Dielectric behaviour of graded spherical cells
with an intrinsic dispersion

Y. T. C. Ko\textsuperscript{1,2}, J. P. Huang\textsuperscript{1,3}, K. W. Yu\textsuperscript{1}

\textsuperscript{1}Department of Physics, The Chinese University of Hong Kong, Shatin, NT, Hong Kong
\textsuperscript{2}Trinity College, University of Cambridge, Cambridge CB2 1TQ, United Kingdom
\textsuperscript{3}Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

Abstract

The dielectric properties of single-shell spherical cells with an intrinsic dielectric dispersion has been investigated. By means of the dielectric dispersion spectral representation (DDSR) for the Clausius-Mossotti (CM) factor, we express the dispersion strengths as well as the characteristic frequencies of the CM factor analytically in terms of the parameters of the cell model. These analytic expressions enable us to assess the influence of various model parameters on the electrokinetics of cells. Various interesting behaviours have been reported. We extend our considerations to a more realistic cell model with a graded core, which can have spatial gradients in the conductivity and/or permittivity. To this end, we address the effects of a graded profile in a small-gradient expansion in the framework of DDSR.

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I. INTRODUCTION

The interaction of the polarization of biological cells with the applied fields has resulted in a wide range of practical applications from manipulation, trapping to separation of biological cells [1], and even nanotechnology [2]. When a biological cell in medium is exposed to an applied electric field, there is an accumulation of charge at the interfaces and hence a dipole moment is induced in the cell. The strength of the polarization depends on the frequency of the applied field as well as on the permittivities and conductivities of cells and medium. The situation becomes more complicated when we consider structured particles because biological cells are usually modeled as conductive spheres (cytosol) with a thin insulating outer shell (membrane), assuming the shell is an isotropic, non-dispersive dielectric with conductive losses. In this case, there are additional frequency-dependent changes in the polarization.

The Clausius-Mossotti (CM) factor determines the polarization of a biological particle in a surrounding medium, and is a measure of the dielectric contrast between the particle and medium. The CM factor is important in biophysical research because it is closely related to the alternating current (ac) electrokinetic behaviors of biological cells, namely, dielectrophoresis [3], electrorotation [4], electro-orientation [5], electrofusion [6], as well as electrodeformation [7]. Any change in the cell’s properties such as the mobile charges, or particle shape as well as the variation of medium conductivity or medium permittivity will change the CM factor, which is in turn reflected in the ac electrokinetic spectra. These spectra show characteristic frequency-dependent changes amongst other complicated features.

Moreover, the conductivities and permittivities can have characteristic frequency dependencies due to the presence of mobile charges in membrane. Thus the constancy of these quantities is only an approximation and these quantities do change with frequency, giving rise to additional dispersions. In this work, we aim to establish a dielectric dispersion spectral representation (DDSR) for the single-shell spherical cell model with an intrinsic dielectric dispersion in the cytosol. The DDSR was pioneered by Maxwell [8] in 1891 in the
context of interfacial polarization. When two media are put in contact (thus forming an interface) and an electric field is applied, polarization charge is induced at the interface due to the dielectric contrast between the two media. Although Maxwell considered a two phase system in which one phase is insulating, it can be readily generalized to a more general case when both media have complex dielectric permittivities.

The DDSR was subsequently extended to spherical particles by Lei et al. [9] and further elaborated by Gao et al. [10] for cell models without shells, the single-shell model has been widely used to mimic a living biological cell as a homogeneous, nondispersive spherical particle surrounded by a thin shell corresponding to the plasma membrane. The DDSR enables us to express the CM factor analytically in terms of a series of sub-dispersions, each of which with analytic expressions for the dispersion strengths and their corresponding characteristic frequencies expressed in terms of the various parameters of the cell model [9,10]. Thus this representation enables us to assess in detail the influence of the various model parameters, including structural, material, as well as dynamic properties of cells, without the need to analyze the full dielectric dispersion spectrum.

