# Electric-field-induced interaction between biological cells or colloidal particles

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Biological cells can be treated as an inhomogeneous particle. In addition to biomaterials, inhomogeneous particles are also important in more traditional colloidal science. By using two energy methods that are based on Legendre polynomials and Green's function, respectively, we investigate the interaction between biological cells or colloidal particles in the presence of an external electric field, in an attempt to investigate the effect of inhomogeneity on crossover frequencies across which the interaction force changes from attraction to repulsion or vice versa. The predictions by the two methods agree with each other very well. It is shown that there exist two kinds of crossover frequencies $\omega_p$, one from attraction to repulsion and the other from repulsion to attraction as external frequencies increase. The first $\omega_p$ strongly depends on the degree of inhomogeneity, while the second $\omega_p$ does not. This work has relevance to manipulation of biological cells or colloidal particles. © *2009 American Institute of Physics*. [DOI: 10.1063/1.3116628]

## I. INTRODUCTION

The interaction between polarized particles is very important in various systems ranging from biological cell suspensions to colloidal electrorheological fluids, which determines their macroscopic physical properties as well as microstructure. Under an external electric field, polarized charges are induced on the surface of the particles. The interaction between these induced charges leads to an anisotropic interaction between the particles. To understand the interparticle force between two polarized particles, some authors have developed two independent theories,[1,2] which are respectively based on Legendre polynomials[1] and Green's function.[2]

However, the problem becomes more complicated due to the presence of inhomogeneities. The graded materials, whose material properties can vary continuously in space, are abundant in nature. Biomaterials such as cells and bones are typical examples as their composition varies through the object. With the advent of fabrication techniques, these materials can be well produced to tailor their properties for specific needs via the design of the material and microstructure gradients. Such a design makes graded materials quite different in physical properties from the homogeneous materials and other conventional composite materials. Moreover, the composite media consisting of graded inclusions can have more interesting properties than those of homogeneous inclusions.[3]

As far as one decade ago, Freyria *et al.*[4] observed a graded cell response when they experimentally studied cell-implant interactions. Recently, motivated by positional information of protein molecules, Honda and Mochizuki[5] performed computer simulations of cell pattern formation showing that graded cells can be generated by cell behavior involving differences in intercellular repulsion.

In this work, we introduce two profiles to describe the graded particles. A differential equation is then used for the equivalent dielectric constant and conductivity, which was demonstrated to fit perfectly with the first-principles approach.[6]

This paper is organized as follows. In Sec. II, we describe the theory and define briefly the effective dielectric constant and conductivity. Two methods for calculating the interaction force are introduced. In Sec. III, some numerical results are displayed. And the discussion of crossover frequencies and potential use based on the theory is followed in Sec. IV.

## II. FORMALISM

### A. Equivalent dielectric constant of an inhomogeneous cell

This theory can be used in any homogeneous particles. But experimentally, biologic cells are mostly graded. The gradation is generic due to inhomogeneous compartments of cells, the cytoplasm often contains organelles or vacuoles. These inhomogeneities are reflected in their dielectric properties. In order to perform numerical calculations, we take the conductivity and dielectric profiles to be[7]

$$\tilde{\sigma}(r) = \tilde{\sigma}(0)(r/a)^n,$$

$$\tilde{\epsilon}(r) = \tilde{\epsilon}(0) + c(r/a), \tag{1}$$

where $n$ and $c$ are profile dependent constants (tuning parameters). The profile is quite physical in the sense that the conductivity can change rapidly near the boundary of cell and a

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power-law profile prevails. The profile constant $n$ can take any positive values and it can be larger than unity. From the above equations it is clear that the conductivity is largest at the boundary. This is the case in real systems as well since the outermost shell (e.g., cell wall) of a cell is always conductive and often has the largest conductivity. On the other hand, the dielectric constant may vary only slightly and thus a linear profile suffices. In particular, the dielectric constant at the center, i.e., $\bar{\epsilon}(0)$, may be larger than that at the boundary. Thus, we will choose $c \leq 0$.

