Published in final edited form as:

Langmuir. 2013 January 29; 29(4): 1303–1317. doi:10.1021/la304032t.

Ion correlations in nanofluidic channels: Effects of ion size, valence, and concentration on voltage- and pressure-driven currents

Jordan Hoffmann¹ and Dirk Gillespie²

¹Johns Hopkins University, Baltimore, MD

²Department of Molecular Biophysics and Physiology, Rush University Medical Center, Chicago, IL

Abstract

The effects of ion-ion and ion-wall correlations in nanochannels are explored, specifically how they influence voltage- and pressure-driven currents and pressure-to-voltage energy conversion. Cations of different diameters (0.15, 0.3, and 0.9 nm) and different valences (+1, +2, and +3) at concentrations ranging from 10^{-6} M to 1 M are considered in 50 nm- and 100 nm-wide nanoslits with wall surface charges ranging from 0 C/m² to −0.3 C/m². These parameters are typical of nanofluidic devices. Ion correlations have significant effects on device properties over large parts of this parameter space. These effects are the result of ion layering (oscillatory concentration profiles) for large monovalent cations and charge inversion (more cations in the first layer near the wall than necessary to neutralize the surface charge) for the multivalent cations. The ions were modeled as charged, hard spheres using density functional theory of fluids and current was computed with the Navier-Stokes equations with two different no-slip conditions.

INTRODUCTION

With continued improvement in fabrication techniques, true nanoscale fluidic device designs have become feasible in the last 20 years (reviewed by Napoli et al.¹). But, the full potential of these devices has yet to be realized. Possible applications of nanoscale fluid devices include molecular level analysis and detection, DNA sequencing, and small point-of-care medical devices, among many others.¹ The ability to generate electrical power from pressure-driven ion flow through these nanodevices^{1–6} has potential uses across many fields because their tiny size potentially gives them high levels of pressure-to-voltage power conversion efficiency.^{5,6}

Fluidic devices on the nanometer scale have significantly different physical properties than their micrometer scale counterparts.¹ Typically in microscale devices, bulk properties of solutions dominate the physical properties. However, in nanoslit devices, the distance between walls in a slit is only one to two orders of magnitude greater than the ion diameter and Debye length. As a result, effects at the solid/liquid interface are significant and can dominate over the bulk properties of the fluid. Currently, effects at the solid/liquid interface

Correspondence to: Dirk Gillespie.

corresponding author: dirk_gillespie@rush.edu.

SUPPORTING INFORMATION AVAILABLE

Figures in which a zero Stern layer height is used are available as online Supplementary Material Figs. S1–S4. These should be compared to the corresponding Figs. 2–5 in the main text where the Stern layer height is defined as the counterion diameter. This information is available free of charge via the Internet at <http://pubs.acs.org/>.

are not well defined. For example, variation in ion size and valence can lead to many unexpected, novel phenomena.^{7,8} To design truly innovative devices, it is essential to develop a working theory that can be used to predict the behavior of fluids in nanodevices over a wide range of conditions.

Theories describing properties of fluids in nanoslit experiments were originally developed for macroscale systems, where the effects of ion-wall and ion-ion correlations many times can be ignored. The majority of these theories make simplifications that do not reproduce known nonlinear results like ion layering and charge inversion. On the other hand, more accurate theories describing nanoscale fluid dynamics, like molecular-level simulations, are too computationally expensive to be useful in determining device properties over very wide parameter ranges. Simpler and less computationally intensive theories that include ion-wall and ion-ion correlations are essential for the successful prediction of new phenomena and device properties. The trick is balancing the necessary physics and computation time.

