2.2 Mass Diffusion in Brain Tissues: a Theoretical Approach

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Diffusion plays a decisive role in brain function. In treating brain disorders, where diffusion is often compromised, understanding the transport of molecules can be essential to effective drug delivery. It became apparent that the classical laws of diffusion, cast in the framework of porous media theory, can deliver an accurate quantitative description of the way that molecules are transported through the brain tissue [2-3].

The diffusion-generated concentration distributions of well-chosen molecules also reveal the structure of brain tissue. This structure is represented by the volume fraction (void space) and the tortuosity (hindrance to diffusion imposed by local boundaries or local viscosity).

Transport phenomena through porous media have been the subject of various studies due to an increasing need for a better understanding of the associated transport processes. The brain contains a complicated network of specialized cells called neurons (or nerve cells) and glia (glial cells), each of which is bounded by a thin membrane. The membrane separates the brain into two compartments: extra cellular space (ECS), and intracellular space (ICS). From the perspective of the transport equations, the densely packed cells of the brain and their interstitial spaces can be regarded as resembling a porous medium with two phases, one permeant and one impermeant. The interstitial spaces remain open under most conditions and the ECS, from a topological viewpoint, is a multiply connected three-dimensional domain. The averaged mass diffusion equation is [2]:

$$\frac{\partial C}{\partial t} = D^{*}\nabla^{2}C + \frac{S}{\varepsilon}$$

where we noted $D^{*} = \frac{D}{\lambda^{2}}$ D - the diffusivity in pure fluid, D* - effective diffusivity in porous medium, λ - tortuosity, t - time, C – concentration of species, ε - volume fraction (porosity) and s - source term.
It can be shown by numerical evaluation of equation [2] with realistic parameters that usually it holds only when C(r,t) as a dependence of position and time the condition r > 2b is satisfied. If it is assumed that the injected material forms a cavity and in this case a numerical solution is required [2]. A set of numerical simulations concerning the concentration profile evolution for three types of idealized cells, considering two possible injection mechanisms will be presented.

The computations were performed for three different idealized cell configurations, for which the tortuosity versus diffusion coefficient variation was reported [5]. The three types of cells are presented, together with their characteristics, in Figure 2.2-1.

Two types of injection source were considered: the case when the injected substance forms a spherical cavity (Figure 2.2-2 a) and the case when the injected substance is confined to the pore space (Figure 2.2-2 b).a)

Figures 2.2-3 a-c present the calculated time evolution of concentration as a function of distance from center of cavity, when the injection is of type (a).

The same type of dependencies, but in the case of an injection of type (b), is depicted in Figures 2.2-4 a-c. The same volume of substance injected as in (a), but it is now confined to the pore space and so initial radius will modify, according to the corresponding porosity value.

A comparison of concentration profiles at two different time values, t= 10 and 100 s, for an injection of type (b) is presented in Figures 2.2-5. The type of comparison between the concentration profiles at the same moment of time gives a better image of the influence of cell parameters on the transport inside the brain tissue.

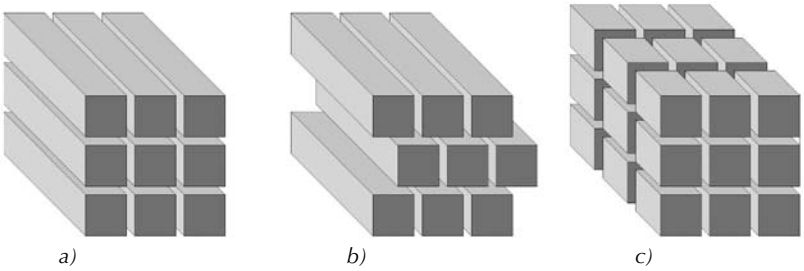

Abb. 2.2-1: *Schematic 3-D structures used in computations a) Type 1: ε=0.2166, λ=1.25, b) Type 2: ε=0.3, λ=2.4, c) Type 3: ε=0.2, λ=2.1 [4]*

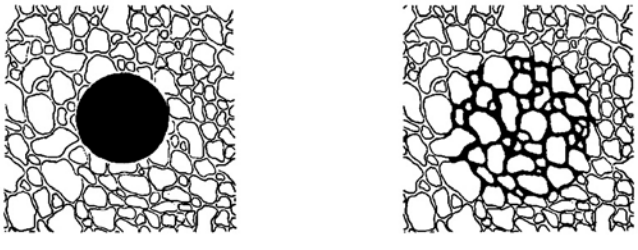

Abb. 2.2-2: *Models of injection source; (a) The injected substance forms a spherical cavity, (b) The injected substance is confined to the pore space [2]*

We can conclude that brain tissues can be treated as a permeable medium for describing the transport of drugs and nutrient substances. The mathematical modelisation and the numerical simulations are successfully applied in the investigation of diffusion processes in tissues, replacing the costly laboratory investigations. By measuring the time evolution of the concentration profile of an injected substance and using suitable fitting procedures, the main parameters (tortuosity, volume fraction) which characterize the tissue can be determined, analyzed and optimized.