To discuss such graded cells, it is necessary to determine the effective properties of graded composite materials under externally applied fields. Thus, we use the differential equation for the equivalent dielectric constant $\bar{\epsilon}(r)$ as[8–10]

$$\frac{d\bar{\epsilon}(r)}{dr} = \frac{[\epsilon(r) - \bar{\epsilon}(r)][l\bar{\epsilon}(r) + (l+1)\epsilon(r)]}{r\epsilon(r)}. \quad (2)$$

Here $\bar{\epsilon}(a)$ is the equivalent dielectric properties of the entire cell and multipole order $l = 1, 2, \ldots$. And the substitution of $l = 1$ into this equation yields just the Tartar formula, derived

for assemblages of spheres with varying radial and tangential conductivity.[11]

If the applied electric field is alternating, the conductivity of the system will be considered, and the dielectric constant will show as a complex form, which actually arises from the Maxwell equation combined with the charge conservation law. In that case, the external electric field can be written as $E_0 \cos(\omega t)\hat{\mathbf{Z}}$, while the complex dielectric constants are given by

$$\epsilon = \tilde{\epsilon} + i\frac{\tilde{\sigma}}{\omega},$$

$$\epsilon_h = \tilde{\epsilon}_h + i\frac{\tilde{\sigma}_h}{\omega}. \quad (3)$$

Here both $\tilde{\epsilon}$ and $\tilde{\epsilon}_h$ ($\tilde{\sigma}$ and $\tilde{\sigma}_h$) are real numbers, and they represent the dielectric constant (conductivity) of the rotating sphere and host medium.

Now we introduce the dispersion form of dielectric constants in Eq. (3) into Eq. (2). Then we obtain two differential equations by separating the real part from the imaginary part,

$$\frac{d\bar{\tilde{\epsilon}}}{dr} = \frac{(l+1)\omega^2\tilde{\epsilon}^3 - \omega^2\tilde{\epsilon}^2\bar{\tilde{\epsilon}} - \tilde{\sigma}\tilde{\epsilon}[\tilde{\sigma} + 2l\bar{\tilde{\sigma}}] + \tilde{\epsilon}[(l+1)\tilde{\sigma}^2 - l\omega^2\bar{\tilde{\epsilon}}^2 + l\bar{\tilde{\sigma}}^2]}{r[\omega^2\tilde{\epsilon}^2 + \tilde{\sigma}^2]},$$

$$\frac{d\bar{\tilde{\sigma}}}{dr} = \frac{\omega^2\tilde{\epsilon}^2[(l+1)\tilde{\sigma} - \bar{\tilde{\sigma}}] - 2l\omega^2\tilde{\epsilon}\bar{\tilde{\epsilon}}\bar{\tilde{\sigma}} + \tilde{\sigma}[(l+1)\tilde{\sigma}^2 + l\omega^2\bar{\tilde{\epsilon}}^2 - \tilde{\sigma}\bar{\tilde{\sigma}} - l\bar{\tilde{\sigma}}^2]}{r[\omega^2\tilde{\epsilon}^2 + \tilde{\sigma}^2]}. \quad (4)$$

Then we can easily get the numerical result with the electronic profile in Eq. (1). $\bar{\tilde{\epsilon}}(a)$ and $\bar{\tilde{\sigma}}(a)$ that we obtain in Eq. (4) can be substitute into Eq. (18) as effective values.

## B. Interaction force between two cells

### 1. Method I

First of all, we try to calculate the interparticle force between two homogeneous cells (we see them as sphere particles). We assume the two particles $a$ and $b$ are arranged along $\hat{\mathbf{Z}}$ axis and at rest in the host medium. A dc electric field $E_0\hat{\mathbf{Z}}$ is applied (as showed in inset of Fig. 1).