Commonly used, less computationally intensive theories like Gouy-Chapman, Poisson-Boltzmann, Bikerman, and Carnahan-Starling fail to show the nonmonotonic concentration profiles seen in atomic simulations.⁹ For example, in ion layering, the cations form very high density layers with a small probability of finding a particle between this layer and the next, producing oscillatory concentration profiles.^{6,10-13} Similarly, nonmonotonic concentration profiles occur in charge inversion. Charge inversion typically occurs only with multivalent counterions and results from a surplus of co-ions in the second ion layer near a high surface charge, causing a sign change of the electrostatic potential due to the change in sign of the net charge profile.^{7,8,14-16}

The classic theories listed above omit the ion-ion and ion-wall correlations necessary to produce the observed oscillatory profiles.⁹ Since charge inversion and ion layering occur in devices fabricated today,^{7,8} different theories are necessary to continue the development of novel nanofluidic devices. Atomic simulations are still too computationally expensive to perform calculations over a wide parameter space, so here we take a middle road between the computational intensity of molecular simulations and the simplifications of earlier theories.

This paper uses Density Functional Theory (DFT) of fluids—not to be confused with Density Functional Theory from quantum mechanics that is used to describe electronic structure. DFT of fluids is thermodynamically derived, taking into account the finite size of ions, as well as a wide range of ion-ion interactions. The use of DFT for nanofluidic devices has been limited (e.g., ^{6,13,17}), perhaps because of the increased computational complexity over simpler models. However, DFT paints an accurate qualitative picture of electrolyte behavior in nanofluidic devices, reproducing the necessary nonlinear results like charge inversion and ion layering.^{15,16} Furthermore, it remains significantly more computationally efficient than atomic simulations. DFT has been applied to multiple real world cases: ion channels,¹⁸⁻²³ electrical double layers,^{15,16,24-26} and simple fluids,²⁷⁻²⁹ in each case reproducing—most times quantitatively—the behavior observed in Monte Carlo simulations^{15,16} as well as reproducing and predicting experimental results.¹⁸⁻²³

DFT takes seconds to minutes to compute in the nanoscale slit geometry, making it an ideal theory to scan a large parameter space.¹⁷ This is useful because in a nanofluidic channel, the number of experimental parameters is near infinite. For example, possible parameters of interest include the surface charge on the device walls, the slit height, as well as the size, valence, and concentration of the ion species. The goal of this paper is to explore the behavior of total voltage conductance (electromigration and advection together), streaming conductance, and pressure-to-voltage power conversion efficiency over a wide range of

concentrations (10^{-6} M to 1 M cation concentrations) and surface charges (from no surface charge to -0.30 C/m²). Calculations were performed for “small” (0.15 nm), “medium” (0.30 nm), and “large” (0.90 nm) diameter cations with valences of +1, +2, and +3. For all experiments the anion was chloride. The calculations were performed for nanoslit devices with a height of 50 or 100 nm, a length of 5 mm, and a width of 50 μ m. These parameters were chosen to encompass the values of real devices (e.g., the use of trivalent ions by van der Heyden et. al⁷ and high surface charges in electrode-embedded devices^{30,31}).

We will describe the general behavior of total conductance, streaming conductance, and power conversion efficiency over this very large parameter space. To our knowledge, this is the first time this has been done using a theory with finite sized ions. We discuss when phenomena like charge inversion and ion layering occur and how they affect device properties (e.g., conductances). We describe how the streaming and total conductance results affect the power conversion efficiency, and how to maximize power conversion efficiency in a nanofluidic device. We also briefly comment on how the results of a 100 nm fluidic device compare to the results at 50 nm and how different Stern layer models affect the results.

THEORY AND METHODS

All of the calculations were performed in a nanofluidic slit geometry. The thinnest dimension, extending from $y = 0$ to $y = H$, is the distance between the two charged walls. In this paper, $H = 50$ and 100 nm. The x -direction is the length of the channel ($0 \leq x \leq L$) and the z -direction the width ($0 \leq z \leq W$). Here, $L = 5$ mm and $W = 50$ μ m.

