A SPATIALLY VARYING MULTI-COMPARTMENT MODEL OF THE REGULATION OF CEREBRAL BLOOD FLOW AND VOLUME

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Introduction

The maintenance of adequate cerebral perfusion is a key aspect of healthy brain function. Dynamic cerebral autoregulation is the mechanism that acts to maintain cerebral blood flow constant in response to short-term changes in arterial blood pressure and is impaired in many cerebrovascular and neurodegenerative diseases. However, little is known about its spatial variability due to the difficulties in measurement of flow/perfusion in the human brain and no mathematical model yet exists of this. A new framework for considering the regulation of perfusion and blood volume in a simplified whole-brain geometry is thus presented and the different types of behaviour that are exhibited are highlighted.

Theory

Three blood compartments (arterial, capillary, and venous) are assumed for simplicity, although additional compartments can be added as required. Conservation of mass in each compartment gives:

$$\frac{\partial \phi_a}{\partial t} + \nabla.(\phi_a \mathbf{u}_a) = -\phi_a \beta_{ac}(p_a - p_c)$$

$$\frac{\partial \phi_c}{\partial t} + \nabla.(\phi_c \mathbf{u}_c) = \phi_a \beta_{ac}(p_a - p_c) - \phi_c \beta_{cv}(p_c - p_v)$$

$$\frac{\partial \phi_v}{\partial t} + \nabla.(\phi_v \mathbf{u}_v) = \phi_c \beta_{cv}(p_c - p_v)$$

where each compartment has volume fraction ϕ_i, pressure p_i and velocity field $\mathbf{u}_i$ respectively. It is assumed that perfusion coupling between compartments is linearly proportional to the volume fraction and the driving pressure difference, with coefficient β_{ij}. Darcy flow is assumed, following the homogenization procedure derived in [1]. It is finally assumed that there is a linear relationship between changes in volume fraction and pressure in each compartment, i.e.:

$$\frac{\phi_i - \bar{\phi}_i}{\bar{\phi}_i} = G_i \frac{p_i - \bar{p}_i}{\bar{p}_i}$$

This enables us to consider the responses of different compartments independently (since they are known to respond differently), providing a more general framework for the control of blood flow and volume. Three cases are considered: first, the pressure-volume relationship is purely passive; second, volume fractions remain constant; third, assuming typical/baseline values for each compartment.

The equations are converted into non-dimensional form, using a characteristic time, t_c, length, L, permeability, K_c, and pressure, $p_{a,c}$. Analysis of the arterial compartment then yields $t_c = 1/\beta_{ac} p_{a,c}$, which has a value of around 60 seconds (values taken from [2]). Elimination of small terms then gives the final non-dimensional form in terms of the 'corrected' pressures and various non-dimensional groups:

$$\frac{\partial p_a}{\partial t} = \left(\frac{K_c}{L^2 \beta_{ac}}\right) \nabla.\{p_a'(\mathbf{K}_a \nabla p_a)\} - p_a'(p_a - p_c)$$

$$\frac{\partial p_c}{\partial t} = \frac{Q_c}{Q_a}\frac{g_a \alpha_a}{g_c \alpha_c} p_a'(p_a - p_c) - \frac{\beta_{cv}}{\beta_{ac}} p_c'(p_c - p_v)$$

$$\frac{\partial p_v}{\partial t} = \left(\frac{K_c}{L^2 \beta_{ac}}\right) \nabla.\{p_v'(\mathbf{K}_v \nabla p_v)\} + \frac{\beta_{cv}}{\beta_{ac}}\frac{Q_v}{Q_c}\frac{g_c \alpha_c}{g_v \alpha_v} p_c'(p_c - p_v)$$

Values and boundary conditions are taken from [2]. The equations are solved in a spherically symmetric annular shell, with properties scaled between grey and white matter as in [2].

Results

A drop in inlet arterial pressure of 10% at time 0 is used to illustrate the model behaviour, as shown in Figure 1 for (spatially averaged) grey matter perfusion. The response times are very different, and a biphasic response is shown for two of the three conditions.

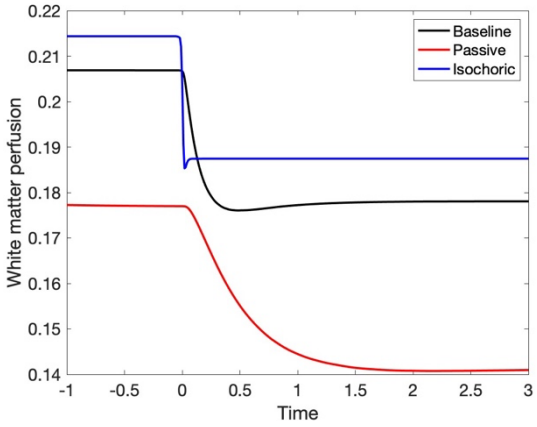

Figure 1: Spatially averaged white matter perfusion in three cases: baseline, passive and isochoric.

Conclusions

A new multi-compartmental framework for spatially varying regulation of cerebral blood flow and volume is presented. Future work will extend this to integrate more active mechanisms of control.

References

1. El-Bouri WK, Payne SJ. J Theor Biol. 2015;380:40-7.
2. Jozsa IT et al. Ann Biomed Eng. 2021;49(12)3647-3665.

Acknowledgements

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