As we know, the electric potential $\Phi$ satisfies the equation

$$\nabla \cdot [\epsilon(r) \nabla \Phi] = 0. \quad (5)$$

For homogeneous particles, it reduces to the Laplace equation. In the paper of method I,[1] the general expressions for $\Phi$ are written down in spherical coordinates $(r, \theta, \varphi)_\alpha$. Here the subscript $\alpha = a, b$ means that the origin of coordinates is the center of particle $\alpha$. The potential in the host region is

$$\Phi_h(\mathbf{r}_\alpha) = A_0 + \sum_{n=1}\left(A_n r_\alpha^n + \frac{B_n}{r_\alpha^{n+1}}\right)P_n(\cos\theta_\alpha), \quad (6)$$

and the potential inside particle $\alpha$ is

$$\Phi_i(\mathbf{r}_\alpha) = C_0 + \sum_{n=1} C_n r_\alpha^n P_n(\cos\theta_\alpha). \quad (7)$$

Because of the symmetry of our system, the influence that comes from $\varphi$ is ignored in Eq. (6) and (7). Applying the
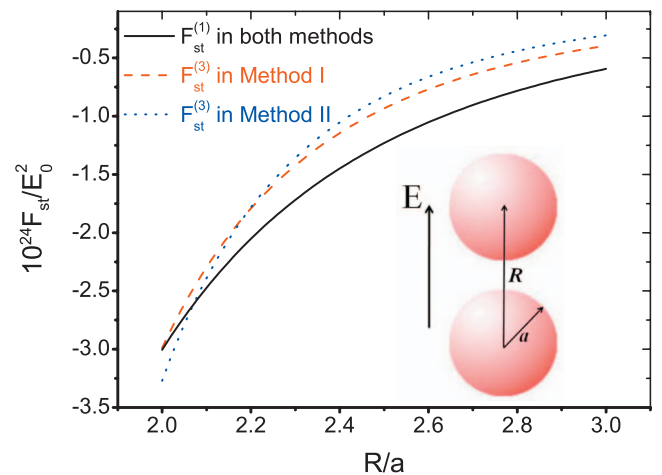


FIG. 1. (Color) The comparison of methods I and II, up to first and third order.

boundary conditions, i.e., the continuity of the potential and the electric displacement on the surface of particles, we can obtain some relations between the unknown coefficients $A_n$, $B_n$, and $C_n$. The only remaining unknown coefficients $C_n$ can be found by constructing a set of Rayleigh identities by the Green's function formulation.[12] According to the Green's function approach, the effects of the polarized charges on the potential at any location can be written as

$$\Phi(\mathbf{r}_\alpha) = E_0 z_\alpha + \frac{1}{4\pi} \sum_{\beta=a,b} \int q_\beta(\mathcal{R}) G(\mathbf{r}_\beta - \mathcal{R}) d\mathcal{R}. \quad (8)$$

The parameter $q(\mathcal{R})$ represents the surface polarized charge which is

$$\sigma = \left. \left( \frac{\partial \Phi_i(\mathbf{r})}{\partial r} - \frac{\partial \Phi_h(\mathbf{r})}{\partial r} \right) \right|_{\text{boundary}}. \quad (9)$$

Comparing Eqs. (6) and (7) with Eq. (8), which represent two different ways of describing the same quantity in regions occupied by the particles, we succeed in getting all the information about the potential of the whole system.

The force exerted on a particle can be found by evaluating the derivative of the energy with respect to particle displacement in space. The change in electrostatic energy due to the introduction of particles into the host medium in the presence of an electric field $\mathbf{E}_0$ is[13,14]

$$W = \frac{1}{8\pi} \int (\mathbf{E} \cdot \mathbf{D}_h - \mathbf{D} \cdot \mathbf{E}_0) d^3x = -\frac{V_a + V_b}{8\pi} C_1 (\epsilon_h - \epsilon) E_0, \quad (10)$$

where $\mathbf{D}_h = \epsilon_h \mathbf{E}_0$ is the displacement field in the host medium in the absence of particles. And for two particles with the same radius and the same dielectric constant, we have

$$C_1 = \frac{-3R^3 E_0}{2a^3 + 2\epsilon/\epsilon_h(R^3 - a^3)} \quad (11)$$

to lowest order. Here $\epsilon$ and $\epsilon_h$ denote the effective dielectric constant of the inhomogeneous sphere and host medium, $a$ is the radii of particles, and $R$ is the distance of particles.

