Abstract

**Electrofluidics in Micro/Nanofluidic Systems**

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This work presents the efforts to study the electrofluidics, with a focus on the electric field-matter interactions in microfluidic and nanofluidic systems for lab-on-a-chip applications. The field of electrofluidics integrates the multidisciplinary knowledge in silicon technology, solid and soft condensed matter physics, fluidics, electrochemistry, and electronics. The fundamental understanding of electrofluidics in engineered micro and nano structures opens up wide opportunities for biomedical sensing and actuation devices integrated on a single chip.

Using spatial and temporal properties of electric fields in top-down engineered micro/nano structures, we successfully demonstrated the precise control over a single macro-ion and a collective group of ions in aqueous solutions. In the manipulation of a single macro-ion, we revisited the long-time overlooked AC electrophoretic (ACEP) phenomena. We proved that the widely held notion of vanishing electrophoretic (EP) effects in AC fields does not apply to spatially non-uniform electric fields. In contrast to dielectrophoretic (DEP) traps, ACEP traps favor the downscaling of the particle size if it is sufficiently charged. We experimentally demonstrated the predicted ACEP trap by recognizing that the ACEP dynamics is equivalent to that of Paul traps working in an aqueous solution. Since all Paul traps realized so far have only been operated in vacuum or gaseous phase, our experimental effort represents the world’s first aqueous Paul trap device. In the manipulation of a collective group of ions, we demonstrated that
the ion transport in nanochannels can be directly gated by DC electric fields, an impossible property in microscale geometries. Successful fabrication techniques were developed to create the nanochannel structures with gating ability. Using the gated nanochannel structures, we demonstrated a field effect reconfigurable nanofluidic diode, whose forward/reverse direction as well as the rectification degree can be significantly modulated. We also demonstrated a solid-state protocell, whose ion selectivity and membrane potential can be modulated by external electric field. Moreover, by recognizing the key role played by the surface charge density in electrofluidic gating of nanochannels, a low-cost, off-chip extended gate field effect transistor (FET) structure to measure the surface charges at the dielectric-electrolyte interface is demonstrated. This technique simplifies and accelerates the process of dielectric selection for effective electrofluidic gating.
Electrofluidics in Micro/Nanofluidic Systems

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I know this probably is the page most of the people will have a look at before reading the thesis. I would like to take advantage of this to thank all who have made the past five years of doing a PhD at Yale an enjoyable journey.

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To my parents and Lei
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Chapter 1 Introduction and overview

1.1 Background

Manipulation of objects in a controlled manner is desirable in a variety of disciplines. For example, physicists are interested in isolating a single atom or ion to study its quantum dynamics, biologists and chemists trap and manipulate a single cell or molecule to examine the intrinsic property in its native environment, and electrical engineers are interested in regulating the flow of a collective of electrons to create certain functions. Over the years, optical, electrical, magnetic, acoustic, and thermal interactions have all been extensively explored to achieve this desired controlled manipulation.

Among all these physical interactions, the electrical force, due to its integration potential, is an increasingly common method for achieving manipulations in aqueous solutions, especially within a lab-on-a-chip (LOC) platform. The marriage of VLSI electronics and micro/nano fluidics is therefore a natural choice to achieve lower fluid volume consumption, faster analysis and response time and massive parallelization. This allows for high-throughput analysis and cost-effective disposable chips.

This interdisciplinary marriage has resulted in the field of so called ‘electrofluidics’. Electrofluidics is both an ‘old’ and ‘new’ science and technology. It is ‘old’ in the sense that various electrokinetic phenomena have been widely studied and utilized in the past. For example, gel electrophoresis is a standard method in separation of nucleic acids [1]. However,
electrofluidics is also an emerging field. First, researchers are discovering new electrokinetic phenomena which have not been recognized before [2] or new electrokinetic behavior that is just recently enabled by advanced fabrication techniques [3]. Second, the interaction of electric field and matter is being exploited for new applications in fields ranging from the detection of chemical or biological agents [4, 5] and biological particle control [6], to energy generation [7-9]. The science and technology developments in electrofluidics are critical to develop various actuation and sensing tools for life science, healthcare, and analytical chemistry.

This thesis mainly focuses on the electrofluidic actuation side and tries to understand how the electric field can be used in the microfluidic and nanofluidic systems to manipulate the particles either individually or collectively. The main contribution of this thesis is as follows.

First, we revisit the long-time overlooked aspect of AC electrokinetics – the AC electrophoretic effect. We theoretically [10] and experimentally [11] demonstrate a planar aqueous Paul trap for trapping a single macro-ions, using spatially non-uniform AC electric fields. This represents the first endeavor for realizing an aqueous Paul trap, which not only allows for trapping a single particle, but also enables a direct analysis of mass to charge ratio for macro-ions in aqueous solutions.

Second, we explore ion transport property through nanoscale channels, enabled by micro and nano fabrication techniques. Electric fields are used to regulate ion transport in nanometer-sized channels, much like the gated electron/hole transport in various semiconductor devices. In particular, we demonstrate a field-effect reconfigurable ionic diode device, aiming for control the preferential flow directions of a collective group of ions [12]. We also demonstrate a solid-state abiotic cell whose membrane potential can be regulated by external electric field [13].
1.2 Overview of work presented

Chapter 2 presents the fundamental aspects of electrostatics and electrokinetics in fluids as well as the electrode-electrolyte interface, the concepts of which will be encountered repeatedly throughout this work. The first part of the thesis (Chapter 3 and Chapter 4) discusses the efforts that have been undertaken to realize an alternating current (AC) electrophoretic trap for confining charged particles in microfluidic systems. Chapter 3 theoretically investigates the dynamics of a particle with both polarizability and net charges in a non-uniform AC electric field. It is found that either electrophoretic (EP) or dielectrophoretic (DEP) effects can dominate the trapping dynamics, depending on the salt concentration used in experiments. This provides important guidance on the design and embodiment of systems to elucidate these effects. Chapter 4 discusses the experimental realization of the world’s first AC electrophoretic trap (aqueous phase Paul trap). The second part of the work (Chapter 5 to Chapter 7) discusses the efforts to realize a direct current (DC) electric field regulated ion transport in nanoscale channels. Chapter 5 discusses a field-effect reconfigurable nanofluidic diode device. The ionic flow driven by a potential gradient exhibits a rectified feature. The forward/reverse directions of the diode as well as the degrees of rectification can be regulated by the application of an orthogonal electric field. Chapter 6 discusses the electric field modulated membrane potential phenomenon, driven by a concentration gradient. Chapter 7 presents a facile method to measure the surface charge densities at dielectric-electrolyte interface, which is one of the most important parameters for effective electrofluidic gating in nanofluidic systems. Finally, Chapter 8 offers conclusions based on the work presented in the preceding chapters and perspectives for future development.
Chapter 2  Fundamental theoretical aspects

This chapter introduces the theory on electrostatics, electrokinetic effects, fluid dynamics, and electrochemistry in liquid solutions, with the intention to present the relevant theoretical background for describing the work throughout this thesis. It starts with the introduction of the ion concentration and potential profile near a charged surface, which can be modeled by the electrical double layer (EDL). This will be followed by reviewing the electrokinetic phenomena in heterogeneous fluids (fluids containing particles). Note that the term ‘particle’ throughout this thesis refers to a wide variety of objects, such as molecules, viruses, proteins, cells, polystyrene beads, and ions, etc. The electric forces on the particles as well as on the fluid will be discussed. Then, the related fluid dynamics that is highly relevant to fluid transportation in micro/nanofluidic systems will be given. Finally, the electrode-electrode interface, which is almost inevitable in any electrofluidic systems, will be briefly reviewed.

2.1 Electrostatics in solutions

2.1.1 Surface charges

When a solid surface is in contact with a polarizable electrolyte solution (e.g., KCl in water), surface charges will appear at the solid surface. This surface charge can be caused by either the dissociation of surface groups (e.g., carboxylate groups or amino groups) or the adsorption of ions in the solution onto the surface [14]. Take the most common material SiO₂ for
instance. When SiO$_2$ is in contact with an aqueous solution, it hydrolyzes to form surface silanol (SiOH) groups at the surface (Figure 2.1), which gives rise to surface charges according to the reactions $\text{SiOH}^+ \rightleftharpoons \text{SiOH} + \text{H}^+$ and $\text{SiOH} \rightleftharpoons \text{SiO}^- + \text{H}^+$. Depending on the pH values of the solution, the SiO$_2$ surface will possess either a positive or a negative surface charge density [15-17]. The pH value at which the surface charges crossover from negative to positive (i.e. no surface charges) is known as the point of zero charge, which is around 3 for SiO$_2$ [16]. Other materials such as SiN$_x$, Al$_2$O$_3$, and the carboxylate-modified surface will also bear surface charges when immersed in the solution due to a similar principle.

![Figure 2.1 Hydrolyzed silanol (SiOH) groups at the SiO$_2$ surface when in contact with aqueous solutions.](image)

The surface charge density $\sigma_s$ [C/m$^2$] can be empirically described by,

$$\sigma_s = \sum_i z_i e / A$$  \hspace{1cm} (2.1)

where $z_i$ is the valence of charge $i$, $e$ is the elementary charge, and $A$ is the surface area.
2.1.2 Electrical double layer (EDL)

Due to the surface charges developed at the solid surface in electrolyte solutions, the electrostatic force will naturally attract oppositely charged ions (counter-ions) and repel like charges (co-ions) in the electrolyte to maintain the electro-neutrality. An electrical double layer (EDL) is therefore formed at equilibrium. EDL refers to two parallel layers of charge in the system. The first layer corresponds to the surface charges as we discussed in section 2.1.1. The second layer is composed of ions attracted to the surface charges via the Coulomb force, effectively screening the first layer. The net result of the EDL is that the overall charge appeared to the observers on the global scale is zero.

The detailed microscopic picture of the second layer has been under research for more than 150 years since its first debut by Helmholtz [18]. There are several theoretical treatments of the EDL. Here we will look at a few 1-D models in the order of their historical developments.

2.1.2.1 Helmholtz model

The earliest EDL model is attributed to Helmholtz [18], who treated the EDL as a simple capacitor. Helmholtz's view of the EDL is shown in Figure 2.2. The surface charge is fully neutralized by a single layer of counter-ions, which resides at a distance that is limited to the radius of the counter-ions. The overall result is the two layers of charge (the origin of the term ‘double layer’) and a linear potential drop confined only to this region. The Helmholtz model does not adequately explain experimental features, since it hypothesizes rigid layers of counter-ions. This actually does not occur in nature.
2.1.2.2 Gouy-Chapman model

Later Gouy [19] and Chapman [20] made significant improvements by introducing a diffusive model of the EDL. In Gouy-Chapman model, ions are modeled as point charges and they obey Poisson-Boltzmann distributions. Counter-ions are not rigidly held, but tend to diffuse following Fick's laws of diffusion. The Gouy-Chapman’s view of the EDL is shown in Figure 2.3. It consists of a rigid charged surface, with a cloud of excessive opposite charge in the solution, the concentration of which decreases with distance from the surface. This is the so-called diffuse layer.
Figure 2.3 Ion distributions and the corresponding potential profile in Gouy-Chapman model. $Q_{\text{surface}}$ and $Q_{\text{diffuse}}$ is the charge at the surface and in the diffuse layer, separately.

The Gouy-Chapman model is still not an entirely accurate picture. The experimental double layer thickness is generally found to be greater than calculated. In other words, the double layer capacitance is overestimated in Gouy-Chapman model.

2.1.2.3 Gouy-Chapman-Stern model
Figure 2.4 Ion distributions and the corresponding potential profile in Gouy-Chapman-Stern model. The ionic environment can be separated into two main layers (Stern layer and the diffuse layer). The Stern layer can further be divided into inner Helmholtz layer and outer Helmholtz layer. The ions in the inner Helmholtz layer are non-hydrated co-ions and counter-ions (the figure shows only a co-ion case) and potential varies linearly with the distance, whereas the outer Helmholtz layer is built up of only hydrated counter-ions and the potential also varies linearly with the distance. All ions in the Stern layer are tightly associated on to the surface and cannot move freely. The diffuse layer (also called Guoy-Chapman layer) consists of mobile co- and counter-ions, like the case in the Gouy-Chapman model. The slip plan is an imaginary interface between the immobile Stern layer and the mobile diffuse layer, which bears the $\zeta$ potential.

The Gouy-Chapman model provides a better approximation of reality than the Helmholtz model, but it still has limited quantitative applications. It assumes that ions behave as point...
charges and they can approach the charged surface indefinitely. This is not true in reality, since ions have finite sizes. Stern [21] recognized the Gouy-Chapman model’s inadequacy and introduced a thin region between the surface and the diffuse layer (a.k.a., Gouy-Chapman layer), which is a layer of bound or tightly associated counter-ions, generally referred to as the Stern layer (a.k.a., compact layer, Helmholtz layer, bound part of the double layer). This region is on the order of one or two hydrated ions thick.

The Stern layer can be further divided into two regions, as shown in Figure 2.4 [22]. The inner layer, the electrical center of which is referred to as the inner Helmholtz plane (IHP), consists of ions which are not hydrated and specifically adsorbed to the surface. The inner Helmholtz plane bears a potential of $\psi_{IHP}$. The outer layer is a layer of bound hydrated ions, the electrical center of which is referred to as the outer Helmholtz plane (OHP). The outer Helmholtz plane bears a potential of $\psi_{OHP}$. The inner layer can contain both co- and counter-ions, while the outer layer only contains counter-ions. As a result, the location of the outer Helmholtz plane is significantly affected by counter-ions hydration.

The imaginary interface between the outer layer of the immobile Stern layer and the mobile diffuse layer is referred to as the slip plane (or shear plane), which bears the zeta ($\zeta$) potential. As one of the most important parameters in micro/nanofluidics, the $\zeta$ potential can be experimentally determined by measuring the electrophoretic mobility (section 2.2.1). It is usually valid to approximate $\psi_{OHP}$ with $\zeta$ potential since the outer Helmholtz plane and the slip plane are very close to each other.

It is easy to see that the surface charges $Q_{\text{surface}}$, the charges in the stern layer $Q_{\text{stern}}$, and the charges in the diffuse layer $Q_{\text{diffuse}}$ (Figure 2.4) obey an electrical neutrality relationship,
\[ Q_{\text{surface}} + Q_{\text{stern}} + Q_{\text{diffuse}} = 0 \] (2.2)

Since the charges in the Stern layer are strongly associated with the surface and contained in a very thin thickness, the surface and the Stern layer can be considered as a single entity with an effective surface charge of \( Q_{\text{effective}} = Q_{\text{surface}} + Q_{\text{stern}} \) and the Gouy-Chapman model can thus be applied into this single entity. The \( \zeta \) potential in the Gouy-Chapman-Stern model (Figure 2.4) becomes the surface potential in the Gouy-Chapman model (Figure 2.3).

2.1.3 Potential and ion concentration profile in the diffuse layer

2.1.3.1 Poisson-Boltzmann equation

So far we have qualitatively elucidated the microscopic ionic environment and the potential profile near a charged surface in electrolyte solutions. Here we will briefly summarize the quantitative potential and ion profile in the diffuse layer (not in the Stern layer). More detailed calculation can be found in classic Colloid Science textbooks [22].

The electrochemical potential \( \Phi_i \) of ion \( i \) in a solution phase at constant pressure and temperature can be expressed as [23],

\[ \Phi_i = \phi_i + z_i F \psi \] (2.3)

where \( \phi_i \) is the chemical potential, \( F \) is the Faraday constant, \( \psi \) is the electric potential, \( z_i \) is the ion valence. The chemical potential \( \phi_i \) can be further expressed as,

\[ \phi_i = \phi_i^0 + RT \ln(\gamma_i c_i / c_0) \] (2.4)

where \( \phi_i^0 \) is the standard chemical potential of ion \( i \), \( R \) is the gas constant, \( T \) is the temperature, \( \gamma_i \) is the activity coefficient, \( c_i \) is the molar concentration of ion \( i \) [mole/L, or molar], and \( c_0 \) is
the standard molarity of 1 molar.

At equilibrium, the electrochemical potential must have no gradient, that is, \( \nabla \Phi_j = 0 \). Using Eq. (2.3) and (2.4), we can therefore obtain the following equation,

\[
\nabla \psi = - \frac{RTc_0}{z_i F} \gamma_a c_i
\]

(2.5)

In the equations above, integration from a point in the bulk solution where \( \psi = 0 \) and \( n_i = n_0 \) (\( n_0 \) [1/m\(^3\)] is the bulk number density, \( n_0 = 10^{-3} N_\text{A}c_i \), results in Boltzmann equation for the local concentration for each type of ion in the diffuse layer,

\[
n_i = n_0 \exp(-z_i e\psi / k_b T)
\]

(2.6)

By considering all ions, the total charge density \( \rho \) (C/m\(^3\)) in the diffuse is given by,

\[
\rho = e \sum_i n_i z_i
\]

(2.7)

The electric potential \( \psi \) is related to the charge density \( \rho \) by Poisson's equation,

\[
\nabla^2 \psi = - \frac{\rho}{\varepsilon_o \varepsilon_r}
\]

(2.8)

where \( \varepsilon_o \) is the permittivity of free space, \( \varepsilon_r \) is the dielectric constant of the liquid (\( \varepsilon_r = 78.5 \) for water at 25°C).

Combining Eq.(2.6), (2.7) and (2.8), we obtain the following Poisson-Boltzmann equation to describes the electrostatic potential profile due to a distribution of different ionic species,

\[
\nabla^2 \psi = - \frac{e}{\varepsilon_o \varepsilon_r} \sum_i n_0 z_i \exp(-z_i e\psi / k_b T)
\]

(2.9)

2.1.3.2 Debye-Hückel approximation
For spherical geometry (e.g. a small particle or an ion), there is no analytical solution to Poisson-Boltzmann equation (2.9). However, the Debye-Hückel theory [24] was developed to give an approximate analytical solution if the potential in the diffuse layer is very small (\(z_i e \psi / k_B T \ll 1\)). Using the first two terms in the series expansion for the exponential term: 
\(e^{-a} = 1 - a\) for small \(a\), Eq. (2.9) becomes,

\[
\nabla^2 \psi = \kappa^2 \psi \tag{2.10}
\]

where

\[
\kappa^2 = \frac{e^2 \sum n_i z_i^2}{\varepsilon_r \varepsilon_0 k_B T} \tag{2.11}
\]

The general solution to Eq. (2.10) is,

\[
\psi = Ae^{\kappa y} + Be^{-\kappa y} \tag{2.12}
\]

Using the boundary conditions \(\lim_{y \to \infty} \psi = 0\), \(\lim_{y \to \infty} \nabla \psi = 0\), and \(\psi(y = 0) = \psi_s\) (here \(\psi_s\) is at the beginning of the diffuse layer, i.e., the \(\zeta\) potential in Figure 2.4), the solution of the Debye-Hückel approximation is given by,

\[
\psi(y) = \psi_s \exp(-\kappa y) \tag{2.13}
\]

Eq. (2.13) states that the potential in the diffuse layer decays exponentially with a characteristic distance, known as the Debye length,

\[
\lambda_D = \kappa^{-1} \tag{2.14}
\]

The Debye length is a very important characteristic length scale which quantitatively describes the thickness of the diffuse layer. For a symmetrical monovalent electrolyte KCl (
\( z_i = \pm 1 \) in water at 25 °C, the value of the Debye length \( \lambda_d \) can be approximately written as [23],

\[
\lambda_d (\text{nm}) = \frac{0.304}{\sqrt{I(\text{molar})}} \tag{2.15}
\]

where \( I \) is the ionic strength, given by

\[
I = \frac{1}{2} \sum_i c_i z_i^2 \tag{2.16}
\]

As a result, the Debye length is a function of ionic strength. The Debye length reduces when the ionic concentration is increased (Figure 2.5).

Figure 2.5 The Debye length as a function of ionic strength for simple KCl electrolyte at room temperature. The inset is a log-log scale.
2.1.3.3 Gouy-Chapman approximation

The Debye-Hückel model assumes that the potential in the diffuse layer is very small \( z_e \psi / k_B T \ll 1 \), which will not be valid for high surface potentials. Under such conditions, the Poisson-Boltzmann equation (2.9) has to be solved numerically. However, for planar surfaces, which is the thin double layer limit for a spherical particle, Gouy [25] and Chapman [20] solved the Poisson-Boltzmann equation (2.9) analytically. It is worth mentioning again that the Poisson-Boltzmann equation is solved for the diffuse part of the double layer only. Under the assumption of a symmetrical electrolyte where the valence of the co-ion is equal to the valence of the counter-ion \( |z^+| = |z^-| = z \), Gouy-Chapman equation is obtained as [14],

\[
\tanh\left(\frac{z_e \psi(y)}{4k_B T}\right) = \tanh\left(\frac{z_e \psi}{4k_B T}\right) \exp(-\kappa y) \tag{2.17}
\]

The equation above is valid for any value of the surface potential \( \psi_s \). For small values of \( \psi_s \), \( \tanh(z_e \psi_s / 4k_B T) \sim z_e \psi_s / 4k_B T \) is valid (Taylor expansion), and Eq. (2.17) reduces to (2.13). The Debye-Hückel model also shows a exponential decay of the potential to the bulk value through a characteristic length scale \( \lambda_D \).

In summary, The Debye-Hückel approximation and the Gouy-Chapman approximation, represent the two limiting cases for thick and thin double layers around a charged surface, respectively. They exhibit a similar exponential potential decay in the diffuse part of the double layer. The resulting ionic concentration profile for each ion can be calculated by using Eq. (2.6) once the potential \( \psi \) is known. As examples, a plot of ion concentrations and electric potential with distance is shown in Figure 2.6 for both the Debye-Hückel model (with \( \psi_s = -10mV \)) and Gouy-Chapman model (with \( \psi_s = -50mV \)).
Figure 2.6 Plot of the electrical potential and the ion concentration as a function of the distance from the surface. The plots are calculated from Eq. (2.6), (2.13), and (2.17). The electrolyte used in the calculation is 10 mM KCl. A surface of potential -10 mV is assumed for Debye-Hückel model (a) and -50 mV for Gouy-Chapman model (b).

2.1.4 Grahame equation

The relation between surface charge $Q_{\text{surface}}$ and surface potential $\psi_s$ in the Gouy-Chapman model (Figure 2.3) can be expressed by the Grahame equation. It is derived by assuming an electro-neutrality condition. Using the one dimensional Poisson equation for a symmetrical electrolyte ($|z^+| = |z^-| = z$), and the boundary conditions of $\lim_{y\to\infty} \nabla \psi = 0$, the Grahame equation is obtained as [26],

$$Q_{\text{surface}} = \sqrt{8\varepsilon_0 \varepsilon_r n_o k_B T} \sinh\left(\frac{ze\psi_s}{2k_B T}\right)$$ (2.18)
where \( n_0 \) is the bulk number density \([1/m^3]\) which is related to the molar concentration \( c_i \) \([\text{mol/L}]\) by \( n_0 = 10^{-3} N_A c_i \). \( Q_{\text{surface}} \) bears the unit of \( \text{C/m}^2 \) and \( \psi_s \) is of unit Volt.

For the case of small surface potential \( \psi_s << 2k_B T / ze \), since \( \sinh(x) \approx x \), Eq. (2.18) can be simplified to the following form by using Eq. (2.14),

\[
Q_{\text{surface}} = \varepsilon_o \varepsilon_r \kappa \psi_s = \varepsilon_o \varepsilon_r \psi_s / \lambda_D
\]  

As a result, measurements of the \( \zeta \) potential can be used to quantify the effective surface charge density \( Q_{\text{effective}} = Q_{\text{surface}} + Q_{\text{stern}} \) (Figure 2.4).

### 2.1.5 Ionic conduction

#### 2.1.5.1 Bulk conductance

The current density \( J_i \) carried by an ion \( i \) with valence \( z_i \) under the electric field \( E \), is given by

\[
J_i = \sigma_i E
\]  

with

\[
\sigma_i = z_i n_i e \mu_i = 10^{-3} z_i e \mu_i N_A c_i
\]  

where \( \sigma_i \) is the electrical conductivity of ion \( i \), \( N_A \) is the Avogadro's constant, \( n_i \) is the number density \([1/m^3]\), \( c_i \) is the molar concentration \([\text{mole/L}]\), \( e \) is the elementary charge \((1.6 \times 10^{-19} \text{ C})\), \( \mu_i \) is the ion mobility \([\text{m}^2/(\text{V} \cdot \text{s})]\) and can be related to the diffusion constant \( D_i \) by,

\[
\mu_i = \frac{e D_i}{k_B T}
\]  

The conductivity of the whole electrolyte solution, without considering the complex
interactions between ions [14], is given by the sum of the contributions of each ion,

\[
\sigma = \sum_i \sigma_i = 10^{-3} e N A \sum_i z_i \mu_i c_i
\]  

(2.23)

2.1.5.2 Surface conductance

The EDL formed around charged surfaces results in an ionic environment that is different from the bulk. This conducting sheet surrounding the charged surface contributes to an additional surface conductance. The surface conductance can be thought of as a two-dimensional analogue of bulk conduction, with the charge movement confined near the surface.

The surface conductance can be further divided into two separate components that come from the Stern layer and the diffuse layer (Figure 2.4). The total surface conduction \( G_s \) can be expressed as the sum of these two [27],

\[
G_s = G_s^{\text{Stern}} + G_s^{\text{Diffuse}}
\]

(2.24)

The Stern layer conductance is typically in the order of 1 nS [28].

For the diffuse layer, the electro-osmotic transport (see section 2.3.1 for details) of charge carriers must be considered, in addition to the drift current. The total surface current in the diffuse layer is therefore the sum of the drift current \( J_{\text{Drift}} \) and the electro-osmosis current \( J_{\text{EO}} \),

\[
J_{\text{Diffuse}} = J_{\text{Drift}} + J_{\text{EO}}
\]

(2.25)

For a sphere particle with radius \( a \), the surface conductivity is related to the surface conductance as [29],

\[
\sigma_{\text{Surface}} = \frac{2G_s}{a}
\]

(2.26)
2.2 Electric forces on the particle

When applying electric fields to a heterogeneous fluid (fluid containing particles), two kinds of electric forces will be generated. The first one is due to the direct interactions between the electric field (AC or DC, uniform or non-uniform) and the particle (charged or non-charged). We will review the kinetics resulting from this interaction in section 2.2. This interaction results in an electrophoretic (EP) force for a charged particle, and a dielectrophoretic (DEP) force for a neutral but polarizable particle. The second electric force generated is due to the interactions of the electric field and the mobile ions in the diffuse layer, which further induces a fluid movement by friction. This so-called electro-osmosis (EO) will be covered in section 2.3.

2.2.1 Electrophoresis

Electrophoresis is the motion of charged particles in solution under the influence of an electric field through Columbic interactions. As we discussed in section 2.1.1, surface charges will appear at the particle surface by either the dissociation of surface groups or the adsorption of ions. For example, most biological particles generally have negative surface charges due to the presence of acid groups on the surface. The electrophoretic movement in a uniform electric field is widely used to characterize and to separate particles. One of the best known examples is gel electrophoresis used to separate DNA molecules based on their size and charge [1].

The Coulomb force on a charged particle is given by,

\[ F_{ep} = QE = \int \sigma ds E \]  \hspace{1cm} (2.27)

where \( Q \) is the net charge on the particle surface, which can be further expressed as the integral of the surface charge density over the particle surface.
According to the double layer theory (section 2.1.2), all surface charges in electrolyte solutions will be screened by a Stern layer of \textit{immobile} ions, and a diffuse layer of \textit{mobile} ions (Figure 2.4), which has the same amount of opposite charges with respect to the surface charge. Note that if all ions in the double layer are fixed to the particles (\textit{immobile}), the particle will appear no net charge and it would not be able to move upon the action of the electric field. This clearly is not the case. As we discussed before, the bare surface charge combined with the fixed Stern layer charge can be considered as a single entity with an effective surface charge of $Q_{\text{surface}} + Q_{\text{stern}}$. The ions beyond the Stern layer are \textit{mobile}.

![Figure 2.7 Forces acting on the charged particle immersed in the electrolyte solution when applying an electric field.](image)

Now let us look at the forces when applying an electric field (Figure 2.7). Apart from the direct Coulomb force $F_{ep}$ on the charged particle, the electric field also exerts a force on the \textit{mobile} ions in the diffuse layer which has a direction opposite to that acting on the charged particle, part of which is transferred to the particle through viscous stress and is known as the
electrophoretic retardation force $F_{\text{ret}}$. The third force acting on the charged particle during its movement is the viscous drag force $F_\xi$ due to the friction of the particle and the liquid. When the charged particle movement is at steady state, the total resulting force should be zero,

$$F_{\text{ep}} + F_{\text{ret}} + F_\xi = 0$$

The electrophoretic mobility $\mu_E$ is defined as a measure of the steady state velocity under a certain electric field,

$$\mu_E = \left| \frac{v}{E} \right| = \frac{v}{E}$$

From the microscopic view of electrophoresis, it is obvious that the electrophoretic mobility is highly dependent on the properties of the diffuse layer. As a matter of fact, the electrophoretic mobility depends on the ratio of particle radius with respect to the Debye length, given by $\kappa a$. Following is to present three different models based on the magnitude of $\kappa a$.

### 2.2.1.1 Hückel Model: thick Double Layer, $\kappa a<<1$

When a particle has a thick double layer, the retardation force from diffuse ions will not be felt by the particle (because the particle is too small in this case). As a result, the net force acting on the particle is the difference between the viscous drag and Coulomb forces.