In this geometry, ions move in the x -direction, and in the y -direction the ions are in equilibrium since there are no currents through the walls. Their concentration profiles are computed from the ions' excess chemical potentials:

$$\rho_i(y) = \rho_i^{\text{bath}} \exp\left(-\frac{z_i e}{kT} \psi(y) - \Delta \mu_i^{\text{ex}}(y) - U_i(y)\right) \quad (1)$$

where ρ_i^{bath} is the concentration in the bath (far from the wall) of ion species i with valence z_i and $\mu_i^{\text{ex}}(y)$ is the excess chemical potential of species i , with the Δ indicating that the bath value has been subtracted off. The excess chemical potential is computed with DFT, as described below. The fundamental charge is e , the Boltzmann constant k , and the absolute temperature T . The mean electrostatic potential ψ is computed from the Poisson equation

$$-\epsilon \epsilon_0 \frac{d^2 \psi}{dy^2}(y) = e \sum_i z_i \rho_i(y) + \sigma \delta(y) + \sigma \delta(H - y) \quad (2)$$

where σ is the surface charge on the wall, δ is the Dirac delta function, ϵ_0 is the permittivity of vacuum, and $\epsilon = 78.4$ is the relative dielectric coefficient. The boundary conditions for Eq. (2)

$$\frac{d\psi}{dy}(\pm\infty) = 0. \quad (3)$$

(In practice, $\pm\infty$ are taken to be finite large distances.) The last term in Eq. (1) is the function U_i that defines that the centers of the hard-sphere ions cannot approach the walls closer than a radius.

DFT of Charged, Hard Spheres

In this paper we use the primitive model of ions where ions are charged, hard spheres with the same dielectric constant as the solvent. This is the simplest model of ions with finite size and has been successfully applied to reproduce/predict experimental data in various field, including activity coefficients³² and ionic currents through biological ion channels,^{18-21,23} nanoslits,¹⁷ and synthetic nanopores.^{8,33}

The idea of DFT is mapping every possible set of ion density profiles $\{\rho_k(y)\}$ into the system's free energy. The concentrations that minimize the free energy functional are those of the system at equilibrium. The existence of such a free energy functional for fluids has been known since the 1970s³⁴ and good approximations of the free energy functional were derived starting ~25 years ago.^{24,35}

Here we present a simplified sketch of DFT for charged, hard spheres with radius R_i for ion species i . The excess chemical potential is split into two components, one for the hard-sphere (HS) core and one for short-range screening (SC) electrostatics correlations:²⁴

$$\mu_i^{\text{ex}}(y) = \mu_i^{\text{HS}}(y) + \mu_i^{\text{SC}}(y). \quad (4)$$

The long-range electrostatics are already included in $\psi(y)$ in Eq. (1).

Modern hard-sphere functionals are based on Rosenfeld's fundamental measure theory approach.³⁵ In the planar geometry, the hard-sphere component of the excess chemical potential is given by

$$\mu_i^{\text{HS}}(y) = kT \sum_{\alpha=0}^5 \int_{y-R_i}^{y+R_i} \frac{\partial \Phi_{\text{HS}}}{\partial n_{\alpha}}(y') \omega_i^{(\alpha)}(y-y') dy' \quad (5)$$

where $\Phi_{\text{HS}}(\{n_{\alpha}\})$ is a function of the locally-averaged concentrations

$$n_{\alpha}(y) = \sum_i \int_{y-R_i}^{y+R_i} \rho_i(y') \omega_i^{(\alpha)}(y'-y) dy' \quad (6)$$

with weight functions

$$\begin{aligned} \omega_i^{(2)}(r) &= 2\pi R_i \\ \omega_i^{(3)}(r) &= \pi(R_i^2 - r^2) \\ \omega_i^{(5)}(r) &= 2\pi r \\ 4\pi R_i^2 \omega_i^{(0)}(r) &= 4\pi R_i \omega_i^{(1)}(r) = \omega_i^{(2)}(r) \\ 4\pi R_i \omega_i^{(4)}(r) &= \omega_i^{(5)}(r). \end{aligned} \quad (7)$$

Different hard-sphere functionals use different Φ_{HS} . In this paper we use the “antisymmetrized” version of Rosenfeld et al.,³⁶ but the results for other choices for Φ_{HS} differ only by a few percent.³⁷

