

A particle flow specific boundary element formulation for microfluidic applications

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Abstract In this study, a special formulation to obtain velocities of particles flowing within a microchannel is presented. The formulation is based on boundary element method, and the large system matrices resulting from the analysis is reduced to a system of linear equations with the unknowns being the rigid-body motion parameters of the particles. This reduction is achieved through matrix multiplications which increases computational efficiency when compared with the solution of a large system of equations. Since the formulation involves mainly matrix multiplications, parallelization is straightforward. With the presented algorithm, only the position of the particle(s) are tracked through the solution of their rigid-body velocities and an explicit time integration to obtain displacements. Due to the boundary-only nature of the boundary element method, the particle flow in close proximity to the channel walls are very effectively modeled without any need for specific model. The presented method is given in 2D, where the 3D formulation is straightforward. To demonstrate the applicability of the method, besides some benchmark problems, two fundamental processes, namely flow cytometry and hydrodynamic-based particle separation, are studied. It is observed that present formulation offers an efficient numerical model to be used for the simulation of the particle trajectory for 2D microfluidic applications and can easily be extended for 3D multiphysics simulations.

Keywords: Boundary element method, microfluidics, particle flow, Stoke's flow

1. Introduction

Manipulation of bioparticles within the microchannels is a key ingredient for many microfluidics-based biomedical and chemical applications. Therefore, for an efficient design of microfluidic systems, the simulation of the motion of the bioparticle(s) with different shapes is crucial. In many applications of microfluidics, particles are under the action of electrical, magnetic and/or acoustic field together with the flow field. Particle trajectory is the result of the interaction of the particle with the fields that are present. One approach to model the particle trajectory within the microchannel is the stress tensor approach. In this approach, the field variables are solved with the presence of the finite-sized particle. The resultant force on the particle can be obtained by integrating the appropriate stress tensor on the particle surface. In each incremental movement of the particle, the field

variables need to be resolved. In many studies, this approach has also been successfully implemented [1,2] to explore the nature of the bioparticle flow within a microchannel.

A rigorous simulation of the particle motion utilizing tensor approach requires massive remeshing. For methods involving domain discretization, such as finite element method (FEM) or finite volume method (FVM) not only the remeshing process is computationally expensive, but also at each remeshing step, some interpolating algorithms relating the field variables in the new mesh in terms of the variables of the old mesh are required which causes some loss in the accuracy. Moreover, the determination of the forces induced on the particles requires the calculation of gradient of the field variables. Therefore, for an accurate calculation of gradient of field variables, fine mesh is required on and within the close neighborhood

of the particle surface. Due to the computationally expensive nature, only 2D models with relatively coarse mesh and the motion of single particle have been worked on using FEM. To overcome the remeshing problem for the simulation of particulate flow at macroscale, immersed boundary method [3] and fictitious domain method [4] have been proposed and implemented. Although these methods are computationally very efficient, to model the particle-particle interaction, some contact modeling is required which has a resolution that cannot be accepted for the simulation at microscale. Moreover, these methods are well established for flow simulations, but very rare studies exist for the coupling of flow with the electrical and/or magnetic fields.

Considering the microchannel networks within the microfluidic devices, typical flow speed is low (resulting in very low Reynolds number) and the inertia forces are negligible (in magnitude) when compared to the pressure or the viscous forces. The flow can be considered as the so-called creeping flow. The governing equations of the creeping flow are those of the Stoke's flow, which are linear partial differential equations suitable for solution with the Boundary Element Method. Since the BEM does not require meshing within the flow region and the exact calculation of the gradient of the field variables, and considering the linearity of the governing equations, it is a preferable tool for the simulation of the trajectory of particles in a microchannel.