The viscous drag force on a particle is given by,

$$F_\xi = -\xi v$$

where $v$ is the velocity of the particle and $\xi$ is the friction coefficient. For a spherical particle with small Reynolds numbers (e.g., very small particles) in a Newtonian fluid, the friction coefficient can be written as,
in which $\eta$ is the dynamic viscosity of the solution (The SI unit of $\eta$ is Pa·s) and $a$ is the particle radius.

For non-spherical objects, the friction coefficient $\xi$ is a complex function of the object geometry. In such cases, the Stokes-Einstein relation provides a simple form between the friction coefficient and the diffusion coefficient $D$,

$$\xi = k_B T / D$$

(2.32)

At steady state, the viscous drag force is balanced against the electric force,

$$Q E = 6 \pi \eta a v$$

(2.33)

According to Eq. (2.29), the electrophoretic mobility is therefore,

$$\mu_E = \frac{Q}{6 \pi \eta a}$$

(2.34)

It is often convenient to express the electrophoretic mobility in terms of the $\zeta$ potential, instead of the charges on the particle. The $\zeta$ potential can be identified for a point charge $Q$ as,

$$\zeta = \frac{Q}{4 \pi \varepsilon_0 \varepsilon_r a}$$

(2.35)

The electrophoretic mobility as a function of $\zeta$ potential is therefore,

$$\mu_E = \frac{2 \varepsilon_0 \varepsilon_r \zeta}{3 \eta}$$

(2.36)

2.2.1.2 Smoluchowski Model: thin Double Layer, $\kappa a \gg 1$

One cannot ignore the effect of the retardation force if the EDL is much thinner than the
particle size. For an EDL that is much thinner compared to the particle radius, one can think of a flat planar surface.

![Figure 2.8 Schematic diagram of the model system for calculating the electrophoretic mobility in the case of very thin double layer ($\kappa a \gg 1$).](image)

For an insulating particle in a conductive solution, the steady state electric field must be tangential to the surface of the particle. Consider here a thin sheet of solution of area $A$ and thickness $dy$, parallel to the surface of the particle, which can be seen as a planner surface (Figure 2.8). The viscous drag force required to shear this sheet at a uniform rate is given by,

$$
F_\xi = \eta A \frac{dv}{dy}
$$

(2.37)

The Coulomb force acting on this sheet solution with charge density $\rho$ is given by,

$$
dF_{cp} = E \rho A dy
$$

(2.38)

Differentiating Eq. (2.37) with respect to $y$ yields,
\[ dF_\xi = \eta A \frac{d^2 v}{dy^2} dy \]  

The force balance between the Coulomb force and viscous drag force \( dF_{ep} = dF_\xi \) gives,

\[ \rho E = \eta \frac{d^2 v}{dy^2} \]  

(2.40)

Substituting the Poisson equation \( \frac{d^2 \psi}{dy^2} = -\frac{\rho}{\varepsilon_s \varepsilon_r} \) into Eq. (2.40), we obtain

\[ \frac{d^2 v}{dy^2} = -\frac{\varepsilon_s \varepsilon_r E}{\eta} \frac{d^2 \psi}{dy^2} \]  

(2.41)

Integrating from \( y = \infty \) to the slip plane where the potential is equal to \( \zeta \) potential and the fluid velocity is zero yields:

\[ v = \frac{\varepsilon_s \varepsilon_r \zeta}{\eta} E \]  

(2.42)

Eq. (2.42) states that there is a velocity difference between the solid surface and the bulk solution. This applies equally to the motion of a particle in a fluid at rest (electrophoresis) or to the electric field-induced motion of fluid on a fixed surface (e.g., electro-osmosis, as we will discuss in section 2.3).

The electrophoretic mobility of the Smoluchowski model is therefore in the form of,

\[ \mu_e = \frac{\varepsilon_0 \varepsilon_r \zeta}{\eta} \]  

(2.43)

2.2.1.3 Henry Model: intermediate Double Layer, \( \kappa a \sim 1 \)

The difference between the low and high limits of \( \kappa a \) (Eq. (2.36) and (2.43)) is only a factor of 3/2. Improvements on the theories have been made by Henry, who took into account the distortion of the field by the particle and also the ratio of the particle conductivity to the
suspending electrolyte conductivity. He developed a general function for describing the electrophoretic mobility [30],

\[
\mu_E = \frac{2\varepsilon_0\varepsilon_r\zeta f(\kappa a)}{3\eta}
\]  

(2.44)

The expression of \( f(\kappa a) \) for low \( \zeta \) potential (\( |\zeta| < 50 \text{ mV} \)) is given by [30, 31],

\[
f(\kappa a) = 1 + \frac{1}{2} \left( 1 + \frac{5}{2\kappa a(1 + 2e^{-\kappa a})} \right)
\]  

(2.45)

This function shows a variation between 1 and 1.5 as \( \kappa a \) varies between 0 and \( \infty \), allowing values of electrophoretic mobility to be more accurately determined between the two limiting cases.

### 2.2.1.4 Further considerations

Further developments of the theory must take into account the effect of the electric field on the structure of the double layer and the surface conductivity of the particle. The relaxation forces must be taken into account. In the absence of an applied electric field, the center of the charged particle and the surrounding EDL is coincident. When an electric field is applied, charge separation will happen in the EDL, resulting in an EDL polarization. It requires a finite time (relaxation time) to restore. As long as the electric field is applied, the force causing the separation is still present and a steady state charge separation is maintained. The resulting dipole exerts an additional force on the particle through an internal electric field. The relaxation effect is negligible for very thin (\( \kappa a > 300 \)) or very thick (\( \kappa a < 0.1 \)) double layers, but can be significant in the intermediate case. This effect is much more pronounced when the double layer conductivity is large compared to the bulk conductivity in the solution (times the particle radius \( a \)). Then one can think of the double layer as a partially conducting Faraday cage that screens
some of the applied field and leads to a lower mobility than expected.

Furthermore, the simplified scenario as we discussed above becomes rather inadequate with polyvalent counter-ions. This is because the Poisson-Boltzmann equation becomes invalid by itself since it is intrinsically a mean-field approach that only deals with average potentials and concentrations. However, due to the strong interactions between polyvalent ions, their movement becomes correlated. The mean-field approach in Poisson-Boltzmann thus becomes problematic. As a matter of fact, a ‘charge inversion’ phenomenon has been observed in which counter-ions with high valence condense onto the surface and actually reverse the sign of its total charge [32].

The analytical challenge of predicting $\mu_e$ becomes much harder for larger $\zeta$ potentials because it is no longer suitable to apply the linearized Poisson-Boltzmann equation. Analytical formula valid for predicting $\mu_e$ under all $\zeta$ potential values, all $\kappa a$ ranges, and a multivalent ionic environment is still a topic of current research.

There are numerous claims in the literatures [33] that electrophoresis in an alternating electric field will lead to no net motion and the electrophoretic effects will vanish upon high frequency AC fields, due to the time integral of the electrophoretic force is zero (Eq. (2.27)). However, this claim is only true if the AC field is uniform (e.g. in capillary electrophoresis or parallel plate geometry [34, 35]). If the electric field is non-uniform, the AC electrophoretic effect can indeed produce useful ponderomotive force, the theory and the experiment of which will be presented in Chapter 3 and Chapter 4, respectively.

2.2.2 Dielectrophoresis

The subject of dielectrophoresis (DEP) is of great interest to the lab-on-a-chip studies and has a great deal of review articles [36, 37] and books [38] dedicated to this topic. In this section,
we will briefly review some salient concepts of DEP.

2.2.2.1 *The induced dipole moment*

Figure 2.9 Schematic diagram of the charge distribution in an induced dipole moment in a uniform electric field, when the suspended particle is (a) more polarizable or (b) less polarizable than the suspending electrolyte. Adapted from Morgan and Green [14]

Assuming a spherical particle suspended in an electrolyte upon the action of a *uniform* electric field, the relative polarizability of the particle and the electrolyte will determine the charge distribution around a particle (Figure 2.9). When the particle is more polarizable than the electrolyte, more charge separation will occur in the particle than that in the electrolyte, as shown in Figure 2.9a. This means that there is an imbalance of charge density on each side of the particle, which gives rise to an effective or induced dipole across the particle. This dipole will be aligned with the applied field if enough time is allowed after applying the electric field. If the external applied electric field is removed, the dipole will disappear, which is why this kind of dipole is called *induced*. However, when the particle is less polarizable than the electrolyte, the induced dipole will be opposite, as shown in Figure 2.9b.
The induced dipole is highly frequency dependent. Figure 2.9 only shows a *steady state* situation. If the applied electric field is reversed, the opposite charge distributions will be established if we wait long enough (typically a few microseconds). At low frequencies, the movement of the *free* charge can keep pace with the changing direction of the field. However, as the field frequency increases there comes a point where the charges no longer have sufficient time to respond. At high frequencies, free charge movement is no longer the dominant mechanism responsible for charging the interface, and instead the polarization of the *bound* charges (permittivity) dominates.

To summarize, the induced dipole moment is dependent on the operating frequency, as well as the conductivity and the permittivity of both particles and suspending mediums, and of course the strength of the electric field. For a homogeneous particle of radius $a$ suspended in a homogeneous medium upon an electric field $E$, the effective induced dipole moment is,

$$ p = 4\pi a^3 \varepsilon_m \left( \frac{\tilde{\varepsilon}_p - \tilde{\varepsilon}_m}{\tilde{\varepsilon}_p + 2\tilde{\varepsilon}_m} \right) E \quad (2.46) $$

where the tidle indicates a complex number, the subscript $m$ and $p$ indicates the medium and the particle, respectively. The complex permittivity $\tilde{\varepsilon}$ can be written as,

$$ \tilde{\varepsilon} = \varepsilon - i \frac{\sigma}{\omega} \quad (2.47) $$

in which $\varepsilon$ is the permittivity, $\sigma$ is the conductivity and $\omega$ is the angular frequency.

It is worth noting that the conductivity of the particle should include the surface conductivity part (see section 2.1.5.2 for discussion), a detailed surface conductance effect on the induced dipole moment is still not fully understood, and remains a current research topic.

### 2.2.2.2 Dielectrophoresis in DC electric field
Figure 2.10 Interactions of the induced dipole with electrical fields. (a) Dipole in a spatially uniform electric field. The particle will not experience a net force since the electric field magnitude for each of the pole is the same. (b) pDEP, the particle will experience a net force toward the electric-field maxima because the electric field magnitude is different for each side of the induced dipole. (c) nDEP, the particle will experience a net force that repels it away from the strongest electric-field.

Whereas electrophoresis (EP) arises from the interaction of a particle’s net charge with an electric field, dielectrophoresis (DEP) is due to the interaction of a particle’s induced dipole and
the spatial gradient of the electric field. Therefore, DEP does not require the particle to be charged but does require a *non-uniform* electric field \((\nabla E \neq 0)\). The general form of a DEP force on a dipole is given by,

\[
F_{\text{dep}} = (p \cdot \nabla)E
\]

If the electric field is uniform (Figure 2.10a), the force on each side of the dipole will be balanced, and there will be no net motion. However, if the electric field is non-uniform (Figure 2.10b), the two forces are not equal and the particle moves. Of course, the direction of motion will depend on the properties of the induced dipole (the relative polarizability of the particle and the electrolyte). For example, Figure 2.10b shows a case where the particle is more polarizable than the electrolyte and the particle will move towards the strongest electric field region. This is known as the positive DEP (pDEP). However, if the particle is less polarizable than the electrolyte, as shown in Figure 2.10c, the resulting DEP force will repel the particle away from the electric field maxima, which is known as the negative DEP (nDEP).

2.2.2.3 *Dielectrophoresis in AC electric field*

As we discussed in section 2.2.2.1, the induced dipole is not only a function of conductivity and permittivity of the particle and the suspending electrolyte, but also a function of frequency. As a result, the direction in which the particle moves will also be frequency dependent.

For a homogeneous particle of radius \(a\) suspended in a homogeneous medium upon an a sinusoidal AC electric field,

\[
E(r, t) = \text{Re}[\hat{E}(r)e^{i\omega t}]
\]

where \(\hat{E}(r)\) is the complex electric-field phasor \((E(r)e^{i\theta})\). If the phase \(\theta\) is constant in the
system, the complex field phasor $\tilde{E}(r)$ can be assumed to be real (denoted as $E(r)$), without loss of generality, as a result,

$$E(r, t) = \text{Re}[E(r)e^{i\omega t}]$$ (2.50)

The resulting instantaneous DEP force can be obtained by using Eq. (2.48), substituting the induced dipole moment with Eq. (2.46),

$$F_{\text{dep}}(r, t) = \left\{ \frac{4\pi a^3 \varepsilon_m}{\bar{\varepsilon}_p + 2\bar{\varepsilon}_m} \right\} \text{Re}[E(r)e^{i\omega t}] \cdot \nabla \text{Re}[E(r)e^{i\omega t}]$$ (2.51)

The time-averaged DEP force is therefore,

$$\left\langle F_{\text{dep}}(r) \right\rangle = \pi a^3 \varepsilon_m \text{Re} \left( \frac{\bar{\varepsilon}_p - \bar{\varepsilon}_m}{\bar{\varepsilon}_p + 2\bar{\varepsilon}_m} \right) \nabla |E(r)|^2$$ (2.52)

Eq. (2.52) shows that the time averaged DEP force depends on the volume of the particle and the gradient of the electric field magnitude squared. It also depends on the permittivity and conductivity of both the particle and the suspending medium, as well as the frequency of the applied electric field, which is combined in the real part of a parameter known as the Clausius-Mossotti (CM) factor, given by

$$\tilde{K}(\omega) = \frac{\bar{\varepsilon}_p - \bar{\varepsilon}_m}{\bar{\varepsilon}_p + 2\bar{\varepsilon}_m}$$ (2.53)

The real part of the Clausius-Mossotti factor defines the frequency dependence and direction of the force. If the relative polarizability of the particle is greater than that of the medium, then $\text{Re}[\tilde{K}(\omega)]$ will be positive (pDEP), and the force will be directed up the field gradient. If the particle is less polarizable than the medium, then $\text{Re}[\tilde{K}(\omega)]$ is negative, and the force will be directed down the field gradient (nDEP). By looking at the expression in Eq. (2.53),
it is easy to see that \( \text{Re}[\tilde{K}(\omega)] \) can only vary between +1 and −1/2. The low frequency and the high frequency limit of the \( \text{Re}[\tilde{K}(\omega)] \) is given by,

\[
\lim_{\omega \to \omega_0} \text{Re}[\tilde{K}(\omega)] = \frac{\sigma_p - \sigma_m}{\sigma_p + 2\sigma_m}
\]

(2.54)

\[
\lim_{\omega \to \infty} \text{Re}[\tilde{K}(\omega)] = \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m}
\]

(2.55)

At a particular frequency, \( \text{Re}[\tilde{K}(\omega)] = 0 \), which will result in a zero DEP force and the particle will remain stationary. This frequency is known as the crossover frequency, given by

\[
f_{co} = \frac{1}{2\pi} \sqrt{\frac{\sigma_p + 2\sigma_m}{\varepsilon_p + 2\varepsilon_m} \left(\frac{\sigma_p - \sigma_m}{\varepsilon_p - \varepsilon_m}\right)}
\]

(2.56)

### 2.2.2.4 Dielectrophoresis with multipoles

In general, not only dipoles but also quadrupoles and higher-order multipoles can be induced in the particle, which must sometimes be taken into account to fully describe the particle behavior. This occurs when the particle is in a region where the field strength varies greatly over the particle size. In general, the DEP force on particles in arbitrarily polarized sinusoidal electric fields can be expressed in a compact tensor expression given by Jones and Washizu [39-41],

\[
\langle F_{DEP}^{(n)}(r) \rangle = \frac{1}{2} \text{Re} \left[ \frac{p_n[\nabla]^n}{{n!}} E \right]
\]

(2.57)

where \( [\cdot]^n \) represents \( n \) dot products operations and \( (\nabla)^n \) represents \( n \) vector gradient operations. As a result, the \( n \)-th order DEP force is given by the interaction of the \( n \)-th order multipole moment \( p_n \) with the \( n \)-th gradient of the electric field. For \( n=1 \), Eq. (2.57) simplifies to the dipole case (Eq. (2.48)), whereas for \( n=0 \), Eq. (2.57) reduces to the Coulomb force (Eq. (2.27)).
2.3 Electric forces on the fluid

2.3.1 DC Electro-osmosis

If an electric field is applied tangential to a charged surface immersed in electrolyte, the ions in the diffuse layer will experience Coulomb forces. The consequence is that these diffuse layer ions move, pulling the fluid along with them through Stokes fiction force and generating a fluid flow. This electric field induced fluid flow is called electro-osmosis (EO). The electro-osmosis is a ‘relative movement’ to the thin double layer electrophoresis (section 2.2.1.2), where the fluid is considered still on a global scale and the particle moves with respect to the fluid. Therefore, the same analysis technique as shown in Figure 2.8 can be used. The velocity of fluid motion is linearly proportional to the applied electric field and the ζ potential (surface charges) as follows,

\[ v_{EO} = -\frac{\varepsilon_0 \varepsilon_r \zeta}{\eta} E \]  

(2.58)

The EO flow velocity profile is zero at the slip plane and rises to a maximum (and constant thereafter) given by Eq. (2.58) at a certain distance away from the surface. This flow profile is known as the plug flow. Figure 2.11 illustrates the velocity profile in an electro-osmotic flow.

The electro-osmotic velocity is independent of channel size, as long as the EDL thickness is much smaller than the characteristic length scale of the channel such that the potential is zero beyond the EDL. However, when the EDL thickness is larger than the channel size (e.g., nanoscale channels with low ionic strength), the EDL from the two surfaces will overlap in the channel and the potential will remain non-zero at the center of a channel. This EDL overlapping changes the plug flow in large channels to the flow that follows the electric potential ψ(y) as,
Figure 2.11 The velocity profile in an electro-osmotic flow when the channel size is much bigger than the EDL thickness.

Figure 2.12 The potential profile $\psi(y)$ for different channel sizes $h$. The calculation is based on $\zeta = -5\text{mV}$ and $\lambda_D = 10\text{nm}$.

\[ v_{EO} = -\frac{\varepsilon_0 \kappa \zeta}{\eta} E (1 - \frac{\psi(y)}{\zeta}) \]  

(2.59)

The potential distribution in the case of EDL overlapping in nanochannels with height $h$, under the Debye-Hückel approximation (low surface potential approximation, see section
2.1.3.2), is given by [22]

\[
\psi(y) = \frac{\zeta \cosh\left(\frac{h}{2} - \frac{y}{\lambda_d}\right)}{\cosh\left(\frac{h}{2\lambda_d}\right)}
\]  

(2.60)

Figure 2.12 shows the electric potential profile for various channel dimensions. Note that for \( h \gg \lambda_d \), Eq. (2.59) reduces to Eq. (2.58).

2.3.2 AC Electro-osmosis

Figure 2.13 Schematic AC electro-osmosis mechanism. The induced charge in the double layer and the corresponding electric field during (a) the first half-cycle of an AC electric field and (b) the second half-cycle of an AC electric field. (c) The interaction of the tangential electric field and the induced charges in the double layer gives rise to a surface fluid flow and a resulting bulk fluid flow.

For a uniform electric field as shown in Figure 2.11, if the electric field alternates the direction at a certain frequency (AC field), the fluid would move in an oscillatory manner with
zero time-averaged displacement. However, things are different when the electric field is non-uniform, which will result in a non-zero time-averaged flow, known as the AC electro-osmosis (ACEO).

Take two coplanar electrodes separated by a narrow gap for example (Figure 2.13), voltages $\pm V$ are applied to each electrode. This gives rise to two things. The first is the induced charges on each electrode. The second is a tangential components of the electric field ($E_{\parallel}$), parallel to the electrode surface. The interactions of the induced charges and $E_{\parallel}$ results in a fluid flow, similar to the DC electro-osmosis (Figure 2.11). Figure 2.13a shows the situation for one half-cycle of an AC electric field. In the other half-cycle (Figure 2.13b), the sign of applied potential, the direction of the tangential electric field and the sign of the induced charge are all reversed. As a result, the direction of the force remains the same and a steady state fluid flow occurs, as shown in Figure 2.13c.

The velocity of ACEO flow is frequency dependent. At very low frequencies, most of the applied potential drops to the interfacial double layer, thus the resulting tangential electric field $E_{\parallel}$ is close to zero, resulting in no fluid motion. At very high frequencies, the ACEO flow also tends to be zero, because there is insufficient time for the induced charge to form in the double layer. Therefore, the fluid motion for ACEO is most pronounced at an intermediate characteristic frequency. Experimentally, the ACEO occurs mainly at the frequency range from Hz to tens of kHz. ACEO flow is not observed above $\sim$100 kHz [14].

**2.4 Fluid dynamics in micro/nanofluidic systems**

The dynamics of the particles are strongly affected by its suspending medium. This can be understood from two aspects. On one hand, if the fluid is stationary on a global scale (such as in
electrophoresis), when the particle moves, the fluid will exert a viscous drag force on the particle opposing the movement. On the other hand, the drag force will pull the particles along with the fluid if the fluid moves. In micro/nanofluidic systems, the fluid flow is usually driven by a pump, or driven by electro-osmosis. In this section, we will summarize the main governing equations of fluid dynamics, especially those that are highly relevant in microfluidic and nanofluidic systems.

2.4.1 Continuity equation

The fluid in the micro/nanofluidics is assumed as a continuous medium. The local density of the fluid obeys the conservation of mass equation, which states that the rate of change of mass in an arbitrary volume is equal to the flux of mass through the surface enclosing the volume. The continuity equation can be written as,

\[ \frac{d \rho_m}{dt} + \rho_m \nabla \cdot \mathbf{v} = 0 \quad (2.61) \]

where \( \rho_m \) is the mass density and \( \mathbf{v} \) is the velocity of the fluid.

If the fluid is incompressible (\( \rho_m \) is independent of space and time, \( d \rho_m / dt = 0 \)), the continuity equation (2.61) is then reduced to,

\[ \nabla \cdot \mathbf{v} = 0 \quad (2.62) \]

which says that the divergence of velocity field is zero everywhere for an incompressible fluid.

2.4.2 Navier-Stokes equation

While continuity equation is derived from the conservation of mass, Navier-Stokes equation is derived from conservation of momentum. For an incompressible homogeneous Newtonian fluid, the Navier-Stokes equation is,
where the physical meaning of each term is shown. At steady state ($\frac{\partial v}{\partial t} = 0$), the ratio of the inertial term $\rho_m (v \cdot \nabla) v$ to the viscous term $\eta \nabla^2 v$ is known as the Reynold's number,

$$Re = \frac{\rho_m v L}{\eta}$$ (2.64)

in which:

- $\rho_m$ is the mass density of the fluid (kg/m$^3$).
- $v$ is the velocity of the particle relative to the fluid (m/s).
- $L$ is a characteristic channel size (m).
- $\eta$ is the dynamic viscosity of the fluid (Pa·s or N·s/m² or kg/(m·s)).

For Reynold’s number much less than 1, the viscous term dominates the dynamics of the fluid and for high Reynold’s number ($>> 1$), the inertial term dominates.

### 2.4.3 Laminar flow

For micro/nanofluidic systems, $Re \ll 1$ and the fluid flow is said to be Laminar flow. One of the main features in the Laminar flow is that the fluid flow follows streamlines and is free of turbulence. The Navier-Stokes equation for the steady state laminar flow can be simplified from Eq. (2.63) as,

$$-\nabla p + \eta \nabla^2 v + f = 0$$ (2.65)

Assume a two-dimensional fluid flow through a chamber of height $h$, length $L$, under the
pressure of $\Delta P$, the steady state laminar flow profile is a parabola. The velocity is zero at the walls and reaches maximum in the center of the channel, which is given by,

$$v_{\text{max}} = \frac{h^2 \Delta P}{8\eta L}$$

(2.66)

It is interesting to note that the EO flow profile (Figure 2.11) is flat (plug flow), while the profile of the pressure-driven flow is parabolic.

2.5 Electrode-electrolyte interface

For most electro-micro/nanofluidic systems, it is inevitable to have the electrode bridge the real world to the liquid. As a result, the electrode-electrolyte interface has to be clearly understood to design, perform and analyze the experiments. This topic is extensively studied in the discipline of electrochemistry. Here we will present a general overview of two types of processes that take place at the electrode-electrolyte interface: the non-Faradaic and Faradaic processes. The electrode-electrolyte interface can be modeled as a capacitor in parallel to a charge transfer resistance, as will be discussed in the following.

2.5.1 Non-Faradaic process

An electrode at which no charge transfer can occur across the electrode-electrolyte interface, regardless of the potential imposed by an outside source of voltage, is called an ideal polarized (or ideal polarizable) electrode (IPE). While no real electrode can behave as an IPE over the whole potential range, some electrode-electrolyte systems can approach ideal polarizability over limited potential ranges. One good example is a gold electrode decorated with self-assembled monolayer of alkanethiol [42].

When an IPE electrode is placed in contact with an electrolyte, the EDL formed at the
interface behaves as a capacitor. The potential decays exponentially from a maximum at the electrode to nearly zero in the bulk solution, through a characteristic length $\lambda_d$. The applied potential can change the charges stored in the capacitor. This phenomenon is known as the electrode polarization in electrochemistry.

The interface between the electrode and the electrolyte can be represented by the double layer capacitance $C_{DL}$, which is the serial capacitance of the Stern layer capacitor $C_S$ and the Gouy-Chapman layer capacitor $C_{GC}$ (Figure 2.4),

$$\frac{1}{C_{DL}} = \frac{1}{C_S} + \frac{1}{C_{GC}}$$

(2.67)

The Stern layer capacitor can be easily modeled by a parallel plate capacitor,

$$C_S = \frac{\varepsilon_0 \varepsilon_r S}{d_s}$$

(2.68)

where $d_s$ is the thickness of the Stern layer (typically 0.5 nm) and $\varepsilon_r S$ is the relative permittivity of Stern layer (usually 6-20, smaller than the bulk since higher ion concentrations lead to a lower permittivity). The Stern layer capacitor can be further divided into an inner Helmholtz capacitor and an outer Helmholtz capacitor.

The Gouy-Chapman capacitor is a differential capacitor and can be obtained as,

$$C_{GC} = \frac{dQ_{diffuse}}{d\psi_s}$$

(2.69)

2.5.2 Faradaic process

Apart from an interfacial capacitance, there can also be a charge transfer across the electrode-electrolyte interface, which causes oxidation or reduction reactions (Faradaic
processes). Electrodes at which Faradaic processes occur are also called charge transfer electrodes. This reaction can take place spontaneously with an open circuit configuration, or can be driven externally by a power source.

For the open circuit setup, the interfacial potential difference at equilibrium when no current flows can be found through thermodynamic analysis, and is given by the Nernst equation,

$$E = E_0 + \frac{RT}{nF} \ln \frac{\alpha_o}{\alpha_r}$$

(2.70)

where $n$ is the stoichiometric number of electrons consumed in the reaction, and $\alpha_i$ is the chemical activity for the ion $i$. The subscript $o$ and $r$ denotes the oxidant and the reductant, respectively.

For the externally driven reaction, the current density $j$ [A/cm²] that flows across the interface is related to the reaction rate as follows,

$$\text{Rate}(\text{mol s}^{-1} \text{ cm}^2) = \frac{dN}{dt} = \frac{j}{nF}$$

(2.71)

In general, the current (or electrode reaction rate) is governed by the rates of the following processes [42],

- Mass transfer (e.g., from the bulk solution to the electrode surface via drift, diffusion and convection).
- Electron transfer at the electrode surface.
- Chemical reactions preceding or following the electron transfer.
- Other surface reactions, such as adsorption and desorption.

The magnitude of the current is often limited by slowest process listed above (the rate-
determining step). It is interesting to point out that the heterogeneous characteristic of the electrode-electrolyte interface is quite similar to the metal-semiconductor interface. The counterparts for the contact resistance in the metal-semiconductor interface [43] is the so called charge transfer resistance in the electrode-electrolyte interface.

2.5.3 Frequency dependence

The above analysis assumes the double layer can always completely form and the charge transfer across the interface is at equilibrium. This is only true when sufficient time is given, since the ions have a finite mobility and the diffusion cannot happen instantaneously.

The picture will be different if the applied potential is alternating. At very low frequencies, in each half of the cycle of the applied potential the double layer has sufficient time to form. As a result, the potential drop across the double layer is inevitable. At very high frequencies, the double layer formation process cannot keep pace with the alternating field, so that the potential across the double layer is minimized. In other words, AC electric field with sufficiently high frequency cannot be screened by the formation of the electrical double layer. In addition, the Faradaic reaction does not have time to occur at high frequency electric fields, which is desirable in many situations.

