Numerical modeling of motion trajectory and deformation behavior of a cell in a nonuniform electric field

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The motion trajectory and deformation behavior of a neutral red blood cell (RBC) in a microchannel subjected to an externally applied nonuniform electric field are numerically investigated, where both the membrane mechanical force and the dielectrophoresis (DEP) force are considered. The simulation results demonstrate that the DEP force is significantly influenced by several factors, namely, the RBC size, electrode potential, electric frequency, RBC permittivity, and conductivity, which finally results in the different behaviors of the cell motion and deformation in the nonuniform electric field. © 2011 American Institute of Physics.
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I. INTRODUCTION

Dielectrophoresis (DEP) is a physical phenomenon, in which the dielectric bodies experience a net force and thus move toward or away from the region with higher electric field strength in response to an applied nonuniform electric field. This net force is known as the DEP force, and it is associated with a variety of parameters, including the dielectric properties of the dielectric body and the surrounding fluid, the shape and size of the dielectric body, as well as the applied electric field.^{1,2} As such, all the dielectric bodies can be purposely manipulated by means of controlling the above parameters, such as microparticles,^{3–6} biological cells,^{7–9} virus,¹⁰ and DNA molecules.¹¹

So far, several analytical approaches have been developed to express the DEP force acting on a dielectric body, which is usually modeled as a spherical particle. The conventional theory uses a dipole approximation,¹² where the dielectric particle is assumed to be very small such that only a dipole is induced on the particle. Although the dipole approximation may provide acceptable results in some cases, the predicted accuracy becomes worse and worse with increasing the size of the dielectric particle because the high-order moments also become dominant for the larger dielectric particle, except the dipole moment. Therefore, the multipole moment method with consideration of the high-order moments was proposed by Washizu¹³ and Washizu and Jones.^{14,15} Subsequently, Schnelle *et al.*¹⁶ investigated the influence of the high-order moments in detail and pointed out that the multipole approximation is more applicable for the large dielectric particles. However, the multipole approximation does not work well to treat the nonspherical dielectric particle. Even for ellipsoidal particles, it becomes more complicated, not to mention the arbitrary particles. Currently, an accurate approach developed is the Maxwell stress tensor (MST) method,¹⁷ in which MST requires an integration over the surface of the dielectric particle to obtain the DEP force. This method is regarded as the most general approach without any assumption required for the shape of dielectric particle and the externally applied electric field. Due to its mathematical complexity, however, this approach is mainly applied in numerical simulations.^{18–20}

Since the calculation of the DEP force is complicated for arbitrary dielectric bodies, so far the DEP application is mostly limited to the very small and rigid spherical particles, and the under-

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standing of DEP phenomenon is still poor for the large and deformable dielectric bodies. Therefore, in the present work, the motion trajectory and deformation behavior of a neutral red blood cell (RBC) in a microchannel are simulated and analyzed in detail when it is subjected to an externally applied nonuniform electric field. Several crucial factors are analyzed for evaluating the effects on the behaviors of cell motion and deformation, including the RBC size, electrode potential, electric frequency, RBC permittivity, and conductivity.

II. MATHEMATICAL MODEL

At the microscale level, it is reasonable to consider both the RBC and the suspending fluid as incompressible fluid such that the incompressible Navier–Stokes (NS) equations are used by treating the two fluids as a single fluid with variable material properties and are given by

$$\nabla \cdot \mathbf{u} = 0, \quad (1)$$

$$\frac{\partial \rho \mathbf{u}}{\partial t} + \nabla \cdot (\rho \mathbf{u} \mathbf{u}) = -\nabla p + \nabla \cdot [\mu(\nabla \mathbf{u} + \nabla \mathbf{u}^T)] + \int_{\Gamma} (\mathbf{f}_m + \mathbf{f}_d) \delta(\mathbf{x} - \mathbf{x}_f) ds, \quad (2)$$

where $\mathbf{u}$ is the velocity, p is the pressure, ρ and μ are the density and viscosity, t and $\mathbf{x}$ are the temporal and spatial variables, and Γ is the RBC membrane. In Eq. (2), the Dirac delta function $\delta(\mathbf{x} - \mathbf{x}_f)$ is used to characterize the DEP and membrane mechanical force strengths acting on the cell membrane $\mathbf{x}_f$ only. The membrane mechanical force strength $\mathbf{f}_m$ is given by²¹