In this study, a formulation to track the motion of the particles within a microchannel flow is presented. The method involves the re-organization of the BE matrices that are evaluated for the flow problem, and through several manipulations, reducing the problem to a linear system of equations where the only unknowns are the motion parameters (eg., the translational and rotational velocities of the centers of gravity) of the particles. With such manipulation, the dimension of the linear system of equations to be solved is reduced drastically, resulting in a comparably fast solution. Since the presented manipulations are

all matrix multiplications, the procedure can easily be parallelized. To assess the formulation presented, a benchmark study from the literature is considered. Some results related with practical microfluidic applications are also presented. The present formulation offers an efficient numerical model to be used for the simulation of the particle trajectory for microfluidic applications, and can easily be extended for 3D multiphysics simulations

2. The Boundary Element Formulation for Stoke's Flow

Defining a modified pressure as:

$$P = p - \rho g \cdot \mathbf{x}, \quad (1)$$

where \mathbf{x} represents the Cartesian coordinates and ρg is the body force, the Stoke's equation (assuming the inertial effects to be negligible) can be rewritten as [5]:

$$-\nabla P + \mu \nabla^2 \mathbf{u} = 0, \quad (2)$$

where \mathbf{u} is the velocity vector (its components will be denoted as u_i) and μ represents the viscosity of the fluid. Denoting the components of the hydrodynamic traction as t_i on the boundary of the solution region, the BE formulation can be obtained in 2D in the integral form [5]:

$$C_{ij}(\mathbf{A})u_j(\mathbf{A}) = \int_C G_{ij}(\mathbf{A},\mathbf{P})t_j(\mathbf{P})dS - \int_C H_{ij}(\mathbf{A},\mathbf{P})u_j(\mathbf{P})dS \quad (3)$$

In Eq. (3), $C_{ij} = \delta_{ij}$ if $\mathbf{A} \in V$, $\delta_{ij}/2$ if \mathbf{A} is on a smooth boundary, and 0 if $\mathbf{A} \notin V$. The 2D fundamental solutions can be found in literature [6]. In Eq. (3) and in the following equations, unless otherwise is explicitly stated, Einstein's summation convention is used.

In this study, for boundary discretization, constant elements are employed where the variation of any field variable over the element is assumed to be constant with the value that it has at the computational node of the element.

When the boundary of the solution region is discretized with N constant elements, Eq. (3) can be written at a fixed point \mathbf{A}_l belonging to the element l as:

$$\frac{1}{2}u_i^l + H_{ij}^{kl}u_j^k = G_{ij}^{kl}t_j^k, \quad (4)$$

where u_i^l and u_k^k are the i^{th} and j^{th} components of the velocity vector evaluated at the nodes of the l^{th} and k^{th} elements respectively, and similarly t_j^k is the j^{th} component of the traction vector evaluated at the node of the k^{th} element ($l, k=1..N$). The terms

$$G_{ij}^{kl} = \int_{C_k} G_{ij}(\mathbf{A}_l, \mathbf{P}_k) ds \quad (5)$$

and

$$H_{ij}^{kl} = \int_{C_k} H_{ij}(\mathbf{A}_l, \mathbf{P}_k) ds \quad (6)$$

where C_k represents the element boundary, and \mathbf{P}_k is the varied (integration) point on the k^{th} element. This equation can be re-written (if diagonals H_{ii}^{ll} are augmented with 1/2) as:

$$H_{ij}^{kl}u_j^k = G_{ij}^{kl}t_j^k \quad (7)$$

This gives a set of $2N$ equations in terms of $4N$ unknowns:

$$\mathbf{H} \cdot \mathbf{u} = \mathbf{G} \cdot \mathbf{t} \quad (8)$$

The imposition of boundary conditions can be achieved by swapping the columns and the solution can be obtained with $2N$ boundary conditions imposed.

2.1 Formulation of particle trajectory

The resultant drag force on the particle can be determined by integrating the hydrodynamic-stress tensor over the particle surface. Once the resultant forces are evaluated, Newton's second law of motion can be utilized to obtain the acceleration of the particle, which then can be integrated to calculate the new position of the particle. This approach can be applied for any geometry and it inherently includes the particle-particle interaction and also the interaction of the particle with the field.

A major drawback of this approach is that the particle velocities are not obtained directly; instead an indirect evaluation through time integration of the acceleration is employed. Moreover, it is computationally expensive, especially if domain discretization is needed (as in FEM), since as the particle moves in the microchannel, the mesh needs to be updated from time-to-time. At this point the BEM introduces special advantages: (i) the particle

velocities are obtained directly, (ii) due to the boundary-only discretization of the BEM, remeshing is much simpler and no interpolation of the internal field variables are required - for an undeformable body, only the mesh on the particle surface needs to be moved in accordance with the calculated velocities. Utilizing this fact, Dustin and Luo [7,8] implemented the BEM to simulate the particle trajectory within a microchannel under the action of electrophoretic and electro-osmotically driven flow field.