2.6 Summary

This chapter provides an overview of the theoretical aspects of electrostatics and electrokinetics in fluidics. The complex interactions among the surface charges, the bound and mobile ions in aqueous phase, the fluid, as well as the electric field (AC or DC) have been discussed. We start by introducing the origin of the surface charges in aqueous solutions. The
steady state ionic environment surrounding this charged surface is described by EDL. The EDL consists of ionic concentrations that are different from the bulk, and as a result, the ionic conduction can be separated into a bulk and a surface component. We then discussed the electric force on the particle, which includes the EP and DEP. The effects of the uniformity and the alternating properties of the electric field on the electric force are particularly discussed. The electric force can also act on the fluid, resulting in an EO flow. The fluid dynamics relevant in micro/nanofluidics is also briefly introduced. Finally, we discuss some basic concepts in electrochemistry regarding the electrode-electrolyte interface.
Chapter 3 AC electrophoretic effect in non-uniform electric field

This chapter presents the theoretical study on one of the overlooked aspects of AC electrokinetics - AC electrophoretic (ACEP) phenomena. The dynamics of a particle with both polarizability and net charges in a non-uniform AC electric trapping field is investigated. It is found that either electrophoretic (EP) or dielectrophoretic (DEP) effects can dominate its dynamics, depending on the experimental conditions (especially the ionic concentration). A dimensionless parameter $\gamma$ is developed to predict the relative strength of EP and DEP effects in a quadrupole AC field. An ACEP ponderomotive force can be used to trap charged particles in ‘salt-free’ or low salt concentration solutions. Most importantly, in contrast to DEP traps, an ACEP trap favors the downscaling of the particle size, provided it is sufficiently charged.

3.1 Introduction

When a particle is placed in an electric field, it experiences an electric force which can be described by [40],

$$F = QE + (p \cdot \nabla)E + \cdots$$  \hspace{1cm} (3.1)

The first term of Eq. (3.1) describes the Coulomb interaction between the net charge $Q$ of the particle and the electric field $E$ and embodies the electrophoretic (EP) phenomenon. The additional terms depict the dielectrophoretic behavior (DEP), which arises from the interaction of the particle’s polarizability and the non-uniformity of the electric field.
It is well known that most polarizable particles (e.g. beads, cells and DNA molecules) suspended in aqueous solutions will develop surface charges (section 2.1.1). As a result, those particles usually possess both polarizability and charges in aqueous solutions. Therefore, when placed in a liquid with a spatially non-uniform electric field, particles experience not only a dielectrophoretic (DEP) force but also an electrophoretic (EP) force [33, 44, 45]. Modern electrokinetic techniques often use an alternating current (AC) method, owing to the absence of Faradic reactions at the electrodes and the formation of the screening double layer at the electrode surface (section 2.5.3).

While the effect of non-uniformity of electric fields is widely appreciated for DEP (section 2.2.2) and electro-osmosis (EO) (section 2.3.2), the impact of the non-uniformity of electric fields on EP behavior is largely overlooked. It is commonly thought that the EP effect will vanish upon high frequency AC electric fields due to the linearity of EP [33, 45, 46]. As a result, EP contributions are not taken into account in most of the high frequency AC electrokinetic experiments [28, 47-49]. Little attention is paid to the EP behavior in AC electric fields.

However, the common thought that the EP effect will vanish in AC fields is true only when the AC field is (i) harmonic, and (ii) uniform. Violation of either of these two conditions will result in a substantial drift motion. Indeed, Dukhin et al. proposed to use an aperiodic (but uniform) AC field to induce drifting motion of charged particles [50]. In fact, it has been realized in several disciplines of physics that a charged particle exposed to an oscillating non-uniform electric field can experience a force proportional to the cycle-averaged intensity gradient. This so-called ponderomotive force [51] plays a significant role in a variety of physical systems such as Paul traps [52], and laser-based particle acceleration [53].

In this chapter, one of the main goals is to show theoretically the non-vanishing
ponderomotive EP effect in fluid environments with high frequency AC electric field (section 3.2, and 3.3), as well as its potential application for trapping charged particles in a quadrupole field (section 3.4).

### 3.2 ACEP dynamics in one-dimension

#### 3.2.1 Secular and oscillating motion

We start our analysis with the one-dimensional EP motion of a homogeneous spherical particle with mass $m$, charge $Q$ and radius $a$ in a high frequency AC electric field. The damping force due to the viscosity of the liquid is of the form $-\xi \dot{x}$ (Eq. (2.30)), where the Stokes drag coefficient $\xi$ can be approximated by $\xi = 6\pi \eta a$ (Eq. (2.31)), and the dot denotes the time derivative. Here we assume that the hydrodynamic memory effect [54] can be neglected for the dragging force (i.e., the friction force is only dependent on the current velocity).

Without loss of generality, we assume the particle moves in an electric potential consisting of two parts:

- a static part $U(x)$, and
- a harmonically oscillating part $V(x) \cos \omega t$, where $\omega$ is the angular frequency.

The magnitude of the harmonically oscillating magnitude $V(x)$ is not assumed small in comparison with $U(x)$. Note that both potentials ($U(x)$ and $V(x)$) have a spatial dependence.

Accordingly, the electric potential gives rise to EP forces with the following two components:

- a static force $F(x) = -Q \frac{\partial}{\partial x} U(x)$, and
• an oscillating force \( f(x,t) = QE_0(x) \cos \omega t \), where \( E_0(x) = -\frac{\partial}{\partial x}V(x) \).

It is clear on physical ground that the particle will move along an averaged smooth trajectory \( S(t) \) on a time scale longer than one oscillating cycle \( \tau = \frac{2\pi}{\omega} \), which is decoupled from the rapidly oscillating micro-motion \( R(S,t) \) (see Appendix in section 3.6 for mathematical validation). Therefore, the particle motion can be written in the form,

\[
X(t) = S(t) + R(S,t)
\] (3.2)

If the amplitude of the rapidly oscillating motion, \( 2QE_0/m\omega^2 \), is much smaller than the characteristic length of the non-uniform electric field, \( E_0/\frac{\partial E_0}{\partial x} \), in other words, if the following inequality is satisfied,

\[
2Q \frac{\partial E_0}{\partial x} \ll m\omega^2
\] (3.3)

the time averaged rapidly oscillating micro-motion should be zero (because the electric field can be considered uniform on the length scale of the micro-motion), therfore,

\[
\langle R(S,t) \rangle = 0
\] (3.4)

in which bracket denotes time averaging.

It is therefore also reasonable to assume

\[
| S | \gg | R |
\] (3.5)

where the dependence on \( t \) and \( S \) are henceforth dropped for brevity.

As a result, the rapidly oscillating motion \( R \) can be considered as a small perturbation to the secular motion \( S \), and thus the equation of motion,
\[ m\ddot{X} = -\xi \dot{X} + F(X) + f(X,t) \]  

(3.6)
can be Taylor-expanded to the first order in \( R \),

\[ m(\ddot{S} + \ddot{R}) = -\xi (\dot{S} + \dot{R}) + F(S) + f(S,t) + R \frac{\partial}{\partial x} (F(x) + f(x,t)) \big|_{s=s} \]  

(3.7)
The rapidly oscillating terms on each side of Eq. (3.7) must be approximately equal,

\[ m\ddot{R} \approx -\xi \dot{R} + f(S,t) \]  

(3.8)
The oscillating term \( R \frac{\partial F(x)}{\partial x} \) is neglected by assuming \( \xi \omega \gg \frac{\partial F(x)}{\partial x} \), which is reasonable for highly damped environments such as water. By integration, we obtain the rapid micro-motion component as,

\[ R(S,t) \approx -\frac{f_o(S)}{m\omega^2 [1 + (\xi / m\omega)^2]} \left( \cos \omega t - \frac{\xi}{m\omega} \sin \omega t \right) \]  

(3.9)
with

\[ f_o(x) = QE_0(x) \]  

(3.10)
The rapid micro-motion \( R(S,t) \) is thus an oscillation of the same frequency as the driving electric field, but with a phase lag \( \theta = \arctan(\xi / m\omega) \). The oscillating amplitude depends on the position of the secular motion through \( f_o(S) \), the driving frequency, the damping coefficient, and the particle mass.

The secular motion \( S(t) \) can therefore be found by averaging Eq. (3.7) over one period of the rapid micro-motion (only \( \ddot{S} \), \( F(S) \), and the term containing \( \cos^2 \) survive after averaging), and by replacing \( f_o(x) \) with \( QE_0(x) \),
50

\[ m\ddot{S} = -\xi \dot{S} + F(S) - \frac{Q^2 E_0(x) \frac{\partial E_0(x)}{\partial x} |_{x=0}}{2\pi\omega^2[1 + (\xi / m\omega)^2]} \]  

(3.11)

So far we have obtained equations regarding both the rapid oscillating micro-motion (Eq. (3.9)) and the secular motion (Eq. (3.11)). It should be noted that this analysis is valid for any viscosity of the medium when Eq. (3.3) is satisfied. As a matter of fact, the inequality in Eq. (3.3) is valid for most experiments performed in aqueous environment around the MHz range [28, 47-49].

### 3.2.2 Uniform AC electric field with no DC component

If the applied AC electric field has no DC component, and the electric field is spatially uniform,

\[ \begin{cases} F(S) = 0 \\ \frac{\partial}{\partial x} E_0(x) = 0 \end{cases} \]  

(3.12)

the secular motion of Eq. (3.11) is then reduced to,

\[ m\ddot{S} = -\xi \dot{S} \]  

(3.13)

By integration, we obtain the solution for Eq. (3.13) as,

\[ S = A_1 e^{-\xi/m} + A_2 \]  

(3.14)

where \( A_1 \) and \( A_2 \) are constants depending on initial conditions. This is simply a transient response and will not contribute to a long timescale drift motion. Since the amplitude of the superimposed rapid micro-motion \( R(S,t) \) is usually negligible at high frequency (\( \sim 1/\omega^2 \), Eq. (3.9)), the high frequency ACEP effect vanishes in this case. No translational motion would be developed. This is consistent with O'Brien's results with a parallel plate geometry (and thus a
uniform electric field) with no DC component [34]. It is thus invalid to directly apply O’Brien’s result for the cases of non-uniform electric fields [35, 55]. It also explains why no separation could happen for capillary zone electrophoresis in a high frequency AC field (because the electric field in the capillary zone electrophoresis is uniform).

### 3.2.3 Non-uniform AC electric field with no DC component

If the applied AC electric field has no DC component, but the electric field is spatially non-uniform,\[ F(S) = 0 \]
\[ \frac{\partial}{\partial x} E_o(x) \neq 0 \] (3.15)

the secular motion of Eq. (3.11) in this case is then reduced to,
\[ m\ddot{S} = -\xi \dot{S} - \frac{Q^2 E_o(x) \frac{\partial E_o(x)}{\partial x}}{2\mu_0^2 \left[1 + (\xi / \mu_0)^2\right]} \] (3.16)

which describes a typical damped harmonic oscillator.

The second term on the right hand side of Eq. (3.16) provides a ponderomotive EP force for the secular motion due to the non-uniformity of the electric field. The particle is directed towards a point with weaker electric field (in other words, the charged particle becomes a low field seeker). Moreover, due to the squared dependence on charge \( Q \) in Eq. (3.16), the repelling of the particle from regions with high electric field intensity happens for both the positive and negative charges.

We need to emphasize that even though the time average over one period of both the force \( f(S,t) \) and the oscillating motion \( R(S,t) \) is zero at a fixed position, \emph{averaging over the micro-}
motion in the non-uniform electric field is the essential mechanism that causes the movement of charged particles.

### 3.2.4 Non-uniform AC electric field with finite DC component

If the applied AC electric field has a finite DC component, and the electric field is spatially non-uniform,

\[
\begin{cases}
F(S) \neq 0 \\
\frac{\partial}{\partial x} E_0(x) \neq 0
\end{cases}
\]  

(3.17)

it is then convenient to express \( F(x) \) and \( E_0(x) \) in Eq. (3.11) by potential energy derivatives and the motion equation is given by,

\[
m\ddot{x} = -\zeta \dot{x} - Q \frac{\partial}{\partial x} (U(x) + \Phi_{sp}(x))|_{x=S}
\]  

(3.18)

where \( \Phi_{sp}(x) \) defines an AC pseudopotential, which is of form,

\[
\Phi_{sp}(x) = \frac{QE_0^2(x)}{4m\omega^2[1 + (\zeta/\omega)^2]}
\]  

(3.19)

As a consequence, the charged particle will move towards the bottom of the effective potential well, the position of which is determined by

\[
\frac{\partial}{\partial x} (U(x) + \Phi_{sp}(x)) = 0
\]  

(3.20)

In other words, the charged particle will be damped towards the bottom of the effective pseudopotential. Since \( f_0(S) \) is a complex function of time, the motion toward and around the bottom of the effective pseudopotential depends on the detailed form of \( E_0(x) \), and other parameters of the system (frequency, viscosity, etc.). The time-dependent dynamics can only be
numerically solved for arbitrarily complex parameter sets.

### 3.2.5 Summary

To this end, we have investigated in detail the EP behavior of a charged particle in an AC electric field which satisfies (Eq. (3.3)),

\[ \omega \gg \sqrt{2Q \frac{\partial E_0}{\partial x} / m} \]  

(3.21)

A translational motion due to the action of a ponderomotive force, is unarguably possible for charged particles in a non-uniform AC field. As a result, simply ignoring the EP effect in AC electric fields will not be correct.

### 3.3 Generalized ponderomotive force

For a more general case, the instantaneous motion equation for a particle experiencing both the dielectrophoretic (DEP) force and the electrophoretic (EP) force is of the form,

\[ m\ddot{\mathbf{r}} - \zeta \dot{\mathbf{r}} + \mathbf{F}_{ep} + \mathbf{F}_{dep} = 0 \]  

(3.22)

where \( \mathbf{F}_{ep} \) and \( \mathbf{F}_{dep} \) are the instantaneous EP force (Eq. (2.27)) and instantaneous DEP force (Eq. (2.48)), respectively.

Although analytical solutions for a general case can not be obtained, information about the relative contribution of the EP force and the DEP force to the particle dynamics can be obtained from a ponderomotive force point of view, which could give a more intuitive physical insight.

#### 3.3.1 Ponderomotive DEP force

The ponderomotive force for DEP effect is well studied [14, 38]. In the point dipole approximation, the ponderomotive force has the form (Eq. (2.52)),
\[ \langle F_{\text{dep}} \rangle = \pi \varepsilon_{\text{m}} a^3 \text{Re}[\tilde{K}(\omega)] \nabla E_0^2(r) \]  

(3.23)

### 3.3.2 Ponderomotive EP force

The ponderomotive force for the EP effect in an AC-only case can be expressed as,

\[ \langle F_{\text{ep}} \rangle = Q(-\nabla \Phi_{sp}) \]  

(3.24)

Substituting Eq. (3.19) into Eq. (3.24), we obtain

\[ \langle F_{\text{ep}} \rangle = \frac{-Q^2 \nabla E_0^2(r)}{4m\omega^2(1 + (\xi/m\omega)^2)} \]  

(3.25)

As a result, spatial non-uniformity of the electric field is critical for both DEP (Eq. (2.52)) and EP (Eq. (3.25)) ponderomotive forces. While the effect of non-uniformity of electric fields is widely appreciated for DEP (section 2.2.2), its impact on EP behavior has so far been largely overlooked.

### 3.4 Trap stiffness in an AC quadrupole field

The relative strength of the EP versus the DEP ponderomotive force will determine the dominant mechanism governing the particle motion. For arbitrarily complex geometry or potentials, this requires a case by case numerical calculation. We here choose a symmetric geometry for illustrative purposes, which is a good approximation to many experimentally realized DEP traps [28, 47-49, 56] and the ACEP traps we will present in Chapter 4.

Assuming a quadrupole AC electric potential,

\[ \varphi(x, y, t) = V \cos(\omega t) \left( \frac{x^2 - y^2}{2r_0^2} \right) \]  

(3.26)

the electric field and the field intensity squared can be derived as (with \( r = xi + yj \) as the position
vector, and $r = |r|$ as its length),

$$E_0(r) = -\nabla \varphi = V \frac{(xi - yj)}{r_0^2}$$  \hspace{1cm} (3.27)

$$|E_0(r)|^2 = V^2 \frac{r^2}{r_0^4}$$  \hspace{1cm} (3.28)

Figure 3.1 Schematics of the quadrupole field. (a) the geometry and the applied potential to generate a quadrupole electric field, (b) the potential profile at $t=0$, (c) the electric field profile at $t=0$, (d) the profile of the electric field intensity squared.

Figure 3.1 shows the geometry, potential, and the electric field profile in a quadrupole field. Note that we have considered the one-dimensional motion in section 3.2. In the case of a
quadrupole electric field, the motions of a particle are independent in each dimension, and the main conclusions from section 3.2 are still valid for each direction in a quadrupole field.

We know from section 3.2 that the charged particle in a non-uniform electric field is a low-field seeker. Therefore this quadrupole AC field can be used to trap the charged particle through a ponderomotive EP force. We also know that the same geometry has been used for trapping neutral particles by a ponderomotive DEP force [28, 47-49, 56]. As a result, it is very interesting to compare the relative trap stiffness of these two mechanisms in a quadrupole AC field.

3.4.1 DEP trap stiffness

The DEP ponderomotive force in a trapping setup can be written as,

\[ \langle F_{dep} \rangle = -k_{dep} r \]  

with \( k_{dep} \) as its trap stiffness (or the spring constant if the trap is thought a spring).

In a quadrupole AC electric potential as shown in Figure 3.1 (Eq. (3.26)), the general ponderomotive DEP force (Eq. (3.23)), when applying Eq. (3.28), can be written as,

\[ \langle F_{dep} \rangle = \text{Re}[\tilde{K}(\omega)] \frac{2\pi \varepsilon_m a^3 V^2}{r_0^4} r \]  

As a result, the DEP trap stiffness in a quadrupole AC electric potential is given by,

\[ k_{dep} = -\text{Re}[\tilde{K}(\omega)] \frac{2\pi \varepsilon_m a^3 V^2}{r_0^4} \]  

In order to hold the particle in the center of the trap (weakest electric field intensity), the ponderomotive DEP force should be a restoring force (i.e. the trap stiffness should be positive). For DEP trapping, this means a negative value of \( \text{Re}[\tilde{K}(\omega)] \) is needed (nDEP, see section 2.2.2.3).
### 3.4.2 EP trap stiffness

The EP ponderomotive force in a quadrupole trapping setup can be written as,

\[ \langle F_{ep} \rangle = -k_{ep} r \tag{3.32} \]

with \( k_{ep} \) as its trap stiffness.

In a quadrupole AC electric potential as shown in Figure 3.1 (Eq. (3.26)), the general ponderomotive EP force (Eq. (3.25)), when applying Eq. (3.28), can be written as,

\[ \langle F_{ep} \rangle = -\frac{Q^2V^2}{2m\omega^2 r_0^4[1+(\xi/m\omega)^2]} r \tag{3.33} \]

As a result, the EP trap stiffness in a quadrupole AC electric potential is given by,

\[ k_{ep} = \frac{Q^2V^2}{2m\omega^2 r_0^4[1+(\xi/m\omega)^2]} \tag{3.34} \]

### 3.4.3 Trap stiffness comparison

To compare the relative strength of the EP and DEP in a quadrupole AC electric potential as shown in Figure 3.1, we define a dimensionless parameter \( \gamma \),

\[ \gamma \equiv \left| \frac{k_{ep}}{k_{dep}} \right| = \frac{Q^2}{4|\text{Re}\{\tilde{K}(\omega)\}|\pi \varepsilon_m^3 m \omega^2[1+(\xi/m\omega)^2]} \tag{3.35} \]

The relative strength of EP and DEP effect can therefore be clarified by the magnitude of the \( \gamma \) parameter:

- \( \gamma \ll 1 \), DEP effect dominates, the EP effect can be safely ignored.
- \( \gamma \gg 1 \), EP effect dominates, the DEP effect can be safely ignored.
- \( \gamma \sim 1 \), both of the EP and DEP effects are important.
Figure 2.1a plots the $\gamma$ value as a function of $Q$ and $a$ at a fixed frequency (1 MHz), while Figure 2.1b shows the $\gamma$ dependence on $Q$ and $\omega$ at a fixed particle size (500 nm radius). It is easy to see that the EP effect can dominate the trapping dynamics in the case of a sufficiently high net charge in a non-uniform electric field.

It is noteworthy that even though the $\gamma$ parameter derived here is based on a quadrupole electric field, the general conclusion that ACEP effect can be used to trap sufficiently charged particles in a non-uniform electric field holds true for other geometries.

3.4.4 Why to realize an ACEP trap

It is very important to realize the fundamental difference on the scaling performance of
both DEP and EP trapping stiffness, as shown in Eq. (3.31) and (3.34).

First, reducing the device size $r_0$ helps to enhance the trapping strength for both EP and DEP in a same fashion ($\sim 1/r_0^4$).

Second, increasing the applied voltage has the same impact on the trap stiffness ($\sim V^2$) and the maximum voltage that can apply is limited by the breakdown field and other electrokinetic effects (such as electro-thermal flow [57]).

Most importantly, the DEP trap strength decreases with the volume of the particle. In contrast, an EP trap prefers smaller particle since the trap stiffness increase with decreasing the mass of the particle, which makes EP very attractive for quantum dot and single molecule trapping. However, in order for this EP trap to happen, the net charge $Q$, as we discussed above, should maintain a certain minimum value.

The observations that the ACEP trap favors the downscaling of the particle size is one of the main driving factors to realize an ACEP trap, rather than a conventional DEP trap [28, 47-49].

3.4.5 How to realize an ACEP trap

The key parameter in the trap stiffness for a ponderomotive EP trap is particle charge appeared to the electric field. Notice that the charge we used in the derivations above is the effective charge rather than the bare charge [58, 59]. A charged surface in contact with a conductive liquid creates an induced EDL. A significant fraction of the particle's charge is neutralized by the strongly bounded counterions in the Stern layer. The charged particle plus the thin Stern layer (which determines the bare charge $Q_{bare}$) is further screened by diffusive
counter-ions within a characteristic Debye length $\lambda_D$ (Figure 2.4).

To determine the effective charge $Q_{\text{eff}}$, we look at the motion of charged particles in an electric field, which is governed by electrostatic forces, friction, and electrophoretic retardation forces. Among them, the electrophoretic retardation force originates from the delayed response of the surrounding ionic atmosphere to the motion of a charged particle. Since $\zeta$-potential can be expressed in terms of the bare charge as [59],

$$\zeta = \frac{Q_{\text{bare}}}{4\pi \varepsilon a (1 + a / \lambda_D)} \quad (3.36)$$

The electrophoretic mobility $\mu_E$ described by Henry's formula (Eq. (2.44)) can therefore be rewritten as,

$$\mu_E = \frac{Q_{\text{bare}}}{6\pi \eta a (1 + a / \lambda_D)} f\left(\frac{a}{\lambda_D}\right) \quad (3.37)$$

The effective charge of particle can thus be estimated from Eq. (2.34) as,

$$Q_{\text{eff}} = \frac{f\left(\frac{a}{\lambda_D}\right)}{(1 + a / \lambda_D)} Q_{\text{bare}} \quad (3.38)$$

At a high ionic concentration $c$, the Debye length ($\lambda_D \sim c^{-1/2}$) becomes very small, as a result, $a / \lambda_D \gg 1$ and $f\left(\frac{a}{\lambda_D}\right) \rightarrow 3/2$ (Eq. (2.45)). Therefore, $Q_{\text{eff}} \ll Q_{\text{bare}}$. The effective charge is greatly reduced in high ionic strength solutions. This reduced effective charge in high ionic strength solutions pushes the $\gamma$ parameter in Figure 2.1 into the DEP dominating region ($\gamma \ll 1$). For most nDEP trapping experiments reported, high salt concentrations were intentionally added to adjust the conductivity of the suspension medium [28, 47-49, 60], therefore EP effects in trapping dynamics could be safely neglected for those experiments.
In contrast, it is easy to see from Eq. (3.38) that $Q_{\text{eff}} \rightarrow Q_{\text{bare}}$ when $a \rightarrow 0$ and/or $\lambda_D \rightarrow \infty$. This happens for ultrasmall particles or very low ionic concentrations. The high value of $Q_{\text{eff}}$ could push the $\gamma$ parameter in Figure 3.2 into the EP dominating region ($\gamma \gg 1$).

As a matter of fact, the ionic concentration dependent effective charge is well known as ‘charge renormalization’ in colloid science [59, 61-64]. The reduced effective charge in high conductivity medium can also be understood from the charge relaxation point of view (section 2.2.1.4). A highly conductive medium makes the EDL behave as conductive sheet (effective Faraday cage) and therefore less charge can be seen by the electric fields.

In conclusion, to experimentally realize a ponderomotive EP trap, the conductivity of the suspending medium is one of the most important parameters to be treated with care.

### 3.5 Summary

This chapter elucidates the concept of the EP effects in AC electric field. In contrary to the common thought that EP effect will vanish in high frequency AC electric field, we show in this chapter that useful ponderomotive EP force can be generated in a spatially non-uniform AC electric field. We derived the general formular for describing this ponderomotive EP force in arbitrary geometry. We also show that the charged particles, upon the action of the ponderomotive force, is a low field seeker and thus can be used to realize a particle trap.

Moreover, the relative contributions of both the ponderomotive DEP and EP effects in a quadrupole trapping field were studied and an important dimensionless parameter $\gamma$ was obtained, which presents a consistent explanation for previous DEP trapping experiments carried out with highly conductive suspending medium. It also offers a design guidance for realizing an ACEP trap in a quadrupole field, which favors small and sufficiently charged particles, in
contrast to DEP trap’s inability to trap smaller particle.

### 3.6 Appendix: Mathematical validation of motion separation

Considering a particle of charge $Q$ and mass $m$ and in a quadrupole electric potential,

$$\phi(x, y, t) = \frac{U - V \cos \omega t}{2r_0^2}(x^2 - y^2) \quad (3.39)$$

which by definition provides a spatially non-uniform electric field, with DC and AC components in $x$-dimension,

$$\Phi(x, t) = -Q \frac{\partial}{\partial x} \phi(x, y, t) = -F(x) + f(x, t) \quad (3.40)$$

where

$$F(x) = -m \omega^2 \frac{a}{4} x \quad (3.41)$$

$$f(x, t) = m \omega^2 \frac{q}{2} x \cos \omega t \quad (3.42)$$

with the dimensionless parameters $a$ and $q$ defined as,

$$\begin{cases}
  a = \frac{4QU}{mr_0^2 \omega^2} \\
  q = \frac{2OV}{mr_0^2 \omega^2}
\end{cases} \quad (3.43)$$

The equation of motion in the $x$ direction is therefore,

$$m\ddot{x} = -\xi \dot{x} + F(x) + f(x, t) \quad (3.44)$$

Introducing a dimensionless viscosity $b$ and a dimensionless time $\tau$ as follows,
\[
\begin{aligned}
\begin{cases}
    b = \frac{2\xi}{\omega} \\
    \tau = \omega t
\end{cases}
\end{aligned}
\tag{3.45}
\]

and replacing

\[
x = \exp(-b\tau/4)P
\tag{3.46}
\]

then Eq. (3.44) takes the form,

\[
\dot{P} = hP + \frac{1}{2}qP\cos\tau
\tag{3.47}
\]

where

\[
h = \frac{b^2 - a}{16 - 4}
\tag{3.48}
\]

Without loss of generality, the solution of Eq. (3.47) can be written in the form of the Floquet expansion,

\[
P(t) = \exp(-i\int_0^\tau \sigma(\tau) d\tau) \sum_{n=-\infty}^{\infty} P_n(\tau) \exp(int)
\tag{3.49}
\]

where \(P_n(\tau)\) and \(\sigma(\tau)\) are slowly varying functions on the time scale such that the external electric field is switched 'on' adiabatically. By equating the same Floquet components and neglecting time derivatives of \(P_n\) and \(\sigma\), the infinite, homogeneous system of equations follows,

\[
-n^2P_n - \sigma^2P_n + 2n\sigma P_n = hP_n + \frac{q}{4}(P_{n+1} + P_{n-1})
\tag{3.50}
\]

where the dependence on \(\tau\) is henceforth dropped for brevity, and \(n\) takes all integers. To secure a nontrivial solution, one equates the infinite tridiagonal determinant of the system with zero. This yields the equation for the infinite number of Floquet-Lyapunov (FL) exponents \(\sigma\), which define an infinite number of solutions for the system.
We will seek the solution for the case of particular experimental interest, \( q << 1 \) (small \( q \), equivalent to the requirement of Eq. (3.3)), under arbitrary dragging parameter \( b \) and DC parameter \( a \). Looking for the non-oscillating \( (P_0) \) and oscillating terms to the lowest non-vanishing powers in \( q \) \( (P_{\pm 1}) \), Eq. (3.50) simplifies into

\[
-\sigma^2 P_0 = hP_0 + \frac{q}{4}(P_1 + P_{-1})
\]

\[
-P_{\pm 1} - \sigma^2 P_{\pm 1} \pm 2\sigma P_{\pm 1} = hP_{\pm 1} + \frac{q}{4} P_0
\]

reducing the infinite homogeneous system into the finite one of order three. Thus

\[
P_1 + P_{-1} = -A \frac{q}{2} P_0 + O(q^2)
\]

which, when replaced in Eq. (3.51), gives the FL exponents

\[
\sigma_{1,2} = \pm i \sqrt{h - \frac{A}{8} q^2} = \pm i \sigma_0
\]

where

\[
A \approx \frac{1}{1 + 4h} + O(q^2)
\]

Note that the above analysis is valid for an arbitrary drag parameter \( b \) and arbitrary DC parameter \( a \). The Eq. (3.52) yields

\[
\begin{align*}
P_1 &= -\frac{q}{4} \frac{1}{1 \mp 2i\sqrt{h}} P_0 \\
P_{-1} &= -\frac{q}{4} \frac{1}{1 \mp 2i\sqrt{h}} P_0
\end{align*}
\]

Notice that it is easy to show that \( P_{\pm 2} \) are proportional to \( q^2 \), \( P_{\pm 3} \) to \( q^3 \), therefore \( P_{\pm 1} \) are
the leading coefficients in expansion of small $q$ of the rapid oscillating part of the Floquet expansion in Eq. (3.49), oscillating with the driving frequency $\omega$.