Coulombic interactions can also be handled accurately in DFT. Here we use the DFT of Gillespie et al.^{38,39} because it is the most accurate at both low and high wall surface charge.^{15,16} Due to space considerations we do not show all the formulas, but the general form for the short-range screening component of the excess chemical potential is

$$\mu_i^{\text{SC}}(y) = M_i(\{\bar{\rho}_k(y)\}) - \sum_j \int_{y-(R_i+R_j)}^{y+(R_i+R_j)} w_{ij}(y-y') [\rho_j(y') - \bar{\rho}_i(y')] dy' \quad (8)$$

where M_i and w_{ij} are analytic functions³⁸ and the “reference fluid density” functional is used to compute the functionals $\bar{\rho}_i(y')$.^{38,39} It has been extensively tested in comparisons against Monte Carlo simulations and has been shown to be extremely accurate.^{15,16}

Current Equations

As we have done previously,^{6,17} we assume that the ion concentrations do not change in the x and z directions (i.e., $\rho_i(\mathbf{x}) = \rho_i(y)$) so that also $\mu_i^{\text{ex}}(\mathbf{x}) = \mu_i^{\text{ex}}(y)$ and $\psi(\mathbf{x}) = \psi(y)$ and that the ions are in equilibrium in the y and z directions. We also assume that a Stern layer defines where the velocity of the ions is 0. The height of the Stern layer is denoted H_s .

Then the electromigration component of the conductance is

$$g_{\text{EM}} = \frac{W}{L} \frac{e^2}{kT} \sum_i z_i^2 D_i \int_{H_s}^{H-H_s} \rho_i(y) dy \quad (9)$$

where D_i is the diffusion coefficient of species i . The advective component of the current assumes that the ion velocity profile $\mathbf{v}(\mathbf{x})$ is described by the steady-state Navier-Stokes equation. With the previous assumptions, $\mathbf{v}(\mathbf{x}) = (u(y), 0, 0)$. With the applied pressure p producing a linear pressure drop down the channel $p(L-x)/L$ and applied voltage V producing the electric field $V(L-x)/L$, the Navier-Stokes equation reduces to

$$\eta \frac{d^2 u}{dy^2} = -\frac{p}{L} - \frac{V}{L} \rho(y) \quad (10)$$

where η is the viscosity and

$$\rho(y) = e \sum_i z_i \rho_i(y) \quad (11)$$

with the boundary conditions

$$u(H_s) = u(H - H_s) = 0. \quad (12)$$

Splitting the velocity into pressure- and voltage-driven components (u_p and u_v , respectively), we have

$$u_p(y) = \frac{p}{2\eta L} (y - H_s)(H - H_s - y) \quad (13)$$

and, using Eqs. (2) and (3),

$$u_v(y) = \frac{\epsilon \epsilon_0 V}{\eta L} (\psi(y) - \psi(H_s)). \quad (14)$$

The streaming (pressure) conductance then is

$$S_{\text{str}} = \frac{W}{p} \int_{H_s}^{H-H_s} \rho(y) u_p(y) dy \quad (15)$$

and the advective component of the total (voltage) conductance is

$$g_{\text{adv}} = \frac{W}{V} \int_{H_s}^{H-H_s} \rho(y) u_v(y) dy. \quad (16)$$

We define the total voltage conductance as the sum of the electromigration and advection conductances:

$$g_{\text{ch}} = g_{\text{EM}} + g_{\text{adv}}. \quad (17)$$

In a microchannel where the double layers at the device walls can be ignored, the advective component is ~ 0 and so

$$g_{\text{ch}}^{\text{micro}} \approx g_{\text{EM}}^{\text{micro}} = \frac{HW}{L} \frac{e^2}{kT} \sum_i z_i^2 D_i \rho_i^{\text{bath}}. \quad (18)$$

For the energy conversion equations described below, we define the fluidic pressure conductance as

$$q_{\text{ch}} = \frac{W}{p} \int_{H_s}^{H-H_s} u_p(y) dy = \frac{W}{12\eta L} (H - 2H_s)^3. \quad (19)$$