For the BE formulation of the particle trajectory, an incremental time stepping is suggested. At each time increment, the fluid flow will be assumed to be steady. This assumption holds if the particle dimensions are sufficiently small when compared with the characteristic dimensions of the problem (for example, channel wall dimensions) and if the change of location of the particle within one time increment is not significant. In this case, the inertial terms in the fluid flow equation can be neglected, and a quasi-steady-state assumption can be made. In the analysis, further assumptions can be stated as: the particle is buoyant, e.g. the net force acting on it (as it freely moves within the medium) is zero, and the mass of the particle and the time rate of change of its velocity is sufficiently small (which is typical for microfluidics applications [9]). Moreover, within the framework of this analysis, the particle is assumed to be rigid.

A special note should be stated here: the purpose of the study is to track the particle trajectory within a microchannel. Therefore, the solution of the field variables on the channel boundaries and the boundaries of the moving particles is of no practical use; what is more important is the rigid motion parameters, eg., translational and rotational velocities, of the particles. For this reason, a special formulation devised from the above given boundary element equation will be presented below. The formulation credits to the studies of Argeso and Mengi [10] on poroelastic and poroviscoelastic media, and Yalcin and Mengi [11] on wave load analysis. The method is named as impedance formulation by the stated

authors. In this study, we will formulate the impedance relation to model the rigid-body motion of particles in Stokes flow.

The imposition of boundary conditions requires, at all points of the defined boundary, the definition of one and only one of the couples (u_n^m, t_n^m) or a combination of the two, where m represents the node number and n is the direction of the component of the vector. When the motion of a particle within the fluid is considered, neither the velocity components nor the traction components nor a combination of the two is known at a given element m . Instead we impose the rigid body motion conditions:

$$u_i = u_i^B + r\omega\hat{t}_i \quad (9)$$

where u_i represents the velocity components of the node on the particle, u_i^B are the velocity components of the center of gravity (CG) of the particle, ω is the angular velocity of the particle about the CG, r represents the distance from the corresponding node to the CG and \hat{t}_i are the components of the unit vector that is normal to the line segment drawn from the CG of the particle to the node (the direction of the normal is selected using right hand rule, counter-clockwise). Writing Eq.(9) at each particle node, a matrix relation as

$$\mathbf{u}_P = \mathbf{M} \cdot \mathbf{u}^B \quad (10)$$

can be written where \mathbf{u}_P is the vector that contains the nodal velocities at the nodes of the particle boundary and \mathbf{u}^B represents the rigid body velocity components at the center of the particle (including the angular velocity). Here, \mathbf{M} is a (2S x 3) coefficient matrix.

The force on any element can be calculated through integration of the traction vectors on that element. In this study, constant elements are employed; therefore this integration can be obtained simply using

$$f_i^s = \int_{C_s} t_i(\mathbf{P}_s) dS = t_i^s L^s \quad (11)$$

where f_i^s are the components of the force vector at the s^{th} node, C_s represents the element boundary, L^s is the length of the element and t_i^s are the traction components. The moment of this force about the CG is given by

$$m^s = r_1^s t_2^s - r_2^s t_1^s \quad (12)$$

where r_i^s are the components of the relative position vector of the element node with respect to the CG and the moment, m , is taken in counterclockwise sense. With Eq.(11) and(12) one can write the matrix relation

$$\mathbf{f}^B = \mathbf{F} \cdot \mathbf{t}_p \quad (13)$$

where \mathbf{t}_p is the vector containing the traction components at each element, \mathbf{f}^B is the augmented (with m) resultant force vector at the CG, and \mathbf{F} is the coefficient matrix.

At this point, we re-partition Eq.(8) to get

$$\begin{bmatrix} \mathbf{H}_{00} & \mathbf{H}_{0P} \\ \mathbf{H}_{P0} & \mathbf{H}_{PP} \end{bmatrix} \begin{Bmatrix} \mathbf{u}_0 \\ \mathbf{u}_P \end{Bmatrix} = \begin{bmatrix} \mathbf{G}_{00} & \mathbf{G}_{0P} \\ \mathbf{G}_{P0} & \mathbf{G}_{PP} \end{bmatrix} \begin{Bmatrix} \mathbf{t}_0 \\ \mathbf{t}_P \end{Bmatrix} \quad (14)$$

Here, the subscript 0 represents the corresponding variables are evaluated on the non-moving boundary and the subscript P represents the same for moving (particle) boundary.