The paper is organized as follows. In the next section, we review the dielectric dispersion spectral representation (DDSR) for the CM factor of an unshelled spherical cell model [9] to establish notations. We express the dispersion strength as well as the characteristic frequency of the CM factor analytically in terms of the parameters of the cell model. Then an intrinsic dielectric dispersion is included in the cell [10]. In Section III, we analyze the single-shell model with a dispersive core and a non-dispersive, insulating shell. We apply DDSR to the CM factor to obtain the analytic expressions for the dispersion strengths and characteristic frequencies. These expressions enable us to assess the influence of various model parameters on the electrokinetics of cells. In Section IV, we examine the influence of the individual parameters, such as the conductivities of the external medium and the cytosol on the dispersion spectra. Various interesting behaviours will be obtained. In Section V, we extend our considerations to a graded core, namely, the core can have spatial gradients in the conductivity and/or permittivity. We address the effects of a graded profile in a
small-gradient expansion in the general framework of DDSR. Discussion and conclusion will be given in Section VI.

II. DIELECTRIC DISPERSION SPECTRAL REPRESENTATION

In this section, we review the dielectric dispersion spectral representation for the CM (Clausius-Mossotti) factor of an unshelled spherical cell model [9]. The dipole moment $p$ of a single sphere in uniform electric field [11]

$$p = \frac{\varepsilon_e U D^3}{8} E_0$$

(1)

where $\varepsilon_e$ is the permittivity of the external medium, $D$ is the diameter of the particle and $E_0$ is the electric field strength. $U$ is the CM factor due to the dielectric discontinuity and follows the equation

$$U = \frac{\varepsilon_i - \varepsilon_e}{\varepsilon_i + 2\varepsilon_e}$$

(2)

where $\varepsilon_i$ is the permittivity of the particle. In AC applied fields, we replace the permittivities with their complex counterparts:

$$\varepsilon_i \rightarrow \varepsilon_i^* = \varepsilon_i + \frac{\sigma_i}{i\omega}$$

(3)

$$\varepsilon_e \rightarrow \varepsilon_e^* = \varepsilon_e + \frac{\sigma_e}{i\omega}$$

(4)

where $i = \sqrt{-1}$, $\sigma_i$ and $\sigma_e$ are conductivities of the particle and of the external medium respectively. Then

$$U \rightarrow U^* = \frac{\varepsilon_i^* - \varepsilon_e^*}{\varepsilon_i^* + 2\varepsilon_e^*}$$

(5)

This gives the dielectric relaxation of a single spherical particle

$$U^* = U + \frac{\Delta \varepsilon}{1 + i\omega/\omega_c}$$

(6)

with the characteristic frequency $\omega_c$ and dispersion strength $\Delta \varepsilon$: 
\[ \omega_c = \frac{\sigma_i + 2\sigma_e}{\epsilon_i + 2\epsilon_e}, \]  
(7)

\[ \Delta \epsilon = \frac{\sigma_i - \sigma_e}{\sigma_i + 2\sigma_e} - \frac{\epsilon_i - \epsilon_e}{\epsilon_i + 2\epsilon_e}. \]  
(8)

It is related to the Maxwell-Wagner structure relaxation \( \omega_c = 10^4 \text{ s}^{-1} \ldots 10^9 \text{ s}^{-1} \).

The angular velocity \( \Omega \) of electroration is

\[ \Omega = -\frac{\epsilon_e E_0^2}{2\eta} \text{Im } U^*, \]  
(9)

where \( \eta \) is the coefficient of viscosity. Note that \( \text{Im } U^* < 0 \) gives co-field rotation while \( \text{Im } U^* > 0 \) gives anti-field rotation.

