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Investigation and improvement of Focusing of Nano-bio-Particle in Viscoelastic Fluid

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Abstract

Nano-bio particle separation has been widely implemented in diagnosis and treatment in the medical area. Nano-bio particles such as virus, DNA, protein and exosome contain significant information that can help in the diagnosis and treatment of diseases like cancer. In this article, viscoelastic fluid in the OldRoyd-b model is simulated in a steady state in COMSOL 6.1 multiphysics in the first stage and to calculate the net of inertial lift force on the particles, a direct numerical approach has been implemented through coupling a FEM solver and a code developed in MATLAB. Considering quadrilateral geometry as an applicable microchannel, the aspect ratio effect on Nano-bio particles focusing in the viscoelastic fluid is investigated in a range of particle size of 100 to 1000 nanometer in Reynolds number 8 and polymer concentration 0.1%. Results show single line focusing has not been seen greatly in the channel with an aspect ratio greater than 1, but complete single line focusing has happened in channel with an aspect ratio of 1 in the dilute viscoelastic flow for particles greater than 500nm up to 1000nm.

Keywords: Nano particle, Bio particle, Viscoelastic, Focusing, Microfluidic.

1. Introduction

Medical malignancies, especially types of cancer including prostate, bladder, colon and kidney cancer are prevalent cancer causes of morbidity and mortality in recent years. Extracellular vesicles (EVs) are lipid bilayer encapsulated particles released by cells into the extracellular space [1,2]. Since EVs work as a safe way to the transmission of important biological information through the whole body, they are now recognized as an important mechanism of cell–cell communication and have opened a new way for scientists to gain a better understanding of cancer biology, novel diagnostics and therapeutic options [3]. EVs are divided into three categories, the first category is exosomes which are called small EVs and the second and third categories are micro vesicles and apoptotic particles, respectively. EVs have many uses, including in diagnostic tools and monitoring and as well as drug delivery. Their most important source is blood and saliva. EVs are an important source of biomarkers for identifying and predicting diseases [4]. Exosome with a diameter in the nanometer order and as an important group of EVs of the extracellular vesicles, contains various important biological molecules, such as lipids, proteins, messenger RNAs, microRNAs noncoding RNAs and nucleic acids that play an important role in intercellular communication [5]. Exosomes have been found a lot in biological fluids such as blood [6], breast milk [7], intra articular fluid [8] and saliva [9,10]. Recent evidence demonstrates that proteomic analysis of exosomes is of great significance in studying metabolic diseases, tumor metastasis and immune regulation, can reflect the physiological or pathological conditions of tissues and organs [5]. The simultaneous presence of different types of extracellular vesicles in biological fluids often affects the analysis of exosome behavior. To develop an understanding of the information carried by the exosome, an urgent need is felt for focusing and separation of exosomes from different types of extracellular vesicles. The separation of nanoparticles in diagnosis, treatment and care is widely used in medical and industrial usage [11,12]. Recently, exosome researches have attracted the attention of many researchers because of their important role in intercellular communication [13]. Of course, the small size of the exosome and the complex nature of the biological fluids has many challenges in particle separation and it is rather difficult to trap and separate them [14]. So effective methods for promotion in this field are essential. The microfluidic method is proposed as a relatively cheap, simple and continuous method for the separation of micro and nanoparticles.

In this paper focusing on nano meter suspended particles up to single line focusing in viscoelastic fluid in square and rectangular cross-sections in straight channels have been investigated in 3D numerically. Using geometries with micro meter dimensions as a micro scale geometry and flows rates in microliters per minute range for focusing on nano bio particles 1000nm up to 100nm is one of the privileges of this article.

1. Theoretical background

Particles suspended in the fluid have experienced various forces. Three main forces have been explained in the following. F_D is the viscous drag force of the fluid for per unit particle mass which is defined according to relation 1, this force which is the result of particles velocity difference and fluid is important at low Reynolds numbers. In relation 1 V_f is the fluid velocity, V_p particle velocity, a is particle diameter and η_s fluid viscosity [15]. The presence of elastic tension N_1, in the fluid leads to a force is titled the elastic force in the fluid and obtained according relation 2 which c is constant. The other force is the inertial lift force which is caused by inertial flow. This force for per unit particle mass is defined according to equation 3 [15,16]. $\dot{\gamma}$ is the shear rate and C_i inertial constant. These forces have applied particles according relation 4.