We assume the vector \mathbf{u}_0 is fully known and \mathbf{t}_0 is fully unknown, which would not affect the formulation, if necessary column changes were made for unknown-known variables. From the first row of Eq.(14) one can obtain

$$\mathbf{t}_0 = \mathbf{G}_{00}^{-1}(\mathbf{H}_{00}\mathbf{u}_0 + \mathbf{H}_{0P}\mathbf{u}_P - \mathbf{G}_{0P}\mathbf{t}_P) \quad (15)$$

With Eq.(15) and the second row of Eq.(14) one can write

$$\mathbf{B}\mathbf{t}_P = \mathbf{A}\mathbf{u}_P + \mathbf{C}\mathbf{u}_0 \quad (16)$$

where

$$\begin{aligned} \mathbf{A} &= [\mathbf{H}_{PP} - \mathbf{G}_{P0}\mathbf{G}_{00}^{-1}\mathbf{H}_{0P}], \\ \mathbf{B} &= [\mathbf{G}_{PP} - \mathbf{G}_{P0}\mathbf{G}_{00}^{-1}\mathbf{G}_{0P}], \text{ and} \\ \mathbf{C} &= [\mathbf{H}_{P0} - \mathbf{G}_{P0}\mathbf{G}_{00}^{-1}\mathbf{H}_{00}] \end{aligned}$$

With Eq.(10), (13) and (16) one can obtain

$$\mathbf{f}^B = \mathbf{F}\mathbf{B}^{-1}\mathbf{A}\mathbf{M}\mathbf{u}^B + \mathbf{F}\mathbf{B}^{-1}\mathbf{C}\mathbf{u}_0 \quad (17)$$

Note that this constitutes a system of three equations for three unknowns, which can be solved easily. In a no-force application, this equation will be solved with the condition that $\mathbf{f}^B = \mathbf{0}$.

Note also that, the formulation can simply be extended to include more particles; in this case, for each particle, the equation will be re-written.

2.2 Computational aspect of the formulation

In the presented formulation, the matrices \mathbf{G}_{00} and \mathbf{H}_{00} are evaluated only once at the beginning of the program. Also, before particle tracking the matrix \mathbf{G}_{00} is inverted only once. In the problems of particle flow within microchannels, the discretization of the non-

moving boundary (the microchannel boundary and those of the fixed boundaries within the microchannel) is done with a large number of elements. Especially, if the particle is (or gets) close to the microchannel walls, then the element sizes should also be decreased to avoid near-singularity problems and increase accuracy. As a result, the stated matrices constitute to a very large portion of the assembled coefficient matrices. With the application of presented procedure, at each time increment, the solution of a very large linear system is avoided - instead through matrix multiplications the system is reduced to a linear system of equations with three

3. Results and Discussion

To validate the BE formulation, a benchmark problem from the literature, the drag force generated on a stationary particle placed in a Poiseuille flow is considered, as in [12]. The schematic drawing of the problem is given in Fig. 1. The non-dimensional drag force with respect to changing geometrical dimensions (for $Re = 0.0002$) is given in Table 1. For comparison, the results from [12] together with the Faxen formula are given in the same table. It should be noted that the Faxen formula, being the analytical solution, is valid for $k(=a/b) \leq 0.5$.

Table 1: Comparison between present study and results from literature for a stationary cylinder in a Poiseuille flow ($Re = 2 \times 10^{-4}$)

$k(=a/b)$	Present Study (PS)	Results from [12]	Faxen results from [12] (FR)	Rel. % error between PS and FR	Rel. % error between [12] and FR
0.010	3.4014	3.5393	3.4057	0.13	3.9
0.025	4.5229	4.7145	4.5282	0.11	4.1
0.050	6.0116	5.9999	6.0214	0.16	0.4
0.100	8.8826	9.1630	8.9060	0.26	2.9
0.200	16.1373	16.3585	16.2072	0.43	0.9
0.400	48.3733	48.8511	48.6229	0.51	0.5
0.800	1210.5227	1256.1650	--	--	--
0.900	7670.6609	7361.3287	--	--	--
0.950	44,442.2830	44,093.1632	--	--	--
0.990	2,104,695.6000	2,116,270.2200	--	--	--
0.995	7,254,008.7218	--	--	--	--
0.999	20,342,810.0056	--	--	--	--

unknowns per each particle.