Using this method to the lowest order approximation, we obtain the expression of the force between the particles,

$$\mathbf{F}_{\text{dc}} = -\frac{9(V_a + V_b)a^3 R^2 (\epsilon - \epsilon_h)^2 \epsilon_h}{4\pi[-2a^3(\epsilon - \epsilon_h) + R^3(\epsilon + 2\epsilon_h)]^2} E_0^2 \hat{\mathbf{Z}}. \quad (12)$$

This force to the lowest order approximation contributed by two induced dipoles. There are also contributions from multipoles, which are quite weak and negligible. To confirm that Eq. (12) is efficient, we have calculated the higher order of $\mathbf{F}_{\text{dc}}$ with the same method. And we find that the numerical results approximated to different order are almost the same (see Fig. 1).

However, it is noticed that for inhomogeneous cells the electric properties varies from place to place, and the potential does not satisfy the Laplace equation because of the graded permittivity profiles. Equation (6) and (7) are no longer the common solutions of Eq. (5). The multipole effect is more pronounced for inhomogeneous cells we considered here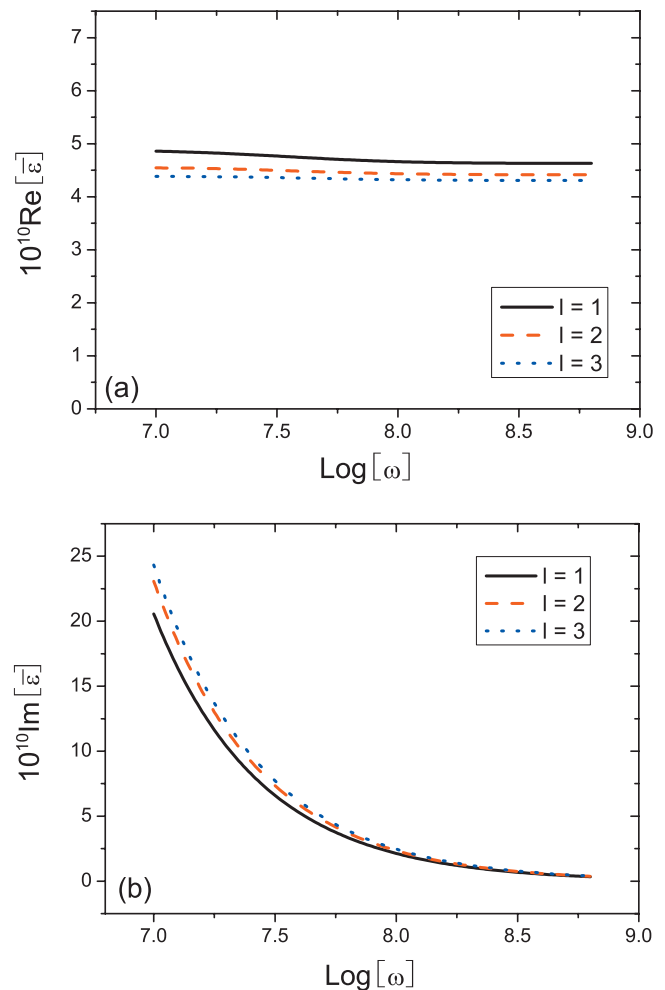.[10] In principle, we have to solve the fully graded electrostatic problem. But fortunately, by calculating the $l$-dependent equivalent permittivity, we find that the curves are very close to one another for relevant frequency of interest (see Fig. 2), and we can safely take only $l=1$ for each multipole level when we calculate the equivalent permittivity as we have done here.