$$\vec{F}_D = 3\pi a\eta_S(\vec{V}_f - \vec{V}_p) \quad (1)$$

$$\vec{F}_e = Ca^3\nabla\vec{N}_1 \quad (2)$$

$$\vec{F}_i = C_i(\dot{\vec{\gamma}})^2\rho a^4 \quad (3)$$

$$\frac{\partial\vec{V}_p}{\partial t} = \vec{F}_D + \vec{F}_e + \vec{F}_i \quad (4)$$

2. Simulation

3D Rectangular channels with different aspect ratios have been simulated in COMSOL Multiphysics finite element software to drive focusing nano particle by using viscoelastic and particle tracing physics. Considering the lifts and drag forces on particles the equations of each physics are mentioned in the previous section (eq1-4). In the first stage, to calculate the net of inertial lift force on the particles, direct numerical approach has been implemented through coupling a FEM solver and a code developed in MATLAB [17], next viscoelastic fluid in OldRoyd-b model is simulated in steady state in COMSOL 6.1 multiphysics. Finally, all forces such as inertial lift force, elastic force and Drag force are obtained and exerted on the particles in COMSOL 6.1 multiphysics. Depending on some parameters, there are 3 ways[1] to simulate particle movement in simulation. When the volume percentage of suspended particles in the fluid is less than 5 percent [18], it is reasonable to ignore their effect on fluid. In this case, because of the nanometer range of particle size and a low number of suspending particles in simulation, the effect of particles on each other and the effect of particles on the fluid have been ignored and the movement of particles is modeled in one way [19]. The particles focusing of 100, 500 and 1000 nm as EVs particles have been simulated in three straight channels with an aspect ratio of 1, 1.5 and 2 according to the geometric and flow characteristics of Table 1. The geometry is according to Figure 1. To elasticize the DI water as a base fluid, PEO polymer with a molecular weight of 400 KD and a concentration of 0.1 percent has been used. The boundary condition is uniform velocity at the inlet and zero pressure at the outlet in the viscoelastic physic, Figure 1. Remain boundaries are the wall. The boundary condition is particle entrance at the inlet and freeze at the outlet in the particle tracing physic. The walls are also in bounce condition. The number of particles released in the channels entrance is 400, 600 and 700 particles for aspect ratios 1, 1.5, and 2 respectively. It is worth noting that particle injection at the entrance is mesh-based and particles are released at the same time. The whole condition for all particles is the same at the entrance and exit of the channel. The initial condition in the movement of particles is the flow velocity. In the time-dependent solution, different time steps have been selected and their results are compared. Due to the less computing time and precise of the result the time step 0.00001 seconds has been selected for all particles. It should be mentioned that constant parameter in equation 2 is 0.0184 [20].

3. Disscution and result

Due to the equipment and fabrication considerations, the rectangular channel is a common and popular micro-channel. For this reason, the role of the aspect ratio of the rectangular cross-section in the straight channel in particle focusing has been studied. Particles in 1000nm up to 100nm have been released in 3 channels with different aspect ratios. In Figure 3 and 4 the particle movement line and final equilibrium position of particles in the outlet in the channels with different aspect ratios have been plotted. In Figure 2, 100 nm particles can migrate up to half the cross-section of the channel in the square geometry. In aspect ratios of 1.5 and 2 the movement toward the center of particles has begun in small sizes of 100 nm particles slowly. By increasing the size of the particles to 500 nm, 3D focusing or single line focusing is almost happening in the square geometry, Figure 2. For sizes greater than 500nm particles, the 3D focusing has completely taken place in square geometry, Figure 3. An increase in particle size leads to an increase in the elastic lift force and consequently to tighter focusing of particles, Figure 2-3. The 3D focusing in geometries with aspect ratios 1.5 and 2 is not visible even up to particle size 2µm. these results

[1] One way, two way, four way

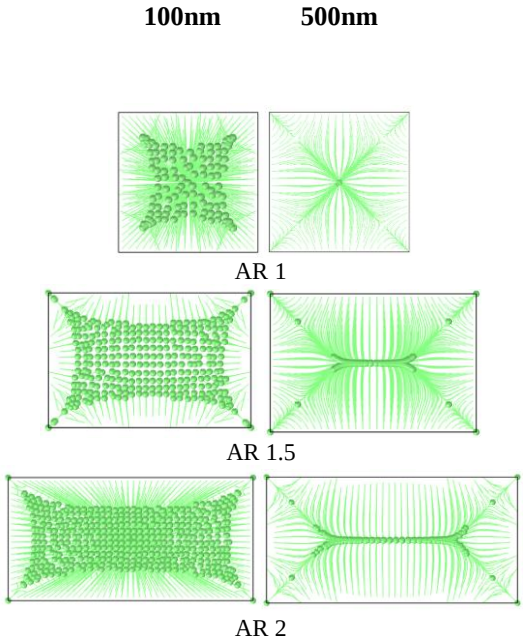

Figure 2. Particle focusing 100 nm and 500nm for aspect ratio 1, 1.5 and 2 at Reynolds number 8 and polymer concentration 0.1 percent in the outlet of the channel