Detailed derivations of all these equations may be found in Ref. ⁶. Whether these equations are applicable either in a nanochannel or coupled to DFT is an important matter to consider. The Navier–Stokes equation assumes that the fluid is a continuous substance. Moreover, quantities like pressure, velocity, and density are assumed to be differentiable. The introduction of something “molecular” like DFT for the ion profiles is perfectly consistent with these assumptions. Ion densities are, by definition, a long-time average of the amount of time an infinitely small volume is occupied by an ion.⁴⁰ Because all the ions in a liquid always move due to thermal motion and their Coulombic interactions, the density used in the Navier–Stokes equation is well-defined even if the ions have a finite volume. The DFT is merely a way to compute that density profile, but it could also be computed using particle simulations techniques.⁴¹

It may be, however, that the assumption that the Navier–Stokes equation holds in 50 nm-wide channels is false. Jiang and Qiao⁴² recently addressed this issue. Using molecular simulations of an ionic liquid, they showed that the Navier–Stokes assumption can fail. In their simulations, the 0.5 nm-diameter Lennard-Jones ions were confined in a 9.2 nm-wide slit with *multi-molar* concentration in the middle of the slit. This produced very strongly correlated anions and cations whose density oscillations interleaved (e.g., cation troughs matched up with anion peaks) to produce velocity profiles inconsistent with the Navier–Stokes equation due to oscillating shearing forces. The ion density profiles in our paper are far from this limit. They do have oscillations, but only for one species (e.g., for cations during ion layering or anions during charge inversion); the other species does not oscillate and therefore their troughs and peaks do not match up, which is what caused the deviation from Navier–Stokes for Jiang and Qiao.⁴² Our oscillations also peter out after only ~ 1 peak so we do not have the long-range ion correlations across the majority of the slit that Jiang and Qiao⁴² did. Moreover, a number of studies have concluded that the Navier–Stokes

approach works very well for slits with heights much smaller than the 50 nm we use.^{43,44} See also the discussion by Jiang and Qiao.⁴²

Energy Conversion

Energy conversion efficiency is described here with the same formalism used by van der Heyden et al.,³ except for the use of DFT to compute the net charge profile (Eq. (11)) instead of PB. Briefly, when pressure is applied, a voltage is created between the two reservoirs at $x = 0$ and $x = L$. When connected to an electrical resistor (with resistance R_{load}) in a circuit, the conversion efficiency ϵ_{load} is the ratio of the output electrical power to the input pumping power:³

$$\epsilon_{\text{load}} \equiv \frac{V^2/R_{\text{load}}}{Qp} = \frac{\alpha r}{(1+r)(1+r(1-\alpha))} \quad (20)$$

where $\alpha = S_{\text{str}}^2/q_{\text{ch}}g_{\text{ch}}$ and $r = g_{\text{ch}}R_{\text{load}}$ is the ratio of load and channel electrical resistances. Efficiency then depends on the load resistance, and maximizing ϵ_{load} with respect to R_{load} gives the maximum efficiency

$$\epsilon_{\text{max}} = \frac{\alpha}{\alpha + 2(\sqrt{1-\alpha} + 1 - \alpha)} \quad (21)$$

for $r = 1/\sqrt{1-\alpha}$. Throughout, we refer to ϵ_{max} as the energy (power) conversion efficiency.

Computational Effort

On a quad-core, third generation, 2.3 GHz Intel i7 computer with 8 GB a simple parameter DFT calculation took ~6 seconds for a 50 nm slit. One of the most complicated parameter sets took <30 seconds to complete. Increasing the slit height to 100 nm caused times to increase by up to a factor 5.

PB Systems for Comparison with DFT

We will compare our DFT results to those of two PB models. The first is the classic PB model with point charges that allows those ions to get infinitely close to the surface charge. Because the ions have zero size, we will refer to this model as PB0. The second is the same as PB0, except that the ions only approach the surface charge to within a distance of closest approach of an ion radius R_i . Because the ions have a distance of closest approach, we will refer to this as DCA-PB.