Since in $P_0(t) = \exp(\pm \int \sigma_0 d\tau)$, $\sigma_0$ can be either real or imaginary. If $\sigma_0$ is imaginary, it produces a secular oscillations of the frequency $\omega \sigma_0$. In the limit $b = 0$, and $a = 0$, $\omega \sigma_0$ equals to $\omega q / 2\sqrt{2}$, a value obviously much smaller than $\omega$ when $q << 1$. This means that a frictionless environment would lead to a oscillating secular motion with a much slower oscillating frequency.

However, when $b > 1$ (typical for aqueous environments), $\omega \sigma_0$ is real, and when combined with the exponent in Eq. (3.46) yields $-(b/4 \mp \sigma_0) < 0$ when $q << 1$. This means that $x(t)$ is proportional to an exponentially decreasing function of time, $\exp[-(b/4 \mp \sigma_0)\omega t]$. It is interesting to note that the two exponent factors are quite different in size:

$$\sigma_1 = (b/4 - \sigma_0) \approx \frac{q^2}{16} \sqrt{h(1+4h)} \ll 1$$  \hspace{1cm} (3.57)

while

$$\sigma_2 = (b/4 + \sigma_0) \approx b/4 + \sqrt{h} \rightarrow b/2 \sim 1$$  \hspace{1cm} (3.58)

This means only the solution corresponding to $\sigma_1$ will define long time motion in water, the other one being a short-time transient.

By neglecting high order terms in $q$, we can now write $P(\tau)$ in Eq. (3.49) as,

$$P^{(i)}(\tau) \approx P_0^{(i)} + (P_1^{(i)} \exp(i\tau) + P_{-1}^{(i)} \exp(-i\tau))$$  \hspace{1cm} (3.59)

where $i=1, 2$ correspond to two eigen solutions in Eq. (3.54),
\[ P^{(1,2)} = \left[ 1 - \frac{q^2}{2(1 + 4\hbar^2)} \right] (\cos \omega t + 2\hbar \sin \omega t) \exp(\pm \omega t) \left( \int_0^t \sigma_0 \, dt \right) \] (3.60)

The full solution for \( x(t) \) is therefore,

\[ x(t) = \exp(-\frac{b^2}{4}) (A_1 P^{(1)} + A_2 P^{(2)}) \] (3.61)

where \( A_1 \) and \( A_2 \) are the integration constants, depending on the initial conditions.

If one assumes zero initial velocity at an initial position \( x_0 \), as well as adiabatic switching on of the external potential, then for \( b \gg q \), the solution takes the form

\[ x(t) = \exp\left[-\left(b^2 / 4 - \sigma_0 \right) \omega t\right] P^{(1)} x_0 \] (3.62)

- When only an AC field is applied (\( a = 0 \)), it follows

\[ x(t) = \exp\left(-\frac{q^2 / b^2}{1 + b^2 / 4} \omega t\right) \left[ 1 - \frac{q^2 / 2}{1 + b^2 / 4} \left( \cos \omega t - \frac{b^2}{2} \sin \omega t \right) \right] x_0 \] (3.63)

- When \( b = 0 \) is also satisfied (frictionless case),

\[ P^{(1,2)} = (1 - \frac{q^2}{2} \cos \omega t) \exp(\pm \frac{\omega t}{2\sqrt{2}}) \int_0^t \sigma \, dt \] (3.64)

which yields

\[ x(t) = x_0 \left( 1 - \frac{q^2}{2} \cos \omega t \right) \cos\left( \frac{\omega t}{2\sqrt{2}} \right) \] (3.65)

defining the secular angular frequency \( \sqrt{2} q \omega / 4 \).
Chapter 4  Paul trapping of charged particles in aqueous solution

This chapter experimentally demonstrates a ponderomotive ACEP trap with a quadrupole electric field (a.k.a., aqueous Paul trap). Radio frequency (RF) voltages are used to generate an alternating focusing/defocusing potential well in two orthogonal directions. Individual charged particles are dynamically confined at nanometer scale in space. Compared with conventional Paul traps working in frictionless vacuum, the aqueous environment associated with damping forces and Brownian noises exerts a fundamental influence on the underlying physics. We investigate the impact of these two effects on the confining dynamics, with the aim to reduce the root-mean-square (rms) value of the positional fluctuations (or to ‘squeeze’ the Brownian noise). We find that the rms fluctuations can be modulated by adjusting the voltages and frequencies. We also demonstrate the scaling properties of the ACEP trap. This technique provides a new alternative for the localization and control of charged particles in an aqueous environment.

4.1 Introduction

4.1.1 Nano-manipulation

Trapping and manipulating single molecule or colloid particle in aqueous solution provides the opportunity to study intrinsic individual characteristics rather than averaged ensemble properties. Over the last decades, a variety of manipulation techniques have been developed to achieve trapping in solutions, including optical tweezers [65], acoustic tweezers [66], and
magnetic tweezers [67]. Electrical forces, due to its integration potential, are increasingly common methods for achieving manipulations in solutions. Electrical forces for manipulating small objects in aqueous solution include electrophoresis (EP) and dielectrophoresis (DEP) (section 2.2). Electrophoretic forces arise from the interaction of an object’s fixed charge and an electric field, whereas dielectrophoresis arises from an object’s polarizability. So far, the electrical trapping of objects in solution has been done primarily by DEP [37, 48, 49, 68]. However, DEP forces are relatively weak, especially for a scaled target since the forces scale with the volume of the trapped object (Eq. (3.30)) [37, 48, 49, 68]. Electrophoretic forces, on the other hand, are much stronger and thus are widely used to separate charged biomolecules such as DNA, RNA and protein. Electrophoretic force depends on the amount of charge rather than polarizability, and is a first order interaction with electric field (Eq. (3.1)).

Even though most macromolecules (DNA molecules for example) suspended in aqueous solutions develop net electric charges (by either the dissociation of chemical groups or the adsorption of ions or molecules from the solution, section 2.1.1), utilization of the direct charge-field interaction to trap objects in aqueous solution has been rarely explored. One notable example of using electrophoretic force to realize a trap is by Cohen et al., who developed an anti-Brownian electrophoretic trap (ABEL) based on a feed-back mechanism [69-71]. This technique requires, however, the target be visible and the sampling rate fast. There is a need to avoid these two requirements, while still take advantage of the strong electrophoretic force.

4.1.2 Paul traps

Earnshaw’s theorem states that a charged particle cannot be stably hold in electrostatic fields due to the saddle shape of the potential that results from Laplace’s equation. Although this would seem to preclude electrophoretic traps, one can get around this problem by using an
alternating electrical field. As we have theoretically shown in Chapter 3, ACEP ponderomotive forces can be used to trap charged particles in aqueous solutions. As a matter of fact, the ACEP ponderomotive force, if it is in a vacuum case, is equivalent to the forces used in the conventional Paul traps [52]. In the following, the term ‘aqueous Paul trap’ is used exchangeable with the term ‘ACEP trap’.

The Paul trap is a standard method in physics to confine ions through spatially inhomogeneous and alternating radio frequency (RF) electrical fields. This principle was later extended to dynamically trap macroscopic charged particles [72]. It has been used in many fields, such as mass spectrometry [73], analytical chemistry [74] and quantum information processing [75].

In contrast to the three-dimensional (3D) Paul traps, a linear Paul trap is compatible with standard micro-fabrication technology and can thus be mass-produced [76]. Linear Paul traps confine the ions radially by a two-dimensional (2D) radio frequency (RF) field and transport the ions axially by an applied axial electric field [77]. However, all Paul traps and the variants [75, 76, 78] experimentally realized so far have only been operated either in vacuum or in gaseous phase. An aqueous Paul trap remains an unexplored area. In fact, there are contradictory predictions whether a Paul trap is applicable in an aqueous environment [78-80]. In this chapter, we will experimentally show the feasibility and the main properties of an ACEP trap (aqueous Paul trap).

4.2 Materials and methods

4.2.1 Device principle
Figure 4.1 Illustration of working principles for the ACEP device under a pure alternating electric field. The $x$ and $y$ axes are normalized by device size $R_0$. $z$ axis is normalized by $V$. At $t=0$, the resulting electric forces (dashed arrows) will focus positively charged particles along $y$ direction and defocus them along the $x$ direction. Half an RF period later, the potential polarity is reversed. If the AC potential changes at the right frequency, the charged particles become stuck in this rapid back-and-forth motion.

The basic principle of the ACEP trapping device is shown in Figure 4.1. At time $t=0$, the applied voltage creates a saddle shape potential such that positive charges will be pushed into the center of the device along the $y$ direction but will be pulled away from the center along the $x$ direction. After half an RF cycle ($t = \pi / \Omega$), the polarity of the potential is reversed and the positive charges are subject to opposite forces. The focusing/defocusing forces alternate between $x$ and $y$ directions with the applied sinusoidal voltage. If the polarity of the voltage changes fast enough, charged particles become stuck in a rapid back-and-forth motion. Note that this mechanism also works for negatively charged particles in a similar way. Because the electric field intensity is at a minimum in the trap center ($x = y = 0$), an effective pseudoforce will push the charged particles (either positively or negatively charged) toward the center, where they become confined in the $x - y$ plane. More mathematical descriptions of this working principle...
can be found in Chapter 2.

4.2.2 Device fabrication

Our planar quadrupole trapping devices are fabricated on a SiO$_2$/Si wafer (Figure 4.2a). The insulating SiO$_2$ layer has a thickness of 3 µm which is thermally grown. LOR 5A resist (Microchem Corp) is spun on the substrate at a speed of 3000 rpm for 1 min, followed by baking at 175°C for 5 min on the hotplate. Another layer of positive photoresist S1808 (Shipley) is then spun on top of the baked LOR. Then a standard UV lithography and developing process is applied to pattern the bi-layer structure. 20-nm-thick Cr and 300-nm-thick Au is e-beam evaporated at the speed of 3 Å/s. The whole wafer is thereafter immersed into the N-Methylpyrrolidone (NMP) solution heated at 60°C to remove the bi-layer photoresist. Finally, the wafer is diced and is ready to be integrated with the microfluidic chamber. The microfluidic chamber is formed by poly(dimethylsiloxane) (PDMS) using SU-8 as a molding master (Figure 4.2 c and d). The detailed protocols can be found in the work by Duffy et al. [81]. Oxygen
plasma treatment was used to permanently bond the PDMS to the device surface and form an anti-evaporation microfluidic channel (Figure 4.2e). An inlet and an outlet were punched through before assembling (Figure 4.2f). Once the device was assembled, it could be repeatedly used for a long time.

Figure 4.3 Planar aqueous Paul trap (ACEP) devices. (a) Scanning electron micrograph (SEM) of the devices before integration with a microfluidic interface. The AC/DC voltages are applied such that the potentials of any two adjacent electrodes are of same magnitude but opposite sign. $2R_0$ denotes the physical size of the device. (b) Finely controlled processing results in smooth sidewalls of the electrodes, which helps to minimized the stray electric fields. (c) Sketch of a functional device with microfluidics integrated (not drawn to scale).

The resulting planar ACEP devices are shown in Figure 4.3, the quadrupole microelectrodes define the confinement region (Figure 4.3a and b), $2R_0$ denotes the physical
size of the devices, which typically varies between 2 µm and 8 µm). The carefully controlled fabrication process results in smooth sidewall profiles (Figure 4.3b). The devices are assembled with polydimethylsiloxane (PDMS) microfluidic chambers to form the functional devices (Figure 4.3c). The assembled devices are wire-bonded and mounted onto a printed circuit board (PCB).

![Figure 4.4 Photograph of experimental setup.](image)

### 4.2.3 Experimental setup

Figure 4.4 and Figure 4.5 show the photograph and the schematic of experimental setups. Voltages in the form of \( \pm[U - V \cos(\Omega t)] \) are used to perform the experiments (Figure 4.3a). Here \( U \) is the DC voltage in series with the time-varying RF sinusoidal voltage of amplitude \( V \) and angular frequency \( \Omega (= 2\pi f) \), and \( f \) is the frequency in Hz. The motion of the charged particles is monitored by an optical microscope (Olympus BX51) and the video is taken by a high-sensitivity digital charge-coupled device (CCD) camera (Olympus DP70) with the highest shutter speed as fast as 1/44000 s.
Figure 4.5 Schematic of the experimental setup. The whole setup is built around a microscope. A LabVIEW (National Instruments) program controls the function generator (FG) to create the AC/DC voltages. The real voltage applied to the device is measured by an oscilloscope (OSC) and recorded by the same LabVIEW program. The electrical connections are through BNC cables (dashed lines. The videos taken by CCD are stored in personal computer (PC) memory in real time.

4.2.4 Video processing method

We use a particle tracking algorithm that has been described in detail elsewhere [82] to extract the motion fluctuations. Videos taken by a high-sensitivity digital CCD camera are decomposed into frame sequences using the software VirtualDub (http://www.virtualdub.org/). The particle tracking is then carried out in NIH ImageJ platform (http://rsb.info.nih.gov/ij/) with a particle tracking plugin tool developed by Levy (https://weeman.inf.ethz.ch/ParticleTracker/). Figure 4.6 illustrates the trajectory extraction process.
However, video based position extraction method does not measure the instantaneous particle position and has a problem of 'motion blur', which results from time-averaging a signal over a finite integration time (shuttle time or acquisition time) [83]. This will lead to the underestimation of the real variance. Wong et al. showed both theoretically and experimentally that the relation between the measured variance $Var(X_m)$ and the real variance $Var(X_r)$ can be linked by motion blur correction function $S(\alpha)$ [83],

$$Var(X_r) = Var(X_m) / S(\alpha)$$  \hspace{1cm} (4.1)

where

$$S(\alpha) = \frac{2}{\alpha} - \frac{2}{\alpha^2} (1 - e^{-\alpha})$$  \hspace{1cm} (4.2)

in which $\alpha$ is a dimensionless parameter, defined by expressing the exposure time $W$ in unit of
the trap relaxation time $\tau$, i.e. $\alpha = W / \tau$.

As for the experimental position variance extraction, we set the shutter speed as 1/80 s and used a 100× objective, leading to an on-screen magnification of 125 nm/pixel. The recording frame rate is 8 fps. We estimate the relaxation time in the experiment as $\tau = \xi / k \sim 1\text{ms}$ (where $\xi = 6\pi \eta r$, the Stokes drag coefficient). As a result, the motion blur correction function value $S(\alpha)|_{\alpha=12.5} = 0.1472$. Therefore, the real variance $\text{Var}(X_r)$ is corrected as, $\text{Var}(X_r) = 6.79 \times \text{Var}(X_m)$, or in terms of standard deviation, $\text{Std}(X_r) = 2.6 \times \text{Std}(X_m)$.

4.2.5 **Particles and solution preparation**

Charged particles used to verify the working principles are polystyrene beads (Polysciences, Warrington, PA). The surfaces of these particles are functionalized with carboxylate groups (-COOH). These COOH surface groups are the origin of the negative charges (-COOH $\rightleftharpoons$ COO$^-+H^+$). Scanning electron microscopy (SEM) reveals that all the particles have a pronounced spherical shape (Figure 4.7).

![Figure 4.7 SEM image of the polystyrene beads used in the test.](image)
As we have discussed in section 3.4.5, the conductivity of the suspending medium is one of the most important parameters in realizing a ponderomotive ACEP trap. A lower solution conductivity is preferred for the AC electrophoretic effect to dominate over the DEP effect.

The solutions used in our experiment are repeatedly washed with deionized (DI) water to obtain a low solution conductivity. The detailed protocol of solution preparation is as follows:

1. The beads were firstly diluted to a density of \(~10^6\) particle/mL by deionized (DI) water (milli-Q grade, resistivity 18 MΩ·cm), in order to eliminate the particle-particle interactions during the experiment.

2. In order to thoroughly remove the residual ions from the stock solution, the beads prepared in step 1 were washed five times in DI water by centrifuging the beads in a 10 mL tube at 13500 G for 10 min, re-suspending in DI water each time.

The prepared solution in the 10 mL tube was extracted and then pumped into the microfluidic chamber. The conductivity of the fresh suspension solution in the 10 mL tube (exposed to air) is measured as 0.1 µS/cm (EC 215 Multi-range Conductivity Meter, Hanna Instruments) and this slowly goes up to maximum 2.0 µS/cm during the course of an experiment (due to the absorption of ambient gas). This measured conductivity variation sets the lower and upper bound for the solution inside the microfluidic chamber. In fact, since the microfluidic channels are not directly exposed to air, little change of the solution conductivity inside the trap chamber is expected. Since the solution conductivity directly affects the effective charge of the particle (see section 3.4.5 for discussion), long-term measurements were carried out on a single trapped particle to investigate the drift of solution conductivity (section 4.3.5).

4.3 Polystyrene bead trapping
4.3.1 Particle confinement

Figure 4.8 presents the trapping results using the planar ACEP trapping devices. The inset (a) of Figure 4.8 shows a typical image for a single trapped charged bead (of mean radius 490 nm). Individual particles can be stably held in the center of the device for up to four hours (due to insignificant change over this time, we did not explore longer). Trapping mostly occurs for a single particle (instead of ensembles) due to inter-particle Coulomb repulsion.

Figure 4.8 Particle trajectories when the trap is on (orange line) and off (blue line) in the \( x \) direction. Inset (a) shows a snapshot of a single particle confined in the center of the device. Inset (b) shows a magnification of fluctuations. Inset (c) is the histogram of the displacements for the orange curve. A Gaussian fit yields a trap stiffness of 4 pN/\( \mu \)m.

The orange curve in Figure 4.8 describes the time trace of the particle trajectory in the \( x \)
direction when trapped under conditions of $V=1.5$ V, $U=0$ V and $f=2.5$ MHz. The blue curve depicts the Brownian motion when the trap is off (no electrical connection). We observe that the particles are not stationarily trapped but trapped with fluctuations (inset (b) of Figure 4.8).

The inset (c) shows the normal distribution of displacements derived from the orange trajectory in Figure 4.8. A Gaussian fit yields effective trap stiffness $k = \frac{k_B T}{\delta^2}$ in the $x$ direction as $4$ pN/μm ($k_B$ is Boltzmann constant and $T$ is the environment temperature). The motion in the $y$ direction shows a similar property. Note that the confinement of approximately $32$ nm is achieved with a $2R_0=8$ μm device. We note that the trap stiffness of $4$ pN/μm is not a characteristic value of this ACEP trap. In fact, the ACEP trap stiffness depends on the operation frequency, voltage, charge and mass of the objects, as shown in Eq. (3.34).

![Graphs showing the effect of applied voltages and frequencies on the confinement of particles.](image)

Figure 4.9 Effect of the applied voltages and frequencies on the confinement of particles. Experiments are performed with 490 nm-radius particles and $R_0=4$ μm devices. No DC voltages are applied ($U=0$ V). (a)
positions of a single particle trapped under a fixed frequency (3 MHz) and three different voltages.

(b) Radial probability histograms \( r = \sqrt{x^2 + y^2} \) corresponding to the data sets in (a). \( P(r) \) is defined such that \( \int P(r)2\pi rdr = 1 \). (c) \( x \sim y \) positions of a single 490 nm radius particle trapped under a fixed voltage \( V = 1.2 \, \text{V} \) and three different frequencies. (d) Radial probability histograms corresponding to the data sets in (c).

Most importantly, the rms fluctuations of the trapped particles can be tuned by externally applied voltages \( U \) and \( V \) and frequencies \( f \). Figure 4.9a and Figure 4.9b show the \( x \sim y \) positions of a trapped particle and the radial probability distributions at a fixed frequency (3 MHz) and three different AC voltages. By adjusting the voltage, the degree of the radial confinement can be modulated. We observed a decrease of rms fluctuations with increasing the AC voltages \( V \) within ranges that we can experimentally achieve.

Figure 4.9c and Figure 4.9d show the \( x \sim y \) positions of a trapped particle and their radial probability distributions under a fixed voltage \( 1.2 \, \text{V} \) and three different frequencies. A slight decrease of rms fluctuations when increasing the frequency is visible for the data presented. However it is not necessarily true that increasing the frequency will reduce the rms fluctuations. As a matter of fact, due to the complexity of achieving an impedance match for the RF circuit, it is very difficult to maintain a fixed voltage for various frequencies during the experiments. Therefore, the frequency dependence cannot be decoupled from the voltage dependence (Figure 4.9a and Figure 4.9b). We do not have a conclusive trend for the frequency dependence at the current stage. Nevertheless, we can experimentally achieve a tight or loose confinement by adjusting the applied voltages and frequencies. In addition, we are also able to repel a confined particle from the trap and to resume confinement after the particle escapes from the trap.
4.3.2 Theoretical modeling

Unlike the case of charged particles in a vacuum Paul trap, which has been extensively studied and described by Mathieu equations [77], the motion of charged particles in an aqueous environment is governed not only by the external electric fields but also by additional damping forces and thermally induced fluctuations (i.e. Brownian motion). The last two forces always appear together according to the fluctuation-dissipation theorem (FDT) [84]. This kind of system, as suggested by Arnold et al. in their study of trapping microparticles in the atmosphere near standard temperature and pressure, necessitates a stochastic approach [85].

Assuming an ideal planar AC/DC quadrupole electric potential, resulting from the applied voltages as shown in Figure 4.3a,

$$\varphi(x, y, t) = (U - V \cos \Omega t) \frac{x^2 - y^2}{2R_0^2}$$

(4.3)

the motion of a homogeneous charged particle with mass $M$, radius $r_p$, and net charge $Q$ in presence of a stochastic force can be written as ($r$ is the particle radial position vector in the $x-y$ plane, $r = xi + yj$),

$$M \frac{d^2r}{dt^2} = -\xi \frac{dr}{dt} + Q(-\nabla \varphi) + N(t),$$

(4.4)

The three terms on the right-hand-side (rhs) of Eq. (4.4) are the damping force, the electric driving force and the Brownian noise force, respectively. The Stokes' drag coefficient $\xi$ can be approximated by $\xi = 6\pi \eta r_p$, where $\eta$ is the dynamic viscosity of the aqueous solution. $N(t)$ is a random force due to thermal fluctuation with the properties of,
\[
\begin{align*}
\langle N(t) \rangle &= 0 \\
\langle N(t)N(t+\tau) \rangle &= 2k_BT\xi\delta(\tau)
\end{align*}
\] (4.5)

where $\delta(\tau)$ is the Dirac delta function.

Rewriting Eq. (4.4) into a parametric dimensionless form, the motion in the $x$ and $y$ direction takes the form of a Langevin equation,

\[
\begin{align*}
\frac{d^2x}{d\tau^2} + b\frac{dx}{d\tau} + (a - 2q \cos 2\tau)x &= g(\tau) \\
\frac{d^2y}{d\tau^2} + b\frac{dy}{d\tau} - (a - 2q \cos 2\tau)y &= g(\tau)
\end{align*}
\] (4.6)

where $\tau = \Omega t / 2$ is a dimensionless scaled time, $a = 4QU / M\xi_0^2\Omega^2$ is the scaled DC voltage, $q = 2QV / M\xi_0^2\Omega^2$ is the scaled AC voltage, $b = 2\xi / M\Omega$ is the scaled damping coefficient, and $g(\tau)$ is the scaled thermal fluctuation force, following a Gaussian distribution with zero mean and standard deviation of $\sqrt{32k_BT\xi / M\Omega^2}$ [86].

It is worth noting that the geometry of the planar ACEP trapping devices is not an ideal linear Paul trap structure, which would require high aspect-ratios for the four electrodes [77]. However, 3D calculations (Figure 4.10) show that the analysis will not be affected significantly as long as the particle remains within the height of the electrodes. Above the electrodes, the potential changes as if the device radius $R_0$ is increased. As a result, we can deal with this non-ideal 2D situation by adopting an effective device radius $R_0^*$. Moreover, the potential profile of the ACEP trapping device is not exactly an ideal quadrupole field because of the existence of higher-order components. Taking these two effects into account, a correction factor $\Gamma$ should be introduced in the expression of $a$ and $q$. 
\[
\begin{align*}
    a &= \frac{4QU}{\Gamma MR^2 \tau^2} \\
    q &= \frac{2QV}{\Gamma MR^2 \tau^2}
\end{align*}
\] (4.7)

The solutions of Eq. (4.6) will determine the dynamics of particles inside the trap. As is well known for Paul traps in vacuum \((b = 0 \text{ and } g(\tau) = 0)\), stable trapping will only occur when parameters \((q, a)\) are within certain regions in the \(q - a\) diagram (where Eq. (4.6) has convergent solutions) [52].

![Electric Potential Distribution](image)

Figure 4.10 The electric potential distribution in \(x - z\) plane calculated for the real 3D geometry. (b) Comparison of the \(x\)-component potential for the real device with finite height (averaged over \(z\) from 0 to 1 \(\mu\)m) and an ideal 2D device at one instant of time \((t = 0)\).

If a viscous medium is present \((b > 0\), for example, air or water\), the stable region in the \(q - a\) diagram will not only be shifted but also be extended [87]. The deterministic damped Mathieu equation without taking thermal fluctuations into consideration reads as the
homogeneous part of Eq. (4.6) (with \( g(\tau) = 0 \)). With this deterministic system, the particles should settle towards the center of the device \((x = y = 0)\) and eventually be trapped without moving when time \( t \to \infty \) if the \((q,a)\) parameters are inside the stability region. This is clearly not the case experimentally, where positional fluctuations are observed (Figure 4.8).

The fluctuations of the trapped particles confirm the necessity to include the stochastic Brownian effect to study the ACEP trapping device. The questions that arise are how this white Brownian noise affects the stability of the trapping dynamics and the rms value of the position fluctuations. We will address these two aspects in the following discussion.

### 4.3.3 Brownian noise effect on trapping stability

Zerbe et al. [88] theoretically showed that the variance of position displacement fluctuations remains bounded for \((q,a)\) parameters that are located within the stability zones of the damped deterministic equation (Eq. (4.6) with \( g(\tau) = 0 \)). As a result, the trapping stability are solely determined by the behavior of the deterministic system and the Brownian noise would not affect the stability boundaries. The \((q,a)\) stability region for various damping factors \( b \) can be numerically determined using Hasegawa and Uehara's method [87]. It is thus very interesting to experimentally map out the stability boundary and compare it with the theoretical predictions.

The principal problem here is that, unlike atomic ions, the particles are neither identical in mass nor charge. Therefore, it requires that all points in stability boundary be derived from a specific single bead throughout the experiment. We are able to record each boundary point in \((V,U)\) coordinates successfully without losing the single trapped particle by carefully adjusting AC and DC voltages at a fixed frequency and by recognizing when the motion is on the verge of no longer being stable. Eq. (4.7) translates the measured boundary from \((V,U)\) coordinates into
$(q,a)$ coordinates by using a fitting parameter $Q/\Gamma M$ (effective charge to mass ratio), where $\Gamma$ is the correction factor mentioned above.

As shown in Figure 4.11, the resulting measured limits of the $(q,a)$ stability boundary reproduce the theoretical calculated boundary very well. This remarkable agreement between the theoretical boundary and experimental data strongly proves that the trapping dynamics are dominated by Paul trap mechanism (which is a ACEP effect), since a DEP trap would not have such a $(q,a)$ stability boundary.

Figure 4.11 Experimental points on the boundary curves of the stability diagram as observed from a single charged particle (experiments performed with a radius of $0.491 \pm 0.0065$ µm at a fixed frequency of 2 MHz). The solid line is the theoretically calculated stability boundary for an effective charge to mass ratio of $4 \times 10^6$ e/amu. The dimensionless damping coefficient $b=2.83$ is calculated by $b = 2\xi / M\Omega$, using known parameters.
Determination of boundary points becomes difficult for large $a$ values since this requires higher DC voltages, and we find experimentally that DC voltages beyond 2.2 V (corresponds to $a\approx1.34$ using $Q/GM$ as $4\times10^{-6}$ e/amu and $R_0$ as 4 $\mu$m will result in detrimental electrochemical reactions of the metal electrodes. Surface modifications or passivations of the electrodes may improve the tolerance of high DC voltages.

![Figure 4.12 Gaussian distribution of fitting $Q/GM$ for total 121 beads from the same solution. The mean value is $4.77\times10^{-6}$ e/amu and standard deviation is $1.95\times10^{-6}$ e/amu.](image)

By using the fitting techniques described above, we are able to evaluate the distribution of effective charge to mass ratio ($Q/GM$) for a collection of beads. We analyze a total of 121 beads from the same suspension solution and extract the $Q/GM$ for each single bead. Figure 4.12 shows a Gaussian distribution for extracted $Q/GM$, with a mean value of $4.77\times10^{-6}$
This value corresponds to around $10^6$ elementary charges on a single bead, which is two orders of magnitude lower than the number of carboxylate surface groups. This discrepancy may be due to the partial dissociation of carboxylate groups and the charge renormalization effect [61].

### 4.3.4 Brownian noise effect on rms fluctuations

Although the serial DC voltages ($U$) can be used to tune the trapping stability and thus the dynamics in the ACEP trapping devices (Figure 4.11), a pure AC field ($U = 0$) is experimentally favorable due to the obvious advantages of an AC over a DC electric field in solution. In particular, the detrimental electrochemical reactions can be avoided in AC fields (section 2.5.3). Thermal convection can also be suppressed because the heating effect of an AC field is less [50]. As a result, AC fields are of more practical interest in the context of aqueous solutions.

