

Kinematics of Non-axially Positioned Vesicles through a Pore

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Kinematics of Non-axially Positioned Vesicles through a Pore

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Abstract We employ finite element method to investigate the kinematics of non-axially positioned vesicles through a pore. To complete the coupling between fluid flow and the vesicle membranes, we use the fluid structure interactions with the arbitrary Lagrangian Eulerian method. Our results demonstrate that the vesicles show different deformations in migration process, in turn an oblique ellipse-shape, slipper-shape, oval-shape. We find that the rotation angle of non-axially positioned vesicles mainly shows the trend of increase, besides the small fluctuation induced by deformation relaxation. Moreover, when the vesicles move towards the axis of the channel, the rotation angle exhibits a decrease because of the decrease of the shear force. However, rotation of axially positioned vesicles hardly occur due to symmetrical shear force. Our results further indicate that the rotation is faster nearby the pore for non-axially positioned vesicles. Our work answers the mapping between the positions of vesicles and deformed states, as well as the change of rotation angle and rotation velocity, which can provide helpful information on the utilization of vesicles in pharmaceutical, chemical, and physiological processes.

Keywords Vesicles; Narrow pore; Rotation angle; Rotation velocity

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INTRODUCTION

Vesicles consist of an internal liquid medium protected by a thin deformable membrane, which can be deformed easily by external forces. Thus, the behavior of vesicles in external flow field is determined by a complex interplay between membrane elasticity and hydrodynamic forces. Studying the resulting rich phenomenology is fundamental for understanding the flow dynamics of this paradigmatic soft matter system, which possesses great application potential in gene therapy^[1–3] and drug delivery.^[1,4,5] In addition, even though biological cells have a more complex architecture, vesicles have often served as a model system to explore the mechanical properties for anucleate cells such as red blood cells.^[6–9] Therefore, studying the deformation and migration of vesicles in microfluidic channels can provide valuable information on the utilization of vesicles in biomedical, chemical and physiological processes.

Much work has been carried out to expound the deformation and migration of vesicles under planar hyperbolic, shear and Poiseuille flow^[10–16] or in constriction of microchannels.^[17–24] The dynamics of vesicle is complicated due to nonlinear couple between vesicle membrane and surrounding fluid. Previous studies have indicated that in shear flow initial spherical vesicle takes an ellipsoidal shape and moves with in-

clination angle respect to flow direction.^[11,13,14,16,25,26] Meanwhile, the shear rate has significant effect on dynamics of vesicle. For instance, the vesicle is wrinkling within specifically range of shear rate, which was induced by compression forces acting onto the membrane.^[13] Moreover, the vesicle will be broken with shear flow strength beyond its tolerance capacity.^[11,27] Furthermore, nonspherical red blood cells (RBCs) and spherical vesicles move in a variety of ways at different shear rates, such as steady tank-treading, swinging, and unsteady tumbling motions.^[28–30] Abkarian *et al.* have obtained cosinoidal variation of the angular velocity of the inclination of vesicle and of RBC versus the inclination angle.^[29]

In addition, vesicle exhibits special dynamics in Poiseuille flow as the fluid velocity is parabolic distribution.^[15,31] The vesicles were initially placed away from the axis of tube, which also exhibited dynamics similar to those in shear flow. However, the decrease in the deviation of distance from the axis leads to the decrease of shear force on the vesicle, which results in the steady nonspherical shape. Moreover, Abkarian *et al.* have indicated that presence of wall significantly changes deformations and motion of vesicles.^[29] Hence, dynamics of vesicle is more intricate in constriction of microchannels due to nonlinear velocity distribution and interaction between vesicle and wall. However, the description of flow-induced kinematics of vesicles through a pore has not been well established, especially on rotating angle and rotating velocity, which is essential in various engineering and biomedical applications.

In this research, we numerically investigate non-axially positioned vesicles through a pore, in particular from a view of

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motion mechanism, using finite element method (FEM), where the fluid-structure interactions (FSIs) are employed to complete the coupling between fluid flow and vesicle membrane. We aim to monitor the motions and deformations of non-axially positioned vesicles through the pore to yield the mapping between the positions of vesicles and deformed states. Moreover, we calculate rotated states in this process, which possesses a variety of applications, such as cell sorting and characterization. In the second section, we present FEM and the corresponding details. In the third section, we illustrate the shape transition of vesicles and fluctuation of rotation angle. We demonstrate that the rotation velocity reaches its maximum nearby the pore. However, the peak of horizontal velocity decreases with the increase of deviation distance. Finally, we draw some conclusions and provide our overview in the last section.