$$\mathbf{f}_m = \left[E_S \frac{d\varepsilon}{ds} + \kappa E_B \frac{d(\kappa - \kappa_0)}{ds} \right] \mathbf{t} + \left[E_B \frac{d^2(\kappa - \kappa_0)}{ds^2} - E_S \varepsilon \kappa \right] \mathbf{n}. \quad (3)$$

where E_S and E_B are the shear modulus and bending stiffness, ε is the tensile strain, κ and κ_0 are the current and resting curvatures of the membrane, and $\mathbf{t}$ and $\mathbf{n}$ are the unit tangent and normal vector along the direction of increasing arc length s . The DEP force strength $\mathbf{f}_d$ is derived by the MST approach¹⁷ as

$$\mathbf{f}_d = \frac{\text{Re}(\tilde{\xi}_f)}{2} |a|^2 \{ 2 \text{Re}(b)(\mathbf{E}_{\text{rms}} \cdot \mathbf{n}) \mathbf{E}_{\text{rms}} + |c \mathbf{E}_{\text{rms}} \cdot \mathbf{n}|^2 \mathbf{n} + d |\mathbf{E}_{\text{rms}}|^2 \mathbf{n} \}, \quad (4)$$

in which $\mathbf{E}_{\text{rms}}$ is the root of mean square of applied electric field, and

$$a = \frac{\tilde{\xi}_f}{\tilde{\xi}_f + P(\tilde{\xi}_b - \tilde{\xi}_f)}, \quad b = \frac{\tilde{\xi}_f^* \tilde{\xi}_b - \tilde{\xi}_f \tilde{\xi}_b^*}{2 \text{Re}(\tilde{\xi}_f) \tilde{\xi}_f}, \quad c = \frac{\tilde{\xi}_b - \tilde{\xi}_f}{\tilde{\xi}_f}, \quad d = \frac{\text{Re}(\tilde{\xi}_b - \tilde{\xi}_f)}{\text{Re}(\tilde{\xi}_f)}, \quad (5)$$

where $\tilde{\xi}_f$ and $\tilde{\xi}_b$ are the complex permittivities of the external fluid and the dielectric body, P is called the depolarization factor, and the subscript $*$ refers to the conjugate complex. Details about the theoretical model can be obtained in the work of Ye *et al.*²² In order to numerically solve the governing equations (1) and (2), a hybrid method²³ by coupling SIMPLER (Semi-Implicit Method for Pressure Linked Equations Revised) (Ref. 24) and SIMPLEC (Semi-Implicit Method for Pressure Linked Equations-Consistent) (Ref. 25) together is used here, which is a finite volume scheme.

III. RESULTS AND DISCUSSION

It is well-known in the dipole approximation that the DEP force acting on a small rigid particle depends on the particle size, electrode potential, electric frequency, as well as dielectric properties of the particle and suspending fluid.^{26,27} A crucial factor, termed the Clausius–Mossotti (CM) factor, is defined as a measure of the DEP force acting on rigid particles. For example, the CM factor of a rigid spherical particle is given by^{26,27}

$$K_{CM} = \frac{\tilde{\xi}_b - \tilde{\xi}_f}{\tilde{\xi}_b + 2\tilde{\xi}_f}, \quad (6)$$

where $\tilde{\xi}_f$ and $\tilde{\xi}_b$ are the complex permittivities of the suspending fluid and dielectric sphere, respectively. When the rigid sphere is polarized higher than the suspending fluid, $\text{Re}[K_{CM}]$ is positive and the sphere moves toward the region of the higher electric field, which is well-known as the positive DEP (p-DEP). On the contrary, the negative DEP (n-DEP) occurs where the sphere is repelled away from the region of the higher electric field, and $\text{Re}[K_{CM}]$ is negative if the rigid sphere is polarized lower than the suspending fluid. In addition, by taking the limit, at low frequency the CM factor in Eq. (6) reduces to

$$K_{CM} = \frac{\sigma_b - \sigma_f}{\sigma_b + 2\sigma_f}. \quad (7)$$

At high frequency, however, it is

$$K_{CM} = \frac{\xi_b - \xi_f}{\xi_b + 2\xi_f}. \quad (8)$$

In this section, the mathematical model is validated by comparing the present predication with the numerical results previously published. After that, the motion trajectory and the deformation behavior of a neutral RBC in an applied nonuniform electric field are simulated and analyzed from the aspects of the RBC size, electrode potential, electric frequency, RBC permittivity at high frequency, and RBC conductivity at low frequency.

