Abstract

This paper investigates the particle-laden flow for nanoparticles dispersed inside various microchannel networks and collected by nanosized cavities by numerical methods using first principle equations. The cavity size is a determining factor to the collection of particles but the particle size is not. Moreover, Brownian motion effect plays a role as the cavity size is small enough (less than 450 nm in present cases).

Introduction

Nanoparticles in biomedical applications are of great interest in recent years but few studies have been conducted on the effectiveness of nanoparticles inhaled/injected into the fluidic networks such as the respiratory and blood circulatory systems of human body. It will be vital to know how these nanoparticles will travel as they are injected into the blood vessel and carried to tissues nearby. For example, tumors have leaky vasculatures and lack an effective lymphatic drainage system and therefore nanoparticles accumulate preferentially at tumor sites through an enhanced permeability and retention effect. In these cases, nanoparticle size may play roles on permeability for transvascular gap which is roughly 400 to 550 nm in hepatoma. The vascularity in hepatoma can be assessed by various imaging techniques. Figure 1 is an angiogram in the arterial phase showing the intratumoral vascularity [1] and this image will be taken as a base for our present study. There are straight and curved capillaries with various diameters, and branches of blood vessel in hepatoma.

Dispersion of nanoparticles with sizes less than 120 nm flowing inside the capillary with diameter of 2 micrometer is the major interest of our present study. This system is mimicked by straight or curved microchannels with or without branches and a cavity is used to mimic the leakage at a tumor site. The travelling paths and the collections of these nanoparticles into the cavity (vasculum) are of interest as these nanoparticles flow along the microchannel (capillary) networks. The micro-fluidic system consists of blood flow in liquid phase and nanoparticles in solid phase. It can be simplified as a typical particle-laden flows in microchannels and a few studies have been done experimentally [2, 3].
Mathematical and Numerical Models

Discrete nanoparticles are tracked by solving the conservation equations of mass, momentum, and energy in a Lagrangian reference frame, e.g., solving equations of motion for discrete particles in the present study. The discrete particles are allowed to exchange momentum and energy with the continuous phase (surrounding blood). Each nanoparticle is a representative on behaviour of multiple identical nanoparticles. The flow fields in blood vessels are obtained by solving first principle conservation equations of mass, momentum, and energy in both particle and liquid phases. Numerical simulations based on first principle equations using CFD technique are conducted to obtain the trajectories of the nanoparticles as discrete nanoparticles are flowing along the microchannels. Furthermore, Brownian motion may be taken into account for the laden particles at the nanoscale.

The governing equations for liquid (blood) flow are described in three dimensions and energy equation is eliminated by assuming isothermal conditions, i.e.

**Continuity Equations for Liquid**

\[
\frac{\partial \rho u}{\partial x} + \frac{\partial \rho v}{\partial y} + \frac{\partial \rho w}{\partial z} = 0
\]

**Momentum Equation for Liquid**

\[
\frac{\partial \rho u^2}{\partial x} + \frac{\partial \rho uv}{\partial y} + \frac{\partial \rho uw}{\partial z} = -\frac{\partial \rho p}{\partial x} + \frac{\partial}{\partial x} \left( \frac{2\mu}{\partial x} \right) \frac{\partial u}{\partial x} + \frac{\partial}{\partial y} \left( \mu \left( \frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) \right) + \frac{\partial}{\partial z} \left( \mu \left( \frac{\partial u}{\partial z} + \frac{\partial w}{\partial x} \right) \right)
\]

\[
\frac{\partial \rho uv}{\partial x} + \frac{\partial \rho v^2}{\partial y} + \frac{\partial \rho vw}{\partial z} = -\frac{\partial \rho p}{\partial y} + \frac{\partial}{\partial y} \left( \mu \left( \frac{\partial v}{\partial y} + \frac{\partial u}{\partial x} \right) \right) + \frac{\partial}{\partial z} \left( \mu \left( \frac{\partial v}{\partial z} + \frac{\partial w}{\partial x} \right) \right)
\]

