FINITE SIMULATIONS OF MICRO-PARTICLE SUPPORTING FOR SINGLE CELL TRAPPING IN MICROFLUIDIC SYSTEM

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Abstract: *Finite element method (FEM) is the most widely used approach in the simulation of micro-nano devices before actual fabrication. Using simulation software, 2D and 3D structures of the device are designed, meshed, and then simulated to optimize their parameters. In this work, we modeled and simulated the hydrodynamic trapping of micro-particle (μP) representing for single-cell in the microfluidic system. Besides, the interaction between μP and fluid, the effect of flow velocity, and the pressure field variation for increasing the trapping efficiency were investigated. Besides, a fully understanding the behavior of micro-particle during the trapping process is exhibited. Based on the achieved results, the optimization of the design will be adjusted as a pre-step before being used for fabrication and experiment. The simulation results are valuable for designing and fabricating the microfluidic platform for single-cell research.*

Keywords: Microfluidic; Single cell trapping; Finite element simulation.

1. INTRODUCTION

In recent year, microfluidic systems have raised much attention of researchers worldwide because of their unique advantages such as less power consumption, small reagent volumes, biocompatibility, and high sensitivity [1, 2]. By miniaturizing structures that are similar to cell size, microfluidic devices have emerged as powerful tools for single-cell studies. Several microfluidics devices have been developed for single-cell separation [3], single-cell culture [4], single-cell analysis [5], and single cancer cell migration [6] in cell biology. In those devices, the prerequisite step is the isolation of single-cells from the cell suspension flow. However, the capability to capture a single-cell in the traps depends on diverse aspects such as the fluid flow from the inlet, the shape of the trap, and the density of the cell flow. To increase cell trapping efficiency, one needs to understand the hydrodynamic behavior of the cell in the fluid flow.

To figure out the motion of the cell inside the microchannel and develop a proper microfluidics system, FEM module has been widely used [7, 8]. By incorporating different complex parameters of the device and the cell, the cell-microfluidic hydrodynamic behavior can be predicted and visualized. As a result, the simulation process help researchers improve their design, reduce the cost, and set up the experiment properly. Among diverse FEM software, COMSOL Multiphysics is a cross-platform finite element analysis for multi-physics simulation [9]. This software allows integrating the microenvironment with a unified workflow for direct simulation of the microfluidics system. Furthermore, it also provides a huge library with different types of physics and materials, which aid in being able to easily change any parameter and switch the environment of the system to suit each experiment individually.

In this paper, we create a FEM simulation model using COMSOL Multiphysics software to model and simulate the hydrodynamic trapping of μP supporting for single-cell trapping in the microfluidic system. To understanding the flow of each μP inside the microchannel, the interaction between particle and fluid, the effect of flow velocity, and the pressure field variation are investigated. We also study the time-dependent simulation of the μP trapping process for increasing trapping efficiency. Based on the achieved

results, the optimization of the design system will be adjusted as the pre-step before being used for cell trapping. The simulation results are valuable for designing and fabricating the microfluidic platform for single-cell research.

2. THEORY

2.1. Fluid flow

The fluid flow in microfluidic systems, if assumed incompressible, is described by the Navier-Stokes equations [10].

$$\rho_f \frac{\partial u_f}{\partial t} + \rho_f (u_f . \nabla) u_f = \nabla . [-p_f I + \mu_f (\nabla u_f) + (\nabla u_f)^T)] + F_f,$$

$$\rho_f \nabla . u_f = 0,$$

where ρ_f denotes the fluid density (kg/m^3), $u_f = (u_f, v_f, w_f)$ the fluid velocity field (m/s, m/s, m/s), t the time (s), p_f the pressure (Pa), $\nabla . ()$ the divergence operator, $\nabla ()$ the gradient operator, I the identity matrix, and μ_f the fluid dynamic viscosity (Pa.s). Moreover, $\rho_f \frac{\partial u_f}{\partial t}$ represents the unsteady inertia force (N/m^2), $\rho_f (u_f . \nabla) u_f$ represents the non-linear inertia force, and F_f is the volume force affecting the fluid (N/m^3, or N/m^2 for a 2D model). For a pressure driven flow without gravitation or other volume forces, $F_f = 0$. Given the values of ρ_f, t, F_f, and μ_f, the Navier-Stokes equations solve for u_f and p_f.