The DCA-PB model is a somewhat underutilized one, in our opinion. The simple act of not allowing the ion centers to touch the wall captures a majority of the effects that DFT does when ion layering or charge inversion are not an issue. Like all PB models, DCA-PB does not produce either phenomenon as DFT does, but the distance of closest approach solves many of the problems of high ion concentrations near electrodes that models like Bikerman's⁴⁵ aim to curb. (For a more general discussion of an exact thermodynamic relationship between ion concentrations at charged walls, see the Appendix.) Moreover, specifying a distance of closest approach makes intuitive sense because the concentration at location x is the concentration of the ions whose *center* is at x , and that ion center can never go infinitely close to a hard wall.⁴⁰

Comparison to Experiments

Any theory should be validated by comparison to experiments. In this case, the theory used here involves three independent components: the use of the primitive model of ions, the

description of ion concentration and electrostatic potential profiles using DFT, and the use of DFT coupled to Navier-Stokes in nanoslits. While these are necessarily intertwined, we try to assess the validity of each with comparisons to experiments in highly-charged systems like those considered in this paper.

The primitive model of ions has been used in at least two highly-charged systems to compute ion currents using Nernst-Planck with ion concentration and electrostatic potential profiles computed with Monte Carlo simulations. In synthetic nanopores, this combination was the first to calculate their Ca^{2+} versus monovalent selectivity using only physically established parameters (i.e., no fitted parameters).³³ Moreover, charge inversion in these nanopores was computed in the same way.⁸ (That study used cobalt sepulchrate(III) (CoSep) as the trivalent cation, as we will below.) Nernst-Planck with Monte Carlo simulations of primitive-model ions has also reproduced a number of experiments in calcium-selective biological ion channels where the charge density from the protein can be >50 M because of the very small volume.⁴⁶ In the L-type calcium channel, this includes experiments with the competition between two monovalent cation species for the negatively charged pore,⁴⁶ as well as competition between two divalent species⁴⁶ and between monovalents and divalents.⁴⁷ Using Dynamic Monte Carlo simulations instead of Nernst-Planck to compute current, selectivity experiments for the neuronal sodium channel were also reproduced.⁴⁸

DFT of primitive-model ions with Nernst-Planck has also been applied to a biological calcium channel, namely the ryanodine receptor.¹⁸⁻²³ This channel is less selective for Ca^{2+} than the L-type calcium channel and has a lower charge density (~ 23 M). DFT not only reproduced experimental data (generally quantitatively), but also predicted a number of nonlinear, counterintuitive results before they were confirmed by experiments.^{18,19,21-23}

Recently, DFT of primitive-model ions was applied to nanochannels with Navier-Stokes used to compute current, in the same way it is in this paper.¹⁷ There, DFT was compared to experiments from Dekker's group that showed charge inversion in pressure-driven flow.⁷ Specifically, the experiments used CoSep and Ca^{2+} to change the sign of the streaming conductance from positive (cation-dominated current) to negative (anion-dominated current).

Fig. 1A recapitulates these CoSep results; the Ca^{2+} results are shown in Ref. ¹⁷. The symbols are the experimental results⁷ and the solid line the DFT results. Here, we used only the parameters stated by van der Heyden et al. for the diameter of CoSep (0.89 nm) and the surface charge of their bare silica device (-0.15 C/m²). Like before,¹⁷ we used the diameter of CoSep as the Stern layer height. The DFT captures the experiments qualitatively, including subtle features like the size of the current (which we could not impose as all the parameters were already set) and the presence of a minimum in the plot of conductance versus CoSep concentration.

This qualitative nature of the fitting of the experiments is worth noting, however. This is an extremely challenging problem for any theory of a nanochannel since the main ions are very large (0.89 nm in diameter), trivalent, and at 100 mM concentrations. For comparison, we have included PB results using twice the distance of closest approach as the Stern layer height, like in the DFT calculation. Neither PB model even gets the correct size for the conductance. Moreover, since PB cannot produce charge inversion, the streaming conductance never changes sign in either the PB0 or DCA-PB models (dotted and dashed lines, respectively, in Fig. 1A). Why the DFT does not do better than it does is probably because the model we are using is very simple. The ions are hard spheres which does not take into account the ions' hydration state. Other important physics is missing as well. For instance, we use a constant surface charge for all CoSep concentrations, but it is known that

the surface charge changes can change with ion composition.^{49,50} Also missing are dielectric interactions of the trivalent ions with the low-dielectric wall. Moreover, it is unclear what the Stern layer height should be or if it changes with concentration.