The rms fluctuation in the $x$ and $y$ directions for the AC only case ($a = 0$) can be expressed as [86],

$$\sqrt{\langle x^2 \rangle} = \sqrt{\langle y^2 \rangle} = \Theta I(b, q)$$  \hspace{1cm} (4.8)

in which

$$\Theta = \sqrt{\frac{16k_BT\xi}{M^2\Omega^3}}$$  \hspace{1cm} (4.9)

and $I(b, q)$ is a function of dimensionless parameters $b$ and $q$.

The rms fluctuations as a function of applied AC voltages ($V$) at a fixed frequency (2 MHz) observed in the experiment is given in Figure 4.13.
Figure 4.13 Dependence of the standard deviation of position fluctuations of trapped bead on AC voltage at fixed frequency.

\[ I(b, q) \text{ for small } q \text{ values can be approximated as } [85], \]

\[ I(b, q) = \sqrt{(4 + b^2)/4bq^2} \] \hspace{1cm} (4.10)

Note that the working parameter \( b \) and maximum possible \( q \) are calculated to be 2.83 and 0.604, respectively. Therefore the \( q \) values in the experiment can be considered small.

The rms fluctuations thus have the dependence on the AC voltage as \( \sqrt{\langle x^2 \rangle} = \sqrt{\langle y^2 \rangle} \propto 1/q \propto 1/V \) for a fixed frequency (fixed damping factor \( b \)) in small \( q \) region. The linear fitting curve in Figure 4.13 demonstrates a remarkable agreement with the predicted linear dependence of rms fluctuations on \( 1/V \).

This dependence is intuitively correct (stronger field gives a tighter trap). However, it is
not necessarily true for the whole AC voltage range. Theoretical studies showed that there always exists a minimal rms fluctuation if proper working parameters $q$ are chosen within the stability region [86]. By taking the experimental parameters as $f = 2$ MHz, $Q / \Gamma M = 4 \times 10^{-6}$ e/amu and $b = 2.83$, we can calculate that the minimal rms fluctuations corresponds to $q = 2.78$ and $V = 9$ V. This AC voltage is beyond our instrument's ability ($V_{\text{max}} = 5$ V) and therefore we only experimentally observe a decrease of rms fluctuations when increasing AC voltages within ranges we can achieve (Figure 4.9).

The rms fluctuation dependence on the driving parameters when $a = 0$ is theoretically studied in several works [86, 88-90]. The magnitude of the minimal fluctuation can be expressed as [86],

$$\delta_{\text{min}} = \sqrt{8k_B T / M \Omega^2}$$  \hspace{1cm} (4.11)

which is dependent only on the environment temperature $T$, the particle mass $M$ and the working frequency $\Omega$. This minimal fluctuation will happen under a situation of [86],

$$q = 0.759\sqrt{4 + b^2}$$  \hspace{1cm} (4.12)

The existence of such a minimum in the positional fluctuation of the stochastically confined motion is of considerable importance since one can significantly reduce the thermal noise effect on the positional uncertainty of the motion. It is noteworthy that the operating parameters ($q, a$) must be inside of the stability region to achieve this minimal fluctuation. The minimal fluctuation for the particle shown in Figure 4.9 would be 0.63 nm (with $M = 520$ fg and working frequency $f = 2$ MHz).

It is apparent from Eq. (4.11) that higher frequency can be adopted to suppress the
positional uncertainty to the greatest extent for the reduced $M$, if the parameters $q$, $a$, and $b$ are kept within the stability region. For example, for a 1k base-pair (bp) double strand DNA (650 Da/bp, charge to mass ratio $3\times10^{-3}$ e/amu), when the working frequency is increased to 442 MHz, the minimal achievable fluctuation is around 2 nm (close to the size of a physical nanopore [91-93]). By careful RF circuit design, this could be experimentally achievable. The practical limits of the confinement is, however, limited by the highest frequency that can be applied without causing detrimental heating or device damage.

### 4.3.5 Long-term trapping performance

![Figure 4.14](image)

Figure 4.14 Long-term trap stiffness for a single trapped bead (particle radius 491 nm and device size $R_0 = 4 \, \mu m$).

Since the solution conductivity directly affects the effective charge of the particle (see section 3.4.5), long-term measurements were carried out on a single trapped particle to
investigate the effect of the drift of solution conductivity on the trapping performances. We find that we can stably trap particles for a minimum of 4 hours (we did not explore longer), and over this time the trap stiffness \( k = k_B T / \delta^3 \) only changed by <3\% (Figure 4.14), indicating a stable solution conductivity during the 4-hour period.

### 4.3.6 Particle size dependence

As we discussed in section 3.4.4, the time averaged DEP force scales with the particle volume. As a result, the DEP trap stiffness will decrease as a function of particle volume. On the contrary, time averaged ACEP force can be estimated by Eq. (3.25). Instead of a simple dependence on the particle volume, the ACEP trap stiffness depends on the charge \( Q \) and mass \( M \) in a complex way.

We used the polystyrene beads with radius ranging from 240 nm to 1.1 \( \mu \)m. All of these beads are surface functionalized with carboxylate groups. Their sizes are well characterized while the surface charge density is undetermined. The surface charges do not necessarily scale with the surface area of the particle. The suspension solution is thoroughly washed using the same procedure described above. All the trap stiffness are extracted under the condition of \( V = 1.5 \) V, \( U = 0 \) V, and \( f = 2.5 \) MHz, using the device with the same size (8 \( \mu \)m between electrode tips). Figure 4.15 shows the measured trap stiffness as a function of the particle radius. As is shown, the trap stiffness does not scale with the particle volume (~\( a^3 \)). In fact, when the particle radius reduces from 0.491 \( \mu \)m to 0.24 \( \mu \)m, the trap stiffness increases from 4 pN/\( \mu \)m to 15.2 pN/\( \mu \)m. This strongly proves that the trapping mechanism cannot be due to the DEP effect, as one would expect a decrease of trap stiffness when decreasing the particle size. We note that the irregular dependence of the trap stiffness on the particle radius in Figure 4.15 comes from the
irregular $Q/M$ ratio for particles with different sizes.

![Figure 4.15 Trap stiffness as a function of the particle radius.](image)

**4.4 Quantum dots trapping**

After successful proof-of-principle demonstration of ACEP trapping of the larger polystyrene beads using the quadrupole devices with a tip-to-tip distance of 8 μm and with ordinary PDMS based microfluidics, we carried out experiments to investigate the possibility of trapping scaled particles (quantum dots with diameter down to 10 nm). This is to test the predictions in section 3.4.4.

The quantum dots we used are carboxyl quantum dots made from CdSe/ZnS core/shell materials with polymer coatings of COOH surface groups (Qdot®, Molecular Probes, Figure 4.16).
The device used to trap the 10 nm quantum dots is of 2 μm tip-to-tip distance. It is found in the experiments that the hydrodynamic force can easily surpass the electric force for quantum dots. Moreover, the imaging of quantum dots inside a thick PDMS chamber is very difficult. As a result, we designed a more advanced microfluidic system to enable the fluorescent imaging of the quantum dots. The efforts include: (1) a thinner PDMS wall to suppress the light diffraction, (2) a more reliable liquid delivery system that eliminates the internal hydrodynamic imbalance built inside the microfluidic channel, and (3) an on-chip channel. Figure 4.17 shows one of the devices with microfluidic channels integrated on chip.
Figure 4.18 Bundles of 10 nm quantum dots trapped in the center of the 2 um device. The dashed line is the electrodes profiles.

With these efforts, we have achieved the trapping of the 10-nm-diameter quantum dot bundles in the center of the device, as shown in Figure 4.18, even though the dynamics of each individual quantum dot cannot be analyzed. The difficulty to see the single particle dynamics is due to the following factors. (1) The refractive index mismatch on light propagation through diffusive layered media (water-PDMS-air-lenses). (2) The florescence is a point light source that can emit light onto the metal electrodes and gets reflected, giving the central trapping area a strong florescence background. (3) The photo bleaching makes the long-term observation very difficult.

4.5 Summary

In summary, we experimentally demonstrate the feasibility of a planar ACEP trap device, as theoretically predicted in Chapter 3. An oscillating quadrupole electric field generates a
pseudo-potential well and the charged particles are dynamically confined into nanometer scale region, whose size can be externally tuned by driving parameters. This technique opens up the possibility of spatially controlling the object in a liquid environment and can lead to lab-on-a-chip systems controlling single molecules which often appear charged when submerged in water.
Chapter 5 Field-effect reconfigurable nanofluidic ionic diodes

Unlike the AC electric field, a direct electric field-charge interaction is not possible beyond the Debye length, due to the electrostatic screening effect. Nanochannels, which have one dimension comparable to or smaller than the Debye length, possess an electrostatic potential that remains nonzero even in the center of the nanochannel. Thus, direct electrostatic control over the charged species in the nanochannel becomes possible. This chapter discusses the effort that uses this unique property in nanochannels to realize a field effect reconfigurable nanofluidic diode. The forward/reverse directions of the diode as well as the degrees of rectification can be regulated by the application of electric field. The electrostatic modulation offers a fully independent and digitally programmable approach for controlling the preferential conduction of ions and molecules in fluids. This device would also serve as a building block for large-scale integration of reconfigurable ionic circuits.

5.1 Introduction: phenomena in nanoscale channels

5.1.1 Potential profiles in nanochannels

With applications ranging from biosensing to the control of molecular transport, synthetic nanopores and nanochannels are the focus of growing scientific interest [94]. Nanochannels are channels with at least one dimension in the nanoscale, ranging from 1 to 100 nm. Besides the size related steric effects, one of the most important features in a liquid phase nanochannel is the
length scale between the Debye length and the channel size. Due to the electrostatic co-ion exclusion (see section 2.1.3), the electric potential at the surface decays to its bulk value over a characteristic length known as the Debye length. The Debye length ($\lambda_D$) decreases as the ion concentration, $n$, increases, $\lambda_D \sim n^{-1/2}$, and is typically 1-100 nm for aqueous solutions. In micrometer-sized channels, the Debye length is usually much smaller than the channel dimensions, and the bulk of the solution is shielded from the surface charge and possesses a zero potential. However, when the EDL thickness is larger than the channel size (e.g., nanoscale channels with low ionic strength), the EDL from the two surfaces will overlap in the channel and the potential will remain non-zero at the center of a channel. The potential distribution in the case of EDL overlapping in nanochannels with height $H$, under the Debye-Hückel approximation (low surface potential approximation, see section 2.1.3.2), is given by [22],

$$
\psi(y) = \frac{\zeta \cosh\left(\frac{(H / 2 - y)}{\lambda_D}\right)}{\cosh\left(\frac{H}{2\lambda_D}\right)}
$$

(4.13)

5.1.2 Permselectivity in nanochannels

Once we know the potential profile in the nanochannel with a characteristic dimension $H$, the local concentration for ion species $i$ inside the nanochannel can be determined by Boltzmann equation (Eq. (2.6)) as,

$$
n_i(y) = n_0 \exp\left(-\frac{z_i e \zeta \cosh\left(\frac{(H / 2 - y)}{\lambda_D}\right)}{k_B T \cosh\left(\frac{H}{2\lambda_D}\right)}\right)
$$

(4.14)

where $n_0$ is the bulk number density.

It can be easily calculated from Eq. (4.14) that excess of counter-ions will be present inside nanochannels at low ionic strength. This enrichment of counter-ions in and exclusion of co-ions
from a nanometer-sized channel due to electrostatic interactions with the surface charge is called
the exclusion enrichment effect [95]. When the exclusion and enrichment of ions occurs in the
nanochannels with low ionic strength, the local concentration of charged species is not
homogeneous in the cross section of the nanochannel (Eq. (4.14)). The exclusion-enrichment
coefficient $\beta_i$ for ion species $i$, which is defined as the ratio of the averaged ion concentration to
the bulk concentration, can thus be defined as [96],

$$
\beta_i = \frac{1}{h} \int_0^h \exp \left( \frac{-z_i e \zeta \cosh \left( \frac{(H - y)}{2 \lambda_D} \right)}{k_B T \cosh \left( \frac{H}{2 \lambda_D} \right)} \right) dy
$$

(4.15)

Eq. (4.15) shows the quantitative exclusion-enrichment coefficient depends on the Debye
length $\lambda_D$, the characteristic dimension of the nanochannel $H$, the $\zeta$ potential at the surface
and the charge valence of the ion $i$. It is easy to see that $\beta_i > 1$ for $z_i \zeta < 0$, which means the
counter-ion concentration get enriched (as compared to the bulk concentration) and $\beta_i < 1$ for
$z_i \zeta > 0$, which means the co-ion concentration get excluded (as compared to the bulk
concentration). This results in the permselectivity of the nanochannel.

### 5.1.3 Active control of permselectivity

One of the most important parameters in quantifying the exclusion-enrichment coefficient
is the $\zeta$ potential at the surface. The $\zeta$ potential can be altered by chemical modifications [97,
98]. A more elegant way to change the $\zeta$ potential is through an active control with field effect
[99, 100]. In the same way the electric field is used in MOSFETs to regulate the electron/hole
population in the silicon conductive channel, cation and anion population in the nanochannels
can thus be manipulated in a similar fashion. This principle has been used to realize ionic field
effect transistors [99-105].
5.1.4 Donnan potential

The phenomena above discuss the ions inside the nanochannel and far away from the nanochannel’s open end. In reality, an interface between the nanochannel and the adjacent electrolyte solution is inevitable. These two parts will reach *steady-state* when the Gibbs free energy in both of them is identical. This electrochemical equilibrium is referred to as the Donnan equilibrium [106, 107], which is obtained when a concentration difference of the ions between the two parts is compensated by an electrical potential difference. The Donnan potential is analogous to the built-in potential in semiconductor diodes.

The electrochemical potential $\Phi_i$ of ion $i$ at constant pressure and temperature for an ideal solution (activity coefficient is unity) can be expressed as (Eq. (2.3)),

$$\Phi_i = \phi_i^0 + RT \ln(c_i / c_0) + z_i F \psi$$  \hspace{1cm} (4.16)

where $\phi_i^0$ is the standard chemical potential of ion $i$, $R$ is the gas constant, $T$ is the temperature, $c_i$ is the *molar concentration* of ion $i$ [mole/L, or molar], and $c_0$ is the standard molarity of 1 molar. $F$ is the Faraday constant, $\psi$ is the electric potential. $z_i$ is the ion valence.

When the nanochannel ($N$) is in equilibrium with its adjacent bulk electrolyte solution ($B$), the electrochemical potential for both parts should be equal,

$$\phi_i^0 + RT \ln(c_i^B / c_0) + z_i F \psi^B = \phi_i^0 + RT \ln(c_i^N / c_0) + z_i F \psi^N$$  \hspace{1cm} (4.17)

As a result, the electric potential difference between the bulk electrolyte solution and the nanochannel region can be calculated as,

$$\psi^{NB} = \psi^N - \psi^B = \frac{RT}{z_i F} \ln\left(\frac{c_i^B}{c_i^N}\right)$$  \hspace{1cm} (4.18)
This potential difference is known as the Donnan potential.

5.1.5 Ionic current rectification

Analogous to a solid-state semiconductor diode for regulating the flow of electrons/holes to one preferential direction, nanofluidic diodes are being developed to achieve the rectified ionic transport - ions favorably move in one direction and are inhibited in the opposite direction. Such rectification effect is of great importance due to its relevance to biological ion channels [108]. Moreover, ionic diodes, together with ionic transistors [99-105] represent the key building blocks for ionic circuits [109, 110], which would allow for regulating [99], sensing [111], concentrating [112], and separating [113] ions and molecules in electrolyte solutions.

Several nanofluidic platforms based on nanopores and nanochannels were reported to produce ionic current rectification by symmetry breaking [114] in geometries [115-118], surface charge distributions (either intrinsic material properties [119, 120] or chemically modified properties [97, 98]), bath concentrations [121], or a combination of them, for example, by positively and negatively patterning charged regions in conical nanopores [122]. Nevertheless, it has not been possible to change the predefined rectifying properties obtained by these approaches once the devices are made. Although several externally tunable methods have been proposed so far, most of them aim to alter the nanochannel wall property by introducing external chemical stimuli, for example, hydronium ions (pH) [123-125], enzymes [126] and polyvalent cations [127]. All these methods require changing the native environment of the solution being transported.

Contrary to the chemical stimuli-responsive schemes, an electric field normal to the nanochannel walls is able to enhance or diminish the ionic concentrations near the surface in situ [99-105], resembling the carrier number modulation in a metal-oxide-semiconductor field effect
transistor (MOSFET). In the following, we are going to explore the possibility of using the field effects to achieve a reconfigurable ionic diode by asymmetrically modulating the cation/anion ratios along the nanochannel.

5.2 Device structure and fabrication

Figure 5.1 Device structure. (a) Schematic of the nanofluidic field effect reconfigurable diodes (FERD). (b) Sketch of the planar layout for the assembled device. Two microfluidic channels deliver the electrolyte solutions to the Cis and Trans reservoirs, formed by SiO₂ trenches with supporting pillars, as shown in the magnified scanning electron microscope (SEM) image. The scale bar in the SEM image is 100 µm. There are 11 parallel nanochannels connecting Cis and Trans reservoirs. The supporting pillars prevent the PDMS from collapsing into the reservoirs. (c) Schematic of the electrical and fluidic connection configurations. The electrical contacts are made of Ag/AgCl electrodes and are integrated with the connecting tubes, serving as a low resistive loss contact. $V_G$ and $V_C$ denotes the voltage on the gate and Cis, respectively. The Trans side is referenced as ground in all measurements in this study. The whole setup is placed in a Faraday cage to shield the electrostatic noise. (d) Photograph of a FERD device with electrical and fluidic connections.
The schematic structure of the nanofluidic field effect reconfigurable diodes (FERD) and the experimental setup is illustrated in Figure 4.1. The FERD is a three terminal device that has a similar structure to a nanofluidic field effect transistor (FET) [99, 100], yet with a critical difference that the gate electrode of FERD is asymmetrically located near one of the microfluidic reservoirs. To make a consistent notion in the following discussion, we denote the microfluidic reservoir that is close to the gate electrode as ‘Cis’ (C) and the other reservoir far away from the gate electrode as ‘Trans’ (T).

We used a sacrificial layer method to produce the nanochannels. Briefly, 11 thin Cr stripes are patterned on top of an insulating SiO₂ layer on a 4 inch silicon wafer. Then a dielectric SiO₂ layer (50-nm-thick) is subsequently deposited by plasma enhanced chemical vapor deposition (PECVD), followed by a rapid thermal annealing (RTA) process to improve the dielectric quality. Asymmetrically positioned gate electrode is thereafter formed by a double layer lift-off process. The control devices with gate electrodes sitting symmetrically along the nanochannel were also fabricated on the same silicon wafer. A thick SiO₂ capping layer is then deposited as the bonding surface between the device and the PDMS stamps. The accessing reservoirs with supporting pillars are etched simultaneously by reactive CHF₃/Ar plasma at a rate of 1 nm/s. The removal of the buried Cr sacrificial layer is a critical step in device fabrication. We have tried both the conventional ‘etch followed by bond’ approach and the ‘bond followed by etch’ approach. The end point detection for the etching process is done by looking at the color contrast under a microscope.
Figure 5.2 The current-voltage (I-V) curve for the device fabricated using ‘etch followed by bond’ scheme. The inset shows the etching process monitored under the microscope.

Figure 5.3 The current-voltage (I-V) curve for the devices fabricated using ‘bond followed by etch’ scheme. The inset shows the sacrificial layer etching process monitored under the microscope.
5.2.1 ‘Etch followed by bond’ approach

The conventional method etches the sacrificial layer first and then integrates the nanochannel device with a microfluidic interface to form a functional device [97, 121, 128]. In this approach, the diced devices are firstly immersed in a chrome etchant solution (Transene, type 1020) heated at 70 °C, and the etching process is monitored under a microscope. A total time of 90 min is enough to remove the entire Cr sacrificial layer (vertical lines in the inset image of Figure 5.2). After the Cr layer is etched away, the device is rinsed with de-ionized (DI) water and dried in an oven. After that the surface of both the device and the PDMS stamp are treated with oxygen plasma and they are bonded together. It is during this bonding process that a certain pressure is needed to press these two pieces together. After the device is integrated, we carry out experiments to see whether the nanochannel functions correctly. 1 M KCl solutions are introduced into the microchannels and the Cis to Trans current is measured as a function of Cis to Trans voltage (Figure 5.2). The measured current is in the order of pico-ampere (pA) and falls very short of the calculated current, which strongly implies a clogged nanochannel. The reasons for the nanochannel collapse may come from two factors, which are the capillary force in the drying process and the pressure exerted during the PDMS bonding process.

5.2.2 ‘Bond followed by etch’ approach

To overcome the collapse problem encountered in the ‘etch and bond’ approach, we develop a new scheme to remove the sacrificial layer. The diced device and the PDMS stamp are firstly treated with oxygen plasma. Then we bond these two pieces together. Connecting tubes are inserted into PDMS inlet and outlet ports. Subsequently, DI water is pumped along the microchannel to wet the Cis/Trans reservoirs. Then the chrome etchant (Transene, type 1020) is pumped along the microchannel and it diffusively etches the embedded sacrificial Cr layer in
The inset images of Figure 5.3 shows the etching process using this new approach. After the etching process being completed, DI water is flushed along the microchannels to rinse the channel. 1 M KCl solutions are introduced into the device and the I-V properties between the Cis and Trans reservoirs are tested (Figure 5.3). The measured current agrees very well with the calculated current. This confirms the success of the ‘bond followed by etch’ scheme. Since there is neither the drying process nor the external pressure applied, the ‘bond followed by etch’ scheme completely avoids the nanochannel collapse problem.

5.3 Nanochannel characterization

5.3.1 Physical characterization

The resulting microscopic view of the nanochannel is shown in Figure 5.4. The cross section of the nanochannel clearly shows the well-developed structure.

![Cross-section SEM image showing the resulting nanochannel.](image)

5.3.2 Electrical characterization

5.3.2.1 Setup
The functional device is wire bonded onto a printed circuit board (PCB) (Figure 5.1d). The Ag/AgCl electrodes are integrated with the connecting tubes, serving as a low resistive loss contact. The whole PCB board is housed inside a light-shielding metal box. The metal box has maximal four BNC connectors (for connection to Cis, Trans and Gate terminals) and four small holes for tubing entering. This setup minimizes the noise from the environment. The whole testing procedure is done using an automatic system. The solutions are delivered by pumps (New Era Pump Systems, Inc) which are controlled by a LabVIEW (National Instruments) program. The current-voltage (I-V) characteristics are measured using HP4156B semiconductor parameter analyzer (SPA).

5.3.2.2 Results

Figure 5.5 Electrical characterization of the nanochannel. (a) Schematic of the electrical connections, the gate terminal is floating, (b) Measured conductance as a function of KCl concentrations for two devices fabricated using the identical process on a same wafer with gate terminal floating (Blue: \( W = 33 \ \mu m, \ L = 100 \ \mu m, \ H = 20 \ \text{nm} \). Red: \( W = 22 \ \mu m, \ L = 100 \ \mu m, \ H = 20 \ \text{nm} \)). Solid lines are the fitting curves with \( \sigma_s = 2 \ \text{mC/m}^2 \). Dashed lines are the bulk prediction that deviates from the experimental data in the low ionic concentration region. The error bars correspond to 10 measurements and are smaller than the size of the symbol used.
We carried out experiments on the electrical characterization of the nanochannels with the gate terminal floating. By measuring the nanochannel conductance as a function of KCl concentration ($C_b$), we observed a linear dependence of channel conductance on $C_b$ in the high concentration regime and a conductance plateau in the low concentration regime (Figure 5.5b). The transition concentration is around 1 mM, at which the corresponding Debye screening length ($\lambda_D$) is around 10 nm, equal to half of the designed nanochannel height. This behavior confirms a surface charge governed ionic transport property [129, 130].

5.3.2.3 Determination of the surface charge density

The conductance of a nanochannel filled with KCl solutions is the superposition of the bulk conductance (section 2.1.5.1) and the double layer conductance (section 2.1.5.2),

$$G = e(\mu_k + \mu_{Cl}) C_b N_A W H / L + 2\mu_k \sigma_s W / L$$  \hspace{1cm} (4.19)

where $W$ [m], $L$ [m] and $H$ [m] are the width, length and height of the nanochannels, respectively. $\mu_k$ [m$^2$/(V·s)] and $\mu_{Cl}$[m$^2$/(V·s)] are the mobility of K$^+$ and Cl$^-$ ions. $C_b$ [mol/m$^3$] is the bulk concentration. $N_A$ [mol$^{-1}$] is the Avogadro constant, $e$[C] is the elementary charge. $\sigma_s$ [C/m$^2$] is the surface charge on the nanochannel walls. By knowing the dimensions of the lithographically defined channels ($W, L$), we can derive the value of $H$ in high concentration regime (bulk conductance part) and the value of surface charge $\sigma_s$ in low concentration regime (double layer conductance part) by fitting the experimental data.

We tested two individual devices fabricated on the same wafer but with different channel width $W$ (2 μm×11 and 3 μm×11, respectively) (Figure 5.5b). Both of them can be well fit by a same $\sigma_s$ (-2 mC/m$^2$), suggesting the surface properties remain consistent and reliable after the
‘bond followed by etch’ process. This \( \sigma_s \) value is close to those reported with the plasma enhanced chemical vapor deposition (PECVD) SiO\(_2\) (\( \sim \)4.5 mC/m\(^2\))\[119, 121\].

5.3.2.4 *Varying the surface charge by pH*

![Figure 5.6 pH dependence of channel conductance at two electrolyte concentrations ([KCl]=100 μM and [KCl]=100 mM). The pH of the electrolyte solution is adjusted by adding hydrochloric acid or potassium hydroxide into 100 μM phosphate buffers. The error bars correspond to 10 measurements.]

Since the surface charge can be modified by changing the solution pH (see section 2.1.1), we further tested the pH dependence of the nanochannel conductance at fixed KCl concentrations (Figure 5.6). At high KCl concentrations (100 mM), changing the pH value has negligible impact on the channel conductance, whereas at low KCl concentrations (100 μM), pH has a pronounced impact. This behavior can be well explained by surface charge governed transport property. At high ionic concentrations, the double layer conductance (which is regulated by pH values) is overwhelmed by the bulk conductance. Therefore, the channel conductance will not change by varying pH. At low KCl concentrations, the channel
conductance is dominated by the double layer and is thus pH-dependent. As $[\text{H}^+]$ for a given electrolyte concentration decreases, the number of SiO$^-$ surface charges increases [17].

### 5.4 Field effect reconfigurability

After verifying that the device conductance is indeed governed by the ion transport in the nanochannels (instead of leakage paths), we went on to investigate the field effect tunability of the three-terminal FERD devices using electrical configurations shown in Figure 5.7a. The channel current as a function of Cis to Trans voltage ($V_{CT}$) was measured under various gate voltages ($V_G$).

Figure 5.7b shows the representative current-voltage ($I-V$) curves obtained with $V_G$ of different polarities, using a 100 µM KCl solution. A clear gate voltage controlled rectifying property is observed. At $V_G=0$ (middle panel, Figure 5.7b), the $I-V$ curve is symmetric with respect to the origin. At a negative gate voltage (left panel, Figure 5.7b), the ionic current in the positive $V_{CT}$ regime is higher than that in the negative $V_{CT}$ regime. While at a positive gate voltage (right panel, Figure 5.7b), the negative $V_{CT}$ conducts more ionic current than the positive $V_{CT}$. Consequently, it is possible to switch the preferential direction of the ionic flow via adjusting the external gate voltage, a novel mechanism of nanofluidic control that has never been shown before.

To further confirm the role of the asymmetric positioning of the gate electrode on the rectifying properties of the device, we measured the $I-V$ characteristics of the control devices (with symmetrically placed gate electrodes), schematically shown in Figure 5.7c. The major structural difference between the FERD devices and the control devices is the location of the
gate terminal. No rectifying features are observed for the control device, which exhibits a symmetric $I-V$ relationship for all $V_G$ polarities (Figure 5.7d). The control device actually shows a typical p-channel transistor behavior, where the conductance of the nanochannel is modulated by the field effect. In a negatively charged SiO$_2$ nanochannel, cations are the majority carriers, which are expected to increase or decrease when subjected to negative or positive electrostatic potentials, respectively. Therefore, the channel conductance will be enhanced at a negative $V_G$ and suppressed at a positive $V_G$. From the comparison of the FERD and the control devices, we conclude that it is indeed the asymmetric positioning of the gate electrode that introduces the rectifying behavior, whose favorable direction is not fixed but switchable via a gate potential.

Figure 5.7 Current-voltage ($I-V$) curves for the FERD devices (top row) as well as the control devices (bottom row) with different gate voltage ($V_G$) polarities. (a) Testing configurations for the FERD device. (b) $I-V$ curves for FERD devices ($W=2 \ \mu m$, $L=100 \ \mu m$, $H=20 \ \text{nm}$) using a $100 \ \mu M$ KCl solution. An apparent gate voltage controlled rectifying property is observed. The inset symbols
schematically show the forward direction switched upon positive and negative gate voltages. (c) Testing configurations for the control transistor device. (d) $I-V$ curves for the control device ($W=3 \, \mu m \times 11$, $L=100 \, \mu m$, $H=20 \, nm$) using a 100 μM KCl solution. Gate voltage can modulate the channel conductance but no rectifying property is observed.