2.2. Boundary and initial conditions

The fluid flows inside the microchannel, driven by the pressure difference between the inlet and the outlet. At the inlet, the flow is defined as laminar flow with a parabolic velocity profile and the mean velocity u_0 (m/s). Defining a parabolic velocity profile ensures a better convergence of the nonlinear solver at the beginning in comparison with constant velocity. A simple definition of the inflow velocity profile U_0 for a rectangular channel is [10].

$$U_0 = u_0 . \frac{6(W - Y)Y}{W^2}$$

where W is the width of the inlet, and Y is the material frame coordinate along the inlet.

The boundary condition at the outlet is defined as vanishing viscous stress along with a Dirichlet condition on the pressure:

$$p_f = 0, \mu_f (\nabla u_f) + (\nabla u_f)^T) n = 0$$

On the walls, such as the simulation domain sidewalls and the fixed obstacles (e.g., traps in our particle-trap array device), no-slip wall condition is applied to the fluid,

$$u_f = 0,$$

and the prescribed mesh displacements of these walls are defined as zero.

For the initial values of the fluid velocity field u_f, pressure p_f, particle displacement field u_s, and particle velocity field $\partial u_s / \partial t$, one can assign specific values if there are good estimations. Otherwise, they can be set as zeros for simplicity.

3. FROM DESIGN TO SIMULATION

3.1. Design of the cell trap

Fig. 1 presents the schematic of a single-cell trap inside a microfluidic channel system.

A full microfluidic device is formed by linking those traps together. The trap has an inlet on the left side and an outlet on the right side. The material has a mass and shape (object) in the channel are made of polydimethylsiloxane (PDMS). A liquid solution (water) carrying μP of radius r = 10 μm that represents for a single cell flowing from the inlet through the channel. In the simulation, the μP is defined "solid" in the equations of the solid mechanics and the fluid-solid interaction, while the object is assumed to be fixed and act as the no-slip boundary to the fluid. Besides, the length and the width of the channel are shorted in compared with the real dimension to reduce the computation while remaining its hydrodynamic characteristics. As the inlet effectively injects single or several μPs into the channel at one time, the inflow can be emulated in the simulation by a generic source of μP placed at a certain distance away from the object. The geometric parameters of the single cell-trap and the present simulation parameters are given in Table 1.

The flow through the device is characterized by the Reynolds number

$$R_e = lU\rho_f / u_f$$

The characteristic length l is the μP's diameter 2r, and U (U << 10 cm/s) is the relative velocity between the steady state flow and the microsphere. Re << 1 the system can be treated at the asymptotic limit of Stokes flow

