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Design, Fabrication and Characterisation of Hierarchical Branching Vascular Networks

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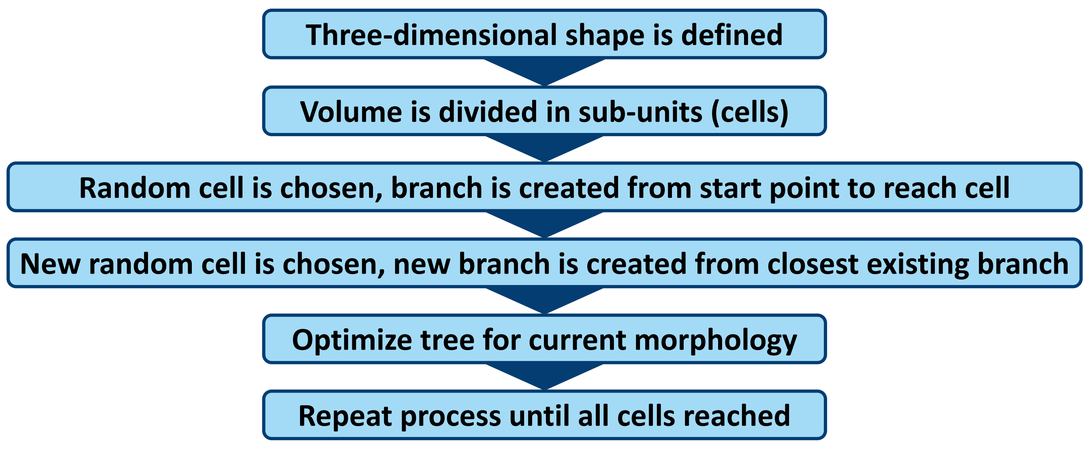
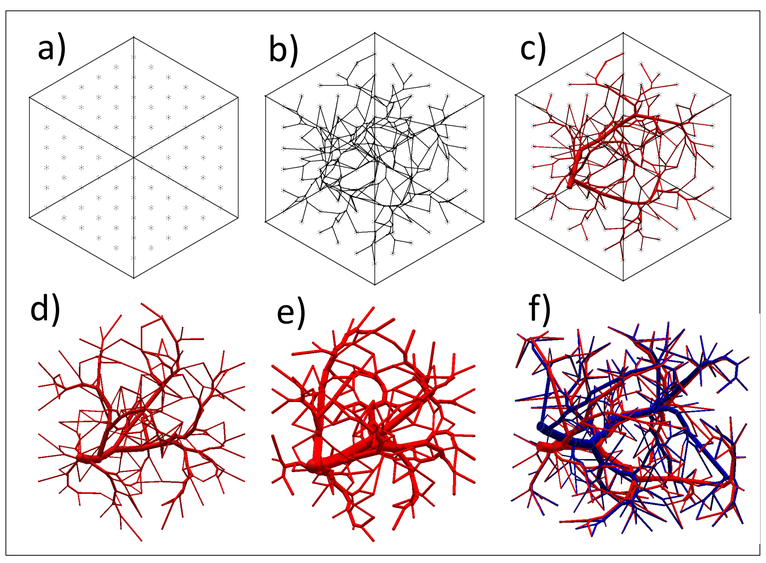
Motivation

Development of engineered artificial tissue has an enormous life-saving potential through the generation of artificial organs for implantation and other research purposes. A current limitation in tissue engineering research is the poor delivery of nutrients and low chances of survival for the cells in the tissue. **The establishment of a functional and hierarchical microvascular network is essential to ensure a proper mass transport (nutrients and waste) within the tissue**. In addition, pre-vascularized tissue aims to accelerate the anastomosis (connection of blood vessels) after surgical implantation of the tissue.