As the particle motion is tracked at each time increment, only the matrix \mathbf{B} is inverted. Since the particle is very small compared with the characteristic dimensions of the problem, the number of elements used in discretizing the particle will be very small; so that the inversion process will not take much computation time. The rest of the formulation involves only matrix multiplications. When compared with the solution of a very large system of equations (eg. using LU decomposition or any other direct or iterative technique) this will constitute to a less computational effort. Since the tracking involves many increments in time, a shorter computational time at each increment will result in a considerable amount of time saving in simulation.

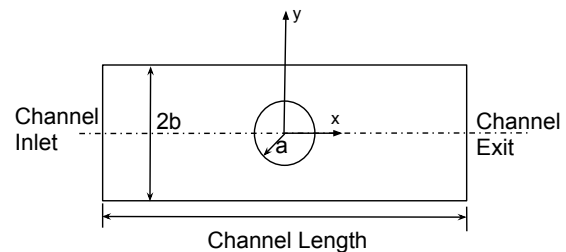


Figure 1: Schematic drawing of the benchmark problem

Following the verification, the current formulation is implemented to simulate particle motion in a microchannel. First, the simulation of the flow of a single circular and an elliptic particle in a microchannel is performed. Afterwards, to demonstrate the effectiveness of the formulation for real application-based problems, the particle motions of many particles are simulated for

flow cytometry and hydrodynamic separation applications. In the simulations, the density of the fluid is taken as 1000kg/m^3 , and the viscosity is taken as 0.001Ns/m^2 which are the typical values for water (for bioparticle based applications, the buffer solutions are water-based solutions). The particle is assumed to be buoyant which is the case for many bioparticles. At the inlet of the channel, uniform velocity of $300\mu\text{m/s}$ is assigned (with these input parameters Reynolds number 10^{-2}).

($D=10\mu\text{m}$) and elliptic (with long-axis diameter of $10\mu\text{m}$ and a short-axis diameter of $6\mu\text{m}$) particles flowing in a microchannel with a length of $500\mu\text{m}$ and a width of $100\mu\text{m}$ are illustrated in Fig. 2. The particles are released from different y -locations. For each time step of 0.25s , the orientations of the particles are shown in the Figs. 2-(a) and 2-(c). To demonstrate the rotation of the particle, one point on the particle is marked with red dot. The x -velocity and the angular speeds of the particles are given in Fig. 2-(b) and 2-(d). For