FIG. 2. (Color) The $l$-dependent equivalent permittivity with $c=-30\epsilon_0$, $n=1$, and $R=2.2a$.

### 2. Method II

To show the validity of method I, we introduce another method developed in Ref. 2 to calculate the same force. They assumed that for an isotropic composite, if the position of the spheres is fixed, the total electrostatic energy may be written in the form

$$W = \frac{V}{8\pi} \epsilon_e E_0^2, \quad (13)$$

where $V$ is the system volume and $\epsilon_e$ is the macroscopic effective dielectric tensor. $\epsilon_e$ may be written in terms of a certain pole spectrum of the composite as[15–17]

$$1 - \frac{\epsilon_e}{\epsilon_h} = \sum_n \frac{B_n}{s - s_n}, \quad (14)$$

where $s = \epsilon_h/(\epsilon_h - \epsilon)$, $s_n$ is a pole, and $B_n$ is the corresponding residue. The poles $s_n$ are confined to the interval $0 \le s_n < 1$.

By long calculation, the total energy takes the form

$$W = \frac{V}{8\pi}\epsilon_h \mathbf{E}_0 \cdot \mathbf{E}_0 - \frac{V_a + V_b}{8\pi}\epsilon_h \langle z | G(s) | z \rangle E_0^2, \quad (15)$$

where

$$G(s) \equiv (sI - \Gamma)^{-1}, \quad (16)$$

$I$ is the identity matrix, and the certain Hermitian operator $\Gamma$ is defined in terms of its operation on an arbitrary function $\phi(\mathbf{r})$ by the relation

$$\Gamma\phi(\mathbf{r}) \equiv \int_{V_a+V_b} d^3\mathbf{r}' \nabla'\left(\frac{1}{|\mathbf{r} - \mathbf{r}'|}\right) \cdot \nabla'\phi(\mathbf{r}'). \quad (17)$$

Then the interparticle force on the sphere is the derivative of the energy.

We find that the analytic form of force in dc field from method II is just the same as Eq. (12) to the first order (i.e., $n_{max} = 1$). Noticing that the first order result just contains the dipole interaction, we need a more accurate result to show the efficacy of the approximation. With our parameters, the numerical results of different methods up to third order (i.e., $n_{max} = 3$) seems close to each other (see Fig. 1). In this condition, we can use Eq. (12) in the further formulate deduction and numerical calculation.

### 3. Force in ac field

As mentioned in Sec. II A, we can just take the complex form of dielectric constant Eq. (3) into expression Eq. (12) in order to get the force under an ac field. Dropping the imaginary part, we obtain the interparticle force in the ac electric field as

$$F_{ac} = \frac{9(V_a + V_b)a^3 R^2}{4\pi} E_0^2 \cos^2(\omega t) \cdot \{9R^6(\tilde{\epsilon}_h \tilde{\sigma} - \tilde{\epsilon}\tilde{\sigma}_h)^2(\tilde{\sigma}_h^2$$
$$+ \tilde{\epsilon}_h^2 \omega^2) - [2a^3\tilde{\epsilon}_h((\tilde{\sigma}_h - \tilde{\sigma})^2 + (\tilde{\epsilon}_h - \tilde{\epsilon})^2\omega^2) + R^3(3(\tilde{\epsilon}_h$$
$$- \tilde{\epsilon})\tilde{\sigma}_h^2 - \tilde{\epsilon}_h(\tilde{\sigma} - \tilde{\sigma}_h)^2 + \tilde{\epsilon}_h(\tilde{\epsilon}_h - \tilde{\epsilon})(2\tilde{\epsilon}_h$$
$$+ \tilde{\epsilon})\omega^2)]^2\}/\{\tilde{\epsilon}_h[(2a^3\tilde{\sigma}_h + 2R^3\tilde{\sigma}_h - 2a^3\tilde{\sigma} + R^3\tilde{\sigma})^2$$
$$+ (2a^3\tilde{\epsilon}_h + 2R^3\tilde{\epsilon}_h - 2a^3\tilde{\epsilon} + R^3\tilde{\epsilon})^2\omega^2]^2\}. \quad (18)$$