\[
\frac{\partial \rho uw}{\partial x} + \frac{\partial \rho vw}{\partial y} + \frac{\partial \rho w^2}{\partial z} = -\frac{\partial \rho p}{\partial z} + \frac{\partial}{\partial z} \left( \mu \left( \frac{\partial w}{\partial z} + \frac{\partial u}{\partial x} \right) \right) + \frac{\partial}{\partial x} \left( \mu \left( \frac{\partial w}{\partial x} + \frac{\partial v}{\partial y} \right) \right) + \frac{\partial}{\partial t} \left( 2\mu \frac{\partial w}{\partial x} \right)
\]

Where \( u, v, \) and \( w \) are velocities in \( x, y, \) and \( z \) directions, respectively, \( \rho \) and \( \mu \) are density and viscosity of liquid (blood), and \( P \) represents pressure.

**Equation of motion for the nanoparticles**

Each nanoparticle experiences acceleration after the balance of drag forces with fluid and body forces with negligible gravity forces according to Lagrangian equations and the equation can be written as

\[
m_p \frac{d\mathbf{v}}{dt} = C_D \rho (U - v)|U - v| \frac{A_p}{2}
\]

Where \( m_p \) is the mass of particle and \( \mathbf{v} \) is the velocity vector of individual nanoparticle with components in \( x-, y-, \) and \( z- \)directions; \( C_D \) is the drag coefficient as the spherical particle travels in surrounding fluids; \( \rho \) and \( U \) are the density and velocity vector of the surrounding fluid, respectively; \( A_p \) represents the particle frontal area and \( A_p = \pi d^2/4 \) for a spherical particle with diameter of \( d \). The local time step used for integrating the equations of motion is estimated based on grid cell residence time and maximum allowable particle velocity.

The drag coefficient for nanoparticles in an incompressible flow is a function of Reynolds number and can be obtained by the following equations (Schiller and Naumann [1933]):

\[
C_D = \frac{24}{Re} \quad \text{for Re} < 1
\]

\[
C_D = \frac{24}{Re} \left(1 + 0.15 \text{Re}^{0.687}\right) \quad \text{for 1 < Re < 10}^3
\]

\[
C_D = 0.44 \quad \text{for Re} > 10^3
\]

where \( \text{Re} = \frac{\rho U - \mathbf{v}}{\mu} D \)

**Brownian Motions**

Since the Brownian motion of nanoparticles at the molecular and nanoscale level is a key mechanism governing the random walk behavior in fluids, effective instantaneous Brownian particle velocity must be taken into account. The Brownian force experienced by nanoparticles can be evaluated as [3]
\[ F_B = R \sqrt{\frac{216 \mu k_B T}{\pi c_c \rho^2 d^3 \Delta t}} \]

Where \( C_c \) is the Cunningham correction factor, \( \mu \) and \( \rho \) are the dynamic viscosity and density of liquid fluid, respectively, \( k_B \) is the Boltzmann constant, \( T \) is the absolute temperature, \( \Delta t \) is the time step, and \( R \) is a Gaussian random number bounded by -1 and +1.

**Results and Discussions**

The capillary vessels are assumed to be classified into three categories (1) straight microchannels, (2) curved microchannels with radius of curvature ranging from 3 to 5 \( \mu \)m, and (3) branched blood vessels with different angles.

I. **Straight microchannel**

A pipe having circular cross-section and a diameter of 2 \( \mu \)m is employed for blood moving with a speed of 0.5 mm/s and the cavity on vessel wall is simulated by a nano-throat to a micro-chamber in the flow system (shown in Fig. 2). The opening width of the nano-throat is ranged from 350 \( \mu \)m to 550 \( \mu \)m.

![Fig. 2: Schematic diagram for nanoparticles flowing in a straight capillary with cavity connected.](image)

Figure 2 shows the percentage of representative particles entrapped into a 450-\( \mu \)m cavity with different representative particle numbers and the results indicate that the employment of 500 particles is appropriate for the simulations.