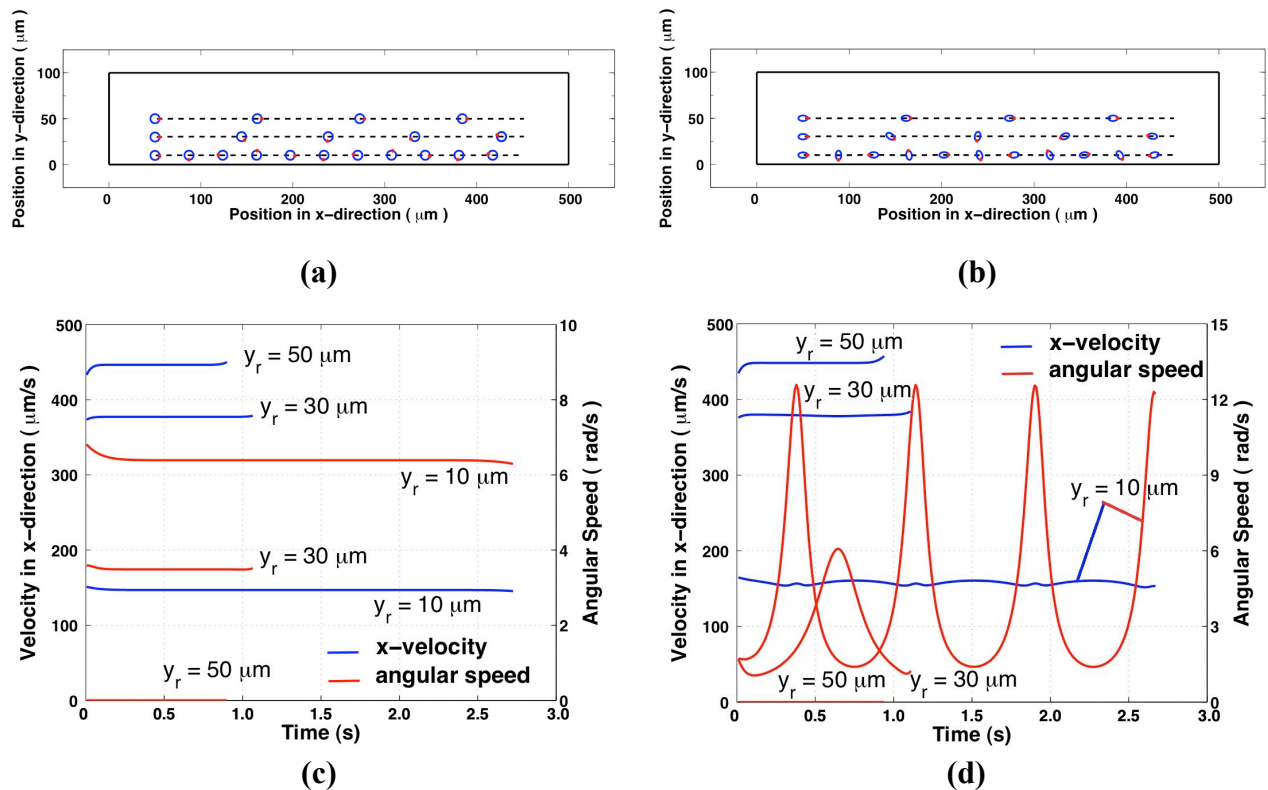


Figure 2: (a) Motion of circular particle in a microchannel released from different y -locations (y_r) (b) x -velocity and angular speed of the circular particle, (c) Motion of elliptic particle in a microchannel released from different y -locations (y_r), (d) x -velocity and angular speed of the elliptic particle

On the channel walls and the particle surface, no-slip boundary condition is applied. Zero hydrodynamic traction at the outlet of the channel is assigned. The simulations were performed on an HP Z400 Workstation (Intel Xeon W3550, Quad Core, 3.06GHz, 16GB RAM). Element size of $2\mu\text{m}$ is used on the channel walls, and 32 elements on the circular particles and 24 elements on the elliptical particles are used. The motion of a circular

circular particle, since it is a particle in a Stoke's flow, the x -velocities and the angular speed of the particles are steady. As the particle moves closer to the centerline it travels with a higher velocity due to the parabolic nature of the velocity profile; therefore, the x -velocity of the particle increases. As the particle moves closer to the channel wall, the symmetry of the flow at the upper and the lower surface of the channel

distorts which results in a higher rotational speed; hence, the angular speed of the particle increases. Since the velocity on the upper half of the particles is higher than the lower half, the rotation of the particles is in the clock-wise direction. Due to the symmetry of the flow field, the particles released from upper half of the channel would have the same trajectory with a counter-clockwise rotation. Similar conclusions to that of spherical particle are valid for the elliptic particle. However, the major difference is the x -velocity and the

restriction when a detection system is attached on the top of the channel to count the number of particles passing through the restriction. In flow cytometry applications, it is important that particles flow one-by-one through the restriction. The common practice for flow cytometry is the use of a specially designed nozzle structure to ensure the pass of the particles one at a time. Recently, there are studies for the on-chip cytometry. For on-chip cytometry, the design of the microchannel network is important for the efficiency of the