Then, when an intrinsic dielectric dispersion is included in the cell \([10]\), we again replace the permittivities with the appropriate complex counterparts:

\[ \epsilon_i^* = \epsilon_i + \frac{\Delta \epsilon_i}{1 + i\omega/\omega_c} + \frac{\sigma_i}{i\omega}, \]  
(10)

\[ \epsilon_e^* = \epsilon_e + \frac{\sigma_e}{i\omega}. \]  
(11)

The corresponding complex CM factor \( U_{\text{int}}^* \) can then be expressed in the dispersion terms as

\[ U_{\text{int}}^* = U_{\text{int}} + \sum_{n=1}^{2} \frac{\Delta \epsilon_n}{1 + i\omega/\omega_n}, \]  
(12)

where \( U_{\text{int}} = (\epsilon_i - \epsilon_e)/(\epsilon_i + 2\epsilon_e) \), \( \Delta \epsilon_n \)s are the dispersion strengths and \( \omega_n \)s are the characteristic frequencies.

To solve for the dispersion strengths and the characteristic frequencies, assume the summation term in Eq. (12) is of the form

\[ U_{\text{int}}^* - U_{\text{int}} = \frac{P_0 + P_1 w}{1 + R_1 w + R_2 w^2} \]  
(13)

\[ = \frac{P_0 + P_1 w}{(1 + w/\omega_1)(1 + w/\omega_2)}, \]  
(14)

where \( w = i\omega \) and, \( P \)s and \( R \)s are constants in terms of the model parameters.

For the characteristic frequencies, solve the following quadratic equation

\[ 1 + R_1 w + R_2 w^2 = 0 \]  
(15)
and the $\omega_n$s are *minus* the solutions to the equation. They come out to be, in terms of the model parameters,

\[
\omega_1 = \frac{1}{2(2\epsilon_e + \epsilon_i)} [2\sigma_e + \sigma_i + (\Delta\epsilon_i + 2\epsilon_e + \epsilon_i)\omega_c + \sqrt{\Gamma}],
\]

\[
\omega_2 = \frac{1}{2(2\epsilon_e + \epsilon_i)} [2\sigma_e + \sigma_i + (\Delta\epsilon_i + 2\epsilon_e + \epsilon_i)\omega_c - \sqrt{\Gamma}],
\]

where

\[
\Gamma = -4(2\epsilon_e + \epsilon_i)(2\sigma_e + \sigma_i)\omega_c + [2\sigma_e + \sigma_i + (\Delta\epsilon_i + 2\epsilon_e + \epsilon_i)\omega_c]^2.
\]

For the dispersion strengths, performing partial fraction can express the summation term in the form of the summation term in Eq. (12). The dispersion strengths turn out to be, in terms of model parameters and characteristic frequencies,

\[
\Delta\epsilon_1 = \frac{3(-\epsilon_i\sigma_e\omega_1 + \epsilon_e\sigma_i\omega_1 + \epsilon_i\sigma_e\omega_c - \epsilon_e\sigma_i\omega_c + \Delta\epsilon_i\epsilon_e\omega_1\omega_c)}{(2\epsilon_e + \epsilon_i)^2\omega_1(\omega_1 - \omega_2)},
\]

\[
\Delta\epsilon_2 = \frac{3(\epsilon_i\sigma_e\omega_2 - \epsilon_e\sigma_i\omega_2 - \epsilon_i\sigma_e\omega_c + \epsilon_e\sigma_i\omega_c - \Delta\epsilon_i\epsilon_e\omega_2\omega_c)}{(2\epsilon_e + \epsilon_i)^2\omega_2(\omega_1 - \omega_2)}.
\]

It is worth remarking that, two dispersion terms appear in Eq. (12): the first term (i.e. when $n = 1$) is due to the phase difference between the cell and the medium, and the second term (i.e. when $n = 2$) is due to the presence of the intrinsic dispersion inside the cell.

This is a special case of the model mentioned in the following section. It is interesting to compare that this model, with no shell, but the same core as the next model, has two dispersion strengths (and the same number of characteristic frequencies), while the next model, with shell, has three dispersion strengths (and the same number of characteristic frequencies).

Similar work was done by Foster *et al.* [12]. For the case of nondispersive particle and medium, our solutions are indeed equivalent to those of Foster *et al.* However, for the case of dispersive particle and nondispersive medium, we quoted the exact analytic solutions while Foster *et al.* only presented the approximate solutions obtained by expanding the exact solutions using Taylor’s expansion (cf. Section b of Ref. [12]).
III. SINGLE-SHELL SPHERICAL CELL MODEL, WITH A DISPERSIVE CORE

The CM (Clausius-Mossotti) factor of an isotropic model with a non-dispersive homogeneous core has been investigated [13,14]. Here we would like to establish the DDSR (dielectric dispersion spectral representation) of an isotropic model with a dispersive homogeneous core covered with a non-dispersive, insulating membrane [15].