Previous Work

The current PhD research is an extension of the 4-month Long Project of the MRes in Ultra Precision Engineering carried out under the supervision of Dr. Athina Markaki. The project involved the development of a method for the automatic generation of three-dimensional vascular structures that fulfil the physiological laws of blood flow and circulation. The vascular structures were built as 3D solid models within a CAD software environment (Autodesk Inventor®) that can be exported for 3D printing.
An algorithm was created and programmed, based on existing computational models for the simulation of arterial trees growth.





a) Cubic 3D shape and cells
b) Tree skeleton inside cubic 3D space, reaching all cells
c) Arterial tree with branch radii applied
c) to **f)** Arterial (red) and Venous (blue) trees, different parameters (216 cells)

Parameter	c)	d)	e)	f)
Tot. Vol [cm³]	27	27	27	27
Cell Vol [cm³]	0.125	0.125	0.125	0.125
In Flow [ml/min]	400	400	400	400
In Pres [mmHg]	95	95	95	95
Cell Pres[mmHg]	60	82	82	82
Viscosity [Pa.s]	0.004	0.004	0.04	0.004
Root diam [mm]	1.127	1.436	2.55	1.44(A) 1.44(V)
Small diam[mm]	0.116	0.082	0.148	0.15(A) 0.16(V)
Process time	~11h	~19h	~19h	+30h

Aims

The main aim is to design, fabricate and characterise biomimetic branching vascular networks within hydrogel materials. Hydrogels are suitable for cell encapsulation and are frequently used in tissue growth or regeneration.
The individual aims can be described as:

- **3D Modelling of vascular networks**, ensuring fulfilment of physiologic laws.
- **Fabrication of vascular networks** within hydrogel structures, exploring different techniques, with focus on inkjet printing.
- **Characterisation of vascularized hydrogel structures**. It is essential to analyse the flow behaviour within the microvascular channels, and effects of the network size/geometry on the flow.

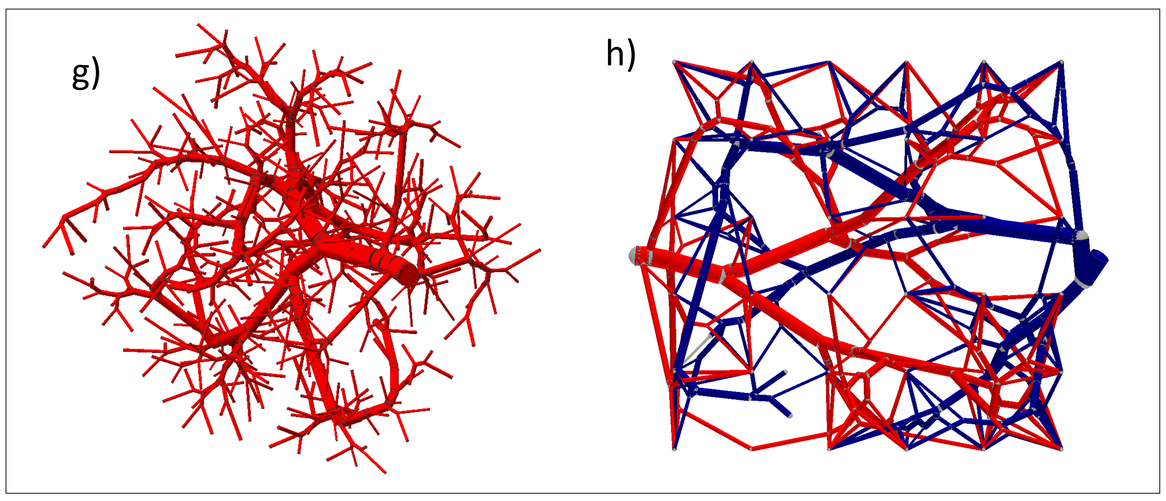
Current status

The current focus is to optimize the algorithm to ensure a functional and physiologically correct network. Some of the improvements that have been applied are:

- Possibility to vary the number of cells and size of 3D shape
- Analysis and correction of pressure for terminal branches
- Matching of radii of Arterial and Venous terminal branches

Some of the problems that are being addressed are:

- Optimization of computing time
- Optimization of Venous tree's morphology
- Avoiding collisions between both trees



g) Arterial tree with 500 cells.

h) Arterial and Venous trees with 216 cells, same terminal radii.

Future Work

After fully optimizing the algorithm and being able to produce the 3D models of vascular networks, the next stage will be to focus on the fabrication process of vascularized hydrogel matrices, and its characterisation.

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