SIMULATION MODEL AND METHOD

We construct a numerical 2D model due to a vesicle always in symmetry plane for non-axially positioned vesicles through a pore, in which a circular vesicle is put into a microchannel (radius is 15 μm and length is 120 μm), where a pore (height is 2 μm and length is 2 μm) exists in the middle of the microchannel as illustrated in Fig. 1. Initially, the vesicle is fixed in the left side of the pore, and then flow fluid will induce deformation and migration of the vesicle.

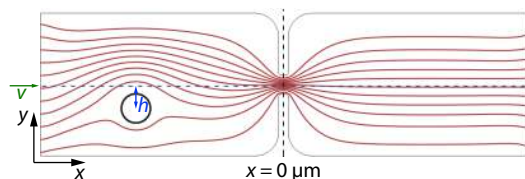


Fig. 1 Schematic representation for the model, in which a vesicle is put into a microchannel (radius is 15 μm and length is 120 μm), where a small pore (radius is 2 μm and length is 2 μm) exists in the middle of the microchannel.

We consider that the membrane of vesicle is isotropically viscoelastic,^[32] in which the deformation and motion are described as follows

$$\rho_{\text{solid}} \frac{\partial^2 \mathbf{u}_{\text{solid}}}{\partial t^2} = \nabla \cdot \boldsymbol{\sigma} + \mathbf{F}_V \quad (1)$$

where ρ_{solid} denotes the density of the membrane, $\mathbf{u}_{\text{solid}}$ is the displacement vector, $\boldsymbol{\sigma}$ is the stress tensor, and $\mathbf{F}_V$ represents the unit volume force. The Kelvin-Voigt model is used to describe viscoelastic behavior of the membrane, in which the relation between stress and elastic strain rate is presented by the following equation

$$\boldsymbol{\sigma} = G\boldsymbol{\varepsilon} + \eta \frac{d\boldsymbol{\varepsilon}}{dt} \quad (2)$$

where $\eta = 0.022 \text{ Pa}\cdot\text{s}$ is the viscosity of membrane, $\boldsymbol{\varepsilon}$ is the strain tensor of membrane, $G = E/2(1 + \nu)$ represents the shear modulus, $\nu = 0.45$ is Poisson's ratio and $E = 180 \text{ Pa}$ represents Young's modulus.

Exterior and interior liquids of vesicle have the same density $\rho_{\text{fluid}} = 1000 \text{ kg/m}^3$ and viscosity $\mu = 0.005 \text{ Pa}\cdot\text{s}$, which are considered as incompressible Newtonian fluids with a laminar

flow. The left-hand side boundary condition is influx with average inlet velocity, and that of right-hand side is outflux with pressure, which is also the same order as velocity of relevant experiment.^[33] The mass and momentum conservation equations are presented as follows

$$\begin{aligned} \rho_{\text{fluid}} \left[\frac{\partial \mathbf{u}_{\text{fluid}}}{\partial t} + (\mathbf{u}_{\text{fluid}} \cdot \nabla) \mathbf{u}_{\text{fluid}} \right] \\ = \nabla [\mu \nabla \mathbf{u}_{\text{fluid}} + \mu (\nabla \mathbf{u}_{\text{fluid}})^T] + \mathbf{F} \end{aligned} \quad (3)$$

where $\mathbf{u}_{\text{fluid}}$ denotes the velocity vector, and $\mathbf{F}$ is the external force.

The fluid-solid interface is boundary of interaction between fluid and membrane, which means the effect of fluid flow on solid and solid displacement and deformation on fluid flow, as described by the following equations

$$\boldsymbol{\sigma} \mathbf{n} = \boldsymbol{\Gamma} \mathbf{n} \quad (4)$$

$$\mathbf{u}_{\text{fluid}} = \mathbf{v}_w \quad (5)$$

$$\mathbf{v}_w = \frac{\partial \mathbf{u}_{\text{solid}}}{\partial t} \quad (6)$$

where $\mathbf{n}$ denotes the unit normal vector of fluid-solid interfaces and $\mathbf{v}_w$ is the solid velocity. $\boldsymbol{\Gamma}$ represents the total force, which is fluid loads on the solid boundary and negative of the reaction force on the fluid.