5.5 Qualitative analysis

![Diagram](image.png)

Figure 5.8 Schematic diagram of cation and anion fluxes under various conditions. The solid red and the empty blue bars represent cation and anion concentrations as well as the corresponding current flux. The length of the bars depicts their amount (not to scale). The resulting ion depletion or accumulation taking place in the center junction of the nanochannel at steady state can be obtained by comparing the amount of ion fluxes flowing into and away from the dashed box.

To understand the asymmetrical-gate controlled nanofluidic diodes, we developed a qualitative interpretation by looking at the change of the transient drift current of both cations and anions inside the nanochannel immediately after $V_{CT}$ bias is applied with different $V_G$ polarities (Figure 5.8). Since the ionic concentration distributions cannot change instantly, they
remain the same as the steady state during this transient period. As a result, the diffusion current is not considered. The solid and empty bars inside the nanochannels in Figure 5.8 correspond to the cation and anion concentrations, respectively. The length of the bars depicts the amount of the ionic concentration as well as the drift current (since the drift current is linearly proportional to the ionic concentrations). According to the Kirchhoff’s current law, the sum of currents flowing into any node should be equal to the sum of currents flowing out of that node, we get \( J_K^C - J_{Cl}^C = J_K^T - J_{Cl}^T \). Therefore the length sum of the two bars in each side of the channel should be equal.

When the gate potential is negative (upper row in Figure 5.8), the cation concentration immediately beneath the gate electrode is enhanced by the electrostatic attraction. With a negative \( V_{CT} \) (upper left panel, Figure 5.8), anions are driven towards the Trans side and the cations towards the Cis side, as indicated by the arrows. Under such a circumstance, the amount of the cation/anion flux flowing out of the center junction of the nanochannel is larger than that flowing into it. As a result, when the system reaches the steady state again, the ions in the channel center will be depleted, resulting in a depletion region with a lower conductance. Conversely, with a positive \( V_{CT} \) bias (upper right panel, Figure 5.8), the flow directions of the ions are reversed. More ions flow into the center junction of the nanochannel while fewer ions flow out. This causes an accumulation of ions in the nanochannel and hence an increase of steady state conductance. Therefore, rectification of ionic transport is established and the preferential ionic current flow direction is from the Cis side to the Trans side when \( V_g < 0 \).

When a positive gate voltage is imposed (lower row in Figure 5.8), the cation concentration near the Cis side of the nanochannel is reduced by the electrostatic repulsion.
Following the same analysis, it is obvious to conclude that a negative $V_{CT}$ conducts more ionic current than a positive $V_{CT}$ of the same magnitude. As a result, rectification of ionic current is also established, but the preferential ionic current direction is reversed as compared to the case of a negative gate potential.

### 5.6 Concentration dependence of the rectifying behavior

#### 5.6.1 Observations

Interestingly, the field effect reconfigurable rectifying behavior shows a strong dependence on ionic concentrations. We recorded the $I_{CT}$ as a function of $V_{CT}$ for $V_G$ ranging from negative to positive values at various KCl concentrations. The rectifying degree ($R = I_{+V} / I_{-V}$, where $V = 1.5$ V) is plotted as a function of $V_G$ (Figure 5.9). The voltage tunability of the FERD devices (i.e., the slope of the $R-V_G$ plot in Figure 5.9) becomes less prominent at both high and low KCl concentrations. With 1 M and 100 mM KCl solutions, no diode characteristics (asymmetric $I-V$ curve) were observed experimentally. The most pronounced voltage tunability happens at intermediate KCl concentrations (1 mM and 10 mM). The rectifying degree shows a monotonically decreasing dependence on $V_G$ when [KCl]<100 mM. Consequently, the forward direction of the nanofluidic diode can be electrically switched by the application of an external gate potential (inset symbols of Figure 5.9), consistent with the results in Figure 5.8.
Figure 5.9 Effect of the ionic concentrations on the rectifying degree under various gate potentials. The error bars correspond to 10 measurements. The inset symbols schematically show the forward direction switched with positive and negative gate voltages.

Another intriguing feature of Figure 5.9 is that, at a fixed gate voltage (e.g., -1.5 V), the highest rectifying degree occurs at the intermediate ion concentrations rather than the lowest concentration regime where surface charge governed ion conduction dominates. This counterintuitive phenomenon has also been observed in the systems of two terminal conical nanopore diodes [117], and nanochannel diodes [97, 119-121, 131]. However, a physical picture is lacking in understanding this behavior.

5.6.2 Physical model

Here we develop a physical model to explain these intriguing phenomena observed in our field effect controlled diodes, with the aim to improve the rectification ratios. Referring to a and considering the averaged concentrations of K$^+$ and Cl$^-$ ions at the two segments of the
nanochannel, we denote the relation in the gated area (subscript $C$) and the un-gated area (subscript $T$) as, $[K]_C = \gamma_C[Cl]_C$, and $[K]_T = \gamma_T[Cl]_T$, where $\gamma$ is the cation/anion ratio. The cation/anion ratio can be determined through the electroneutrality and the law of conservation of mass as (see Appendix section 5.10),

$$
\begin{align*}
\gamma_C &= (-s_C + \sqrt{s_C^2 + 4C_b^2})^2 / 4C_b^2 \\
\gamma_T &= (-s_T + \sqrt{s_T^2 + 4C_b^2})^2 / 4C_b^2
\end{align*}
$$

(4.20)

in which

$$
\begin{align*}
s_C &= (2\sigma_s - \varepsilon_0\varepsilon_{ax} V_g / d_{ax}) / ehN_A \\
s_T &= 2\sigma_s / ehN_A
\end{align*}
$$

(4.21)

$\varepsilon_{ax}$ and $d_{ax}$ are the permittivity and the thickness of dielectric SiO$_2$, respectively. By using the total current continuity at the micro/nano channel interfaces, we can obtain the ratios of cation (anion) flux via the Cis side over the cation (anion) flux via the Trans side of the nanochannel as (see Appendix in section 5.10),

$$
\begin{align*}
\rho_K &= J^{KC}_C / J^{KT}_T = 1 + \gamma_C^{-1} / 1 + \gamma_T^{-1} \\
\rho_{Cl} &= J^{Cl}_C / J^{Cl}_T = 1 + \gamma_C / 1 + \gamma_T
\end{align*}
$$

(4.22)

To observe a rectifying behavior, $\rho_K \neq 1$ and $\rho_{Cl} \neq 1$ are required in the nanochannels (i.e., the two solid bars, or the two empty bars in Figure 5.8 should be unequal in length). In fact, the further the value of $\rho_K$ and $\rho_{Cl}$ deviates from unity, the more pronounced is the rectification. Apparently, $\rho_K$ or $\rho_{Cl}$ is a function of $V_g$, $C_b$ and $\sigma_s$, which is plotted in Figure 5.10. At very high concentrations ( $C_b$ >100mM), the averaged ion concentrations in the nanochannel are
dominated by the bulk rather than the surface and hence are barely affected by the external potential. Therefore, $\gamma_c \sim 1$ and $\gamma_T \sim 1$ (bulk property), which results in $\rho_K = \rho_{Cl} = 1$ and no rectifying behavior would be observed. At very low concentrations ($C_b < 100\mu$M), we obtain $\rho_K \sim 1$ and $\rho_{Cl} \neq 1$. However, since $K^+$ is the majority carrier which dominates the total ionic flux, the rectifying effect is less significant. At intermediate concentrations ($C_b \sim 1$ mM), where $\rho_K \neq 1$ and $\rho_{Cl} \neq 1$, the most profound rectifying behavior is expected.

Figure 5.10 Calculated ratios of cation flux ($\rho_K$) and ratios of anion flux ($\rho_{Cl}$) via the Cis and Trans side of the nanochannel as a function of gate potential $V_G$ and bulk concentration $C_b$. The surface charge density used in the calculation is $\sigma_s = -2$ mC/m$^2$.

### 5.7 Improvement of the device performance

#### 5.7.1 Principles

The above analysis implies the strategies that can be adopted to improve the gate tunable
rectifying effect. Higher rectifying effect will happen when $\gamma_C \ll 1 \ll \gamma_T$ or $\gamma_T \ll 1 \ll \gamma_C$. For an intrinsically negatively charged nanochannel SiO$_2$ wall, it is obvious that $\gamma_T \gg 1$. To achieve $\gamma_C \ll 1$, the charge polarity beneath the gate electrode needs to be reversed, which requires $\varepsilon_0 \varepsilon_a V_g / d_{ox} > 2|\sigma_s|$. Take $\sigma_s = -2$ mC/m$^2$ for example, the minimal gate voltage required for charge polarity reversal is about 9 V. This is inaccessible in our current devices due to the gate leakage and breakdown limitations. However, if a surround-gate architecture (i.e., with both the top gate and the back gate) is used, the minimal gate voltage needed to reverse the charge polarity would be reduced by half. In addition, for a better control over cation/anion ratios, a low surface charge density is desirable. This is because an inherent high surface charge density in nanochannels resembles degenerate doping in a semiconductor or high surface state density of a FET, making the electrostatic control of the ionic concentrations in the nanochannel difficult [99]. By neutralizing the intrinsic surface charge through chemical modifications, it would allow for more efficient gate modulation in the Cis side. A separate gate on top of the Trans segment would further permit the cation/anion modulation in the Trans side. Therefore, by placing dual gate electrodes along the channel length, one can have more flexibility to tune the rectifying property via the dual gates. Moreover, reducing the nanochannel dimensions down to sub-10 nm would allow the diodes to function at a more realistic ionic concentrations (for example, physiological conditions, ~10-100 mM) [100].

In summary, an ideal structure for field effect reconfigurable nanofluidic diodes would be dual split-gates with a gate-all-around structure and a sub-10 nm nanochannels of a neutral surface.

### 5.7.2 Experiments
Figure 5.11 (a) SEM image of the dual split-gate FERD devices ($W=1 \mu m \times 11$, $L=116 \mu m$, $H=8 \text{ nm}$). The scale bar is 100 $\mu m$. The nanochannel wall is chemically modified to be less charged and hydrophilic. The separation between the two gates is 4 $\mu m$. (b) Testing configurations for the dual gate FERD device. (c) Measured conductance as a function of KCl concentrations for the nanochannel before and after surface modification. This dimensions for this nanochannel are $W=11 \mu m$, $L=116 \mu m$, $H=8 \text{ nm}$. The surface charge is reduced from an intrinsic value of -1.6 mC/m$^2$ to -0.3 mC/m$^2$ after the modification.

To experimentally verify these predictions, we fabricated another wafer of devices with a dual gate structure (Figure 5.11a and b) and an 8-nm-thick nanochannel (determined by the thickness of the sacrificial Cr layer). The surface charge of the as-fabricated nanochannel is estimated as $\sigma_s=-1.6 \text{ mC/m}^2$ (Figure 5.11c). This native surface charge density is reduced by sequentially treating the nanochannel wall with 3-Glycidoxypropyltrimethoxysilane (GPTS) and ethanolamine. The detailed procedure for reducing the native surface charge density is as follows:

1. Flushing the microchannel with ethanol (Sigma-Aldrich, category # 459836) for 3 hours.

2. Flushing the microchannel with 2% v/v 3-Glycidoxypropyltrimethoxysilane (GPTS)
3. Flushing the microchannel with 50 mM ethanolamine (Sigma-Aldrich, category # 411000) for 1.5 hours.

The resulting nanochannel surface is highly hydrophilic and the modified surface charge is estimated as $\sigma_s = -0.3 \text{ mC/m}^2$ (Figure 5.11c).

### 5.7.3 Results

With this surface modified dual gate device and an electrical setup schematically shown in Figure 5.11b, we recorded the $I_{CT}$ as a function of $V_{CT}$ for $V_G$ ranging from negative to positive values at various KCl concentrations. Figure 5.12a shows typical $I_{CT}$-$V_{CT}$ curves at different gate voltages $V_G$, for a given ionic concentration (1mM). The rectifying ratio ($R = I_{+V} / I_{-V}$, where $V = 1 \text{ V}$) is plotted as a function of $V_G$ for seven different KCl concentrations (Figure 5.12b). The dual gate device with the chemically modified surface shows a tremendously improved rectification ratio. At $V_G = -1 \text{ V}$, the rectification ratio reaches ~83 for 1mM KCl, much higher than that of the single gate device shown in Figure 5.7a (a ratio of ~1.2 under the same conditions). We note that the rectification ratio can be even higher under larger reference $V_{CT}$ biases. Interestingly, the dual gate device also exhibits a higher rectifying degree at the intermediate ion concentrations under a fixed gate voltage (e.g., $V_G = -1 \text{ V}$ in Figure 5.12b).
Figure 5.12 Improved field effect tunability over the ionic diode property with devices of a dual split-gate structure. (a) Typical $I_{CT} - V_{CT}$ curves at different gate voltages $V_G$ (-1 V, 0 V, +1 V), for a given ionic concentration (1 mM). (b) Measured rectifying degree (referenced at $V_{CT} = \pm 1$ V) as a function of $V_G$ for KCl concentrations ranging from 1 μM to 1 M.

### 5.8 Quantitative analysis

The steady state distributions of the cation/anion concentration and the ionic current under different $V_G$ and $V_{CT}$ biases are calculated by solving the coupled 2D Poisson-Nernst-Planck (PNP) equations within the COMSOL script environment.

#### 5.8.1 Simulation system
Figure 5.13 shows the system that we use in the simulation. We use three modules in the COMSOL environment: Electrostatics (AC/DC Module), Nernst-Planck without electroneutrality for calculation of K\(^+\) ions (Chemical Engineering Module) and Nernst-Planck without electroneutrality for calculation of Cl\(^-\) ions (Chemical Engineering Module).

![Simulation system](image)

Figure 5.13 Simulation system used in the numerical calculation. It contains an 8-µm-long, 20-nm-high nanochannel (domain 3) connected by two 1×1 µm\(^2\) square reservoirs (domain 1 and 2). In addition, there is a SiO\(_2\) dielectric domain (domain 4) which is 50-nm-thick and 4-µm-long. The length of the nanochannel used for calculation is less than the real device (100 µm) in order to reduce the simulation time. Note the figure is not drawn to scale.

### 5.8.2 Governing equations

The quantitative analysis of the ion transport through the nanopores and nanochannels is generally calculated by concurrently solving the coupled Poisson, Nernst-Planck, and Navier-Stokes equations [132-136]. Since the contribution of electro-osmosis is usually very small compared to the diffusive components, the Navier-Stokes equations can be neglected [131, 136]. We calculated the steady state distributions of cation/anion concentrations by self-consistently solving the coupled Poisson-Nernst-Planck (PNP) equations. In order to take into account the field effect arising from the externally imposed gate potential, the electric potential inside the gate dielectric is also solved simultaneously.
The governing equations and the corresponding boundary conditions are listed as follows (Table 5.1 summarizes all the parameters used in the simulation),

5.8.2.1 **Electrostatics**

(1) Governing equations (Poisson equation):

For domain 1, 2 and 3:

$$\varepsilon_0 \varepsilon_m \nabla^2 V = -\sum_i F_{z_i} e_i$$  \hspace{1cm} (4.23)

For domain 4:

$$\varepsilon_0 \varepsilon_{SiO_2} \nabla^2 \varphi = 0$$  \hspace{1cm} (4.24)

(2) Boundary conditions:

The Dirichlet boundary condition is used for the potentials at the ends of the two reservoirs, \(V(x = -5\mu m) = V_C\) and \(V(x = 5\mu m) = V_T\). The gate electrode (top side of domain 4) has Dirichlet boundary condition as \(V = V_G\). Neumann boundary conditions are applied for all the other reservoir walls, \(-\varepsilon_0 \varepsilon_w n \cdot \nabla V = 0\). The nanochannel walls which are not in contact with the gate dielectric have the boundary condition as \(-\varepsilon_0 \varepsilon_n n \cdot \nabla V = \sigma_x\). The Neumann boundary condition is imposed on the interface between the gate dielectric and nanochannel as

\[-\varepsilon_0 \varepsilon_w n \cdot \nabla V + \varepsilon_0 \varepsilon_{SiO_2} n \cdot \nabla \varphi = \sigma_x.\]

5.8.2.2 **Steady state Nernst-Planck equation for either K⁺ or Cl⁻**

(1) Governing equations:

For domain 1, 2 and 3:
\[ \nabla \cdot N_i = \nabla \cdot (-D_i \nabla c_i - z_i u_i c_i \nabla V) = 0 \quad (4.25) \]

For domain 4: inactive.

(2) Boundary conditions:

The Dirichlet boundary condition is used for the ionic concentrations at the ends of the two reservoirs, \( c_i(x = \pm 5 \mu m) = C_b \). The normal ionic fluxes through all the other walls are set to be zero, \( n \cdot N_i = 0 \).

### 5.8.3 Current and concentration extraction

After solving the coupled PNP equations, the ionic concentration and potential distributions can be extracted. The resulting ionic current \( J_i \) of \( i^{th} \) species through the nanochannel can be integrated as,

\[ J_i = \int z_i F N_i dS \quad (4.26) \]

where \( S \) is a cross-sectional area of the nanochannel. The total ionic current can thus be obtained as,

\[ J = \sum_i J_i \quad (4.27) \]

The averaged \( K^+ \) and \( Cl^- \) concentrations along the \( x \) direction is calculated by,

\[ < c_i(x) > = \int_{y=-H/2}^{y=H/2} c_i(x, y) dy / H \quad (4.28) \]

where \( H \) is the channel height.
Table 5.1 Parameters used in the numerical simulation.

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<th>Value</th>
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<tr>
<td>$N_i$</td>
<td>Mass flux density of $i^{th}$ species</td>
<td></td>
<td>mol/(m$^2$·s)</td>
</tr>
<tr>
<td>$u_i$</td>
<td>Ionic mobility of $i^{th}$ species</td>
<td>7.62e-8 ($K^+$) 7.92e-8 ($Cl^-$)</td>
<td>m$^2$/(V·s)</td>
</tr>
<tr>
<td>$V$</td>
<td>Potentials in the liquid</td>
<td></td>
<td>V</td>
</tr>
<tr>
<td>$V_C$</td>
<td>Potential in the Cis reservoir</td>
<td></td>
<td>V</td>
</tr>
<tr>
<td>$V_T$</td>
<td>Potential in the Trans reservoir</td>
<td></td>
<td>V</td>
</tr>
<tr>
<td>$V_G$</td>
<td>Gate potential</td>
<td></td>
<td>V</td>
</tr>
<tr>
<td>$z_i$</td>
<td>Charge number</td>
<td>+1 ($K^+$), -1($Cl^-$)</td>
<td>No unit</td>
</tr>
</tbody>
</table>

5.8.4 Results

The calculated concentration profiles under different $V_G$ and $V_{CT}$ polarities are shown in
Figure 5.14. The quantitative steady state ion profile agrees well with the qualitative transient analysis in Figure 5.8. The ion enrichment and depletion effect at the micro/nano channel interface [112] is also observed in the calculated results ($x = \pm 4\mu m$). This entrance effect only contributes a small portion of the total conductance and is not responsible for the field effect tunable rectifying property.

The qualitative trend that the tunable rectifying property is most prominent at intermediate ion concentrations and weakened at both low and high ionic concentrations is also observed in the numerical calculations (Figure 5.15).

Figure 5.14 Quantitatively calculated steady state profiles of the ion concentrations along the channel length under different $V_{CT}$ and $V_{G}$ polarities at 1 mM KCl. The averaged $K^+$ and Cl$^-$ concentrations is calculated by Eq. (4.28). The surface charge density used in the calculation is $\sigma_s = -2$ mC/m2.
Figure 5.15 Normalized nanochannel conductance ($\frac{G}{G_{\text{max}}}$) as a function of $V_G$ and $V_{CT}$ for various bulk concentrations ($C_b$). The inset lines are the rectifying ratio at $V_{CT}=\pm 2$ V. The asymmetry of the surface plot about the $V_{CT}=0$ V indicates a rectifying property. It can be seen that the gate voltage tunable rectifying property is most prominent at intermediate ion concentrations (e.g. 1 mM and 10 mM), and is weakened at both low and high ionic concentrations.

5.9 Summary

In conclusion, we proposed and demonstrated a field effect reconfigurable nanofluidic diode based upon an asymmetric field effect. This general concept could conceivably be applied to similar thin-body solid-state devices (e.g., silicon-on-insulator or semiconducting nanowires). Compared to any existing nanofluidic control systems including stimuli-responsive tuning, the electrostatic modulation platform offers the full potential for logical programming of rectified transport of ionic and molecular species. Unlike the nanofluidic field effect transistor, where only the amount of ions/molecules is regulated by an electrostatic potential, the FERD can be used to control both directions and magnitudes of ion/molecule transport. FERD represents a
fundamentally novel system and may function as the building block to create an on-demand, reconfigurable, large-scale integrated nanofluidic circuits for digitally-programmed manipulation of biomolecules such as polynucleotides and proteins.

5.10 Appendix: Derivations of $\rho_K$ and $\rho_{Cl}$

For the un-gated area (subscript $T$), according to the charge neutrality condition, we can obtain,

$$[K]_r - [Cl]_r = \frac{2\sigma_s}{ehN_A} \tag{4.29}$$

According to the law of the conservation of mass, we obtain the other relationship,

$$[K]_r [Cl]_r = C_b^2 \tag{4.30}$$

Therefore, the averaged cation/anion concentrations under the un-gated area can be determined as,

$$\begin{cases} 
[K]_r = \frac{s_T}{2} + \sqrt{\left(\frac{s_T}{2}\right)^2 + C_b^2} \\
[Cl]_r = \frac{s_T}{2} + \sqrt{\left(\frac{s_T}{2}\right)^2 + C_b^2}
\end{cases} \tag{4.31}$$

in which

$$s_T = 2\sigma_s / ehN_A \tag{4.32}$$

is the surface charge concentration. As a result,

$$\gamma_T \equiv \frac{[K]_r}{[Cl]_r} = \frac{(-s_T + \sqrt{s_T^2 + 4C_b^2})^2}{4C_b^2} \tag{4.33}$$

For the gated area, it is reasonable to assume that all the gate voltage is dropped on the gate dielectric. According to the charge neutrality condition, we can get,
\[
[K]_c - [Cl]_c = \frac{2\sigma_s - \varepsilon_0 \varepsilon_{SiO_2} V_g / d_{SiO_2}}{ehN_A}
\]  
(4.34)

By applying the law of the conservation of mass, we obtain,

\[
[K]_c [Cl]_c = C_b^2
\]
(4.35)

Therefore, the averaged cation/anion concentrations under the gated area can be determined as,

\[
\begin{align*}
[K]_c &= \frac{s_c}{2} + \sqrt{\left(\frac{s_c}{2}\right)^2 + C_b^2} \\
[Cl]_c &= \frac{s_c}{2} + \sqrt{\left(\frac{s_c}{2}\right)^2 + C_b^2}
\end{align*}
\]
(4.36)

where

\[
s_c = \frac{2\sigma_s - \varepsilon_0 \varepsilon_{SiO_2} V_g / d_{SiO_2}}{ehN_A}
\]
(4.37)

As a result,

\[
\gamma_c \equiv \frac{[K]_c}{[Cl]_c} = \frac{(-s_c + \sqrt{s_c^2 + 4C_b^2})^2}{4C_b^2}
\]
(4.38)

According to the total current continuity at the micro/nano channel interfaces in the Trans side, we obtain,

\[
J_T^K - J_T^{Cl} = J_{TBluk}^K - J_{TBluk}^{Cl}
\]
(4.39)

\(J_{TBluk}^K\) and \(J_{TBluk}^{Cl}\) is the K\(^+\) and Cl\(^-\) current flux in the Trans reservoir and can be assumed to have the relation of \(J_{TBluk}^K = -J_{TBluk}^{Cl}\) because of an equal K\(^+\) and Cl\(^-\) concentration and a similar K\(^+\) and Cl\(^-\) mobilities in the bulk. Moreover, it is easy to see that in the nanochannel, \(J_T^K / J_T^{Cl} = -[K]_T / [Cl]_T = -\gamma_T\), therefore,
Similarly, we get the following relationship at the interface of Cis reservoir and the nanochannel,

\[
\begin{align*}
\frac{J^K_T}{J^K_{Bulk}} &= 2 \left(1 + \gamma_T^{-1}\right) \\
\frac{J^{CI}_T}{J^{CI}_{Bulk}} &= 2 \left(1 + \gamma_T^{-1}\right)
\end{align*}
\tag{4.40}
\]

It is easy to see that \(J^K_{Bulk} = J^K_{C_{Bulk}}\) and \(J^{CI}_{Bulk} = J^{CI}_{C_{Bulk}}\). Therefore, we can obtain the ratios of cation (anion) flux via the Cis side over the cation (anion) flux via the Trans side of the nanochannel as,

\[
\begin{align*}
\rho_K &= \frac{J^K_C}{J^K_T} = \frac{1 + \gamma_C^{-1}}{1 + \gamma_T^{-1}} \\
\rho_{CI} &= \frac{J^{CI}_C}{J^{CI}_T} = \frac{1 + \gamma_C}{1 + \gamma_T}
\end{align*}
\tag{4.42}
\]
Chapter 6  

Exitable artificial solid-state ion channels

In Chapter 5, we have discussed the horizontal ion transport through the nanochannel under the influence of a voltage gradient. This chapter will discuss a second kind of driving forces, which is the concentration gradient. This is inspired by the membrane potential phenomena in the cells, where ion channels are embedded. Biological ion channels are molecular devices that allow for a rapid flow of ions across the cell membrane. Normal physiological functions, such as generating action potentials for cell-to-cell communication, are highly dependent on ion channels that can open and close in response to external stimuli. Mimicking these biological functions using synthetic structures is a rapidly progressing yet challenging area. This chapter presents the field effect modulation of the membrane potential in mechanically and chemically robust solid-state ion channels, an abiotic analogue to the voltage-gated ion channels in living systems.

6.1 Introduction

Construction of protocells (artificial cells with a minimum set of components to reproduce one or several cell functions) provides a novel platform to understand the complex biological-physical-chemical processes in a living biological cell. The most indispensable components in constructing protocells are the cell membranes in which ion channels are embedded to facilitate chemical and electrical communication with the extracellular environment.
Most of the work so far has used soft materials such as phospholipids and polymersomes to implement the ion channel elements [139, 140]. Although these soft materials are native relatives to living cell membranes and have proved to be very useful for a range of interesting experiments [109], they exhibit a number of disadvantages such as limited stability under various pH, salt concentration, temperature and mechanical stress conditions. Fabrication of the membranes from solid-state materials presents obvious advantages over their soft matter counterparts, such as very high stability, adjustable surface properties and the potential for integration into devices and networks. Indeed, development of mechanically and chemically robust solid-state nanopores [141] and nanochannels [3] has already been a rapidly growing area of research due to various practical applications, such as single molecule sensors [142], energy conversion [7] and desalination [113].

One of the most important characteristics in biological ion channels is its selectivity, which allows only specific kind of ions to pass through. The mechanism by which many biological channels achieve selectivity is on the molecular level. For example, in voltage-gated ion channels [143], a conformational change will be initiated when the proteins bearing charged amino acids inside the ion channel relocates upon changes in the transmembrane electric field. Direct implementing physical conformational variation in solid-state platforms is a daunting task [144]. Instead, the electrostatic interactions, described by Poisson-Nernst-Planck equations [133, 136, 145], are widely used to achieve the charge selectivity in solid-state structures [103, 146].

Inspired by the action potential generation behavior in voltage-gated ion channels, we here propose and demonstrate a solid-state protocell built from top-down fabricated artificial solid-state ion channels (ASIC), whose membrane potential can be modulated by an orthogonal electric field. Previous experimental studies in solid-state nanochannels have considered almost
exclusively the voltage driven phenomena, that is, the passage of ions through the nanochannels upon a potential gradient (i.e., the current-voltage relationship [109, 141, 146, 147], like the case we discussed in Chapter 5). The membrane potential phenomenon, essentially an open circuit and concentration driven process, has been barely investigated in artificial ion channel systems [7, 9, 139]. This study adds another dimension to the unique properties of the regulated selective ion transport through a nanoscale channel.

6.2 Device structure

The protocell we envision to reproduce the membrane potential phenomena in biological cells (Figure 6.1a) is schematically shown in Figure 6.1b. It is a three terminal device that is similar to a nanofluidic field effect transistor (FET) [103, 146], except that the longitudinal driving force is a concentration gradient instead of a potential gradient. Note that the gate terminal covers the entire nanochannel region.

It is well known that biological voltage-gated ion channels consist of three basic parts: a voltage sensor, a conducting pathway and a gate that can physically open/close [143]. The protocell device (Figure 6.1b) has all these functional components. The capacitor between the stimulation gate and the nanochannel provides a mechanism for voltage sensing. The electrostatic potential inside the nanochannel forms a virtual potential gate, regulating the ion permeability through the nanochannel (conducting pathway). The orthogonal electric field, produced by the stimulation voltage ($V_s$), is expected to mediate the ionic selectivity through electrostatic principles.

Standard micro-processing techniques are used to fabricate the protocell devices (Figure 6.1c). A same sacrificial layer removal method with a ‘bond followed by etch’ scheme is utilized
to reliably produce the nanochannels (Figure 6.1d). The device fabrication is similar to those described in section 5.2.

