A combined in silico/in vitro approach for studying mass transport across the blood brain barrier

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ABSTRACT

The delivery of therapeutic agents to the brain is mostly impaired by the blood brain barrier (BBB), consisting of an intricate network of blood vessels that supports the selective distribution of nutrients to the central nervous system. Small animal models of brain tumors and neurological diseases are expensive, time-consuming, unpredictable, and not easily reproducible from one laboratory to another. In this context, a microfluidic device has been developed to resemble the complex geometrical and biological features of BBB. This is realized by combining optical lithography with replica molding techniques. The device consists of two channels with a common porous interface. One channel mimics the blood vessel and is coated with microvascular endothelial cells, whereas the second channel represents the extravascular matrix and host glioblastoma multiforme cells (U-87 MG) and normal brain cells. The porous interface is generated by a single array of rectangular pillars which separate the two compartments (vascular and extra-vascular) and serve to modulate BBB permeability. This microfluidic device is used to study the transport of fluorescently labeled nanoparticles under a continuous, laminar flow. The nanoparticle dynamics is also predicted using a Lattice Boltzmann method (LBM). The integration of *in silico* and *in vitro* assays can help in predicting and testing the transport efficiency across BBB and therapeutic efficacy of different agents.