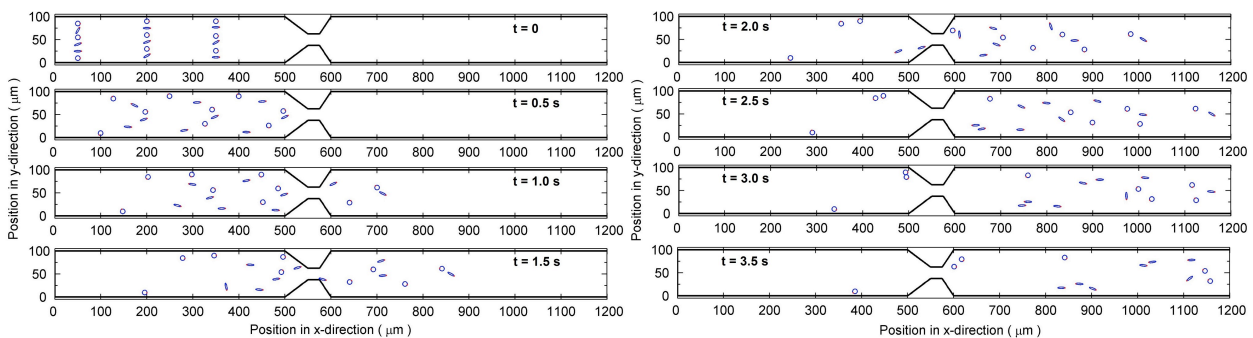


Figure 3: Simulation of the particles in a microchannel for a flow cytometry application (flow is from left to right) (dotted lines indicate the position of the particles at the previous time)

angular speed of the particle. For the angular speed, there exists a steady periodic behavior due to the geometry of the particle. The magnitude of the angular speed depends on the instantaneous orientation of the particle. For the x -velocity, a steady behavior can be observed when the particle is flowing away from the wall. However, as the particle is flowing in the vicinity of the wall, x -velocity has a steady periodic behavior. The effect of the interaction of the particle with the wall can be observed in the figure: there appears a small disturbance in the x -velocity at the point of maximum angular velocity which corresponds to the orientation of the particle where the long axis is perpendicular to the wall (i.e. the spacing between the particle and the wall reaches a minimum). As seen from the figures both the translational and rotational motion of a particle can be captured rigorously with the current formulation.

3.1. Flow cytometry

Flow cytometry is a process where particles are forced to flow through a

device. To demonstrate the applicability of the current numerical model, a practical case for an on-chip cytometry is simulated. Flow of eighteen particles in a microchannel with a length of 1600μm and a width of 100μm is considered. The particles are located at different initial positions. The shapes of the particles are circular ($D=10\mu\text{m}$) and elliptical (with long-axis diameter of 15.6 μm and a short-axis diameter of 3.2μm) to resemble the flow of cells and bacteria. To perform the counting, a restriction is placed at a location 500μm from the inlet with a spacing of 25μm. Time step is taken as 0.001s. The motion of the particles is shown in Fig. 3. As seen from the figure, the current formulation can predict the trajectory of the particles. Due to the laminar nature of the flow velocity, particles are flowing with different velocities, and as they approach to the restriction, there exists a sucking phenomena which results in the one-by-one pass of the particles. One important characteristic of the bioparticles is that their size is not a fixed quantity; rather there exists a size distribution for a given type of cells. With

the current formulation, the size of the particles can vary, the effect of the particle size on the flow through the restriction can be obtained. Although it is not clear from the figure, red dots are also included to show the rotational behavior of the particles.

3.2. Hydrodynamic particle separation

Particle separation is important in many biological applications. Although there exist many methods like dielectrophoresis, magnetophoresis, acoustophoresis for particle

current formulation can predict the trajectory of the particles, and also the performance of the separation. While the particles are turning the corner of the hurdle, they are pushed by the corner. The particles released at the bottom flow closer to the wall, therefore they move very close to the corner. As a result, circular particles follow at a different streamline than that of the elliptic particles after the hurdle. For the case of the particles released from the above, their flow is not close to the corner enough to achieve hydrodynamic separation.

