Colominas, I., Gomex, H. *Computational Modeling of Tumor- Induced Angiogenesis.* Archives of Computational Methods in Engineering, 24(4), 1071-1102, 2017. doi:`https://doi.org/10.1007/s11831-016-9199-7`.

[2] Vilanova, G., Colominas, I., Gomex, H. *A mathematical model of angiogenesis: growth, regression and regrowth.* J. R. Soc. Interface. 14: 20160918. doi: `https://doi.org/10.1098/rsif.2016.0918`