## III. NUMERICAL RESULTS

As discussed before, Fig. 1 offers the evidence that the method I we used in the whole paper is valid. In Fig. 2, we prove numerically that the equivalent permittivities are almost the same to each multipole level. As a result, we can simply take $l=1$ into Eq. (2) when we calculate the equivalent permittivity. The reason why the imaginary part in Fig. 2 is even better is very simple. With the rapidly varying conductivity profile, the conductivity is only important at the cell boundary, which forms a thin shell. Thus a single $l$-independent equivalent conductivity suffices.

To inhomogeneous particles (e.g., biologic cells), the force changes with the profile constants $c$ and $n$. Such a change is displayed in Fig. 3. Noting that the negative sign means the particles are attracting each other, we find there is repulsion in a higher frequency range. And the repulsive
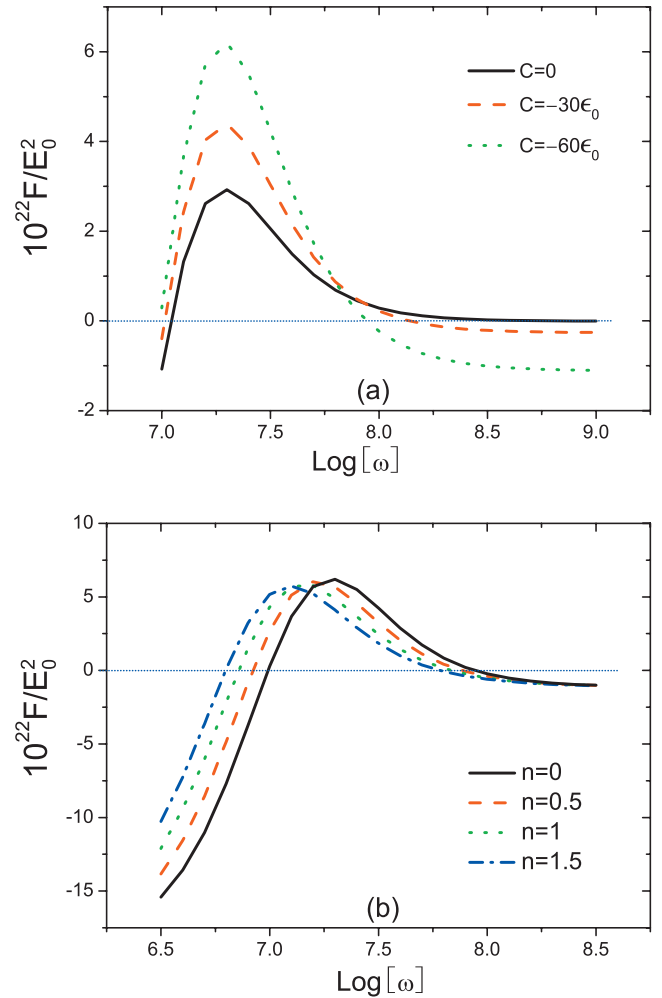


FIG. 3. (Color) The interparticles force for profile constants at different values, for (a) constants $n=0$, constants $c$ at $c=0$, $c=-30\epsilon_0$, and $c=-60\epsilon_0$, respectively, and (b) constants $c=-60\epsilon_0$, constants $n$ at $n=0$, $n=0.5$, $n=1$, and $n=1.5$, respectively. Two crossover frequencies at which force turns to zero can be found in each line. Parameters: $a=5$ $\mu$m, $R=12$ $\mu$m, $\tilde{\epsilon}=75\epsilon_0$, $\tilde{\epsilon}_h=80\epsilon_0$, $\tilde{\sigma}=2.8\times10^{-2}$ S/m, and $\tilde{\sigma}_h=2.8\times10^{-4}$ S/m.