Simulations are performed to estimate the percentage of nanoparticles with sizes ranging from 10 nm to 120 nm entrapped to the neighboring cavity with sizes ranging from 350 to 550 nm. The results are shown in Fig. 5. The density of the fluid is set at 1025 kg/m\(^3\), and its viscosity is set at 0.0015 kg/ms (close to that of human plasma). The density of nanoparticle is 7870 kg/m\(^3\) (the density of iron). Slightly more particles are entrapped to the cavity for larger-sized particle (up to 40 nm) and the increase of the cavity size increases the percentage of particles entrapped in the nearby cavity. Brownian motion effect plays roles for cavity sizes of 350 nm and 450 nm but the effect is insignificant if the cavity size is increased to 550 nm. General speaking, the particle size is not a dominating factor but the cavity size is. For the next two channel configurations, cavity of 450 nm and particle size of 40 nm are chosen to optimize the settings.

II. **Curved microchannel**

If the microchannel is curved, centrifugal force will affect the movement of laden particles and thus the particle entrained. In our present study, the microchannel turns 120 degree with radius of curvature ranging from 3 \( \mu \)m to 5 \( \mu \)m. Figures 6(a) and 6(b) show the computational grids and the corresponding velocity fields inside the flow channels with different radius of curvature. Figure 7 illustrates the distribution of the laden nanoparticles along the flow channels and more particles are observed to be attracted to the inner side of the channel, thus the
collection of nanoparticles at the inner side is more effective than that at outer side of the channel.

III. Branched capillary
The diameters of main vessel ($r_{\text{vessel}}$) and its branches ($r_{\text{branch } i}$) are related to Murray’s law, i.e.
\[ r_{\text{vessel}}^3 = r_{\text{branch } 1}^3 + r_{\text{branch } 2}^3 + \ldots + r_{\text{branch } n}^3 \]
to minimize the power needed for a branching vessels system [5].
In the present study, the vessel is branched into two capillaries with angles ranging from 60° to 120°. It is observed that more particles are attached to the outer side of the channel for all angles and a larger departing angle results in a higher collection percentage as shown in Fig. 8. It is also obtained that Brownian motion plays role on the percentage of particle collection at outer side of the branched network.

Conclusions
Numerical study on transport of nanoparticles (10 to 120 nm) in microchannels of 2 micrometer diameter to nearby cavity of size from 350 to 550 nm is conducted. The flow system of continuous phase is obtained using first principle equations of mass, momentum equation in Eulerian reference frame and the movements of nanoparticles is obtained using a Lagrangian approach. The entrainment of nanoparticles is more affected by the size of cavity than the size of nanoparticle. The effect from Brownian motion plays roles if the cavity is less than 550 nm in size. The radius of curvature of a curved capillary and the departing angle of a branched capillary are also the determining parameters to the collection of nanoparticles.

Acknowledgement
The authors appreciate the support from National Science Council, Republic of China under contract NSC-90-2323-B-007-010

References

[4] Li &Ahmadi, 1992
Fig. 5: The relationship between size of nanoparticles and percentage of particles entrapped to the cavity (various symbols represent the computed value if Brownian motion is accounted).

Fig. 6: (a) Computational grids and (b) Velocity contour of vessels with different radius of curvature.

Fig. 7(a): Nanoparticles in a vessel with radius of curvature as (from left to right) 3000 nm, 4000 nm, and 5000 nm.

Fig. 7(b): Nanoparticles with Brownian motion in a vessel with a radius of curvature as 4000 nm.

Fig. 7(c): Collection of particles at (i) inner side and (ii) outer side of curved microchannel.
Fig. 8(a): Traveling trajectories of nanoparticles in branched microchannel with 3 different departing angles at 4 different time steps

Fig. 8(b): Collection of particles at (i) inner side and (ii) outer side of branched microchannel