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BOOK OF ABSTRACTS

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Modelling Changes In Diffusion Through The Brain Extracellular Space

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Extracellular space occupies about 20% of nervous tissue volume and works as the microenvironment of the nerve cells. Extracellular space directly or indirectly affects neuronal and glial cell functions and works as an important communication channel [1-3]. Diffusion through ECS may be described through an effective diffusion coefficient, which in turn depends on ECS porosity, ε, and tortuosity, τ. Brain tissue diffusion modelling is more complicated than in the case of diffusion modelling in physical systems such as porous media, for several reasons: 1) ECS has a rather complicated physical structure; 2) brain tissue responds dynamically to changes in environmental conditions; 3) there is increasing evidence of selective segregation of large molecules that might exclude them from certain ECS regions. Finally, ECS τ and ε change dramatically in several pathological states[1]. A large set of experimental data on diffusion in ECS for different physiological conditions have been accumulated in the specialised literature. In the present research, diffusion data together with ε and τ were collected and analysed in the form of τ vs. ε correlation. Based on effective diffusion data collected from over 200 measurements, done under different brain conditions by several authors, upper and lower τ bounds, related with "topologically" dense and loose cell packing, were defined. Using boundary limits, a possible range of τ variation was obtained for ECS ε ranging from 0.05 up to 0.6. A tortuosity index (n) in the form of τ and ε logarithms ratio was introduced. This index may be easily adopted for recalculation of τ or ε if only one of these parameters is known. As a result of data analysis and modelling, it was concluded that under external conditions, for instance, oxygen depletion, the ECS porosity decreases and cells (presumably through membrane rearrangements) adjust the void space to keep the diffusion within a defined range, which gives the living tissue the ability to support the diffusion level up to two or more times higher than in conventional granular bed packing. Thus, even with a dramatic ECS decrease, the cellular system is still able to support a given diffusion by decreasing τ. The obtained results clearly show the existence of three clusters: a region of normal brain functioning – both for young and adult brains - for values of ε comprised between 0.15 and 0.30 and two regions of abnormal brain behaviour to the left and to the right of the normal region, corresponding to different behaviours – ageing, tumours, anoxia, brain death, etc. The present approach allows to define the optimal range of ε and τ to assure the best ECS diffusion efficiency for a specified macromolecule. This might be important in brain clinical treatment.

[1] Syková, E., 1997, The extracellular space in the CNS: Its regulation, volume and geometry in normal and pathological neuronal function, *The Neuroscientist*, Vol. 3, No.1, pp. 28-41.
[2] Syková, E., Mazel, T., and Simonová, Z., 1998, Diffusion constraints and neuro-glial interaction during aging, *Experimental Gerontology*, Vol. 33, No.7-8, pp. 837-851.
[3] Syková, E. and Chvatal, A., 2000, Glial cells and volume transmission in the CNS, *Neurochemistry Int.*, Vol. 36, pp. 397-409.