force glows to its peak then decreases quickly and turns to attractive force again with the increasing frequency of the ac external field. As a result, the turning points appear important in physics. We call the turning frequencies as crossover frequencies. There are two kinds of crossover frequencies in each cell profile. The first crossover frequency turns the interaction force from repulsive to attractive, and the second one turns the repulsive force back to attractive force. The crossover frequencies also depend on these profile constants. The two frequencies redshift with the increasing $c$ and blueshift with the increasing $n$. When the applied frequency is high enough, the electrons in the dielectric particles (cells) will not respond to the field because of the limited conductivity and the force tends to a fixed value. Moreover, the large mismatch of the media and cell dielectric constants leads to a higher force. In Fig. 3(a), the maximum of the force is increasing with a large $c$.

Figure 4 displays the detail of first crossover frequency at which the force shifts from attraction to repulsion, while Fig. 5 shows the property of the second crossover frequency at which the force shifts from repulsion to attraction. We also
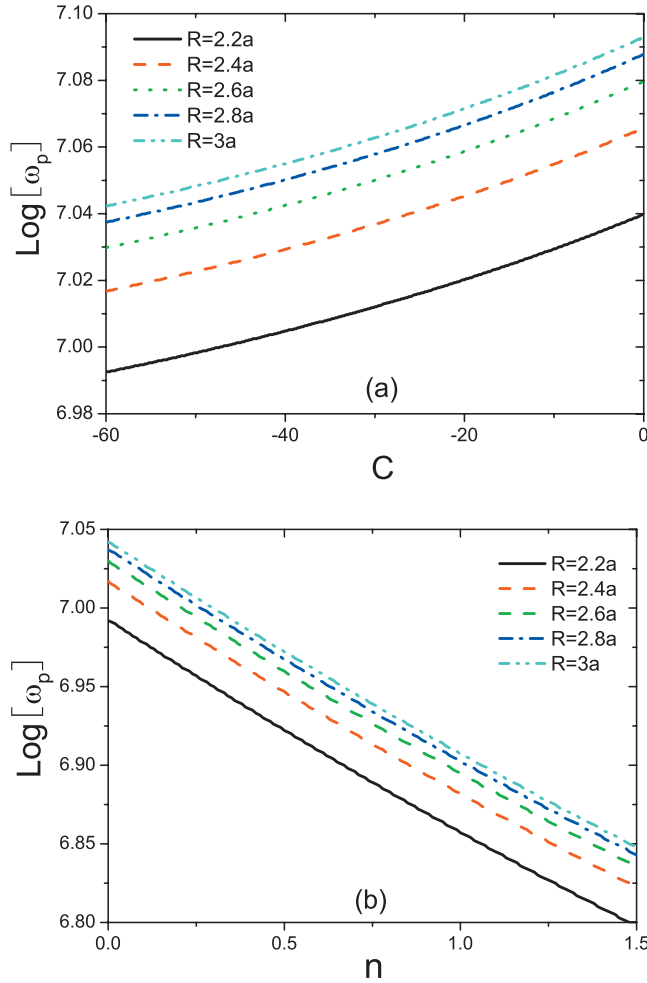
FIG. 4. (Color) The first crossover frequency $\omega_p$ (from attractive force to repulsive force) vs profile constants: (a) constants $c$ and (b) constants $n$. Different colors refer to different particle distances $R$. Parameters: $a$ =5 $\mu$m, $\tilde{\epsilon}=75\epsilon_0$, $\tilde{\epsilon}_h=80\epsilon_0$, $\tilde{\sigma}=2.8\times10^{-2}$ S/m, and $\tilde{\sigma}_h=2.8\times10^{-4}$ S/m.
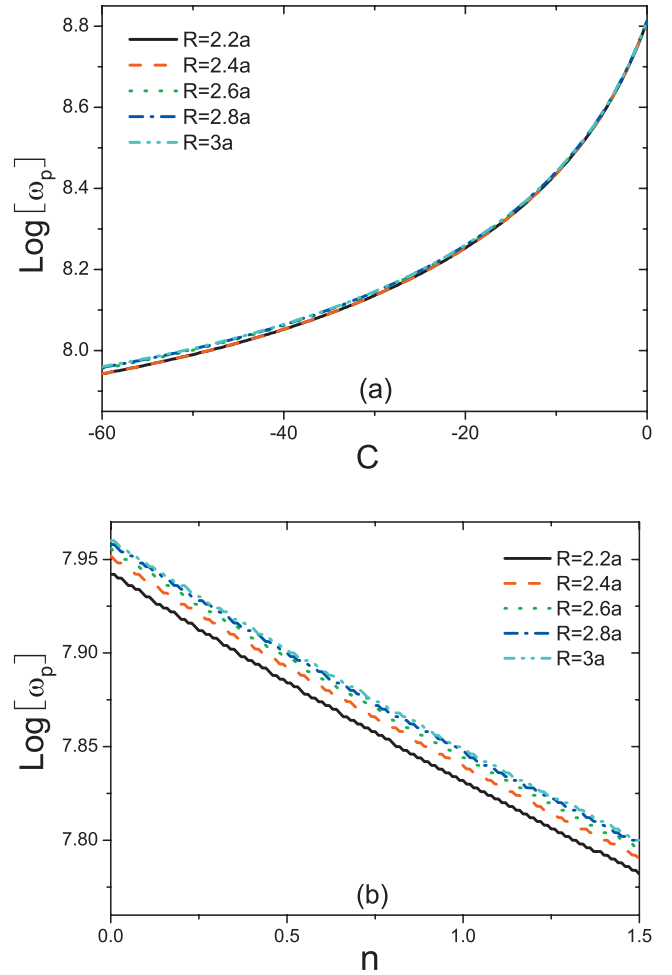