The idea of DDSR is to mathematically extract the analytic expressions of the dispersion strengths and the corresponding characteristic frequencies from the CM factor. The CM factor for a single-shell spherical cell with isotropic, lossless dielectric membrane is [13,14]

$$U_{iso} = \frac{(2\epsilon_m + \epsilon_i)(\epsilon_m - \epsilon_e)(2\epsilon_m + \epsilon_e)R_e^3 + (\epsilon_i - \epsilon_m)(2\epsilon_m + \epsilon_e)R_i^3}{(2\epsilon_m + \epsilon_i)(2\epsilon_e + \epsilon_m)R_e^3 + 2(\epsilon_i - \epsilon_m)(\epsilon_m - \epsilon_e)R_i^3},$$ \hspace{1cm} (21)

where \(\epsilon\) is permittivity and \(R\) the radius; the subscripts \(e, m\) and \(i\) correspond to the external medium, the membrane and the cytosol respectively.

For adaptation to our concerned model, the real constants \(\epsilon_e, \epsilon_m\) and \(\epsilon_i\) are replaced by the complex counterparts

$$\epsilon_i^* = \epsilon_i + \frac{\Delta\epsilon_i}{1 + i\omega/\omega_d} + \frac{\sigma_i}{i\omega},$$ \hspace{1cm} (22)

$$\epsilon_m^* = \epsilon_m + \frac{\sigma_m}{i\omega},$$ \hspace{1cm} (23)

$$\epsilon_e^* = \epsilon_e + \frac{\sigma_e}{i\omega}.$$ \hspace{1cm} (24)

The complex \(\epsilon_i^*\) contains the dispersive term \((\Delta\epsilon_i/1+i\omega/\omega_d)\) to account for the intrinsic dispersive nature of the cytosol, while both the membrane and the external medium are non-dispersive.

The CM factor becomes complex and can be written as

$$U^*_{dis} = U_{iso} + \sum_{t=1}^{3} \frac{\Delta\epsilon_t}{1 + i\omega/\omega_t},$$ \hspace{1cm} (25)

where \(\Delta\epsilon_t\) is the dispersion strengths, and \(\omega_t\) is the characteristic frequencies.

\(\Delta\epsilon_t\) and \(\omega_t\) can be solved easily using Mathematica. Assume the summation part to be of the form
\[ U_{\text{dis}}^* - U_{\text{iso}} = \frac{B_0 + B_1 w + B_2 w^2}{1 + A_1 w + A_2 w^2 + A_3 w^3} \]
\[ = \frac{B_0 + B_1 w + B_2 w^2}{(1 + w/\omega_1)(1 + w/\omega_2)(1 + w/\omega_3)}. \]

where \( w = i\omega \) and the \( A_s \) and \( B_s \) are constants in terms of the parameters of the model. Performing partial fraction can express this term in the form of the summation in Eq. (25).

To solve for \( \omega_t \), solve the cubic equation

\[ 1 + A_1 w + A_2 w^2 + A w^3 = 0 \quad (28) \]

\( \omega_t \)'s are \textit{minus} the solutions to this equation.

\( \Delta \epsilon_1 \) in terms of the constants \( B_s \) and \( \omega_t \) is

\[ \Delta \epsilon_1 = \frac{(B_0 + \omega_1(-B_1 + B_2 \omega_1))\omega_2\omega_3}{(\omega_1 - \omega_2)(\omega_1 - \omega_3)} \quad (29) \]

The rest of the \( \Delta \epsilon_t \)'s follow by cyclic permutation of the variables, namely, \( 1 \to 2, 2 \to 3 \) and \( 3 \to 1 \).