A. Validations

The mathematical model is validated by comparing the present simulation results with the previously published numerical predictions by Cao *et al.*,²⁸ where the levitation height of the latex beads was measured as a function of the applied potential at the electrodes. The parameter values reported by Cao *et al.*²⁸ for the permittivity and conductivity of the latex beads and suspending fluid, $\xi_b = 2.55\xi_0$ (ξ_0 is the vacuum permittivity), $\sigma_b = 0.2$ mS/m, $\xi_f = 78\xi_0$, and $\sigma_f = 10$ mS/m, are also used in the present validation without modification. At the electric frequency $f = 1$ MHz, the levitation heights of the latex beads with radii of 0.5 and 2.0 μm are plotted in Fig. 1 and then compared with the numerical results of Cao *et al.*²⁸ Here, a good agreement between them is achieved, although the deformation of the latex beads is considered in the present model. However, the radius of the latex beads is significantly smaller than the channel width, such that the deformation of latex beads is negligibly small.

B. Effect of RBC size

The motion and deformation of the four RBCs with different radii are investigated, as shown in Fig. 2, where $r = 4.5, 3.91, 3.0$, and 2.0 μm . It is found that the cell deformation becomes smaller and smaller with decreasing the RBC size, such that the deformation of the RBC with a radius of 2.0 μm is almost negligible. This may be explained by the fact that the DEP force acting on a dielectric body is proportional to its volume. As such, the dielectric body is often treated as a rigid one in most studies of the DEP phenomenon, when its size is very small compared with the characteristic length.

C. Effect of electrode potential

In order to investigate the effect of electrode potential on the motion trajectory and deformation behavior of RBC, the four electrode potentials, $V_0 = 0.5, 1.0, 2.0$, and -1.0 V, are used. Figure 3 shows the motion and deformation of the RBC subject to the excitation of the four electrode potentials, where the RBC deformation becomes more and more obvious with increasing the

FIG. 1. Comparison of the levitation heights of the latex beads with radii of 0.5 and 2.0 μm predicted by the present model and numerical results reported by Cao *et al.* (Ref. 28).

electrode potential. The shape and location of RBC remain almost unchanged under the excitation of $V_0=0.5$ V, while the RBC deforms and ascends remarkably at $V_0=2.0$ V. It is noted that the RBC deformation at $V_0=1.0$ V is identical to that at $V_0=-1.0$ V, meaning that the RBC performance is independent of the polarity of the applied electric field. All these behaviors may be explained well by the relationship between the DEP force strength and the electric field strength,

FIG. 2. Motion and deformation of RBCs with different sizes r , where each RBC snapshot corresponds to the topmost dimensionless time $\bar{t}$.

FIG. 3. Motion and deformation of RBCs subject to the different excitations of electrode potential V_0 .

as shown in Fig. 4. With increasing the electrode potential, the DEP force strength is increased, such that the RBC deformation becomes more and more obvious. However, the distribution of the DEP force strength remains unchanged if the polarity of the applied electric field strength is reversed. In other words, the DEP force is independent of the polarity of the applied electric field, which is a well-known characteristic of DEP.^{26,27}

D. Effect of electric frequency

For a rigid spherical dielectric body, it is found from Eqs. (7) and (8) that the DEP force depends on the conductivities of the spherical body and suspending fluid at low frequency and on the permittivities only at high frequency. The present electric frequency is taken as $f=10^3$, 10^6 , 10^8 , 10^9 , and 10^{10} Hz, respectively. Figure 5 shows the motion and deformation of the RBC in the

FIG. 4. Distributions of the DEP force strength acting on the RBC membranes at $\bar{t}=5.0$ subject to the different excitations of electrode potential V_0 .