FIG. 5. (Color) The second crossover frequency $\omega_p$ (from repulsive force to attractive force) vs profile constants: (a) constants $c$ and (b) constants $n$. Different colors refer to different particle distances $R$. Parameters: $a$ =5 $\mu$m, $\tilde{\epsilon}=75\epsilon_0$, $\tilde{\epsilon}_h=80\epsilon_0$, $\tilde{\sigma}=2.8\times10^{-2}$ S/m, and $\tilde{\sigma}_h=2.8\times10^{-4}$ S/m.

display the change of crossover frequency with different distances between particles in Figs. 4 and 5. We find that the first crossover frequencies increase greatly to a further distance when the distances are short compared to the radius of particles.

## IV. DISCUSSIONS

The crossover frequency is an important property of colloid particles. A lot of works studied the crossover frequency especially in some dielectrophoresis (DEP) experiments.[18–21] In a certain frequency, the force changes from positive to negative DEP. In experiments, the frequency is varied until the particle motion is no longer toward low-field intensity, and instead is toward high-field intensity regions; this is straightforward to observe. The source of the crossover frequency in the DEP phenomena is also from the complex dielectric constants in form of Eq. (3). These forms indicates that the dielectric constants change with the frequency, as well as any other properties (e.g., the interaction force). Thus, it is quite easy to control the system by shifting the frequency of applied field experimentally. Considering the interaction force we discussed, we expect to see different electric orientation in different frequency ranges.[22]

Such interaction between particles can improve the trapping efficiency of a DEP device by causing nearly particles to come together. However, in some applications of DEP, it is desirable to manipulate particles individually, and thus these interactions are not desirable. For instance, in devices used for separating particles based on their sizes, the particle-particle interactions are not desirable as they cause all particles, irrespective of their sizes, to aggregates. So, one[23] studied the ratio of the particle-particle and DEP forces in order to control the relative magnitude of these two contributions to the total electrostatic force. They found that the ratio decreases with increasing particle size and increasing gap between the particles.

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