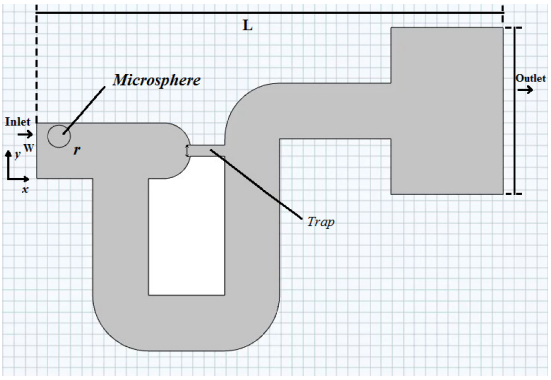


Figure 1. *The design of a single cell trap.*

Table 1. *The dimension of microfluidic channel and other initial parameters.*

v_0	450 [μm/s]	4.5E-4 m/s	Inlet mean velocity at stationary state
L	420 [μm]	4.2E-4 m	Channel length
W	50 [μm]	0.5E-4 m	Channel width (Inlet)
H	20 [μm]	2E-5 m	Channel height
r	10 [μm]	1E-5 m	Radius of μP
Pos1_Y	38 [μm]	3.8E-5 m	Y position of μP
Pos1_X	20 [μm]	2.0E-5 m	X position of μP
Water_rho	1E3 [kg/m^3]	1000 kg/m^3	Water density
Water_mu	1E-3 [Pa.s]	0.001 Pa·s	Water viscosity
Obj_rho	970 [kg/m^3]	970 kg/m^3	Object density
Obj_E	3 [GPa]	3E9 Pa	Object Young's Modulus
Obj_v	0.49	0.49	Object Poisson's Ratio
Microsphere_rho	1050 [kg/m^3]	1050 kg/m^3	Microsphere density
Microsphere_E	3 [MPa]	3E6 Pa	Microsphere Young's Modulus
Microsphere_v	0.33	0.33	Microsphere Poisson's Ratio
Trap	10 [μm]	0.1E-4 m	Trap of Particle

3.2. Mesh creation

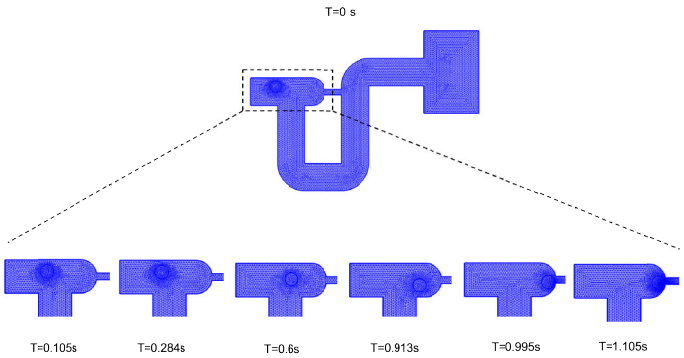


Figure 2. *Mesh and geometry movement and deformation at several time points (t=0 s, 0.105 s, 0.284 s,0.6 s, 0.913 s, 0.995 s, and 1.105 s).*

Fig. 2 shows the mesh creation for solving the model. The mesh was created by free triangle shape with the non-uniform distribution. Herein, the mesh is denser and smaller in the interface of particle-fluid while it is looser and larger in the other part of the fluid. This means that the deformation of the mesh will focus on more important interaction governing the behavior of the μP in the fluid. The mesh distribution around the μP is uniform. Figure also depicts the deformation of the mesh during the movement of the μP in the microchannel. When the particle moves, the mesh deform continuously along the direction of the particle pathway.

4. SIMULATION RESULTS AND DISCUSSION

This section presents the simulation results of the single-cell trap structure based on hydrodynamic trapping phenomenon inside the microchannel. Firstly, the distribution of flow velocity was investigated both in 2D and 3D configurations with the variation of the trap width (W). Secondly, the simulation of the μP displacement during the trapping process is described. Finally, the correlation between particle velocity and particle displacement is illustrated. Based on the simulation results, some important factors are considered before starting the fabrication steps such as the microchannel dimension or the geometries of the trap.

4.1. Simulation in 2D

Fig. 3 illustrates the distribution of flow velocity inside the microchannel in the 2D model.

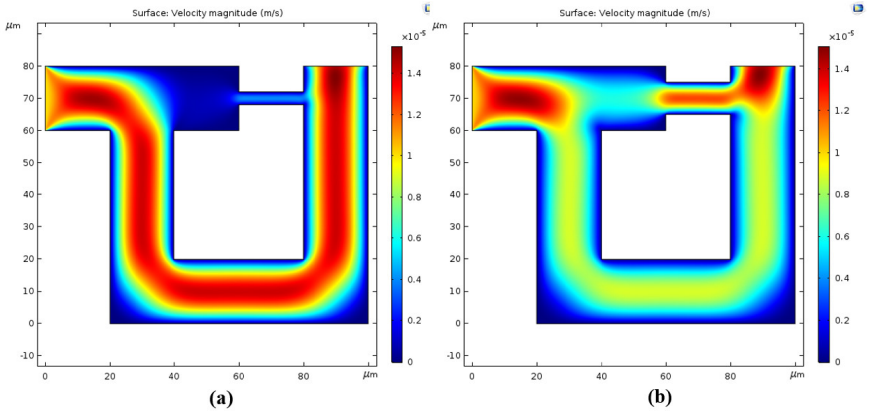


Figure 3. *The 2D model of flow velocity distribution inside the microchannel: (a) the W = 4 μm and (b) the W = 10 μm.*

We simulated with various values of trap width ranging from 4 µm to 12 µm. When the W is smaller than 8 µm, the flow velocity is low as indicated in Fig. 3a by the dark to light blue. It means that the pathway through the trapping region is non-favorable. For a larger trap width, the flow velocity in the trapping region is comparable with the remaining pathway. Based on the simulation results with diverse values of W, a high possibility for cell trapping can be achieved with the W in the range of 10÷12 µm as shown in Fig. 3b.