\textbf{IV. THE INFLUENCE OF INDIVIDUAL PARAMETERS}

This model depends on the thickness of the membrane, the permittivities and conductivities of three different regions (i.e. the cytosol, the membrane and the external medium) and the properties of the cytosol dispersion. Using \textit{Mathematica} these parameters can be varied individually. Each time only one parameter is varied, while the rest are kept at the values in Table I. These variations show interesting behaviours.

As shown in the figures, there are three sub-dispersions: \( \Delta \epsilon_1 \) being the co-field peak related to the cytosol, \( \Delta \epsilon_2 \) being the anti-field peak related to the membrane and \( \Delta \epsilon_3 \) being the anti-field peak related to the intrinsic dispersion of the cytosol.

In Fig. 1, the high-frequency co-field dispersion strength \( \Delta \epsilon_1 \) remains relatively constant from \( \sigma_e = 1 \times 10^{-5} \text{S/m} \) to about \( \sigma_e = 0.01 \text{S/m} \) and then decreases with increasing \( \sigma_e \), due to a significant reduction in the conductivity contrast between the cytosol and the external...
medium. Its corresponding characteristic frequency $\omega_1$ also remains relatively constant in the mentioned range and then increases with increasing $\sigma_e$. The anti-field dispersion strengths $\Delta\epsilon_2$ and $\Delta\epsilon_3$ and their corresponding characteristic frequencies $\omega_2$ and $\omega_3$ show more interesting behaviours. $\Delta\epsilon_2$ and $\Delta\epsilon_3$ swap at between $\sigma_e = 0.00018 \text{ S/m}$ and $\sigma_e = 0.00019 \text{ S/m}$, while $\omega_2$ and $\omega_3$ show level-repulsion, i.e. their values gain closer, being closest at the same value of $\sigma_e$ as when the swapping occurs, and then their values move apart again. This phenomenon is very common in many physical systems and is frequently observed in atomic physics. These interesting phenomena are evidences that both $\Delta\epsilon_2$ and $\Delta\epsilon_3$ are real (as opposed to virtual solutions arising from inaccurate calculations) and are common in varying many of the parameters, as shown below.

In Fig. 2, increasing $\sigma_i$ causes $\Delta\epsilon_1$ to increase from negative (anti-field) to positive (co-field) and then remain constant, $\Delta\epsilon_2$ to decrease to a constant value and $\Delta\epsilon_3$ to remain constant throughout. $\omega_1$ increases monotonically while $\omega_2$ and $\omega_3$ remains roughly constant.

In Fig. 3, varying $\omega_d$ has negligible effect on $\Delta\epsilon_1$ and thus also $\omega_1$. In fact, $\Delta\epsilon_2$ and $\Delta\epsilon_3$ are not very much affected if not for the swapping occurring at about $\omega_d = 30000 \text{ rad/s}$. Their corresponding characteristic frequencies also show level-repulsion, as in previous cases, with the closest point also at about $\omega_d = 30000 \text{ rad/s}$.

In Fig. 4, $\Delta\epsilon_1$ and $\Delta\epsilon_3$ (and also their corresponding characteristic frequencies $\omega_1$ and $\omega_3$) show negligible variations. Both $\Delta\epsilon_2$ and $\omega_2$ remain relatively constant before increasing. They being the only affected ones because they are, as well as the concerned parameter $\sigma_m$, related to the membrane.

Compared with the isotropic mobile charge model with a non-dispersive homogeneous core previously investigated, it is interesting that the variations of different permittivities and conductivities show remarkably similar results, with the most noticeable difference that the swapping and the level-repulsion did not occur in the previous model.

Fig. 5 shows the real and imaginary parts of the CM factor against the field frequency for several values of the medium conductivity, in an attempt to illustrate the results in Fig. 1. In this figure, two dispersions are observed. In fact, as shown in Fig. 1, the third dispersion
strength is small enough to be neglected, and hence the third dispersion in Fig. 5 cannot be shown, as expected. Similarly, we are able to adjust the other parameters respectively, like the cytosolic conductivity, circular frequency of cytosol dispersion and external conductivity, in order to illustrate the results in Figs. 2~4. However, all of them should show a framework similar to Fig. 5, and hence are omitted.