Figure 6.1 Device principles and experimental setup. (a) Schematic of typical intracellular and extracellular fluid with different ionic concentrations. The cell is in a charge polarization state due to the selective ion transport in ion channels, bringing about a resting membrane potential. (b) Cross-section sketch of the solid-state protocell. A stimulation voltage normal to the nanochannel walls (step 1) alters the ion selectivity in the nanochannel (step 2), resulting in a modulated transmembrane potential ($\Delta V_{ct}$) (step 3). (c) Sketch of the planar layout for the assembled device. Two microfluidic channels pump the electrolyte solutions to the cis and trans reservoirs, formed by SiO$_2$ trenches with supporting pillars (preventing PDMS collapse), as shown in the magnified scanning electron microscope (SEM) image. (d) Cross-section SEM image showing a single solid-state ion channels with a height of 17 nm and a width of 1 $\mu$m.

6.3 Quasi-static behavior
6.3.1 Working principle

The steady-state membrane potential $\Delta V_{ct}$ developed across an ion selective membrane (Figure 6.1b) can be described by [148],

$$\Delta V_{ct} = (2t^+ - 1) \frac{RT}{F} \ln \frac{[trans]}{[cis]}$$

(5.1)

Where $R$, $T$, and $F$ are universal gas constant, absolute temperature and Faraday constant, respectively. $[x]$ denotes the salt concentration in the $x$ side ($x=$cis or trans). $t^+$ is the cation transport number, that is, the ratio of cations to all ions in the channel.

With increasing $V_s$, cation/anion concentration will be diminished/enhanced accordingly. Therefore $t^+$ is a monotonic decreasing function of $V_s$, bounded within 0 and 1 (Figure 6.2). The stimulation voltages at which $t^+ \rightarrow 1$ (pure cation selectivity), $t^+ = 1/2$ (no selectivity) and $t^+ \rightarrow 0$
(pure anion selectivity) is defined as $V_{sp}$, $V_N$ and $V_{sn}$, respectively (Figure 6.2). By modulating the steady-state $t^+$ through stimulation voltage $V_s$, it is therefore feasible to modulate the membrane potential $\Delta V_{ct}$.

### 6.3.2 Experimental results

We first carried out quasi-static experiments to verify the above working principles. It is worth noting here that for the measurement shown in Figure 6.1b, one cannot ignore that each Ag/AgCl probing electrode is in contact with solutions of different concentrations and therefore they bear different electrode/electrolyte potentials [139, 149]. The measurement gives the potential difference of the whole cell from which the electrode potential difference must be subtracted in order to obtain the intrinsic $\Delta V_{ct}$ value (Figure 6.3). All $\Delta V_{ct}$ values presented in this study are after this electrode potential difference correction, unless otherwise noted.

Figure 6.4 exhibits the steady-state $\Delta V_{ct}$ as a function of $V_s$ at low salt concentration conditions, with the device of a reduced surface charge density ($\sigma_s$) as -0.28 mC/m$^2$ (Using the same surface modification technique as discussed in section 5.7.2). Figure 6.4 reveals a set of informative features as predicted by Eq. (5.1). No membrane potential appears if there is no cis-trans concentration gradient. When $[\text{cis}] < [\text{trans}]$, $\Delta V_{ct}$ exhibits the same trend as $t^+$, while for $[\text{cis}] > [\text{trans}]$, the trend between $\Delta V_{ct}$ and $t^+$ becomes opposite. Moreover, $\Delta V_{ct}$ can be modulated into different polarities, thanks to $t^+ > 1/2$ when $V_s = -1.5$ V and $t^+ < 1/2$ when $V_s = 1.5$ V (the $V_{sp}$, $V_N$ and $V_{sn}$ value can be extracted from the measurements as -0.15 V, 0.64 V and 1.25 V, respectively).
Figure 6.3 Schematic of the potential profiles in the system of a nanochannel connected by two solutions with different concentrations, probed by Ag/AgCl electrodes. Each Ag/AgCl probing electrode is in contact with solutions of different concentrations and therefore they bear different electrode/electrolyte potentials, shown as $V_{e,c}$ and $V_{e,t}$. The electrical setup measures necessarily the potential difference of the whole cell ($\Delta V_{ct,measured}$, red arrow bar) from which the electrode potential difference must be subtracted in order to obtain the $\Delta V_{ct,intrinsic}$ value (blue arrow bar).

Figure 6.4 Steady-state results in the low salt concentration regime with the device of $\sigma_s$=-0.28 mC/m².

Each $\Delta V_{ct}$ is recorded 5 seconds later after applying $V_s$. 
The quasi-static $\Delta V_{ct}$ modulation is also salt concentration dependent. The red squares in Figure 6.5 show the steady-state $\Delta V_{ct}$ - $V_s$ relationships for [trans] ranging from 10 $\mu$M to 1 M and [cis] fixed at 10 $\mu$M, using the same device of $\sigma_s = -0.28$ mC/m$^2$. As can be seen, when increasing the trans concentration, it is harder and harder to experimentally access the $V_{sp}$ and $V_{sn}$ voltages because of the smaller Debye length compared with the nanochannel dimensions, leading to a situation where creating a unipolar ion environment becomes impossible. The $V_N$ values can be extracted from the $\Delta V_{ct} = 0$ point, which gives the same value of 0.64 V.

![Figure 6.5 Salt concentration dependence of the quasi-static modulation for $\sigma_s = 0.28$ mC/m$^2$ (red squares) and for $\sigma_s = -1.6$ mC/m$^2$ (blue triangles). The legend denotes [cis]/[trans] conditions. The modulation efficiency ($d \Delta V_{ct} / dV_s$) decreases tremendously in highly charged nanochannels.](image)

Another factor that affects the quasi-static behavior is the surface charge density on the nanochannel walls. The blue triangles in Figure 6.5 present the results for the device with $\sigma_s = -1.6$ mC/m$^2$ (determined using the same techniques as shown in section 5.3.2.3). With such a high negative surface charge, the nanochannel is dominated by cations ($i^+ > 1/2$), since $V_s$ within $\pm 1.5$ V is too small to reverse the charge polarity (the smallest absolute $V_s$ required to reverse is approximately $2\sigma_s d_{ax} / \varepsilon_0 \varepsilon_{ax}$, which is around 4.7 V for $\sigma_s = -1.6$ mC/m$^2$ and $d_{ax} = 50$ nm). As a
result, \( \Delta V_{ct} \) can only be modulated within the positive range for \([\text{tans}]>[\text{cis}]\) (Eq. (5.1)). The maximum modulation range of \( \Delta V_{ct} \) in \( \sigma_s = -1.6 \text{ mC/m}^2 \) is much less than that in \( \sigma_s = -0.28 \text{ mC/m}^2 \), when \( V_s \) ranges from -1.5 V to 1.5 V. This inefficient modulation in the high surface charge density sample is due to the same reason as we discussed in section 5.7. Therefore, a nanochannel with lower surface charge density is favorable for an efficient modulation of \( \Delta V_{ct} \).

A thorough quasi-static \( \Delta V_{ct} - V_s \) measurement at various \( \text{cis} \) and \( \text{trans} \) concentrations (ranging from 10 \( \mu \text{M} \) to 1 M, respectively) are performed for devices with high and low surface charge densities (Figure 6.6).

Figure 6.6 Quasi-static modulation of \( \Delta V_{ct} \) through stimulation voltage \( V_s \) for \( \text{cis} \) and \( \text{trans} \) concentrations ranging from 10 \( \mu \text{M} \) to 1 M (KCl). (a) Results on the as-fabricated device with intrinsic \( \sigma_s \) as -1.6 mC/m\(^2\). The test is done using a device with channel length \( L = 116 \text{ mcm} \), and width \( W = 11 \text{ mcm} \). After applying each \( V_s \) (ranging from -1.5 V to 1.5 V, with step 50 mV), \( \Delta V_{ct} \) is recorded 5 seconds later for the system to reach its equilibrium state. A clear regulation of \( \Delta V_{ct} \) through \( V_s \) is observed, especially for some combinations of \([\text{cis}]\) and \([\text{trans}]\). (b) Results on the surface-modified device with
reduced $\sigma_s$ as -0.28 mC/m². The general features are similar to the native device. However, the dynamic range of $\Delta V_{ct}$ can now be modulated into different polarities.

### 6.3.3 Theoretical results

#### 6.3.3.1 Teorell–Meyer–Sievers (TMS) model

Teorell–Meyer–Sievers (TMS) theory deals with the ion transport through a membrane consisting of a matrix of fixed charges [150-152]. It states that the total membrane potential is equal to the sum of two Donnan potentials (see section 5.1.4) at the membrane boundaries and a Nernst-Planck diffusion potential within the membrane, which can be expressed as [151],

$$\Delta V_{ct} = V_c - V_t = \frac{RT}{F} \ln \frac{R_C}{R_T} + \frac{RT}{F} \gamma \ln \frac{C_t(R_C D_C + R_T^{-1} D_T)}{C_c(R_C D_C + R_T^{-1} D_T)} \tag{5.2}$$

where $R$, $T$, and $F$ are universal gas constant, absolute temperature and Faraday constant, respectively.

In the Donnan potential component, $R_x$ is the Donnan ratio at the nanochannel/micro reservoir interface in the $x$ side ($c$: cis side, $t$: trans side) and can be expressed as,

$$R_x = -s / 2C_x + \sqrt{1 + (s / 2C_x)^2} \tag{5.3}$$

where $C_x$ is the micro reservoir concentration in the $x$ side, $s$ is the ionic concentration in the nanochannel and can be expressed as

$$s = \frac{2\sigma_s + \varepsilon_0 \varepsilon_m V_s / d_{ex}}{eHN_A} \tag{5.4}$$

in which $\sigma_s$ is the surface charge density, $H$ is the nanochannel height, $\varepsilon$ and $d$ is the
dielectric constant and thickness, respectively, $V_s$ is the stimulative voltage, and $N_A$ is the Avogadro constant.

In the diffusion potential component, $\gamma$ reflects the diffusion coefficient differences between the cations and the anions,

$$\gamma = \frac{D_+ - D_-}{D_+ + D_-}$$  \hspace{1cm} (5.5)$$

where $D_+$ and $D_-$ is the diffusion coefficient of the cations and anions, respectively. By knowing all the parameters, it is able to calculate the $V_s - \Delta V_{ct}$ relation from the TMS model. It needs to be noted that the TMS model assumes a uniform distribution of fixed charge [150-152].

### 6.3.3.2 Space charge (SC) model

The steady-state distributions of the cation/anion concentration (SC model [150, 152]) and the open-circuit potential under different $V_s$ are calculated by solving the coupled two dimensional (2D) Poisson-Nernst-Planck (PNP) equations using COMSOL script environment. Figure 6.7 shows the system that we use in the simulation.

![Figure 6.7 Simulation system used in the numerical calculation. It contains a nanochannel of length $L$ (μm) and height 20 nm (domain 2) connected by two 10×10 μm² square reservoirs (domain 1 and 4). In](image)
addition, there is a SiO₂ dielectric domain (domain 3) which has a thickness of 50 nm and length of \((L - 6)\) μm. The length of the nanochannel used for calculation is the same as the real device in order to make valid comparisons. Note the figure is not drawn to scale.

We use three modules in the COMSOL environment: Electrostatics (AC/DC Module), Nernst-Planck without electroneutrality for calculation of \(K^+\) ions (Chemical Engineering Module) and Nernst-Planck without electroneutrality for calculation of \(Cl^-\) ions (Chemical Engineering Module). The governing equations and the corresponding boundary conditions are listed as follows (Most of the parameters used in the simulation are summarized in Table 5.1),

6.3.3.2.1 Electrostatics

(1) Governing equations (Poisson equation):

For domain 1, 2 and 4:

\[ \varepsilon_0 \varepsilon_w \nabla^2 V = - \sum_i F_z_i c_i \]  
(5.6)

For domain 3:

\[ \varepsilon_0 \varepsilon_{st} \nabla^2 \phi = 0 \]  
(5.7)

(2) Boundary conditions:

The Dirichlet boundary condition is used in the trans side, \(V(x = L + 10) = 0\). The cis side boundary condition is set as floating potential, where the potential is extracted as the \(\Delta V_{ct}\) value. The gate electrode (top side of domain 4) has Dirichlet boundary condition as \(V = V_g\). Neumann boundary conditions are applied for all the other reservoir walls, \(-\varepsilon_0 \varepsilon_w n \cdot \nabla V = 0\). The nanochannel walls which are not in contact with the gate dielectric have the boundary condition as \(-\varepsilon_0 \varepsilon_w n \cdot \nabla V = \sigma_v\). The Neumann boundary condition is imposed on the interface between the
gate dielectric and nanochannel as 

\[-\varepsilon_0\varepsilon_r n \cdot \nabla V + \varepsilon_0 \varepsilon_a n \cdot \nabla \varphi = \sigma_s.\]

### 6.3.3.2 Steady state Nernst-Planck equation for either $K^+$ or $Cl^-$

(1) Governing equations:

For domain 1, 2 and 4:

\[
\nabla \cdot N_i = \nabla \cdot ( -D_i \nabla c_i - z_i \mu_i c_i \nabla V ) = 0 \tag{5.8}
\]

For domain 3: inactive.

(2) Boundary conditions:

The Dirichlet boundary condition is used for the ionic concentrations at the ends of the two reservoirs, 

\[
c_i(x = -L/2 -10) = C_{cis} \quad \text{and} \quad c_i(x = L/2 +10) = C_{trans}. \]

The normal ionic fluxes through all the other walls are set to be zero, 

\[n \cdot N_i = 0.\]

### 6.3.3.3 Model comparisons

A reasonable quantitative agreement is attainable by numerical calculations from both classical Teorell-Meyer-Sievers (TMS) model and space charge (SC) model [150-152]. Figure 6.8 shows the steady-state membrane potential comparisons between the experiments and the theoretical calculations. The larger quantitative discrepancy in the TMS model than that in the SC model is because SC model assumes a radial distribution of the electric potential and ion concentration in space while TMS model ignores the radial non-uniformity of ion concentrations inside the nanochannel.
Figure 6.8 Reasonable quantitative agreement between the quasi-static experimental data (black) and the theoretical predictions from both the classical Teorell-Meyer-Sievers (TMS) model (red) and space charge (SC) model (blue) for (a) as-fabricated device with $\sigma_s=1.6$ mC/m$^2$, and (b) surface-modified device with $\sigma_s=-0.28$ mC/m$^2$.

### 6.4 Transient behavior

#### 6.4.1 Transient dynamics

The above quasi-static analysis applies only if the stimulation voltage $V_s$ changes at a rate slower than that required for all ions to redistribute themselves via drift and diffusion. If a voltage ramp is applied, the modulation behavior will depend on the magnitude of $dV_s/dt$. We investigate here an extreme case with a step $V_s$ to characterize the device transient behavior.

A representative $\Delta V_{ct}$ waveform as a function of time is shown in Figure 6.9. The stimulation voltage $V_s$ is stepped from -1.5 V to 1.5 V (Figure 6.9, inset a). Immediately following the applied step, $\Delta V_{ct}$ rises from an equilibrium value (state 1) of $-69.7\pm4.40$ mV, to a peak value of 452.74 mV, and then decays to another equilibrium value (state 2) of $-30.3\pm4.20$
mV with a characteristic relaxation time $\tau$.

Figure 6.9 Transient behavior of $\Delta V_{ct}$ upon a step change in the stimulation voltage. Typical transient $\Delta V_{ct}$ characteristics when applying a step voltage to the $V_s$ at time $t = 0$. The characteristic relaxation time $\tau$ to reach a new equilibrium state can be determined by least square exponential fitting. Insets: (a) Schematic of the $V_s$ step. (b) Protocell cross-section with a nanochannel height $H$ and length $L$. (c) Equivalent circuit of the protocell. (d) Potential profiles in the system at time $t = 0^-$, $0^+$, and $\infty$, respectively. The trans side is grounded. The potential difference in the trans side is much higher than the cis side in this concentration configurations. The time course of $\Delta V_{ct}$ is also schematically shown, which qualitatively agrees with the experimental observations.

The variation of $\Delta V_{ct}$ following a step in stimulation voltage $V_s$ can be understood by looking at the device structure (Figure 6.9, inset b) and its equivalent circuit (Figure 6.9, inset c).
A micro/nano channel interface acts as an ionic diode, with a cation selective nanochannel as a $p$ region \([147]\). Therefore, the two micro/nano channel interfaces can be treated as two diodes \([153]\), connecting anode-to-anode through the nanochannel, capacitively coupled to the stimulation electrode through a capacitor $C_{an}$ (Figure 6.9, inset c). Let us now consider one of the diodes. When a charge-selective nanochannel is in isothermal Donnan equilibrium with an adjacent microfluidic reservoir, a Donnan potential will appear at the micro/nano channel interface and can be expressed as \([96]\),

$$
V_D = \frac{RT}{z_i F} \ln \frac{c_i^{nc}}{c_i^{bulk}}
$$

(5.9)

where $z_i$ is the valence of ion $i$, $c_i^{nc}$ and $c_i^{bulk}$ is the concentration of ion $i$ in the nanochannel and in the reservoir, respectively. This Donnan potential is analogous to the built-in potential in semiconductor diodes. It can be seen that the higher the reservoir concentration, the lower the Donnan potential. For the case of $[\text{cis}]/[\text{trans}]=100 \text{ mM}/100 \text{ µM},$ the Donnan potential in the $\text{trans}$ side is much higher than the $\text{cis}$ side.

Referring to the inset d of Figure 6.9, immediately after the $V_s$ step is applied ($t=0^-$), the floating nanochannel body potential will exactly follow the rapid change in $V_s$ (dashed purple line). As a result, $\Delta V_{ct}$ will experience the same abrupt change as in $V_s$, up to the amount allowed by RC time constant limitations (i.e., $\Delta V_{ct}$ at $t=0^-$ ($\sim 0.5\text{ V}$) is less than the step change in $V_s$ (3 V)). Following this, the potentials in the system will attempt to reach steady-state as ions redistribute themselves via Poisson-Nernst-Planck principles \([133, 134, 136]\) (dashed blue line). This equivalent picture thus successfully explains the observed time evolution of $\Delta V_{ct}$. For completeness, Figure 6.10 shows a similar but inverted behavior for a falling edge step in $V_s$, \([\text{cis}]/[\text{trans}]=100 \text{ µM}/100 \text{ mM}\)
6.4.2 Bias history dependence

When applying an abrupt step stimulation voltage (Figure 6.11a), the ionic concentration and potential distribution in the nanochannel is disturbed from equilibrium. In a hydroxyl group terminated SiO2 nanochannel filled with KCl solution, there are three possible physicochemical processes happening during this transient period [102] (Figure 6.11b):

1. protonation or deprotonation upon external electric field,
2. adsorption or desorption of counter ions in the Stern layer,
3. ion exchange between the nanochannel and reservoirs.

These three dynamic processes taken together determine the characteristic time required to reach a new equilibrium.
Figure 6.11 Bias history dependence of the transient characteristic relaxation time. (a) The time sequence of $V_s$ used to test the protocell device. The dashed lines depict no voltage being applied. The device is firstly biased with voltage $V_1$ for a period of $t_{pb}$ (pre-bias time), followed by a sudden change into another level of $V_2$. (b) Microscopic kinetics during a transient $V_s$ step. (c) The pre-bias time dependence of the relaxation time under a constant voltage step. (d) The voltage step amplitude dependence of the relaxation time with a fixed pre-bias time. (e) Contour plot showing the characteristic relaxation time as a function of both the pre-bias time and the voltage step amplitude.

Processes 1 and 2 are channel surface-related radial dynamics that are dependent on the bias history of $V_s$. We found in the experiments that the characteristic relaxation time $\tau$ is dependent on both the pre-bias time ($t_{pb}$) and the step amplitude ($\Delta V_{step}$) of $V_s$ (Figure 6.11a). With a fixed voltage step, the longer the pre-bias time, the slower it is to reach a new equilibrium (Figure 6.11c), while for a fixed pre-bias time, a larger step voltage in $V_s$ results in a larger $\tau$ value (Figure 6.11d). Figure 6.11e further shows the characteristic relaxation time is indeed
affected by both $t_{pb}$ and $\Delta V_{\text{step}}$.

This dependence of $\tau$ on the $V_s$ history is because the amount of the transiently generated/diminished H$^+$ or K$^+$ is strongly affected by the pre-bias time and the voltage step amplitude. For example, Eijkel et al. showed that the capacitive release or uptake of protons at the dielectric-electrolyte interface is positively proportional to the applied voltage [154], whereas Han et al. showed that the small but inevitable leakage current related water electrolysis produces a change of proton concentration, affected by both the bias voltage and time [155]. An excessive amount of the transient ions requires a longer time to remove before reaching another equilibrium state. It is thus important that any valid comparison on the relaxation time must be performed with the same bias history to ensure a comparable starting microenvironment.

### 6.4.3 Channel length dependence

Process 3 is an axial kinetic process which is governed by the ambipolar drift-diffusion equation without generation and recombination [146]. The characteristic time in this process can be estimated as $\tau \sim L^2 / 4D_a$, where $L$ is the diffusion length and $D_a$ is the ambipolar diffusion coefficient.

Figure 6.13 shows the characteristic time as a function of nanochannel length ranging from 17 µm to 116 µm, with $\Delta V_{\text{step}}$ and $t_{pb}$ being constant (decoupling the axial process from the radial process to make the comparison valid). The parabolic fitting curve in Figure 6.13 demonstrates a remarkable agreement with the predicted parabolic dependence of $\tau$ on the channel length.
Figure 6.12 Nanochannel length dependence of the characteristic relaxation time. The solid line shows a parabolic fitting of the relaxation time as a function of nanochannel length.

6.4.4 Bath concentration dependence

The axial kinetics (process 3) is also dependent on the reservoir concentrations. We measured the characteristic time for different salt concentrations. As shown in Figure 6.13, the case of $[\text{cis}]=100$ mM takes less time to reach equilibrium than the case of $[\text{cis}]=10$ mM at a same $\Delta V_{\text{step}}$ (both with $[\text{trans}]=100$ μM). This reduced $\tau$ value at higher cis concentration is because of two factors. First, the higher the cis concentration, the more pronounced Debye screening in the cis side of the nanochannel. The effective channel length is therefore reduced in the $[\text{cis}]=100$ mM case, resulting in a short diffusion time. Second, the relative change of the ion concentration in the $[\text{cis}]=100$ mM case is much smaller than in the $[\text{cis}]=10$ mM case (as shown in the calculated results in Figure 6.14). As a result, less time is needed to reach a new equilibrium in the high concentration case.

Figure 6.13 also shows the slope of the $\tau \sim \Delta V_{\text{step}}$ is dependent on the salt concentrations.
This can be explained by the model proposed by Eijkel \textit{et al.}, where the amount of protons transiently generated upon an applied gate voltage can be expressed as \[154],

\[ N = V_s C_{ox} C_{\text{buff}} / (C_{\text{buff}} + C_{DL}) \]  

(5.10)

in which \( C_{\text{buff}} \) is the surface intrinsic (chemical) buffer capacitance and \( C_{DL} \) is the double layer capacitance. As a result, \( d\tau / dV_s \sim dN / dV_s \sim 1 / (C_{\text{buff}} + C_{DL}) \). Increasing the salt concentration will lead to an increase of \( C_{DL} \) and thus a decreased \( d\tau / dV_s \), consistent with Figure 6.13.

![Figure 6.13](image)

Figure 6.13 Bath concentration dependence of the characteristic relaxation time. The \textit{trans} side is fixed with 100 \( \mu \)M KCl. The test is done with a device of channel length \( L = 31 \mu \)m and \( \sigma_s = -1.6 \) mC/m\(^2\).
Figure 6.14 Simulated concentration profiles and the relative concentration change between two equilibrium states under two different bath concentration conditions. The length of the nanochannel used in the simulation is 61 μm.

6.4.5 Surface charge density dependence

We also investigate the effect of nanochannel surface charge density on the characteristic time. Figure 6.15 shows that it takes longer time for the low surface charge density device (with $\sigma_s = -0.28$ mC/m$^2$) to reach a new equilibrium than the native device (with $\sigma_s = -1.6$ mC/m$^2$). This can also be understood by looking at the relative ion concentration change in the nanochannel. With a reduced $\sigma_s$, a larger relative concentration change occurs because of the more effective ion population modulation. A numerical calculation shows that the relative concentration change is indeed higher in the nanochannel with a less charged surface (Figure
The slope of the $\tau \sim \Delta V_{\text{step}}$ is less dependent on the surface charge densities at intermediate $\Delta V_{\text{step}}$, as expected by $d\tau / dV_s \sim 1/(C_{\text{buff}} + C_{DL})$. This result, combined with the data shown in Figure 6.5, indicates that there is a trade-off between the stimulation efficiency and speed, owing to the surface charge effect.

Figure 6.15 Surface charge density dependence of the characteristic relaxation time. The test is carried out on the same device before and after the surface chemical modification, with $L = 61 \, \mu m$ and $[\text{cis}] / [\text{trans}] = 100 \, \text{mM} / 100 \, \mu M$. 
Figure 6.16 Simulated concentration profiles and the relative concentration change between two equilibrium states under two different surface charge density conditions. The length of the nanochannel used in the simulation is 61 μm.

6.5 Frequency dependent switching behavior

The step analysis suggests the maximum continuous operation speed for the protocell device. The dynamic behavior of the protocell in continuous operation must be frequency dependent. Once the ASIC is disturbed from steady-state, the ability to reach a new equilibrium before the next clock cycle is determined by the switching period. Increasing frequency will produce less changes in ionic concentrations from one cycle to the other, since the radial surface reaction and the axial drift-diffusion does not have enough time to respond. Therefore, it can be expected that the modulation of the ion-contributed $\Delta V_{eq}$ will disappear at high frequencies.
Figure 6.17 Frequency dependence of the continuous switching behavior. The stimulation voltage is switched back-and-forth between -1.5 V and 1.5 V (first row). The corresponding $\Delta V_{ct}$ waveform shows a strong dependence on the operation frequency. The dashed green and solid red arrows denote the potential value right before the falling edge and the rising edge, respectively. This test indicates a maximum operation frequency around 1 Hz for this particular device ($L = 17 \ \mu m$, $\sigma_s = -1.8 \ \text{mC/m2}$, and $[\text{cis}]/[\text{trans}] = 100 \ \text{mM}/100 \ \text{µM}$).

Figure 6.17 shows the $\Delta V_{ct}$ waveforms in continuous switching operations under various frequencies. At lower frequencies (10 mHz -1 Hz), $\Delta V_{ct}$ can always be modulated stably between two steady-state values (indicated by two arrows, -31 mV and -43 mV). At higher frequencies (>1 Hz), each clock-cycle is too short for the system to reach an ionic equilibrium.
and therefore the membrane potential $\Delta V_{ct}$ value cannot be modulated between two steady-state values. The modulation of $\Delta V_{ct}$ at higher frequencies mostly comes from the electronic contributions instead of ionic ones, owing to the close coupling of the floating nanochannel body potential to $V_s$ at the rising or falling edges (Figure 6.9c). These results indicate a protocell device of maximum operation frequency around 1 Hz, which can be further increased towards the maximum action potential frequency in biological nerve cells (~200 Hz) by shrinking the device length (i.e., adopting a gated nanopore structure [104]) and tailoring the surface charges.

### 6.6 Summary

In summary, we have demonstrated a solid-state protocell with engineered ion channels, whose ion selectivity and membrane potential can be modulated by external electric field, harvesting the major components in a biological voltage-gated ion channel. It can also be viewed as a universal ion exchange membrane [156], where similar membrane potential modulation has been observed. The experimental results on quasi-statically converting the transmembrane ion gradients into potential validate the voltage regulated selectivity mechanism. Critical factors that affect the modulation efficiency and transient modulation speed are also identified, which has an immediate indication to the transient performances in nanofluidic FETs [102, 146] and chemical charge coupled devices [157]. As a concentration driven system, the top-down fabricated solid-state protocells provide an excellent engineered model platform to study the membrane phenomena in biological samples, which would lead to the creation of engineered nerve cells and neuron networks due to this approach’s potential of integration and surface tailoring. It also has practical indications to desalination and energy generation using solid-state structures.
Chapter 7 Quantify surface charges at dielectric-electrolyte interfaces

As is shown in Chapter 5 and Chapter 6, the intrinsic charging status at the dielectric-electrolyte interface (DEI) plays a critical role for electrofluidic gating in microfluidics and nanofluidics, which offers the opportunities for integration of wet ionics with dry electronics. A convenient approach to quantitatively probe the surface charges at the DEI for material pre-selection purpose has been lacking so far. This chapter presents a low-cost, off-chip extended gate field effect transistor configuration for direct electrostatic probing the charging status at the DEI. Capacitive coupling between the surface charges and the floating extended gate is utilized for signal transducing. The relationship between the surface charge density and the experimentally accessible quantities is given by device modeling. The multiplexing ability makes measuring a local instead of a globally averaged surface charge possible.

7.1 Introduction

The electrofluidic gating [158] approach we discussed in Chapter 5 and Chapter 6 leverages both the structural and functional properties of MOSFETs, offering the opportunities for seamlessly integrating wet ionics with dry electronics. However, most of the channel-forming dielectric materials will spontaneously obtain surface charges when brought into contact with an aqueous phase electrolyte. These intrinsic surface charges function similarly as the surface states
in semiconductors. Therefore, the surface charge density at the DEI is one of the most important parameters for effective electrofluidic gating [12, 99].

