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To cite this version:

Maxime Berg, Oliver Bracko, Yohan Davit, Michel Quintard, Nozomi Nishimura, et al.. A new model for molecule exchange in the brain microvascular system: consequences of capillary occlusions in Alzheimer's disease. Journal of Cerebral Blood Flow and Metabolism, 2019, 39 (1_suppl), pp.301-302. 10.1177/0271678X19851020 . hal-03498724

HAL Id: hal-03498724

https://hal.science/hal-03498724v1

Submitted on 21 Dec 2021

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https://doi.org/10.1177/0271678X19851020

To cite this version:

Berg, Maxime and Bracko, Oliver and Davit, Yohan and Quintard, Michel and Nishimura, Nozomi and Schaffer, Christopher B. and Lorthois, Sylvie A new model for molecule exchange in the brain microvascular system: consequences of capillary occlusions in Alzheimer's disease. (2019) Journal of Cerebral Blood Flow and Metabolism, 39 (1_suppl). 301-302. ISSN 0271-678X

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A new model for molecule exchange in the brain microvascular system: consequences of capillary occlusions in alzheimers disease

M. Berg[1], O. Bracko[2], Y. Davit[1], M. Quintard[1], N. Nishimura[2], C.B. Schaffer[2] and S. Lorthois[1]

[1] *Institut de Mécanique des Fluides de Toulouse, IMFT, Université de Toulouse, CNRS, Toulouse, France*

[2] *Meinig School of Biomedical Engineering, Cornell University, USA*

Abstract

The brain microvascular system is a key actor in Alzheimer's disease (AD) development. Indeed, a significant decrease of cerebral blood flow is the earliest biomarker of AD [1].

In vivo TPLSM of cortical vasculature in APP/PS1 mice suggests the mechanism underlying the blood flow reduction is capillary occlusions. Leucocytes adhere to inflamed vessel walls and limit the flow.

The impact of capillary occlusions on blood flow has been quantified numerically in large (>10000 vessels) anatomical networks in humans and mice [2]. The regional blood flow has been found to depend linearly with no threshold effect on the fraction of capillary occlusions, so that a small fraction of stalls (2-4%) yields a significant decrease in blood flow (5-12%).

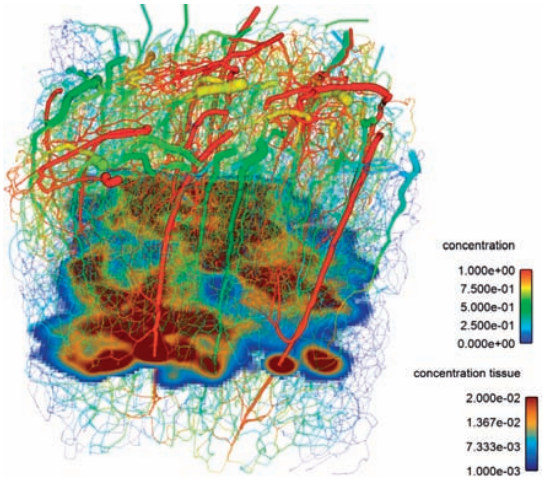
Such flow decrease has a strong impact on nutrient delivery and waste clearance. That is why we devised a new model to study the effect of capillary stalling on molecule

transport. The geometry of anatomical networks is too complex to use classic numerical approaches like finite elements. Instead, our model, inspired by pore-network approaches, reduces computational costs while capturing most of the underlying physics.

To derive this model, we apply upscaling methods [3] to the 3D transport equations within each vessel to obtain 1D average equations along the axis. Contrary to previous models, this new formulation describes accurately radial concentration gradients, capturing effects like longitudinal dispersion.

We further use a Green's function formulation inpired by [4] to calculate the concentration fields inside the tissue where diffusion and reaction occur. The coupling between vessels and tissues is modelled using a membrane condition [5] representing the blood brain barrier.

This new molecule transport model is coupled with our previously validated blood flow model to examine the effects of capillary stalling [2] on molecular exchange in transient and stationary regimes in anatomical networks. In particular, in stationnary regimes, we demonstrate an increase of the extraction coefficient with the proportion of stalled capillaries, which does not compensate for the associated blood flow reduction.



Acknowledgements

ERC Brain Micro Flow (GA 616102). NIH-IMAT (Award Number R21CA214299).

References

1. Iturria-Medina et al. 2016. Early role of vascular dysregulation on late-onset Alzheimer's disease based on multifactorial data-driven analysis. Nature Communications.
2. Cruz Hernández et al. Capillary occlusions reduce cortical blood flow and impair memory in Alzheimer's mouse models. In press. Nature Neuroscience.
3. Davit et al. 2013. Homogenization via formal multiscale asymptotics and volume averaging: How do the two techniques compare? Advances in Water Resources.
4. Secomb et al. 2004. Green's function methods for analysis of oxygen delivery to tissue by microvascular networks. Annals of biomedical engineering.
5. Fraser et al. 2015. Impact of incremental perfusion loss on oxygen transport in a capillary network mathematical model. Microcirculation.