Supplementary Text

Theoretical and Simulation Analysis

There have been a number of attempts to create a gradient electric field using a planar interdigitated electrode array patterned on an insulating substrate, as shown in Fig. 1(a). A planar electrode array is an effective structure for separating and the preliminary trapping of particles that is easy to implement. The simulated electric flux density distribution around an interdigitated electrode array shows that most of the charge on the electrodes is at the edges of the electrodes (Fig. 1(b)). According to the following equation, this can be simplified as illustrated in Fig. 1(c),

$$D_N = \rho_{\rm S} \tag{1}$$

where D_N is the electric flux density in the direction normal to the electrode surface, and ρ_S is the surface charge density.

From a theoretical perspective, an interdigitated electrode array with an applied voltage can be modeled more simply as line charges $\pm \rho_L$ placed on both edges of the electrodes, as shown in Fig. 1(c). Using this simplified model, the electric field intensity, \vec{E} , of the line charge placed between the suspension medium and the insulating substrate is

$$\vec{E} = \frac{\rho_L}{\pi(\varepsilon_m + \varepsilon_s)R} \vec{a}_\rho \tag{2}$$

where ε_m and ε_s are the permittivities of the medium and substrate, *R* is the distance from the line charge, and \vec{a}_{ρ} is a unit vector in the radial direction from the line charge.

When an AC voltage v_{in} is applied to interdigitated electrodes with a width and spacing of 2*d*, as shown in Fig. 1(a), the line charge density, ρ_L , becomes

$$\rho_{L} = \frac{\pi(\varepsilon_{m} + \varepsilon_{s})}{2\ln\left(\frac{8d}{\pi a}\right)} v_{in}$$
(3)

where a is the effective radius of the line electrode in Fig. 1(c).

In the case of planar electrodes fabricated using metal evaporation, the effective radius, a, of the line electrode can be approximated as the thickness of the electrode itself. For a cell passing through an interdigitated electrodes from x = -2d to x = 2d, as shown in Fig. 2(a), we can simply disregard the electric field intensity from remote electrodes at $|x| \ge 5d$. Using eqn (2) and (3), the electric field intensity, \vec{E} , acting on the cell can be approximated as

$$\vec{E} \approx \frac{\rho_L}{\pi(\varepsilon_m + \varepsilon_s)} \vec{A} \tag{4}$$

where
$$\vec{A} = \mp \frac{(x+3d)\vec{a}_x + z\vec{a}_z}{(x+3d)^2 + z^2} \pm \frac{(x+d)\vec{a}_x + z\vec{a}_z}{(x+d)^2 + z^2} \pm \frac{(x-d)\vec{a}_x + z\vec{a}_z}{(x-d)^2 + z^2} \mp \frac{(x-3d)\vec{a}_x + z\vec{a}_z}{(x-3d)^2 + z^2}$$
 (5)

and z is the levitation height of the cell from the electrode array.

Fig. 2(b) compares the calculated and simulated values of $|\vec{E}|^2$ from x = -2d to x = 2d at different levitation heights of z = 5, 7.5 and 10 µm. The geometrical values we used for the theoretical calculation and simulation were a = 0.2 µm for the effective radius of the electrode, which is also the thickness of the electrode, $\varepsilon_m = 80\varepsilon_0$ and $\varepsilon_s = 3.9\varepsilon_0$ for the permittivities of the medium and substrate, respectively, and 2d = 50 µm for the width and spacing of the interdigitated electrodes. As shown in Fig. 2(b), using the simplified line charge model in Fig. 1(c), which neglects charges placed on the inside of the electrodes, the calculated result is generally lower than the simulated result. Although the absolute magnitude of the two results differs, the overall shapes of the two results match closely. That is, the peak-to-peak value of $|\vec{E}|^2$, which plays a practical role in the DEP force explained in eqn (6), is roughly same for both the theoretical and simulated results.

