NUMERICAL MODELING OF THERAPEUTIC PARTICLE DIFFUSION IN TISSUE

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Introduction

Tissue can be considered as a complex medium through which transport of molecules occurs. Diffusion within this medium is a process of great interest in technology and medicine. Transport is affected not only by internal microstructural geometry, but also by physico-chemical interactions between the solid phase and the transported molecules or particles. Here we are exploring how structure of collagen, which is a natural biological polymer constituting the structure of capillary walls, affects diffusion of 80 nm liposome (LPS) and 1 nm size chemotherapeutic molecule doxorubicin (DMX).

Methods

First, we have developed and verified a hierarchical model [Ziemys *et al 2011, 2012*] which couples Molecular Dynamics (MD) [Ziemys *et al 2010*] and the Finite Element (FE) [Kojic *et al 2008*] method for simulation of molecular diffusion within nanochannels.

Then we have generalized this model to diffusion within a porous medium with complex internal microstructure. It would be desirable to have an equivalent continuum model with material parameters which adequately represent the diffusion within microstructure. We introduced a numerical homogenization procedure to evaluate a set of material parameters of a homogenous medium, which provide the same diffusion rate as the detailed microstructural model [Kojic *et al 2011a, 2011b*].

It is demonstrated that parameters of the equivalent diffusion model are the true material properties depending only on the internal structure of the composite medium and on the characteristics of the interaction between molecules and solid surfaces. [Kojic *et al 2013*].

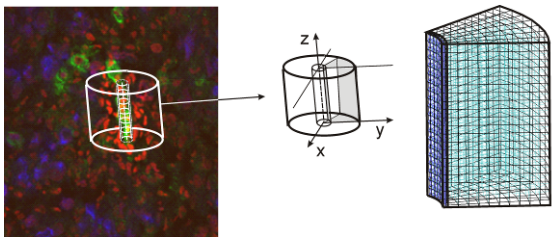

Figure 1: Schematics of the cylindrical diffusion domain around capillary (left), segment of the domain used in the calculation (center) and FE mesh for the collagen sleeve and sink regions (right).

Results

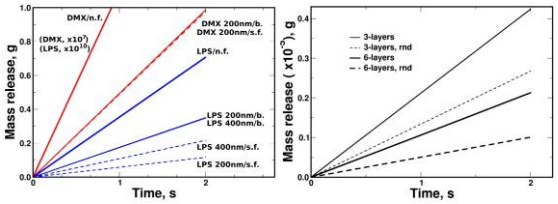

Figure 2: The effects of fibers and interface on DMX and LPS fluxes through 3 collagen sheets of 200 and 400 nm mesh-size (left) and LPS mass release affected by collagen mesh randomness.

Discussion

LPS exhibited substantially smaller flux through collagen sleeves of 3 mesh layers and smaller than 200 nm mesh sizes. The randomness of mesh structure showed reduction of mass flux for both molecules. We found that pharmacokinetics of free DMX and DMX loaded into liposomes are different, with different mass flux through collagen mesh. This finding explains higher efficacy of particle-based drug carriers.

References

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