4.2. Simulation in 3D

The similar results are recorded when we further study the 3D model with corresponding the trap width as in the 2D model. Based on the simulation result, the high possibility to use this structure for cell trapping can be achieved with the same values of W. Fig. 4 presents the simulation result with corresponding W = 10 µm.

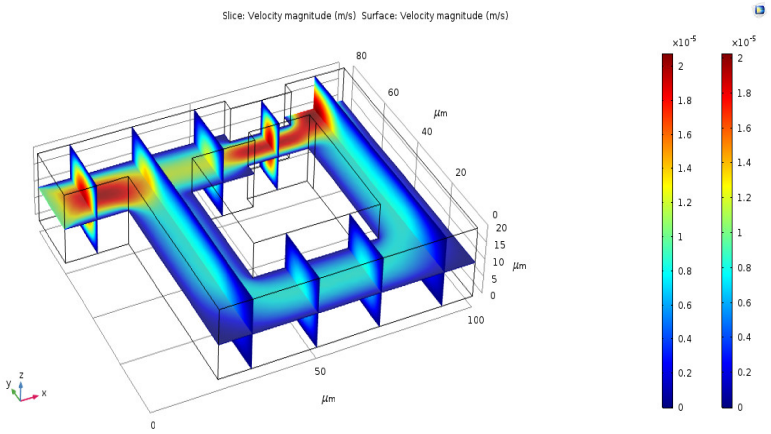


Figure 4. *The 3D model of flow velocity distribution* inside the microchannel with W = 10 µm.

4.3. Study of µP movement on time

4.3.1. The variation of flow velocity on time

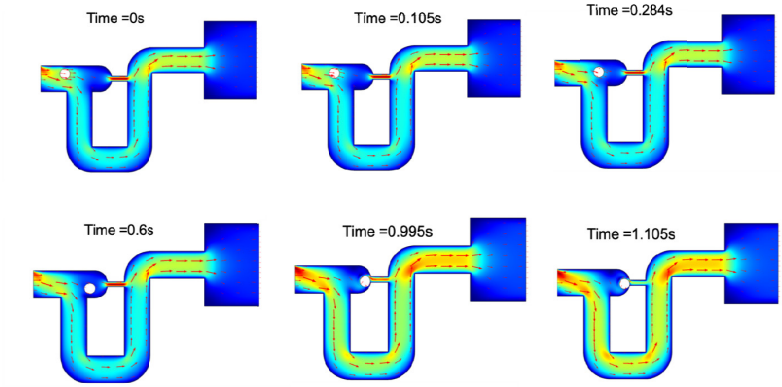


Figure 5. *The flow velocity field at several time points (t = 0 s, 0.105 s, 0.284 s, 0.6 s, 0.995 s, and 1.105 s). The displacement of µP during the trapping process is presented as well. The arrows indicate flow directions and the magnitudes of flow are indicated by the color.*

Fig. 5 presents the simulated flow velocity at several times (t = 0 s, 0.105 s, 0.284 s, 0.6 s, 0.995 s, and 1.105 s). The displacement of µP during the trapping process is presented as well. Herein, the arrows indicate the flow direction and the colour represents for the magnitude of the flow. We can see that at the beginning of the transport process, almost all flows go through the big channel, and therefore, it governs the particle movement to

comes near the trapping structure. When the particle comes nearer the round shape, it is still governed by two streams formed by both big and small channels. At the end of the trapping process, the particle blocks the small channel (the flow velocity reduces). However, a point needs to be considered here is that the particle is not perfectly placed in the trap due to the shape. Thus, the shape of the trapping part should be a triangle or funnel shape to optimize the simulation model.