V. SMALL-GRADIENT EXPANSION

After investigating models with homogeneous cores, it is natural for us to proceed to investigate models with non-homogeneous cores. Here we choose to investigate a model that consists of a dispersive core with graded dielectric profile, and a non-dispersive membrane. We consider a graded permittivity profile

\[ \epsilon_i(r) = \epsilon_i + ar + O[a]^2, \quad 0 \leq r \leq R_i, \]

where \( a \) is a gradient, which has the unit as permittivity per unit length. We start from Eq.(21) and replace the cytosolic permittivity by an equivalent permittivity \( \bar{\epsilon}_i(r) \) [16]

\[ \bar{\epsilon}_i(r) = \epsilon_i + \frac{3}{4} a R_i + O[a]^2. \]

As shown below, \( \bar{\epsilon}_i(r) \) can formally be calculated using the small-gradient expansion of the differential effective dipole approximation (DEDA) [16,17].

After the substitution, we can expand the CM factor using Taylor’s expansion, up to the second order:

\[ U(a) = U(0) + aU'(0) + O[a]^2. \]

The first term is the same as \( U_{iso} \), while the second term is the correction due to the graded profile.

We now extract the DDSR of the second term as usual, by replacing the permittivities by their complex counterparts as in Eqs.(22)–(24), using the following substitution
Using these substitutions, we can see that the dielectric profile is

\[ \epsilon_i^*(r) = \epsilon_i + \frac{\sigma_i + ar}{i\omega} + O[a]^2 \]  

(34)

Assume the second term has the form

\[ aU'(0) = \frac{C_0 + C_1 w + C_2 w^2 + C_3 w^3}{1 + D_1 w + D_2 w^2 + D_3 w^3 + D_4 w^4} \]

\[ = \frac{C_0 + C_1 w + C_2 w^2 + C_3 w^3}{((1 + w/\omega_1)(1 + w/\omega_2))^2} \]  

(35)

(36)

where \( w = i\omega \) and \( C \)s and \( D \)s are constants in terms of the parameters of the model.

Although the denominator is a quartic equation, there are only two distinct solutions for the characteristic frequency. This is due to the differentiation performed in the Taylor’s expansion, causing each frequency to split into a repeated root.

By partial fraction \( aU'(0) \) takes the form

\[ \sum_{q=1}^{2} \frac{\Delta \epsilon_q}{1 + \frac{w}{\omega_q}} + \sum_{q=1}^{2} \frac{\Delta^2 \epsilon_q}{(1 + \frac{w}{\omega_q})^2} \]  

(37)

To avoid confusion, it should be remarked that \( \Delta^2 \epsilon_q \) does not equal the square of \( \Delta \epsilon_q \).

To solve for \( \omega_q \), solve the quartic equation

\[ (1 + D_1 w + D_2 w^2)^2 = 0. \]  

(38)

\( \omega_q \)s are \emph{minus} the solutions to this equation.

\( \Delta \epsilon_1 \) and \( \Delta^2 \epsilon_1 \) in terms of the constants \( C \)s and the characteristic frequencies \( \omega_q \)s are

\[ \Delta \epsilon_1 = \frac{\omega_1 \omega_2^2 (2C_0 - C_1(\omega_1 + \omega_2) + \omega_1(C_3 \omega_1(\omega_1 - 3\omega_2) + 2C_2 \omega_2))}{(\omega_1 - \omega_2)^3}, \]

\[ \Delta^2 \epsilon_1 = \frac{(C_0 - \omega_1(C_1 + \omega_1(-C_2 + C_3 \omega_1)))\omega_2^2}{(\omega_1 - \omega_2)^2}. \]

(39)

(40)

\( \Delta \epsilon_2 \) and \( \Delta^2 \epsilon_2 \) can be obtained by replacing \( \omega_1 \) with \( \omega_2 \) and \( \omega_2 \) with \( \omega_1 \).