The rotation and motion of vesicle in non-uniform shear flow are represented as

$$\theta = \begin{cases} \arccos \frac{y_2 - y_1}{\sqrt{(y_2 - y_1)^2 + (x_2 - x_1)^2}} & x_2 - x_1 \geq 0 \\ 2\pi - \arccos \frac{y_2 - y_1}{\sqrt{(y_2 - y_1)^2 + (x_2 - x_1)^2}} & x_2 - x_1 < 0 \end{cases} \quad (7)$$

$$\omega = \frac{\partial \theta}{\partial t} \quad (8)$$

$$\mathbf{v}_x = \frac{\partial \mathbf{u}_{\text{solid}x}}{\partial t} \quad (9)$$

where θ denotes rotation angle of the point on membrane around the center of mass, x_1 , x_2 and y_1 , y_2 are abscissa and ordinate of the center of mass and point on membrane, respectively, ω is angular velocity of vesicle, and $\mathbf{u}_{\text{solid}x}$ and $\mathbf{v}_x$ represent horizontal displacement and horizontal velocity of vesicle, respectively.

In this work, the corners are smoothed to improve mesh quality and automatic remeshing is switched on to enhance the model convergence and computing precision. The finite element method (FEM) is used to solve governing equations on the unstructured meshes, where FSIs are used to couple between vesicle membrane and fluid flow. The arbitrary Lagrangian Eulerian (ALE) method is employed to describe the movement of the meshes associated with FSIs, in which the nodes of the computational mesh have freedom of motion,^[34] that is, the new coordinates of the deformed grid related to solids are calculated based on the moving boundaries of geometry and mesh smoothing in ALE method. And the Newton iteration method is used to carry out numerical iterative. In addition, we introduce a repulsive zone of thickness 0.1 μm on the boundaries of walls, which consists of a distribution of springs to avoid topological structure change of geometric model and singular when the solid boundaries of walls and the vesicle membrane are too close or even contact between them.^[35] Whenever the vesicle membrane enters the repuls-

ive zone, it will be pushed away along the normal direction of the boundary. Finally, we use the transient study and PARDISO solver to compute the governing equations with COMSOL Multiphysics 5.3a package.

RESULTS AND DISCUSSION

As shown in Fig. 2, we monitor the rotations, deformations and migrations of vesicles through the pore in Poiseuille flow to investigate the kinematics of non-axially positioned vesicles. For the vesicle with $r = 1 \mu\text{m}$ fixed away from middle of microchannel with deviation distance $h = 10 \mu\text{m}$, we find that with the vesicle gradually approaching the pore, its shape changes from circle to ellipse inclined with respect to the axis of microchannel. Then, when the vesicle enters into the pore, it exhibits slipper-like shape and its location is close to the bottom of the pore (depending on the original deviation direction). After passing through the pore, the vesicle keeps an oval-shape and moves towards the bottom of the channel (also depending on the original deviation direction). In the whole process of crossing, the vesicle's membrane rotates around it, which could be visualized clearly as the red dot in Fig. 2. Similar phenomenon is also found for smaller original deviation distance $h = 5 \mu\text{m}$, while the extent of deformation and rotation decreases. When the vesicle is originally positioned at the middle of microchannel, it will be only deformed without rotation during the crossing process. In addition, larger vesicle ($r = 3 \mu\text{m}$) also exhibits similar kinematics. Moreover, the rotations of vesicle are always clockwise for non-axial positioned vesicles (Fig. 2), which is attributed to the Poiseuille flow in the microchannel. The velocity of flow is greater in the middle and decreases towards the wall, which results in the inhomogeneous stress on the vesicle membrane. Therefore, if we put the vesicle into the lower part of the microchannel, the vesicle will rotate clockwise. On the contrary, it will show counter clockwise rotation.

Theoretically, when the vesicles are positioned away from the axis, they will bear an unbalanced shear force owing to the asymmetric distribution of flow field (as demonstrated in Fig. 1), which will further drive the deformation and rotation of vesicles. Moreover, the unbalanced shear force is closely related with the deviation distance and vesicles' size, which is the reason why the extent of deformation is different and rotation for different deviation distance and size of vesicles.

To investigate nonuniform flow field effect on migration of vesicles, we obtain horizontal velocity of center of mass of vesicle along horizontal position. The horizontal direction is