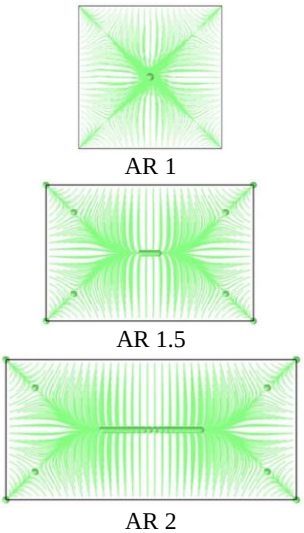

Figure 2. Particle focusing 1000nm for aspect ratio 1, 1.5 and 2 at Reynolds number 8 and polymer concentration 0.1 percent in the outlet of the channel

are consistent with previous results [21,22].

Particle movement in square geometry is more focused than the other two channels in the viscoelastic fluid and this happened because of the stronger shear rate in this geometry in the similar situation [23]. As mentioned above, particles in rectangular channels with aspect ratios 1.5 and 2 can't be focused in the center of the channel greatly [23] and they have settled the positions in center and the position between corner and center as well [24]. It is concluded from Figure 2-3, the aspect ratio variations affect strongly in particle behavior. By increasing the aspect ratio, the velocity profile becomes flatter and this leads to the weakening of the shear rate and the elastic lift force because the elastic and inertial forces applied to the particle, have a strong dependence on the shear rate. On the other hand, due to the dependence of the elastic force on the third power of the particle, the diameter of the particle also is effective in increasing or reducing this force. Large particles have a faster lateral migration. Depending on the mentioned factors, it can be concluded that particles with larger diameters have a larger elastic lift force and for particles with a smaller diameter, the elastic lift force is smaller. This result is obtained that for square geometry and larger size of particles, there is the greatest focusing as 3D [25] focusing or single line focusing; this event is visible in figures 2-3. On the other hand, results represent that in rectangular geometries as a larger scale channel, 3D focusing has not been seen greatly [21].

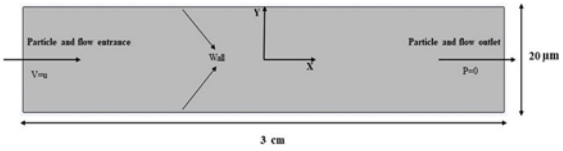

Figure1. The geometry of the present work for three channels with height of 20µm and width of 20µm, 30µm and 40µm

Table 1- geometric and flow characteristics

parameter	quantity
Re	8
Q ($^{\mu l}/_{min}$)	0.388
λ (s)	0.00055
η_s(Pa*s)	0.00041
η_p(Pa*s)	0.001
C	0.1%
ρ_p(kg/m^3)	1050
ρ_s(kg/m^3)	995
M_w (kDa)	400
width (µm)	40; 30; 20

4. conclusions

EVs have been increasingly utilized as diagnostic, prognostic and predictive biomarkers. To analyze EVs isolation, biological nanoparticles focusing on quadrilateral straight geometries have been examined successfully with a passive viscoelastic fluid method in the first stage of this work. As the particle size decreases, focusing is a challenging issue. On the other hand, in nano particle application reduction the size of the channel is difficult or even impossible to build a channel. Fabricate large scale methods for exosome and nano particle should be given more attention. Single line focusing, which is the best pattern of particle focus, is well visible in a square geometry with a cross-section of 20 x 20 µm square with an aspect ratio of 1 and a Reynolds number of 8 for particles between 500 and 1000 nm. In the geometry with aspect ratio of 1.5 and 2, no single concentration has occurred, which can be used to improve the concentration of particles in geometries with aspect ratio higher than 1, by increasing the concentration of polymer within the allowed range and increasing the flow rate, as well as combining passive methods with each other or with active methods is also used

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