We are now in a position to show how to find \( \bar{\epsilon}_i(r) \) from DEDA [16,17]. For the dipole factor of a graded spherical particle, the following differential equation holds [16,17]
\[
\frac{db}{dr} = -\frac{1}{3r \epsilon_e \epsilon_i(r)} [(1 + 2b) \epsilon_e - (1 - b) \epsilon_i(r)] \left[(1 + 2b) \epsilon_e + 2(1 - b) \epsilon_i(r)\right]
\]

(41)

where \(b\) is the dipole factor, \(r\) is the radius, and \(\epsilon_i(r)\) is the dielectric profile.

Since

\[
b(r) = \frac{\bar{\epsilon}_i(r) - \epsilon_e}{\epsilon_i(r) + 2 \epsilon_e}
\]

(42)
solving for \(b(r)\) is equivalent to solving for \(\bar{\epsilon}_i(r)\).

Since we are doing a small-gradient expansion, \(b(r)\) can be expressed as

\[
b(r) = b_0 + b_1 + O[a]^2
\]

(43)

where

\[
b_0 = \frac{\epsilon_i - \epsilon_e}{\epsilon_i + 2 \epsilon_e}
\]

(44)

and \(b_1\) can be solved from the differential equation

\[
\frac{db_1}{dr} = -\frac{3[(\epsilon_i + 2 \epsilon_e)^2 b_1 - 3 \epsilon_e a r]}{r(\epsilon_i + 2 \epsilon_e)^2}.
\]

(45)

The solution reads

\[
b_1 = \frac{9a \epsilon_e}{4(\epsilon_i + 2 \epsilon_e)^2}
\]

(46)

using the initial condition at \(r = 0\).

After putting all the pieces together, \(\bar{\epsilon}_i(r)\) comes out as in Eq. (31).

Using the parameters as shown in Table I and \(a = 0.025/R_i\) (where \(R_i = R_e - d\) and is the internal radius), we have done some numerical calculations. This value of \(a\) corresponds to a change of 10% over the internal radius. The results are shown in Table II. These are corrections to the calculations in the previous session due to a small gradient. The characteristic frequencies remain the same as in the previous isotropic electrostatic model (except now each is a repeated root), while the dispersion strengths are smaller than those in the previous model by one to two order of magnitude. This shows that our small-gradient expansion is valid.
VI. DISCUSSION AND CONCLUSION

Here a few comments are in order. In view of our recent success in the DDSR of single-shell spherical cell model, we are prepared to illustrate the DDSR in various different situations. We would like to extend DDSR to cell suspensions of higher concentration. At a higher concentration, we expect mutual interactions among cells and the dielectric behaviors can change significantly. We may extend DDSR to polydisperse cells, because the cells may have different sizes and/or permittivities. The polydispersity can have nontrivial impact on their dielectric behaviors. Eventually we have to overcome the analytic continuation, and analyze the dispersion spectrum of the full anisotropic mobile charge model and the graded cell model.

Regarding the applicability of the Clausius-Mossotti approach, one can solve the electrostatic problem first, and then extend to complex permittivities accordingly, as pointed out by Jones [1]. As a matter of fact, there are already theories of e.g. Maxwell and Wagner, and Rayleigh for heterogeneous dielectrics [18]. In this regard, it is of value to compare these theories with the present approach.

In the present paper, we have discussed isolated particles in the dilute limit. In fact, for higher volume fractions, we can use the effective-medium theories instead [10], like Maxwell-Garnett approximation or Effective Medium Approximation.

Throughout the paper, the cells under consideration exist in the form of a spherical shape. In this connection, we may include the shape effect as well. More precisely, we can extend the graded spheroidal cell model of Huang et al. [17] to include an intrinsic dispersion in the core. This is a nontrivial extension and we believe the non-spherical shape will have significant impact on the dispersion spectrum. We can consider the following agenda: (1) homogeneous spheroidal cell with intrinsic dispersion, without shell [10]; (2) graded spheroidal cell with intrinsic dispersion, without shell. Also, item 2 will be studied in the small-gradient expansion.

