Proceedings of ASME 2010 First Global Congress on NanoEngineering for Medicine and Biology
NEMB2010
February 7-10, 2010 Houston, TX, USA

NEMB2010-13253

A Hybrid Model for Nanoparticle Targeted Delivery in Blood Flow

Yaling Liu*
University of Texas at Arlington
Arlington, TX, USA
*Email: yaling.liu@uta.edu

Jifu Tan
University of Texas at Arlington
Arlington, TX, USA
jifu.tan@mavs.uta.edu

Samar Shah
University of Texas at Arlington
Arlington, TX, USA
samarshah84@gmail.com

INTRODUCTION

Nanoparticle targeted delivery in vascular system involves the interplay of transport, hydrodynamic force, and multivalent interactions with targeted biosurfaces. Current theoretical studies in nanoparticle therapeutic delivery are limited to nanoparticle suspensions in a Newtonian fluid without blood cells [1-3]. However, blood is a complex biological fluid made of components such as red blood cells (RBC), monocytes, platelets, proteins, etc. The existence of blood cells in the core region of blood streams might change the nanoparticle dispersion and binding through cell-nanoparticle interaction. It is thus important to understand how blood cells influence nanoparticles motion and binding.

METHOD

The dispersion of the nanoparticles in a tube with flow can be described by the Taylor-Aris theory. However, the interaction between nanoparticle and blood cells might lead to a dispersion and binding process different from that in a pure fluid. A combined Immersed Finite Element [4] and particle Brownian dynamics model is developed to simulate nanoparticles transportation and binding inside a small vessel. In this study, the RBCs are modeled as flexible three-dimensional thin structures enclosing a fluid [5, 6]. A Mooney–Rivlin strain energy function is used to depict the material behavior of the RBC membrane. The number of RBCs inside the unit-cell simulation domain is determined by the domain volume to achieve a RBC concentration close to the hematocrit of human blood (between 40 and 45%). The motion of nanoparticles is governed by Brownian adhesion dynamics [7]. The RBCs and its interaction with fluid flow is modeled by IFEM formulation [5, 6]. A short-range repulsive Morse potential will be used to avoid overlapping among nanoparticles and between nanoparticles and RBCs.

RESULTS

Fig. 1A shows a preliminary result on nanoparticle distribution across the vessel. It is clearly shown that the nanoparticle distribution is not uniform due to the existence of the RBCs inside the vessel. The cell-free layer near the vessel wall surface leads to a peak in local nanoparticle concentration. Nanoparticle binding rate is also largely influenced by the existence of RBCs. Fig. 1B shows preliminary results of nanoparticle binding with and without RBCs considered. The binding rate with RBCs is 50% higher than that without RBCs, which demonstrates that the particulate nature of blood is favorable for nanoparticle delivery.

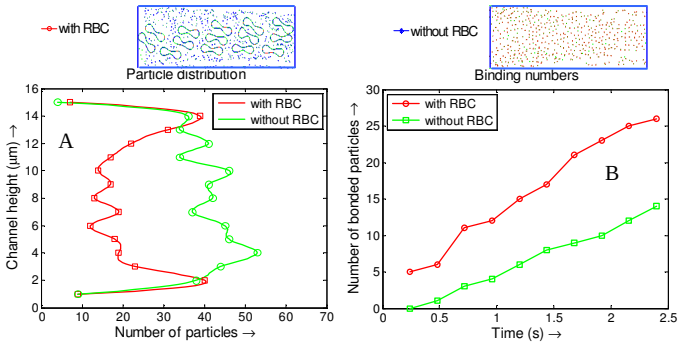

Fig. 1. (A) Nanoparticle distribution profile with and without RBCs; (B) Nanoparticle binding time histories with and without RBCs.

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