Though electrostatic force microscopy (EFM) has been utilized to probe the surface charges in aqueous solutions [159], it requires bulky instrumentation and a quantitative measurement is difficult. In the nanofluidic platform, the conventional method to derive the surface charge density information at the DEI is by plotting the nanochannel conductance against ionic concentrations on a log-log scale (Figure 5.5). The effective surface charge can be extracted from the plateau in that plot at the low ionic concentration region where surface charge dominates the ionic transport [3, 129, 130]. This approach is quite suitable for characterizing the nanochannel after its formation. Nevertheless, it becomes rather inconvenient and tedious to examine various channel-forming dielectric materials beforehand. A faster and simpler method is desirable for such a material pre-selection purpose.

Direct charge detection by field effect has been the scaffold for various FET based biosensors since the invention of the ion selective field effect transistor (ISFET) [4]. The problem of using a conventional ISFET configuration for the above-mentioned material pre-selection purpose is multifold. The most severe one is the reliability issues due to the direct contact of the electrolytes with the FETs.

An extended gate structure, where the sensing area is placed away (either laterally or vertically) from the active region of on-chip integrated FETs, has been widely adopted to solve the chemical contamination problem [160]. Though successful, the extended gate structure with on-chip FETs is ill-suited for the channel-forming material pre-selection purpose due to the following reasons. First, the transistors cannot be repeatedly used because dielectric materials cannot be easily stripped once deposited. Second, the sample preparation is time-consuming
since it involves a complex CMOS fabrication process. Third, common FET based sensors require a liquid filled reference electrode, such as a saturated calomel electrode or Ag/AgCl electrode, to set the potential of the electrochemical system. Such a reference electrode cannot be easily integrated in a standard CMOS process, preventing the realization of really low-cost, disposable devices for material pre-selection purpose.

This chapter will introduce an off-chip extended gate (OCEG) architecture for directly probing the surface charges at the DEI, getting rid of most of the aforementioned problems in the on-chip extended gate structures. Capacitive coupling between surface charges at the DEI and a floating gate is utilized for signal transduction. Successful quantitative local surface charge measurements are demonstrated by examining two most frequently used dielectric materials (silicon dioxide and silicon nitride) under various pH and ionic concentration conditions.

7.2 Theory

7.2.1 Device principle

Figure 7.1 shows the schematic of the OCEG configuration. The front-end probing chips, containing an array of independent sensing and control electrodes, were massively manufactured by conventional lift off process (Figure 7.2). The front-end probing chip and the back-end sensing transistors are integrated on a single printed circuit board (PCB), accompanying signal amplification and data acquisition interface for personal computers (Figure 7.3). The modular configuration of a separate front-end probing chip and a back-end transistor chip has clear advantages in terms of cost and disposability.
Figure 7.1 Schematic of the off-chip extended gate configuration. It consists of two independent parts: a disposable front-end probing chip and a reusable back-end sensing transistor chip. The dielectric material under investigation is deposited on top of the front-end chip by any necessary means. Surface charges developed at the dielectric-electrolyte interface (DEI) capacitively modulate the potential of the floating sensing electrode ($V_s$) underneath and thus the drain current in the back-end transistors.
Figure 7.2 Scanning electron microscope (SEM) of the fabricated front-end probing chip, which consists of an array of sensing/control electrode sets. The magnified SEM image shows a single sensing electrode and its corresponding control electrode.

Figure 7.3 Photograph of the printed circuit board (PCB) setup. The front-end probing chip is used in a plug-and-play fashion. The whole setup is placed in a Faraday cage to shield the electrostatic noise.

When electrolyte is brought into contact with the dielectric material under investigation, surface charges will develop at the DEI according to site-binding theory [16]. These surface
charges capacitively affect the potential of the floating sensing electrode \((V_S)\) underneath. This capacitive coupling process can be understood from a charging by induction picture. The presence of the surface charges at the DEI induces charge polarization in the conductive sensing electrode, which further produces an electric field across the gate oxide of the transistor, modulating the drain current accordingly. By measuring the drain current change, it is therefore able to detect the charging status at the DEI.

![Electrolyte bulk](image)

Figure 7.4 The equivalent small signal circuit model of the system. The total amount of the surface charge \(Q_S\) is redistributed to the two parallel capacitors \((C_{DL} \text{ and } C_{DS})\) according to the capacitor’s ratio. The actual potential at the floating sensing electrode \((V_S)\) is concurrently determined by both \(V_C\) and the surface charges developed at the DEI.

### 7.2.2 Device modeling
To find out a quantitative and predictive dependence of sensing electrode potential $V_S$ on the surface charges, an equivalent small signal circuit model is developed, as shown in Figure 7.4. The total image charges induced by the surface charges are distributed into two capacitors, the electric double-layer capacitor, $C_{DL}$, and the capacitor between sensing electrode and DEI, $C_{DS}$. The amount of charges each capacitor obtains depends on the ratio of $C_{DL}$ and $C_{DS}$. The induced charge on the sensing electrode ($Q_{S,DS}$) thus reads,

$$Q_{S,DS} = -\frac{C_{DS}}{C_{DS} + C_{DL}} \sigma_s A_s$$  \hspace{1cm} (6.1)

where $A_s$ is the overlapped area between the sensing electrodes and the electrolyte, and $\sigma_s$ is the surface charge density at the DEI (the quantity of interest here).

Since the sensing electrode is electrically isolated, the total net charges within the sensing electrode must remain zero, unless a charge injection or ejection process (e.g., tunneling) is involved. According to the charge conservation principle, we get the following relationship at the sensing electrode node in Figure 7.4,

$$Q_{A,DS} + (V_S - V_C)C_{CS} + V_S C_{SB} = 0$$  \hspace{1cm} (6.2)

where $V_C$ is the voltage applied on the control electrode, $C_{CS}$ is capacitor between the control and the sensing electrode. $C_{SB}$ is the lumped capacitance between the sensing electrode and silicon body of MOSFET. Note that all voltages above are referenced with respect to potential in the silicon body, which is ground in this study.

By combining the Eq. (6.1) and Eq. (6.2), the potential at the sensing electrode can be written as,
$$V_S = \frac{A_s C_{DS}}{(C_{DS} + C_{DL})(C_{CS} + C_{SB})} \sigma_S + \frac{C_{CS}}{C_{CS} + C_{SB}} V_C$$  \hspace{1cm} (6.3)$$

Eq. (6.3) represents the relationship between the $V_S$, $V_C$, and $\sigma_S$ at the DEI. It states that the ultimate sensing electrode potential is a linear superposition of two independent contributions, the surface charges and the control electrode voltage. Indeed, the control electrode offers an extra degree of freedom in device operation by applying an independent $V_C$, which functions similarly as a capacitively coupled reference electrode in FET sensors [161]. The transistor’s quiescent working point can be independently set by an appropriate $V_C$. The sensing transistor can thus be tuned to ensure maximum sensitivity. This principle is very similar to the chemoreceptive neuron MOS transistors [162] and the charge modulated FET sensors [163].

### 7.2.3 Measurement protocol

To further relate the sensing electrode potential $V_S$ with the experimentally accessible quality (i.e., the drain current $I_d$), we note that the general form of the $I-V$ characteristics of a MOSFET can be expressed as $I_d = f(V_{gs}, V_{ds})$ for sub-threshold, linear and saturated region [43], where $V_{gs}$ equals the sensing electrode potential $V_S$, and $V_{ds}$ is the drain voltage of the MOSFET. The $I_d-V_{gs}$ curve at a constant $V_{ds}$ could be tested thoroughly off-line before performing any surface charge measurements (Figure 6.1a), serving as a look-up table for converting the measured drain current $I_d$ back into $V_S$ value (and thus the surface charge density, using Eq. (6.3)) when carrying out the real surface charge measurements (Figure 6.1b).
Figure 7.5 Methods to extract the floating sensing electrode potential ($V_S$) from the measured $I_d$ value at various electrolyte conditions. (a) Procedures to find the corresponding floating sensing electrode potential at various pH conditions. Each drain current baseline is used to extract $V_S$ by using the $I_d - V_{gs}$ curve tested off-line before performing any surface charge measurements. (b) Time course of the drain current $I_d$ for SiNx sample under various pH conditions.

7.3 Materials and methods

7.3.1 Device fabrication

The front-end probing chips, containing independent sensing and control electrodes (50 nm Au with 10 nm of Cr as adhesive layer), were massively manufactured by conventional electron beam evaporation and lift off process on a 4 inch Si wafer with 3-µm-thick SiO2 as isolating layer. Hybrid optical lithography and e-beam lithography was employed to ensure both low cost and high spatial resolution. After depositing the dielectric material of interest, the front-end probing chip was wire-bonded with a ceramic chip carrier. A PDMS based microfluidic system was adopted to deliver the electrolyte solution.

7.3.2 Materials
SiO₂ with thickness ranging from 73.8 nm to 168.5 nm and SiNₓ with thickness ranging from 43 nm to 197.1 nm were deposited by plasma enhanced chemical vapor deposition (PECVD) at 400°C. The reactive gases for depositing SiO₂ are silane (SiH₄) and nitrous oxide (N₂O). The reactive gases for depositing SiNₓ are silane and ammonia (NH₃). The chamber pressure for both depositions is 2 Torr. The electrolyte we used is Dulbecco's Phosphate Buffered Saline (Catalog Number 14190-136, Invitrogen), the pH of which is adjusted by adding hydrochloric acid or potassium hydroxide into this buffer. The back-end sensing transistors are commercially available n-channel MOSFET with zero volt threshold voltage (ALD110800, Advanced Linear Devices).

### 7.3.3 Electrical measurement

The whole measurement procedure is done using an automated system at room temperature. The drain current for each sensing electrode, at a constant drain voltage (100 mV), is amplified with operational amplifiers (Op-amps) and recorded in a multiplexed fashion using an 8-channel data acquisition card (NI PXI-4224, National Instrument). Figure 7.6 shows the schematic of the readout circuit for probing the charging status at the dielectric-electrolyte interface.
The voltage on the control electrode is applied as 0 V to maximize the sensitivity. The whole testing system is housed inside a homemade light-shielding Faraday cage. This shielding is essential for a stable electric measurement since the bulk of the electrolyte is in a floating potential. We found that the whole testing system is extremely sensitive to the surrounding electrostatic environment. The electrolyte was delivered by pumps (New Era Pump Systems, Inc.), controlled by a LabVIEW (National Instruments) program. The final drain current is obtained at least 10 min after the solution is brought into the DEI, allowing the charging process reaches an equilibrium state.

7.4 Results and discussion

7.4.1 Effect of pH on the surface charge density

To verify the validity of device principle, we first tested the pH effect on the surface charge at the DEI. According to the well-accepted site-binding model [16], the dielectric surface
has ionizable sites that react directly with the electrolyte to bind or release hydrogen ions. The surface therefore becomes more or less charged depending on the pH. As a demonstration of using the OCEG structure to probe charging status at the DEI, we measured the pH dependence of the sensing electrode potential at a constant ionic strength (0.001×PBS buffer) for both SiO₂ and SiNₓ samples and extracted σₛ based on Eq. (6.3).

![Figure 7.7 Measured sensing electrode potential (upper panels) and the extracted surface charge density σₛ (averaged over the four thicknesses, lower panels) as a function of pH for (a) SiO₂ sample and (b) SiNₓ sample. The measurement is performed at a constant ionic strength (0.001×PBS solutions).](image)

### 7.4.1.1 Silicon dioxide

Figure 7.7a show the measured sensing electrode potential as well as σₛ for SiO₂ at various pH conditions. The SiO₂/electrolyte interface becomes more negatively charged as the pH increases. When SiO₂ is in contact with an aqueous solution, it hydrolyzes to form surface
silanol (SiOH) groups. The amphoteric nature of the silanol groups causes the variation of the oxide surface charge when varying the pH according to the reactions $SiOH^+ \rightleftharpoons SiOH + H^+$ and $SiOH \rightleftharpoons SiO^- + H^+$. Increasing the pH therefore results in a more negatively charged surface. The surface charge density at the SiO$_2$/PBS interface varies from -2.8±0.7 mC/m$^2$ to -13.7±4.82 mC/m$^2$ when changing pH from 5 to 9. In comparison, the surface charge density at the PECVD SiO$_2$/electrolyte interface, derived by plotting the nanochannel conductance against the ionic concentrations in the log-log scale, is estimated to be -2 mC/m$^2$ [12] at pH 7. The reasonable agreement between these two surface charge density measurement methods confirms the validity of our simple OCEG structure. The point of zero charge (pzc) of SiO$_2$ in the 0.001×PBS solution is extrapolated to be around 4.27±0.08 by linear fitting of the experimental data shown in Figure 7.7a, which is a little higher than the pzc of typical silicon oxide material (~2-4).

7.4.1.2 Silicon nitride

Figure 7.7b show the results for the SiN$_x$/PBS interface. A negative shift of the surface charge density as increasing the pH is also observed. However, the polarity of the surface charge is reversed at pH~6.5, indicating the SiN$_x$ deposited by our PECVD has a pzc around 6.5. The surface charge density at the SiN$_x$/PBS interface ranges from 4.21±2.45 mC/m$^2$ to -4.42±2.2 mC/m$^2$ when changing pH from 5 to 9. Silicon nitride is known to produce both a basic primary amine sites SiNH$_2$ ( $SiNH^+_3 \rightleftharpoons SiNH_2 + H^+$ ) and an amphoteric silanol sites [15]. The amphoteric silanol sites are from the oxidation of the silicon nitride surface. The primary amine sites SiNH$_2$ are expected to have a pK of around 10. Since the pzc of SiN$_x$ sample has a value lower than 10, it can be assumed that all the amine sites are positively charged at the pzc of SiN$_x$ sample. As a result, the silanol sites tend to donate a proton to the amine sites at most pH values.
The pzc of SiNₓ (pH 6.5) occurs at the pH where the negative charge on the silanol sites balances the fixed positive charge on the amine sites. The surface site theory can be used to calculate the ratio of the number of amine sites to silanol sites on the SiNₓ/PBS interface [164],

\[
\frac{N_{NH_2}^{NH_2}}{N_{OH}^{OH}} = 2 \sqrt{\frac{K_{a2}}{K_{a1}}} \sinh[2.303(pH_{pzc} - pH_{pzc}^{OH})] \tag{6.4}
\]

where \( K_{a1} \) and \( K_{a2} \) are the surface equilibrium constants of the acid/base reactions of the amphoteric silanol sites, \( pH_{pzc} \) is the zero charge point for SiNₓ sample and \( pH_{pzc}^{OH} \) is the zero charge point for silanol sites only. A typical value [164] for the dissociation constants \( 2\sqrt{K_{a2}/K_{a1}} \) is \( 7 \times 10^{-4} \). Using the experimentally derived value of \( pH_{pzc}^{OH} \) as 4.27 and \( pH_{pzc} \) as 6.5, the ratio of \( N_{NH_2}^{NH_2} / N_{OH}^{OH} \) is calculated to be around 6%. It is therefore apparent that PECVD nitride surfaces are highly populated with silanol sites, instead of the amine sites. The tendency of SiNₓ surfaces to oxidize has been shown extensively before [165].

### 7.4.2 Surface charge extraction at different ionic concentrations

Having verified the capability of using OCEG architecture to quantitatively detect the surface charges, we carried out experiments on the influence of different ionic concentrations under a constant pH value (pH=7) to further relate the experimentally accessible \( V_s \) with \( \sigma_s \) at arbitrary ionic strengths. Figure 7.8 shows the measured floating sensing electrode potential \( V_s \) as a function of the PBS concentration for both SiO₂ and SiNₓ materials. A clear increase of the absolute value of the \( V_s \) when decreasing the PBS buffer concentrations was observed.
Figure 7.8 Measured sensing electrode potential as a function of ionic strength for (a) SiO$_2$ with four different thicknesses and (b) SiN$_x$ with four different thicknesses. Note that 1×PBS corresponds to an ionic strength of about 150 mM. The pH is fixed at 7 for all data points.

To understand this dependence and relate the surface charge density $\sigma_s$ with the measured $V_s$ under different ionic strength, we need to recall Eq. (6.3). Since the control electrode potential applied is 0 V, the second term on the right hand side of Eq. (6.3) can therefore be dropped. Moreover, it is reasonable to assume $C_{SB} \gg C_{CS}$ in our devices, since the thickness of MOSFET gate oxide (50 nm) is much thinner than the distance between sensing and control electrode (>1 μm). Therefore, Eq. (6.3) can be reduced to a simpler approximation form of,

$$V_s = \alpha \frac{A \sigma_s}{C_{SB}}$$

(6.5)
in which 

\[
\alpha = (1 + C_{DL}/C_{DS})^{-1}
\]  

(6.6)

It is easy to show that \( C_{DL}/C_{DS} = \varepsilon_c t / \varepsilon_d \lambda_D \), where \( \varepsilon_c \) and \( \varepsilon_d \) is the relative permittivity of electrolyte and dielectric, respectively, and \( t \) and \( \lambda_D \) is the dielectric thickness and Debye length, respectively. At room temperature, one can consider in water the relation, \( \lambda_D = 0.304 / \sqrt{c} \), where \( \lambda_D \) is expressed in nanometers (nm) and \( c \) is the ionic strength expressed in molar [23]. Since 1×PBS corresponding to an ionic strength around 150 mM, we therefore have \( \lambda_D = 0.785 / \sqrt{XPBS} \). As a result, the factor \( \alpha \) can be expressed as,

\[
\alpha = (1 + 1.274 t \sqrt{XPBS} \varepsilon_c / \varepsilon_d )^{-1}
\]  

(6.7)

where \( t \) is in nm. For a fixed dielectric thickness \( t \), decreasing PBS concentrations will increase the factor \( \alpha \) and thus increase the absolute value of the floating gate potential, consistent with the results shown in Figure 7.8.

Table 7.1 Surface charge density extracted by least squares fitting

<table>
<thead>
<tr>
<th>Dielectric</th>
<th>Thickness (nm)</th>
<th>Fitted ( \sigma_S ) (mC/m²)</th>
<th>Dielectric</th>
<th>Thickness (nm)</th>
<th>Fitted ( \sigma_S ) (mC/m²)</th>
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</thead>
<tbody>
<tr>
<td>SiO(_2)</td>
<td>73.8</td>
<td>-1.17</td>
<td>SiN(_x)</td>
<td>43.0</td>
<td>-0.144</td>
</tr>
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<td></td>
<td>97.8</td>
<td>-1.47</td>
<td></td>
<td>99.3</td>
<td>-0.241</td>
</tr>
<tr>
<td></td>
<td>133.2</td>
<td>-1.88</td>
<td></td>
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<td>-2.30</td>
<td></td>
<td>197.1</td>
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</table>

By fitting the experimentally derived PBS concentration versus \( V_s \) curve using the know parameters (\( C_{SB} = 12 \) pF and \( A_s = 1.4 \times 10^{-8} \) m\(^2\)), it is possible to extract a value for \( \sigma_s \). Table 7.1 shows the \( \sigma_s \) found by the least squares fitting for SiO\(_2\) and SiN\(_x\) materials. The averaged surface charge density for SiO\(_2\) is estimated to be \(-1.7\pm0.492\) mC/m\(^2\) and for SiN\(_x\) is -
0.24±0.0743 mC/m² at pH 7. The lower surface charge density developed at the SiNₓ surface than that of the SiO₂ surface can be understood from the different pzc value for PECVD SiO₂ (4.27) and PECVD SiNₓ (6.5).

7.5 Array implementation

Figure 7.9 Measured spatial surface charge distribution on a same chip (1×8 array) with various pH values. The dielectric material under investigation is the 73.8-nm-thick SiO₂ deposited by plasma-enhanced chemical vapor deposition (PECVD). The measurement is performed with a constant ionic strength at 0.001×PBS solutions. The percentage number indicates the surface charge density variations over the eight channels.

Finally, the ability to quantitatively measure the surface charge density is not limited to a globally averaged value. The flexibility of the electrode patterning enables the multiplexed measurements for mapping out the spatially distributed localized surface charge. Figure 7.9
shows measured spatial surface charge distribution on a same chip under various pH conditions. The sample under test is the 73.8-nm-thick SiO$_2$ and the electrolyte used is $0.001\times$PBS. The variation of surface charge densities probed by each sensing electrode is less than 10% in all pH conditions. It is worth noting that the number of the sensing electrodes is not limited to eight channels. A two dimensional (2D) mapping of the surface charge distributions is possible by using 2D sensing electrodes with finer spatial resolution, using a similar technique as multielectrode arrays (MEAs).

### 7.6 Conclusions

In summary, we have demonstrated a facile OCEG configuration for quantitatively probing the charging status at the dielectric-electrolyte interface for material pre-selection purposes. The use of the OCEG configuration allows the separation of wet ionics from dry electronics and completely eliminates reliability issues. The integrated control electrodes, which allows for adjusting a transistor’s quiescent working point, offers an extra degree of freedom in device operation and circumvents the requirement for a bulky reference electrode. An analytical model to extract the surface charge density is developed. Experiments on two different dielectric materials have successfully demonstrated a reliable quantitative surface charge analysis. It is worth noting that even though the motivation here is to detect the charging status at the DEI, the OCEG architecture can be applied to any charge based sensing schemes (e.g., biosensors).
Chapter 8  Conclusions and future perspectives

8.1 Conclusions

This thesis presents the efforts of understanding and applying the electric field-matter interactions in the microfluidic and nanofluidic systems (electrofluidics). Electrofluidics is of high importance to a variety of emerging fields, such as lab on a chip devices, bioMEMS and bioNEMS. These emerging fields can benefit from studying of electrofluidics due to the following two reasons:

(1) There are electrokinetic phenomena that have not been discovered or have been overlooked before. Understanding of these phenomena will lead to new applications that have not been explored before.

(2) There are undiscovered behaviors that occur at previously inaccessible size scales. New electro-physico-chemical process appears when the system size scales from micrometer to nanometer region.

Both factors can lead to new applications that have not been possible before.

This work brings electrofluidics into new regimes both scientifically and technologically by working exactly on these two aspects, which corresponds to two main parts that presented in this thesis: (1) theory and experiment of AC electrophoretic phenomena, and (2) gated ion transport in nanochannels.
In the effort to explore the new electrokinetic phenomena, we carried out the theoretical study on one of the overlooked aspects of AC electrokinetics - ACEP phenomena. It is shown for the first time that the EP effects will not vanish in non-uniform high frequency AC fields. The dynamics of a particle with both polarizability and net charges in a non-uniform AC electric trapping field is investigated. It is found that either EP or DEP effects can dominate its dynamics, depending on the experimental conditions (especially the ionic concentration). A dimensionless parameter is developed to predict the relative strength of EP and DEP effects in a quadrupole AC field. An ACEP ponderomotive force can be used to trap charged particles in ‘salt-free’ or low salt concentration solutions. Most importantly, in contrast to DEP traps, an ACEP trap favors the downscaling of the particle size, provided it is sufficiently charged.

This theoretical effort has been accompanied in parallel with the experimental effort to demonstrate ACEP traps with quadrupole electric fields. This experimental effort represents the world’s first aqueous Paul trap realized on a chip. Compared with conventional Paul traps working in frictionless vacuum, the aqueous environment associated with damping forces and Brownian noise exerts a fundamental influence on the underlying physics. We investigate the impact of these two effects on the confining dynamics. We find that the rms fluctuations can be suppressed by adjusting the voltages and frequencies. We also demonstrate the scaling properties of the ACEP trap. This technique provides a new alternative for the localization and control of charged particles in an aqueous environment.

The control of macro-ions by AC electric field in aqueous Paul traps naturally leads the following question. Is it possible to use a DC electric field to manipulate charged species? What does it require to do so? These questions are directly linked to our second efforts in this thesis, which is on gated ion transport in nanochannels.
Due to the electrostatic screening effect, a direct electric field-ion interaction is not possible beyond the Debye length. In micrometer-sized channels, the Debye length is usually much smaller than the channel dimensions, and the bulk of the solution is shielded from the surface charge. However, nanochannels, which have one dimension comparable to or smaller than the Debye length, possess an electrostatic potential that remains nonzero even in the center of the nanochannel. Thus, direct electrostatic control over the ions in the nanochannel becomes possible. This property offers a unique opportunity in using the field effect to regulate the ionic transport in the nanochannel, which can be driven by either a potential gradient or a concentration gradient.

Regarding the potential gradient driven system, we realized a field effect reconfigurable ionic diode. The forward/reverse directions of the diode as well as the degrees of rectification can be regulated by the application of gate voltages. The electrostatic modulation offers a fully independent and digitally programmable approach for controlling the preferential flow directions for ions and molecules in fluids. This device would serve as a building block for large-scale integration of reconfigurable ionic circuits.

Regarding the concentration gradient driven system, we demonstrated a solid-state protocell with engineered ion channels, whose ion selectivity and membrane potential can be modulated by external electric field, harvesting the major components in a biological voltage-gated ion channel. It can also be viewed as a universal ion exchange membrane [156]. As a concentration driven system, the top-down fabricated solid-state protocells provide an excellent engineered model platform to study the membrane phenomena in biological samples, which would lead to the creation of engineered nerve cells and neuron networks.

The charging status at the dielectric-electrolyte interface (DEI) is found to play a critical
role in electrofluidic gating in nanofluidics. We demonstrated a facile approach to measure the surface charges at the DEI for material pre-selection purpose. This is done by using a low-cost, off-chip extended gate FET configuration.

In summary, the main contributions of this thesis are as follows.

(1) On theory, we discovered the missing AC electrophoretic phenomena. This greatly advances our understandings of the electrokinetic phenomena.

(2) We experimentally realized the first aqueous Paul trap device and investigated its various properties. This device is not only a trapping tool but also an analytical tool.

(3) We experimentally realized a field effect ionic reconfigurable diode whose functionality can be altered in a post-fabrication fashion.

(4) We experimentally realized an artificial solid-state ion channel, whose membrane potential can be modulated by external electric field, harvesting the major components in a biological voltage-gated ion channel.

(5) We provided a facile technique to quickly prober the surface charging status at the dielectric-electrolyte interface, which is a major concern in electrofluidic gating.

8.2 Future perspectives

Several aspects are important to be addressed by future research.

Regarding the aqueous Paul trap, the planar aqueous Paul trap demonstrated great success in trapping a single particle ranging from micrometer size to tens of nanometer size. However, it is important to keep in mind that the aqueous Paul trap device can also be used as a measurement tool. Since the dynamics of the macro-ion is strongly dependent on the charge-to-mass ($Q/M$)
ratio of the particle, the Q/M variations induced by adsorption of the analyte molecules to the particle surface is therefore expected to change the particle dynamics. This can be utilized as the foundations for analytical devices, and has the possibility to observe charge dynamics and processes in situ. An enticing possibility is to incorporate capacitive sense electrodes along with the trap electrodes for an entire electronic system.

Second, we have shown the dynamics for the particle with a well-defined shape (sphere), it remains unclear what will the dynamics look like for irregular particles, such as protein and nucleotide molecules, as well as deformable cells. This topic is worth the effort since it brings the aqueous Paul trap one more step closer to real world applications. To achieve this goal, advanced optical setup to resolve the trapping dynamics of a single molecule would greatly advance this technology.

Third, it is very important to improve the throughput for the aqueous Paul trap device. The device so far deals with a single macro ions at a time. It would be a more promising technology if the devices can be arranged in an array so that multiple macro ions can be manipulated and analyzed simultaneously. An important aspect is to add additional translocation electrodes into the structure, to sequentially manipulate and load particles (in the z-direction).

On the nanostructure-enabled novel ionic transport phenomena, there are many interesting physical and chemical processes as well as real world applications waiting to be explored.

First of all, this thesis has shown the transport of simple symmetric monovalent KCl electrolyte. We used KCl because it is a simple physical system that can be easily understood by mean field theory (Poisson-Boltzmann theory). However, the real applications may involve multivalent ion species such as Ca$^{2+}$ and Mg$^{2+}$. The simplified scenario of a mean field theory becomes inadequate because of the strong interactions between multivalent ions. As a matter of
fact, ‘charge inversion’ phenomenon has been observed in which counter-ions with high valence condense onto the surface and actually reverse the sign of its total charge [127, 166, 167]. It is very intriguing to understand the ion-ion and ion-wall interactions for multivalent ions in the nanochannel. This has a critical role in understanding ion-selective transport in biological systems.

Second, the nanochannels can also be used as biosensing platforms, other than the actuation that we have shown in this thesis. This can be done by using the following schemes. (1) A coulter-counter type principle (resistive pulse sensing) for single molecular analysis [168]; or, (2) Measuring the channel conductance variation caused by the adsorption of analyte molecules onto the wall. This change in channel conductance can be induced by either the change in the wall surface properties or the change in the nanochannel geometries [169].

Third, combing the nanofluidic channel with advanced optics would make single molecule analysis possible. In a nanometer sized channel, a reduced focal volume will lead to a situation that only one molecule is in the focal volume at a time [170, 171]. This makes single molecule detection possible. Beyond this, an integrated optical waveguide can be placed on the same nanofluidic chip for a real lab on a chip analysis [172].

All in all, the future of electrofluidics is very bright. By combing the interdisciplinary knowledge in electronics, optics, physics, chemistry, fluidics, as well as biochemistry, it provides an unprecedented possibility of a new generation of highly specific, sensitive, selective and reliable biomedical sensing/actuating systems integrated on a single chip.
Bibliography


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