4.3.2. The particle velocity and deplacements

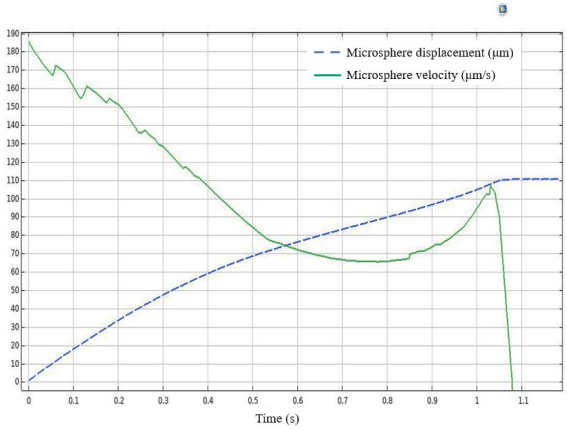


Figure 6. *The particle velocity and displacement as a function of time during the trapping process.*

Fig. 6 shows the movement of the μP during the trapping process. Following the microparticle velocity (green line) as a function of time, it is clear to see that the μP has a maximum velocity at the beginning of the process and reduces gradually. It can be explained that the μP has the same velocity of the flow at the beginning of the process. By the time, when the μP comes to the trap, the μP is mostly governed by the small channel and partly by the big one, which leads to the reduction of the velocity. At the end of the trapping process, the velocity was down to 0 meaning that the μP is completely trapped. The graph also shows the displacement of the μP during the process (blue dash line). In the end, the displacement of the μP is constant at a certain value indicating it stands at the same position in the trap.

5. CONCLUSION

In this study, we have successfully achieved a simulation model for trapping a single μP representing for a single-cell in the microfluidic channel using the COMSOL Multiphysics software. The 20 μm diameter μP is trapped by the hydrodynamic force governed by fluid flows. The time for trapping a μP is less than 1.2 seconds. Besides, the flow velocities inside the microchannel in both 2D and 3D models were investigated. The relationship of the particle velocity indicates that the flow in the big channel is predominant at the beginning of the process. Then, by the time, the flow is predominant at the small channel and reduces significantly its speed when the particle comes near the trap. The research results help design a proper microfluidic system for the single-cell experiment.

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TÓM TẮT

MÔ PHỎNG VI HẠT MINH HỌA CHO QUÁ TRÌNH BẮT GIỮ ĐƠN TẾ BÀO TRONG KÊNH VI LƯU BẰNG PHƯƠNG PHÁP MÔ PHỎNG CÁC PHẦN TỬ HỮU HẠN

Phương pháp mô phỏng phần tử hữu hạn (FEM) thường được sử dụng rộng rãi trong mô phỏng các linh kiện micro và nano trước khi được chế tạo. Bằng việc sử dụng các phần mềm mô phỏng, các cấu trúc 2D và 3D của linh kiện được thiết kế và mô phỏng để tối ưu hóa các tham số của chúng. Trong nghiên cứu này, chúng tôi tiến hành mô phỏng cấu trúc bắt giữ vi hạt dựa trên nguyên lý thủy động học làm tiền đề cho việc bắt giữ các đơn tế bào trong kênh vi lưu. Trong quá trình mô phỏng, sự tương tác giữa vi hạt và dòng chảy, sự thay đổi của trường áp suất và tốc độ dòng chảy trong vi kênh được nghiên cứu một cách chi tiết. Bên cạnh đó, quá trình dịch chuyển của vi hạt minh họa cho các đơn tế bào bên trong hệ vi lưu tới vị trí các bẫy được minh họa một cách chi tiết. Dựa trên kết quả mô phỏng, các tham số liên quan đến thiết kế của các bẫy được tối ưu trước khi tiến hành chế tạo và thí nghiệm . Các kết quả mô phỏng trong nghiên cứu này giữ vai trò quan trọng để tối ưu hóa thiết kế hệ vi lưu trước khi được chế tạo thực nghiệm.

Từ khóa: Vi lưu; Bắt giữ đơn tế bào; Mô phỏng các phần tử hữu hạn.

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