center of mass position, where $x = 0 \mu\text{m}$ indicates the midpoint of the pore. For radius of vesicle $r = 1 \mu\text{m}$ (Fig. 3a1), we find that the horizontal velocity far from the pore is almost constant, and after the vesicle passing through the pore it is always greater than before for non-axially positioned vesicles but increases rapidly near the pore and reaches peak at about $x = 0 \mu\text{m}$. The horizontal velocity of vesicles near the middle of microchannel is always higher than others. The velocity difference is decreased with increase of radius of vesicle after passing the pore. Especially, the horizontal velocities of radii of vesicle $r = 3, 4 \mu\text{m}$ are almost the same. For radii of vesicle $r = 2, 3, 4 \mu\text{m}$, we obtain three fluctuation curves similar to that of radius of vesicle $r = 1 \mu\text{m}$. These are attributed to the fact that fluid flow velocity presents stable parabolic distribution far from the pore but increases rapidly near the pore to keep consistent flux. However, after the non-axially positioned vesicle passes through the pore, it will enter the region with the higher velocity because deformations and rotations of the vesicle reduce vertical pushing force from the flow. While passing the pore, the pushing force decreases with increase of vesicle size because of symmetrical flow field distribution. The increase of inlet velocity obviously enhances horizontal velocity of the vesicle (Fig. 3b). The horizontal velocity of vesicle decreases before reaching the pore when vesicle is placed closer to the pore (Fig. 3c). This is because the flow velocity decreases when getting closer to the pore. The horizontal velocity of vesicle exhibits a small fluctuation with radii of vesicle $r = 2, 3, 4 \mu\text{m}$ after passing through the pore. This phenomenon is induced by deformation relaxation of vesicles.

To quantitatively describe rotation of the vesicle, we calculate the rotation angle of the specified point on the vesicle membrane around the center of mass of vesicle. In fact, the selection of observation point has slight influence on the results because of the deformations of vesicle shape. Fig. 4(a1) presents fluctuation of rotation angle of vesicle along horizontal position for radius $r = 1 \mu\text{m}$. In Fig. 4(a1), the rotation angle of vesicle is monotonically increasing when the vesicle passes through the pore for deviation distance $h = 10 \mu\text{m}$. The fluctuation of rotation angle is low when the vesicle keeps away from the pore. However, the rotation angle exhibits a dramatic increase nearby the narrow pore. The rotation angle of vesicle is also monotonically increasing when the vesicle passes through the pore for deviation distance $h = 5 \mu\text{m}$, which is similar to that of deviation distance $h = 10 \mu\text{m}$. However, the rotation angle of vesicle deviation distance $h =$

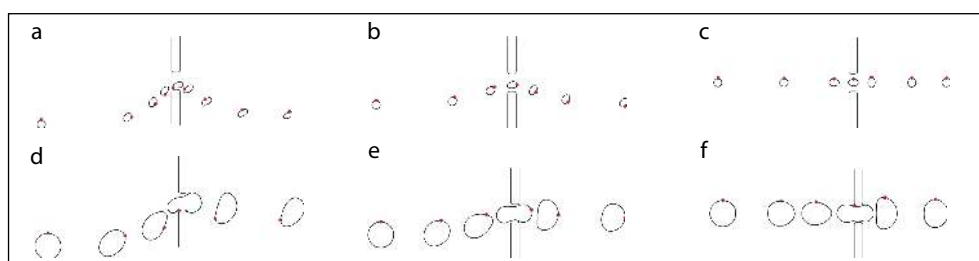


Fig. 2 Rotations, deformations and migrations of vesicles into the pore for deviation distance from axis of microchannel: (a, d) $10 \mu\text{m}$, (b, e) $5 \mu\text{m}$, (c, f) $0 \mu\text{m}$, with the conditions of radii of vesicles $r = 1$ or $3 \mu\text{m}$ and inlet velocity $v = 10 \mu\text{m/s}$.

