Connecting Arterial Blood Flow to Tissue Perfusion for In

Silico Trials of Acute Ischaemic Stroke

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1 Introduction

Predicting infarct volume is necessary to develop *in silico* trials for the treatment of acute ischaemic stroke. This requires modelling of blood flow across length scales incorporating three orders of magnitude, from the large arteries, to the arterioles, the pial surface vessels, to the penetrating vessels and the microcirculation.

Blood flow in large vessels are typically modelled using lumped parameter or 1-D blood flow models, whereas the microcirculation is typically modelled as a porous medium[1]. However, the patient-specific geometry of large vessels is known, the features of the microcirculation are captured statistically. Therefore, there is an information gap between the large vessels and the microcirculation. Here, we present a method to couple blood flow in large blood vessels to cerebral tissue perfusion. A tissue perfusion model is also being developed but is outside the scope of this abstract¹. For more details and derivations of the models, see [1, 2].

2 Methods

The coupling, between arterial blood flow and tissue perfusion, presents several challenges. Firstly, medical images often suffer from low resolution. Secondly, information about the perfusion territories of the cerebral arteries can be determined but is limited[3]. Scans from stroke patients are often done quickly to get an assessment of the stroke severity. As a result, the scans typically only contain the circle of Willis and a few of the major cerebral arteries. This presents a problem as this does not provide enough information for the coupling between arterial blood flow and tissue perfusion in detail. The diameter of the cortical blood vessels is below 0.1 mm and below the resolution of MRI and CT imaging.

Figure 1a shows a schematic representation of the large arteries starting at the heart. We include the arteries starting at the heart such that we can capture the redirection of flow in the event of a stroke The major cerebral arteries are extended with high-resolution segmentations, shown in Figure 1b. The high resolution segmentations of patient-specific cerebral arteries are taken from a publicly available database presented by Wright *et al.*[4]. Extending the patient anatomy with these data sets can alleviate the problem of missing vessels. The patient

¹This is presented in another CompBioMed abstract by Józsa *et al.*, 2019.



Figure 1: (a) Schematic of the vasculature starting at the heart, the red circle. Each vessel is labelled by a number and their name (not shown) and is characterized by their length, radii and Young's modulus. (b)Detailed cerebral vasculature shown as centrelines, colour coded by major vessel branch. The major vessels are the middle, anterior and posterior cerebral arteries and the circle of Willis. Data taken and modified from [4]. (c) Segmentation of the circle of Willis from a stroke patient. Centrelines (green) are extracted and used in the 1-D blood flow model. The red spheres correspond to the large vessel ends in grey in Figure 1b. Data supplied by the Academic Medical Center in Amsterdam.

segmentations, Figure 1c, are used to personalize the vascular network. Once the patient anatomy is extended to the smaller cerebral arteries, we can begin to map the flow in the arteries to the brain.

The heart provides the inlet boundary conditions to the model, the red circle in Figure 1a, while a 3-element windkessel model is used at each outlet. The final outlets of the merged anatomy are the 5 grey vessel ends in Figure 1a and the 93 vessel ends in 1b. A stroke can be simulated by setting the flow velocity to zero in the 1-D blood flow model. The outlets of the 1-D blood flow model provide blood flow to the perfusion territories of the brain.

Detailed information about the perfusion territories of the arteries is limited and not available for individual patients. Most research on brain areas focuses on the functional regions of the cortex. By making a few assumptions, we can compute an estimate for the perfusion territory. We assume that the brain is perfused through the cortical surface (or pial surface)[5]. From arterial spin labelling measurements, we know roughly the perfusion territories of the major cerebral arteries[3]. We therefore first map the pial surface to the nearest major vessels, see Figure 1b. If we assume that brain tissue can be modelled as a highly folded sheet of uniform thickness, the problem is reduced to finding the regions on the pial surface perfused by the arteries.

The mapping problem is now a problem of finding the size and position of the perfusion region of each outlet of the 1-D blood flow model. At each outlet, we generate a bifurcating tree until a cut-off radius using Murray's law. We assume that each cut-off point perfuses an equal volume of tissue. This gives us an estimate for the size of the perfusion territory of an outlet in terms of number of volume elements.

The pial surface is represented as triangulated mesh which we randomly sample in such a way that each sampled element represents an equal sized area on the mesh within the major regions. From the bifurcating tree, we know how many of the sampled elements belong to each outlet. The sampled elements are assigned to the nearest outlet based on their separation on the surface. This is an iterative algorithm to account for the mismatch between the pial surface and the outlet. The outlet position is updated by taking the centre point of the assigned surface elements as a new guess. The pseudo code is given by:

- 1. Determine the number of surface elements per outlet
- 2. Map each outlet to the pial surface
- 3. Minimize the outlet-element distance within the sets
- 4. Update the outlets
- 5. Iterate until convergence

The clustering algorithm ensures that the size of the perfusion territories are scaled based on the radius of the vessel that perfuses it. The algorithm is a modified version of the k-means algorithm with constraints on the number of elements per cluster. Flow is distributed evenly across the perfusion territory of an outlet. The flow distribution is used in the tissue perfusion model as a boundary condition.

3 Results

A typical 1-D blood flow model can have on the order of 100 outlets and 4000 surface elements depending on a cut-off radius of the bifurcating tree. Figure 2a and 2b show the results from the clustering algorithm for one randomly selected patient. The perfusion territory of each outlet of the 1-D blood flow model is mapped to the pial surface. The regions mapped to the major vessels (Figure 2a) are similar to those found in literature[3]. Figure 2b shows the perfusion territories determined for each outlet of the 1-D blood flow model. Figure 2c visualises the mean flow rate for a patient with a clot in the right middle cerebral artery. The figure shows that a patient with such a clot has no blood flowing to the right side of the brain, meaning that



Figure 2: (a) Mapping of the pial surface to the six major cerebral arteries (middle, anterior, and posterior cerebral arteries on each side). These are found by backtracing the outlets. (b) The pial surface with perfusion territories for each cerebral outlet of the 1-D model, see Figure 1b. Each colour represents a perfusion region for one of the 93 outlets. (c) Results from the 1-D blood flow model and the clustering algorithm. Mean flow rate at each of the 93 outlets. Shown is a case with a clot in the right middle cerebral artery (Right), flow to the perfusion territory has dropped to zero. Flow rate shown in log-scale to emphasise the difference in perfusion.

tissue there is at risk of dying if left untreated.

4 Conclusion

Modelling stroke and predicting infarct volume requires the coupling of multiple models on different scales. Coupling these models is necessary to predict the effects of a stroke. A method to couple patient-specific blood flow models to a tissue perfusion model is presented here. The coupling algorithm uses a geometric construction to estimate the area of each perfusion territory and maps these onto the pial surface. Additional work has to be done on the incorporation of feedback between the 1-D blood flow model and the tissue perfusion model. We also want to perform validation and uncertainty quantification on the level of the individual models and as an integrated whole.

References

- [1] W. K. El-Bouri and S. J. Payne, Journal of Theoretical Biology, 380:40-47, 2015.
- [2] E. Boileau et al., International Journal for Numerical Methods in Biomedical Engineering, 31(10):1–33, 2015.
- [3] N. S. Hartkamp et al., NMR in Biomedicine, 26(8):901–912, 2013.
- [4] S. N. Wright et al., NeuroImage, 82:170–181, 2013.
- [5] P. Blinder et al., Proceedings of the National Academy of Sciences, 107(28):12670-12675, 2010.