AXONAL UNDULATION ROLE FOR TORTUOSITY IN WHITE MATTER

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Introduction

Convection-enhanced delivery (CED) is a surgical technique that offers a minimally invasive treatment for patients affected by brain tumors. It consists in injecting therapeutics directly into the parenchyma. However, its effectiveness relies on complex numerical models that need to be built on reliable parameters. A critical parameter is tortuosity, which is a measure of the hindrance to the diffusion of a molecule due to the extracellular space (ECS) geometry. However, the relationship between the axons' geometry and the effective diffusivity, is currently unclear. This work starts from an already existing Monte Carlo based study [1] which investigated the role of ECS volume ratio and width in an axisymmetric model (the axons were simplified as straight parallel cylinders). The present contribution adds a new and more realistic insight that considers also axonal undulation.

Methods

A white matter geometrical model was built considering axon diameter distribution (ADD) and myelin sheath width of a monkey corpus callosum [2]. The undulation was defined as a sinusoidal curve with amplitude 5 µm and wavelength 20 µm [3] (Fig. 1). The model met four fundamental physiological requirements: ADD, ECS volume ratio, ECS width and axonal undulation.

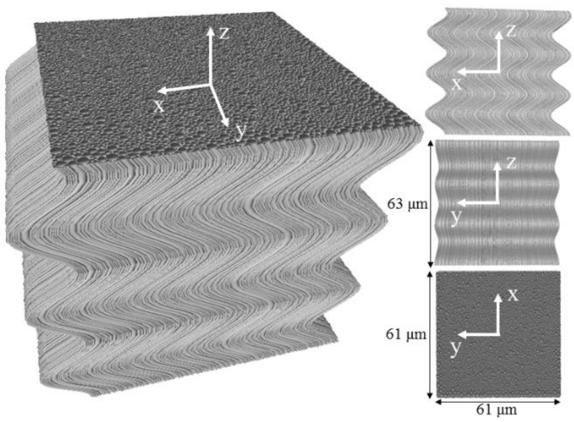

Figure 1: Geometrical model: the axons are represented as parallel cylinders with a sinusoidal axis.

Tortuosity (λ), computed as described in [1], is defined as:

$$\lambda=\sqrt{D/D^*} \qquad (1)$$

where D is the free diffusion coefficient and D* is the effective diffusion coefficient due to the hindering effect of the ECS geometry.

Results

Fig. 2 shows that tortuosity in every direction increases as the ECS volume ratio and width decrease. Tortuosity values, in the x and y directions, are comparable to the axisymmetric model [1]. On the other hand, comparing e.g. λ_z computed in the present model with the equivalent value obtained for the axisymmetric model, it is clear that the axonal curvature adds a decisive contribution to tortuosity.

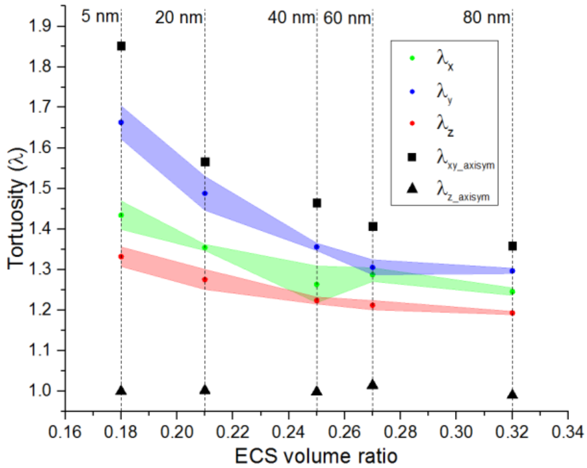

Figure 2: Tortuosity as a function of ECS volume ratio and width in the x (λ_x), y (λ_y) and z (λ_z) directions of the present model compared with the axisymmetric model (λ_{xy_axisym} and λ_{z_axisym}) [1].

Discussion

In this study, we have shown that including the axonal undulation allows a more realistic evaluation of the tortuosity in the white matter. This work represents an additional step towards a more comprehensive understanding of how the drug delivery depends on the cellular geometrical organization.

References

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