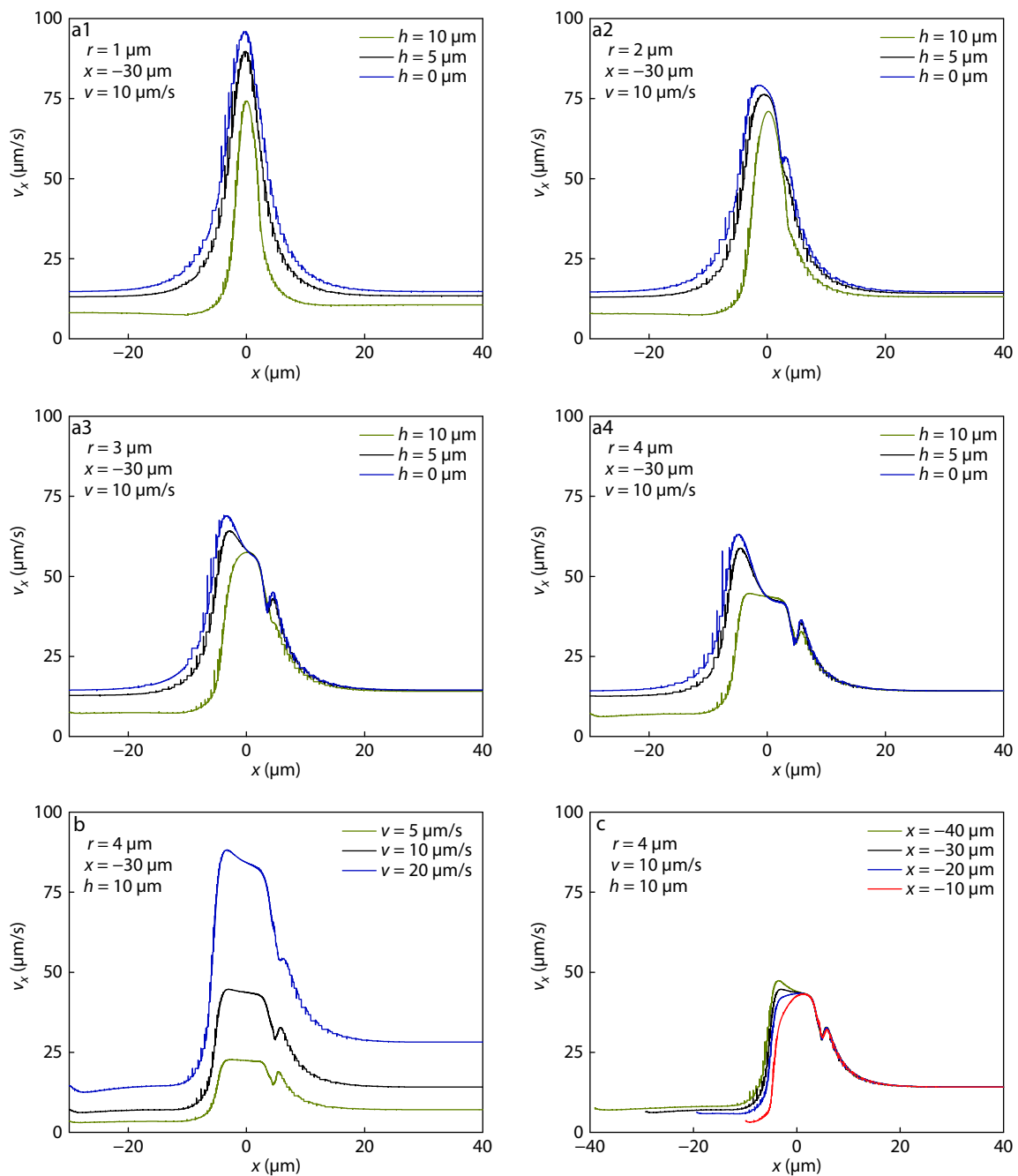


Fig. 3 Horizontal velocity of center of mass of vesicle along horizontal position for radii of vesicles (a1) 1 μm , (a2) 2 μm , (a3) 3 μm , (a4) 4 μm with the inlet velocity $v = 10 \mu\text{m/s}$ and initial horizontal position $x = -30 \mu\text{m}$; (b) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and initial horizontal position $x = -30 \mu\text{m}$; (c) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and inlet velocity $v = 10 \mu\text{m/s}$ ($x = 0 \mu\text{m}$ is the midpoint of the pore).

5 μm is smaller than that of deviation distance $h = 10 \mu\text{m}$. The vesicle is not rotating when it is placed at axis of microchannel ($h = 0 \mu\text{m}$). We obtain tiny fluctuation of rotation angle of vesicle. This is because the flow strength is weak at the position far away from the pore, but it is intense nearby the pore to ensure constant of flux. Thus, the vesicle bears higher shear force nearby the pore. The shear rate around vesicle decreases as the deviation distance of vesicle decreases. For the vesicle deviation distance $h = 0 \mu\text{m}$, the symmetrical shear

force is exerted on vesicles. Therefore, the vesicle is only deformed, but without rotation. The deformation of vesicle induces tiny fluctuation of rotation angle. For radii of vesicle $r = 2, 3, 4 \mu\text{m}$, we obtain similar change of rotation angle. However, the rotation angle decreases with increase of vesicles size for the same position, for shear force induces greater deformation for bigger vesicle. Hence, more work done by shear forces is stored as strain energy. The deformations and relaxations of vesicles induce decrease of rotation angle

