APPLICATION OF OUR MULTISCALE DIFFUSION MODEL TO DETERMINATION OF DRUG DISTRIBUTION WITHIN TUMOR

Miljan Milosevic*[1], Milos Kojic[1,2], Dejan Petrovic[1], Nikola Kojic[3], Mauro Ferrari[2] and Arturas Ziemys[2]

[1] Belgrade Metropolitan University – Bioengineering Research and Development Center BioIRC Kragujevac; Prvoslava Stojanovica 6, 34000 Kragujevac, Serbia; miljan.m@kg.ac.rs, racanac@kg.ac.rs,

[2] Houston Methodist Research Institute, The Department of Nanomedicine, 6670 Bertner Ave., R7-117, Houston, TX 77030; mkojic@tmhs.org, mferari@tmhs.org, aziemys@tmhs.org

[3] Center for Engineering in Medicine and Surgical Services, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114; kojic@mit.edu

Key Words: *Multiscale diffusion model, Numerical homogenization procedure, Partitioning conditions.*

We have developed a multiscale diffusion model which couples molecular dynamics (MD) and continuum finite element (FE) method. Our model is based on a novel numerical homogenization procedure. The equivalent diffusion parameters of the continuum model consist of commonly used equivalent diffusion coefficients and new equivalent distances from the solid surface. Tissue can be considered as a composite medium through which occurs transport of molecules. Diffusion within this medium is affected not only by internal microstructural geometry, but also by physico-chemical interactions between solid phase (proteins, fibers) and transported molecules or particles. We implemented this multiscale model [1] - [5] to various conditions of diffusion through complex media. Here, we studied transport of molecules through tumor tissue. We considered diffusion in the vicinity of a capillary through which molecules are transported by convection. The partitioning conditions, which arise from biological barriers, are included in the model. Effects of collagen mesh density within tissue on transported molecule concentration profiles and mass content in different domains are presented, which also incorporate partitioning relations.

REFERENCES

[1] A. Ziemys, M. Kojic, M. Milosevic, N. Kojic, F. Hussain, M. Ferrari, A. Grattoni, Hierarchical modeling of diffusive transport through nanochannels by coupling molecular dynamics with finite element method, *Journal of Computational Physics*, **230**, 5722–5731, 2011.

[2] M. Kojic, M. Milosevic, N. Kojic, M. Ferrari, A. Ziemys, On diffusion in nanospace, *J. Serbian Soc. Comp. Mechanics*, **5** (1), 84-109, 2011.

[3] M. Kojic, A. Ziemys, M. Milosevic, V. Isailovic, N. Kojic, M. Rosic, N. Filipovic, M.Ferrari, Transport in biological systems, J. Serbian Soc. Comp. Mechanics, **5**(2), 101-128, 2011.

[4] A. Ziemys, M. Kojic, M. Milosevic, M. Ferrari, Interfacial effects on nanoconfined

diffusive mass transport regimes, *Physical Review Letters*, Vol. 108(23), 236102, ISSN: 0031-9007. DOI: .1103/PhysRevLett.108.236102, 2012.
[5] M. Kojic , M. Milosevic, N. Kojic , K. Kim , M. Ferrari, A. Ziemys, A multiscale MD–FE model of diffusion in composite media with internal surface interaction based on numerical homogenization procedure, Comput. Methods Appl. Mech. Engrg. 269, 123–138, 2014.