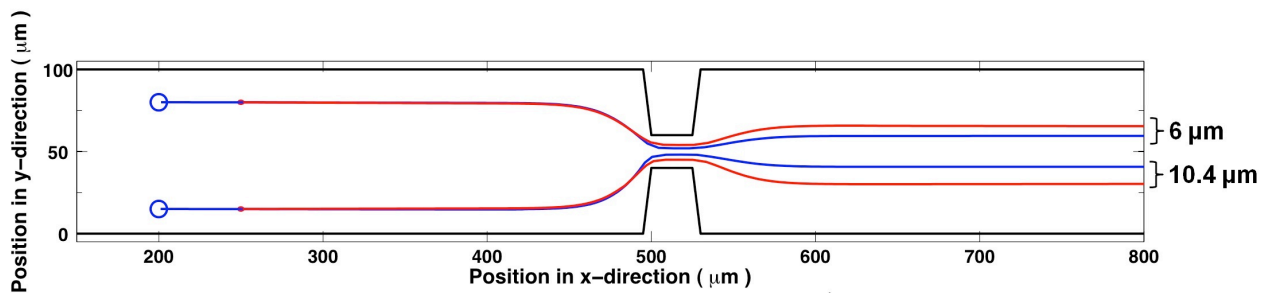


Figure 4: Trajectory of the centers of the particles (**blue:** circular particles, **red:** elliptic particles)

separation, hydrodynamic separation [13] is one of the robust methods in which the change in the flow characteristics by modifying the microchannel geometry affects the motion of the particles depending on their sizes and shapes. For a successful separation there needs to be appreciable size difference between the particles, though. However, there are some practical applications in which there exists size difference between the particles of interest to be separated. One example is the separation of the blood cells (typically 8-15 μm) and bacteria (typically 1-3 μm) in urine, or whole milk.

In this case, flow of four particles in a microchannel with a length of 1600 μm and a width of 100 μm is considered. The particles are located at different initial positions. The shapes of the particles are circular ($D=10\mu\text{m}$) and elliptic (with long-axis diameter of 5 μm and a short-axis diameter of 3 μm) to resemble the flow of cells and bacteria. Time step is taken as 0.005s. To perform the hydrodynamic separation a restriction is placed (which is a common approach in the literature [13]) at the middle with a spacing of 25 μm . The trajectory of the center points of the particles is also included in Fig. 4. As seen from the figure, the

This is a clear image to demonstrate how the current formulation can be utilized to assess the performance of a hydrodynamic separation. With this current tool, an optimized design can be achieved by analyzing different cases with different geometry and/or flow rate.

4. Summary and Outlook

In this study, a new formulation to track the motion of the particle(s) within a microchannel is presented. The method is presented in 2D pressure-driven flow, but it can easily be extended to 3D. To evaluate the translational and rotational velocities at the particle CG, the system matrices of the BEM are employed. Through matrix manipulations, the system of equations are reduced drastically which also decreases the computational effort. Current model is compared with some benchmark problems from the literature and excellent consistency is achieved. Comparison of the BEM with the FEM is also presented. To demonstrate the applicability of the method, two fundamental processes namely microfluidic flow cytometry and hydrodynamic-based particle separation are demonstrated.

The novelties and advantages of the presented formulation can be stated as:

- Instead of solving the large linear system of equations arising from the BE formulation of Stokes flow, through matrix manipulations, the size of the system of equations is reduced to a form where the unknowns are only the motion parameters (e.g., translational and rotational velocities at the CG) of the particles. This introduces only three unknown per particle, which, when compared with the original system of equations, is a small system to be solved.
- The solution of a linear system of equations using direct (e.g., LU decomposition) or iterative (e.g., Gauss-Seidel) methods lack efficient parallel algorithms. In the presented method, a large system matrix is inverted only once (at the beginning) and rest of the algorithm involves only matrix multiplications at each time step and an inversion of a comparably very small system matrix. Noting that matrix multiplications can easily and very effectively be parallelized, both in CPU and in GPU, the presented method is expected to be suitable for parallel programming. This property of the method would be very beneficial especially for 3D problems.
- The final form of equations is presented in an impedance form; the forces on the particles are directly related to the velocity components of the particles through a matrix relation. This presents several opportunities for future research; e.g., instead of taking the resultant forces to be zero, any external force resulting from the interaction of the particles with other external fields (such as electrical/magnetic/acoustical, etc.) can be given to obtain the particle velocities. This will expand the applicability of the formulation for multiphysics problems which is very common in microfluidic applications.

A main disadvantage of the presented method is that it does not solve for the field variables on the boundary, which is not a very critical issue when tracking particles. This may be thought of as a post-processing step, if flow parameters are required at a calculated position

of the particles.

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