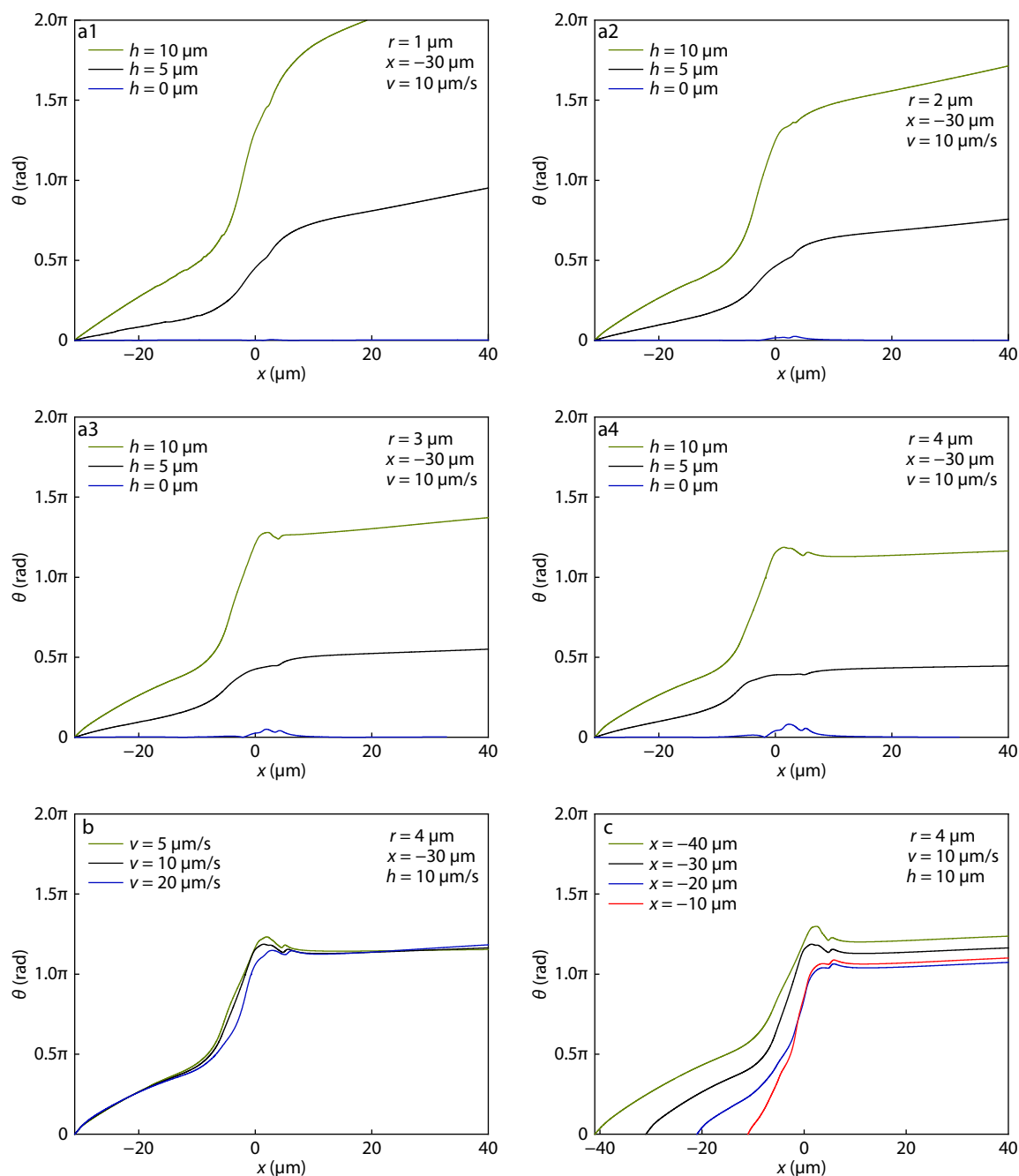


Fig. 4 Rotation angle of vesicle membranes along horizontal position for radii of vesicles (a1) 1 μm , (a2) 2 μm , (a3) 3 μm , (a4) 4 μm with the inlet velocity $v = 10 \mu\text{m/s}$ and initial horizontal position $x = -30 \mu\text{m}$; (b) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and initial horizontal position $x = -30 \mu\text{m}$; (c) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and inlet velocity $v = 10 \mu\text{m/s}$ ($x = 0 \mu\text{m}$ is the midpoint of the pore).

nearby the pore when radii of vesicle are $r = 2, 3, 4 \mu\text{m}$ and deviation distance is $h = 10 \mu\text{m}$. The decrease of deviation distance reduces this influence.