References

[1] Der Autor wurde bereits unter 4.6 vorgestellt

[2] Ch. Nicholson, Diffusion and related transport mechanisms in brain tissue, Rep. Prog. Phys. 64 (2001) pag.815-884 doi: 10.1088/0034-4885/64/7/202

[3] A.W. El-Kareh, S.L. Braunstein, T.W. Secomb, Effect of cell arrangement and interstitial volume fraction on the diffusivity of monoclonal antibodies in tissue, Biophys. J. © Biophysical Society, Volume 64, May 1993 pag.1638-1646

[4] A.-R.A. Khaled, K. Vafai, The role of porous media in modeling flow and heat transfer in biological tissues, International Journal of Heat and Mass Transfer, Volume 46, Issue 26, December 2003, Pages 4989-5003, doi:10.1016/S0017-9310(03)00301-6

[5] L. Dai, R.M. Miura, A Lattice Cellular Automata Model for Ion Diffusion in the Brain-Cell Microenvironment and Determination of Tortuosity and Volume Fraction, SIAM J. Appl. Math. 59, (1999) pp. 2247-2273

[6] www.freefem.org (Dez. 2010)

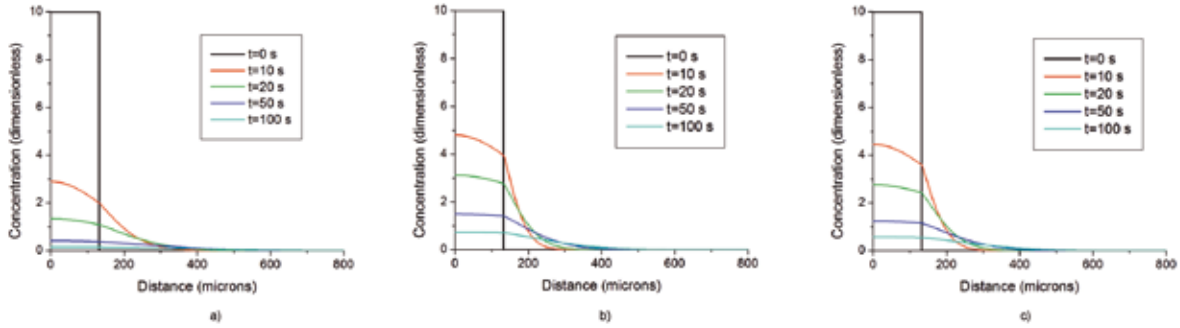

Abb. 2.2-3: *Time evolution of concentration as a function of distance from center of cavity when the injection is of type (a) for the three types of schematic cells*

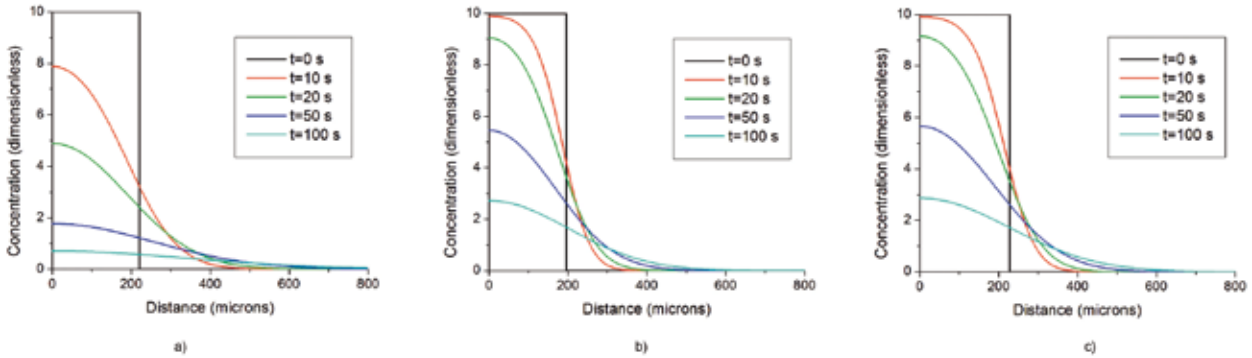

Abb. 2.2-4: *Time evolution of concentration as a function of distance from center of cavity when the injection is of type (b) for the three types of schematic cells*

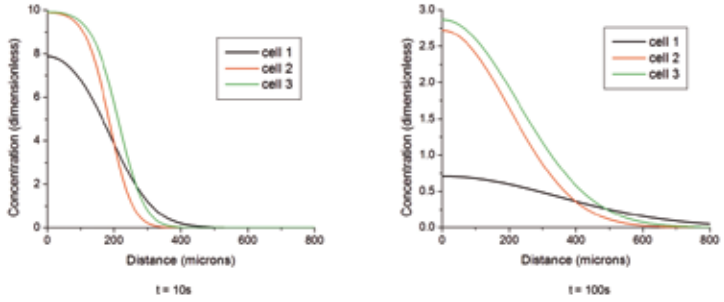

Abb. 2.2-5: *Comparison of concentration profiles at two different time values t = 10 and 100 s, In the case of a (b)-type injection*