FIG. 5. Motion and deformation of RBCs subject to the nonuniform electric field with different frequencies f .

nonuniform electric field with the five frequencies. In the former two cases ($f=10^3$ and 10^6 Hz), similar behaviors are observed, where the RBCs are attracted toward the electrodes, i.e., they experience the p-DEP phenomenon. In the latter two cases ($f=10^9$ and 10^{10} Hz), the RBCs still have similar behaviors, but they move away from the electrodes, which is the n-DEP phenomenon. In other words, the RBC performance is independent of the frequency at the regions of the low and high frequencies, respectively. Similar to a rigid particle, the RBC undergoes the p-DEP phenomenon at low frequency according to Eq. (7), when the conductivity of RBC is larger than that of the suspending fluid. However, it experiences the n-DEP phenomenon at high frequency according to Eq. (8), when the permittivity of RBC is smaller than that of the suspending fluid. In the middle case ($f=10^8$ Hz), the motion of RBC seems to be in the n-DEP state because the RBC slightly moves away from the electrodes.

E. Effect of RBC permittivity

Since the effect of the RBC permittivity is highly significant at high frequency, the three permittivities, $\xi_b=57\xi_0$, $80\xi_0$, and $103\xi_0$, are considered at a frequency of 10^9 Hz. Figure 6 shows the motion and deformation of RBCs in these three cases. It is found that the RBC moves gradually away from the electrodes when the permittivity of RBC is smaller than that of the suspending fluid. In other words, the RBC experiences the n-DEP phenomenon when it is polarized less than the suspending fluid. On the contrary, a descending trend of the RBC toward the electrodes is observed when the permittivity of RBC is larger than that of the suspending fluid, where the p-DEP phenomenon occurs, as the RBC is polarized more than the suspending fluid. However, only the translational motion occurs due to the transport flow, when the RBC has the same permittivity as that of the suspending fluid. These different motion behaviors are attributed

FIG. 6. Motion and deformation of RBCs with different permittivities ξ_b at a frequency of 10^9 Hz.

to the different distributions of the DEP force strength, as shown in Fig. 7. In the first case, the DEP force strength at the lower part is larger than that at the upper part, and its direction is inward, such that the resultant force acting on the RBC is directed away from the electrodes. As a result, the RBC moves away from the electrodes. However, the direction of the DEP force strength is outward in the third case, and thus the resultant force is directed toward the electrodes. Therefore, the RBC is attracted toward the electrodes. In the second case, there is no DEP force acting on the RBC so no deformation occurs. In addition, the lower part of the RBC becomes smaller and smaller in the first case due to the distribution of the DEP force strength, while the upper part becomes wider and wider to maintain the conservation of the RBC area, as shown in Fig. 7(a). However, the opposite deformation is found in the third case, as shown in Fig. 7(c).

FIG. 7. Distributions of the DEP force strength acting on the membranes of RBCs with different permittivities ξ_b at $\bar{t}=5.0$.

FIG. 8. Motion and deformation of RBCs with different conductivities σ_b at a frequency of 10^6 Hz

F. Effect of RBC conductivity

Since the effect of the RBC conductivity is very significant at low frequency, the three conductivities, $\sigma_b=0.3$, 0.4 , and 0.52 S/m, are considered at a frequency of 10^6 Hz. Figure 8 shows the motion and deformation of RBCs in these three cases, in which the first two RBCs move away from the electrodes, while the last one is attracted toward the electrodes. In other words, the RBC with smaller conductivity than that of the suspending fluid experiences the n-DEP phenomenon. Otherwise, the p-DEP phenomenon occurs.

IV. CONCLUSIONS

The motion trajectory and deformation behavior of a neutral RBC in an applied nonuniform electric field are numerically investigated in terms of the RBC size, electrode potential, electric frequency, RBC permittivity, and conductivity. The simulation results show that the RBC behavior depends on the conductivities of the RBC and suspending fluid at low frequency and on the permittivities at high frequency. At low frequency, the RBC experiences a positive DEP phenomenon, when the conductivity of the RBC is larger than that of the suspending fluid, in which it moves toward the electrodes. At high frequency, however, the RBC undergoes a negative DEP phenomenon, when the permittivity of the RBC is smaller than that of the suspending fluid, where it moves away from the electrodes. In addition, the motion trajectory and deformation behavior of the RBC are very sensitive to the RBC size and electrode potential because they directly influence the DEP force strength. The DEP force strength decreases with decreasing the RBC size, and then the RBC deforms slightly. The RBC deformation becomes more and more significant with increasing the electrode potential since the DEP force strength also increases.

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