For deviation distance $h = 10 \mu\text{m}$ and radius of vesicle $r = 4 \mu\text{m}$, effect of inlet velocity on rotation angle is shown in Fig. 4(b). We find that different inlet velocities have certain effect on the rotation angle near the pore, where the increase of inlet velocity leads to decrease of rotation angle. In Fig. 4(c), the vesicle is fixed at different horizontal positions

for radius of vesicle $r = 4 \mu\text{m}$ and deviation distance $h = 10 \mu\text{m}$. When the vesicles are fixed far away from the pore, the rotation angle increases continuously with the vesicle approaching the pore. The farther the vesicle away from the pore, the longer the rotation time. Hence, the rotation angle is decreasing with increase of horizontal position x except for $x = -10 \mu\text{m}$. When horizontal position is $x = -10 \mu\text{m}$, the vesicle bears strong enough shear force that propel rotation angle higher than $x = -20 \mu\text{m}$.

The rotation angle of vesicle membrane shows complex variation. Thus, we calculate the rotation velocity of vesicle membrane to characterize angle change. In Fig. 5(a1) ($r = 1 \mu\text{m}$), the rotation velocity of vesicle is almost constant when vesicle keeps away from the pore. The rotation velocity shows dramatic fluctuation nearby the narrow pore. It increases with increase of deviation distance, and reaches up to 28 rad/s nearby the pore for deviation distance $h = 10 \mu\text{m}$. That is much higher than rotation velocity of deviation distance $h =$

$5 \mu\text{m}$. Because flow strength is stronger nearby the narrow pore than far away from the pore, vesicle rotation is faster nearby the narrow pore. The shear rate is stronger nearby wall of microchannel, for the flow field distribution is hyperbolic. The vesicle is placed at axis of microchannel, and the rotation velocity is equal to 0 when vesicle keeps away from the pore. The rotation velocity nearby the pore is attributed to deformation and relaxation of vesicle. We obtain similar results in Fig. 5(a1) for radii $r = 2, 3, 4 \mu\text{m}$. However, the rotation