In view of the present interesting results, the corresponding experiment is suggested to
be done. In doing so, one may use coated colloids having a graded core.

In summary, we have considered a single-shell model with an inhomogeneous graded cytosol. Realistic cells must be inhomogeneous due to the compartment in the interior of cells. In such a model, the cytosol can have a conductivity profile which varies along the radius of the cell. A small conductivity-gradient expansion for the DDSR of single-shell graded cell model has been done, based on the differential effective dipole approximation [16,17]. We have assessed the effects of a conductivity gradient in the cytosol on the dispersion spectrum.

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| Parameters                          | Symbols | Numerical Values |
|------------------------------------|---------|-----------------|
| Cell radius                        | \( R_e \) | 9.5 \( \mu \)m |
| Membrane thickness                 | \( d \)  | 8 nm            |
| External permittivity              | \( \epsilon_e \) | 80\( \epsilon_0 \) |
| External conductivity              | \( \sigma_e \) | 1 mS/m          |
| Cytosolic permittivity             | \( \epsilon_i \) | 120\( \epsilon_0 \) |
| Cytosolic conductivity             | \( \sigma_i \) | 0.25 S/m        |
| Cytosolic dielectric increment     | \( \Delta \epsilon_i \) | 800\( \epsilon_0 \) |
| Membrane permittivity              | \( \epsilon_m \) | 7.23\( \epsilon_0 \) |
| Membrane conductivity              | \( \sigma_m \) | 4 \times 10^{-7} S/m |
| Circular frequency of cytosol dispersion | \( \omega_d \) | 10^4 rad/s |

**TABLE I. Parameters used for model calculations**

| Solutions                          | Symbols | Absolute numerical Values |
|------------------------------------|---------|---------------------------|
| Characteristic frequencies         | \( \omega_1 \) | 1.03 \times 10^8 rad/s    |
|                                    | \( \omega_2 \) | 3.18 \times 10^4 rad/s    |
|                                    | \( \omega_3 \) | 1.00 \times 10^4 rad/s    |
| Dielectric dispersion strengths    | \( \Delta \epsilon_1 \) | 0.0621                    |
|                                    | \( \Delta \epsilon_2 \) | -0.00133                  |
|                                    | \( \Delta \epsilon_3 \) | 1.42 \times 10^{-8}       |
|                                    | \( \Delta^2 \epsilon_1 \) | -0.0613                   |
|                                    | \( \Delta^2 \epsilon_2 \) | 0.000539                  |
|                                    | \( \Delta^2 \epsilon_3 \) | 2.02 \times 10^{-12}      |

**TABLE II. Results from small-gradient model calculations**
FIGURES

FIG. 1. The dispersion strengths ($\Delta\epsilon_1 \sim \Delta\epsilon_3$) and the characteristic frequencies ($\omega_1 \sim \omega_3$) as a function of the conductivity of the external medium $\sigma_e$.

FIG. 2. Same as Fig. 1, but as a function of the conductivity of the cytosol $\sigma_i$. Typical $\sigma_i$ values range from 0.2 to 1 S/m.

FIG. 3. Same as Fig. 1, but as a function of the circular frequency of the cytosol dispersion $\omega_d$.

FIG. 4. Same as Fig. 1, but as a function of the conductivity of the membrane $\sigma_m$.

FIG. 5. Real and imaginary parts of the CM factor as a function of the circular frequency of the external field. $\text{Re}\{\cdots\}$ ($\text{Im}\{\cdots\}$) denotes the real (imaginary) part of $\cdots$. 
The effect of varying $\sigma_e$ on $\Delta \varepsilon$

The effect of varying $\sigma_e$ on $\omega$

Fig. 1
The effect of varying $\sigma_i$ on $\Delta \varepsilon$

The effect of varying $\sigma_i$ on $\omega$

Fig. 2
The effect of varying $\omega_d$ on $\Delta \varepsilon$

Fig. 3
The effect of varying $\sigma_m$ on $\Delta \varepsilon$

The effect of varying $\sigma_m$ on $\omega$

Fig. 4
Fig. 5