Accepted Manuscript

Multiscale smeared finite element model for mass transport in biological tissue: From blood vessels to cells and cellular organelles

M. Kojic, M. Milosevic, V. Simic, E.J. Koay, N. Kojic, A. Ziemys, M. Ferrari

PII: S0010-4825(18)30135-5

DOI: 10.1016/j.compbiomed.2018.05.022

Reference: CBM 2973

To appear in: *Computers in Biology and Medicine*

Received Date: 26 April 2018

Revised Date: 19 May 2018

Accepted Date: 19 May 2018

Please cite this article as: M. Kojic, M. Milosevic, V. Simic, E.J. Koay, N. Kojic, A. Ziemys, M. Ferrari, Multiscale smeared finite element model for mass transport in biological tissue: From blood vessels to cells and cellular organelles, *Computers in Biology and Medicine* (2018), doi: 10.1016/j.compbiomed.2018.05.022.

Multiscale smeared finite element model for mass transport in biological tissue: from blood vessels to cells and cellular organelles

M. Kojic[a,b,c*], M. Milosevic[b] , V. Simic[b], E.J. Koay[e], N. Kojic[d], A. Ziemys[a] , M. Ferrari[a],

[a]Houston Methodist Research Institute, The Department of Nanomedicine, 6670 Bertner Ave., R7-117, Houston, TX 77030.

[b]Bioengineering Research and Development Center BioIRC Kragujevac, Prvoslava Stojanovica 6, 3400 Kragujevac, Serbia.

[c]Serbian Academy of Sciences and Arts, Knez Mihailova 35, 11000 Belgrade, Serbia.

[d]Center for Engineering in Medicine and Surgical Services, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114.

[e]Department of Radiation Oncology, MD Anderson Cancer Center, Houston, TX 77030.

* Corresponding author: Milos Kojic

Houston Methodist Research Institute,

The Department of Nanomedicine,

6670 Bertner Ave., R7-117, Houston, TX 77030

mkojic42@gmail.com

phone: 713 441 7355; fax: 713 441 7438

One of the basic and vital processes in living organisms is mass exchange, which occurs on several levels: it goes from blood vessels to cells and organelles within cells. On that path, molecules, as oxygen, metabolic products, drugs, etc. traverse different macro and micro environments – blood, extracellular/intracellular space, and interior of organelles; and also biological barriers such as walls of blood vessels and membranes of cells and organelles. Many aspects of this mass transport remain unknown, particularly the biophysical mechanisms governing drug delivery. The main research approach relies on laboratory and clinical investigations. In parallel, considerable efforts have been directed to develop computational tools for additional insight into the intricate process of mass exchange and transport. Along these lines, we have recently formulated a composite smeared finite element (CSFE) which is composed of the smeared continuum pressure and concentration fields of the capillary and lymphatic system, and of these fields within tissue. The element offers an elegant and simple procedure which opens up new lines of inquiry and can be applied to large systems such as organs and tumors models. Here, we extend this concept to a multiscale scheme which concurrently couples domains that span from large blood vessels, capillaries and lymph, to cell cytosol and further to organelles of nanometer size. These spatial physical domains are coupled by the appropriate connectivity elements representing biological barriers. The composite finite element has