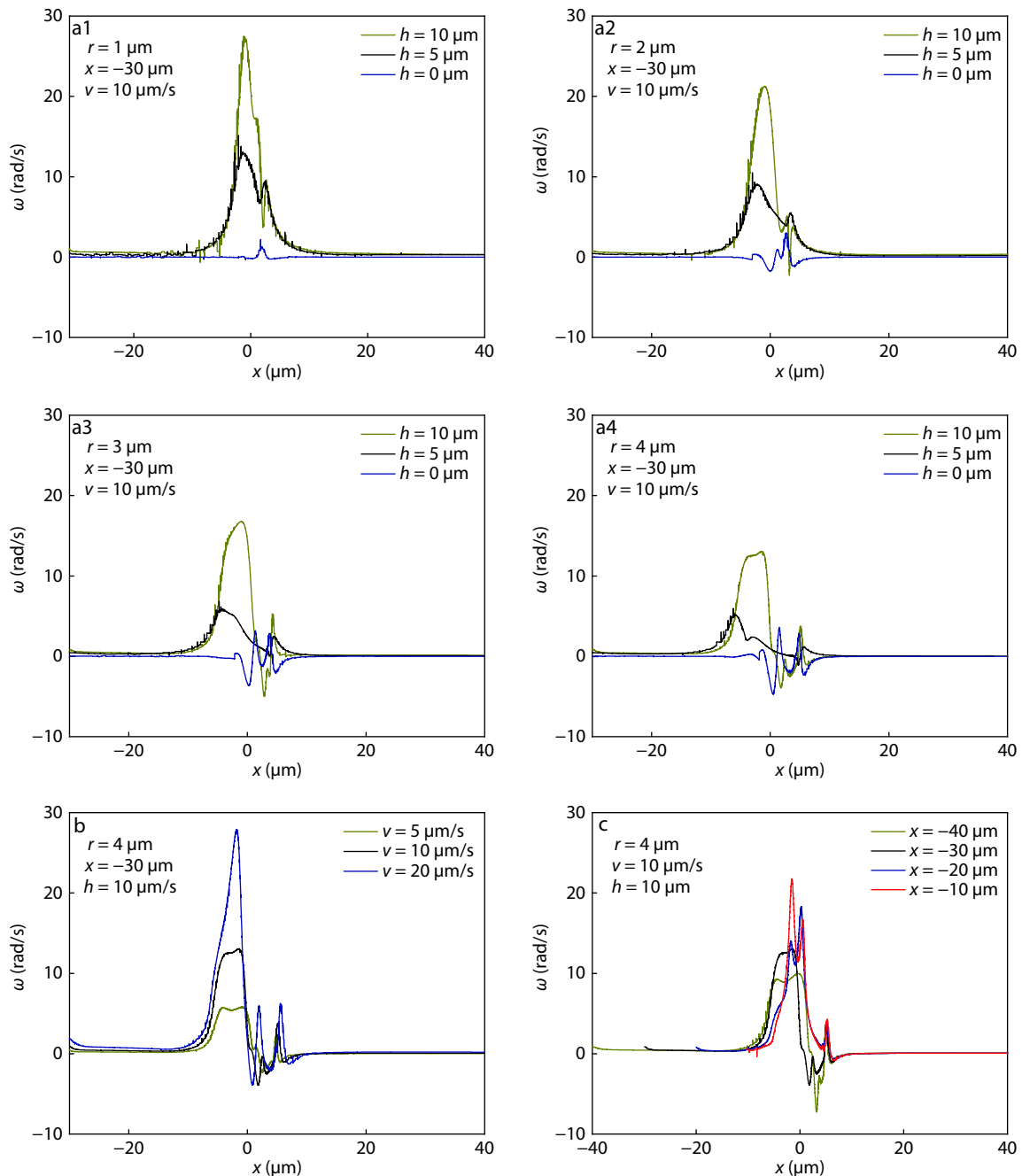


Fig. 5 Rotation velocity of vesicle membranes along horizontal position for radii of vesicles (a1) $1 \mu\text{m}$, (a2) $2 \mu\text{m}$, (a3) $3 \mu\text{m}$, (a4) $4 \mu\text{m}$ with the inlet velocity $v = 10 \mu\text{m/s}$ and initial horizontal position $x = -30 \mu\text{m}$; (b) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and initial horizontal position $x = -30 \mu\text{m}$; (c) for deviation distance $h = 10 \mu\text{m}$ with the radius of vesicles $r = 4 \mu\text{m}$ and inlet velocity $v = 10 \mu\text{m/s}$ ($x = 0 \mu\text{m}$ is the midpoint of the pore).

velocity decreases with increase of vesicle radius. The rotation velocity of vesicle radius $r = 4 \mu\text{m}$ is reduced to 15 rad/s for deviation distance $h = 10 \mu\text{m}$. The rotation velocity of vesicle radii $r = 2, 3, 4 \mu\text{m}$ shows negative value for deviation distance $h = 10 \mu\text{m}$. This is the result of deformation and relaxation of the vesicle. Fig. 5(b) indicates effect of inlet velocity on rotation velocity for deviation distance $h = 10 \mu\text{m}$. The rotation velocity increases with increase of inlet velocity. It is up to 28 rad/s for mean inlet velocity of $20 \mu\text{m/s}$ because the increase of inlet velocity enhances flow strength. Moreover, the presence of pore creates non-uniform flow field distribution. Thus, we study the influence of horizontal position on rotation velocity for deviation distance $h = 10 \mu\text{m}$. The result presents that the maximum of rotation velocity is increasing as the vesicle approaches the pore.

Our simple theoretical model can describe the microscopic images of translocation dynamics of vesicles or cells, which is very helpful for us to understand the relevant processes. For example, our simulations find that when the initial position of the same vesicle is different, the dynamic behavior exhibits great difference. Moreover, the strain energy also shows a great difference, which proves that to improve the accuracy of cell selection, their initial positions are also very important.

CONCLUSIONS

In this work, using finite element method, we numerically investigate the motion mechanism of non-axially positioned vesicles passing through a pore. The fluid-structure interactions are employed to complete the coupling between vesicle membrane and fluid flow with the arbitrary Lagrangian-Eulerian method. We monitor the motions, rotations and deformations of vesicles into the pore to yield the mapping between the positions and rotations of vesicle, and deformed states. Our results demonstrate that the non-axially positioned vesicle shows similar shape change from ellipse-shape to slipper-shape, and from slipper-shape to oval-shape. In addition, the horizontal velocity decreases with increase of deviation distance. Furthermore, we find that the rotation angle of non-axially positioned vesicle is complex when passing through the pore. The rotation angle increases linearly far away from the pore, but increases rapidly nearby the pore. In addition, the rotation angle exhibits an increase with increase of deviation distance. Our results further indicate that the rotation velocity is constant far away from the pore, but shows drastic increase nearby the pore, where the increase of deviation distance enhances rotation velocity. These are attributed to hyperbolic distribution of flow field and presence of pore. Our work not only creates mapping between the positions of the vesicles and deformed states, but also displays the change of horizontal velocity, rotation angle and rotation velocity. In this context, we expect that extensive studies on the non-spherical structure of vesicles or the non-Newtonian and compressible behaviors of fluids would be of particular interest,^[10,36,37] which can provide an extensive understanding on the utilization of vesicles in pharmaceutical, physiological, and chemical processes.

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