The time-averaged x-directional DEP force, F_{DEP} in Fig. 2(a), is given by,³

$$F_{DEP} = \frac{3}{2} \varepsilon_m V_c \operatorname{Re}[f_{CM}] \frac{\partial \left| \vec{E} \right|^2}{\partial x}$$
(6)

$$f_{CM} = \frac{\varepsilon_c^*(\omega) - \varepsilon_m^*(\omega)}{\varepsilon_c^*(\omega) + 2\varepsilon_m^*(\omega)}$$
(7)

where V_c is the cell volume, f_{CM} is the Clausius-Mossitti factor, and $\varepsilon_c^*(\omega)$ and $\varepsilon_m^*(\omega)$ are the complex permittivities of the cell and suspension medium, respectively. Parameter ω is the radian frequency of the electrical field. Each permittivity takes the form $\varepsilon^* = \varepsilon - j(\sigma/\omega)$, where $j = \sqrt{-1}$, ε is the dielectric constant of the material, and σ is its electrical conductivity. From eqn (3)-(5), eqn (6) can be rewritten as

$$F_{DEP} = \frac{3\varepsilon_m V_c \operatorname{Re}[f_{CM}] v_{in}^2}{8 \left[\ln \left(\frac{8d}{\pi a} \right) \right]^2} \frac{\partial \left| \vec{A} \right|^2}{\partial x} = k \frac{\partial \left| \vec{A} \right|^2}{\partial x}, \quad \text{where } k = \frac{3\varepsilon_m V_c \operatorname{Re}[f_{CM}] v_{in}^2}{8 \left[\ln \left(\frac{8d}{\pi a} \right) \right]^2}$$
(8)

Fig. 2(c) shows the calculated x-directional DEP force on a cell passing from x = -2d to x = 2d in Fig. 2(a). The peak DEP force generated slightly inwards from the electrode edge is somewhat larger than that generated toward the outside of the electrode edge. This agrees with Fig. 2(b), which shows that the peak-to-peak value of $|\vec{E}|^2$ created over the electrode is larger than that created between the electrodes.

The total force vector on the cell becomes

$$\vec{F} = \vec{F}_{DEP} + \vec{F}_f = \left(F_{DEP} + F_f \sin\theta\right) \vec{a}_x - F_f \cos\theta \,\vec{a}_y \tag{9}$$

where F_f is the fluidic drag force on a cell. The velocity of the cell, \vec{v} , is

$$\vec{v} = \frac{\vec{F}}{12\eta(A/l)} = \beta \left[\left(F_{DEP} + F_f \sin \theta \right) \vec{a}_x - F_f \cos \theta \, \vec{a}_y \right], \quad \text{where } \beta = \frac{1}{12\eta(A/l)}$$
(10)

where η is the apparent viscosity of the cell in the suspension medium, A is the maximum crosssection area presented perpendicular to the velocity, and l is the characteristic length of the cell in the direction of the velocity vector. If the levitation height z is constant, then the velocity, \vec{v} , is

$$\vec{v} = \frac{d\vec{r}}{dt} = \frac{dx}{dt}\vec{a}_x + \frac{dy}{dt}\vec{a}_y$$
(11)

From eqn (10) and (11), the x- and y-directional components match, and

$$dx = \beta \left(k \frac{\partial |\vec{A}|^2}{\partial x} + F_f \sin \theta \right) dt \quad \text{and}$$
(12)

$$y = -\beta F_f \cos \theta t \,. \tag{13}$$

In Fig. 2(a), del y' can be obtained using the numerical results of eqn (12) and (13), as

$$del y' = x\cos\theta + y\sin\theta.$$
(14)

Fig. 2(d) shows the numerical calculation of del y' at different levitation heights z. This shows that a cell, which is passing over the interdigitated electrode array with an angle of θ between the electrode and direction of flow, is driven in the lateral direction, as illustrated in Fig. 2(a). The lateral force is determined by the magnitude of the DEP force on the cells, as shown in Fig. 2(d); this is determined by the applied frequency and the levitation height z, as explained in eqn (8).

From eqn (7), for a highly conductive suspension medium, such as physiological solution with a conductivity of 17 mS cm⁻¹, the real part of the Clausius-Mossitti factor for the blood cells, based on these dielectric parameters from Yang's studies,^{4,5,30} is about –0.5 for an applied electric frequency of < 2 MHz. That is, the DEP force acting on blood cells suspended in the physiological medium is typically negative for the frequency range < 5 MHz, causing the blood cells to move upward in the microchannel. As a result, under given conditions for a range of frequencies < 2 MHz, del y' is determined largely by the levitation height of the blood cell. In blood, the typical mass densities of human RBCs and WBCs are approximately 1130 and $1050~1080 \text{ kg/m}^3$, respectively.³¹⁻³³ Therefore, the DEP levitation height,^{34,35} which is settled by z-

directional DEP force and gravitation, of RBCs is typically lower than that of WBCs, and the DEP force

acting on RBCs will be stronger than that acting on WBCs.