To assess the DFT theory even more for this CoSep system, we present new comparisons to the experiments of van der Heyden et al.⁷ In addition to using only CoSep and Ca^{2+} as the cations, they also added varying concentrations of K^+ to the system, letting it compete with CoSep in screening the surface charge. Fig. 1B show this comparison of DFT (solid lines) and the DCA-PB model (dashed lines) to the experimental results (symbols). The DFT reproduces both the sizes of the conductances, as well as the maximum each curve has and the K^+ concentration at which it occurs. Therefore, the DFT correctly reproduces the competition between K^+ and CoSep, while the DCA-PB does not. The differences between the DFT and experimental conductances are the same as in the pure CoSep case. This is indicated with the arrows labeled with circled 1 and 2 in Figs. 1A and 1B.

Lastly, we note that ion-ion correlations in an electrical double layer calculated with DFT have been directly experimentally tested and the agreement was excellent.⁵¹

Collectively this comparison to experiments indicates that the primitive model of ions and the DFT description of them is a reasonable model for ions in a nanochannel. As with all such simple models, the results that we show below are probably only be qualitatively good, especially for multivalent ions (Fig. 1). Therefore, one should analyze trends seen in the calculations, rather than the exact numbers. We will present and analyze our results on this level.

RESULTS

In this paper, we show DFT calculations of the total conductance, streaming conductance, and power conversion efficiency for a wide range of surface charges (-0.30 C/m^2 to 0 C/m^2) and concentrations (10^{-6} M to 1 M). The results show some general trends, but also highlight differences resulting from cation size and valence. Most of the calculations show that monovalents behave qualitatively different than di- and trivalent cations. Typically, adding the second valence charge has a significant qualitative effect, however then adding a third valence charge often only changes the picture quantitatively.

Total Voltage Conductance

We first describe the general trends of total conductance (Eq. (17)) and the nonlinear regions that appear for the multivalent cations (Fig. 2). We then look at the total conductance compared to the bulk value to see how the different parameters change the value relative to the bath/microchannel baseline (Fig. 3).

In Figure 2, we see that as concentration decreases, generally the total conductance decreases. In the high concentration regime, the total conductance is large. Therefore, in Fig. 2 we introduced a 200 pS cutoff and so the high concentration regime is solid red. (This cutoff was necessary to resolve finer details in the rest of the figure.) Within this red region, the total conductance falls from a maximum value of well over 1000 pS to approximately 200 pS over a two order of magnitude change in concentration (data not shown). After the steep initial decline, the fall is much more gradual, only changing by ~ 1 order of magnitude over a 10,000 fold change in concentration. The steep change in total conductance is due to the electromigration term dominating at high concentrations and the conductance leveling off at low concentrations, trends seen in experiments as well as PB models.⁵² Another general trend for the nine cations is that as the surface charge gets larger, the total

conductance increases (Fig. 2). Most other trends are not as easily generalized over all 9 of the different cations because they depend on cation size or valence.

For example, Figure 2 shows that the surface charge that produces the greatest total conductance is related to cation size: for the mono- and divalent cations, total conductance increases with increased concentration, however the density of the contours tends to decrease as cation size and valence increase. The large monovalent cation is the exception to the trend due to ion layering (see Discussion below). For the trivalent cations, a local maximum is attained with respect to surface charge in the low concentration regime (Fig. 2, row 3).

For the trivalent cations in the low concentration regime, as one moves from left to right (from the small to the large cations), the position of the total conductance maximum shifts towards a smaller surface charge. Specifically, the small trivalent cation has the local total conductance maximum near a surface charge of -0.15 C/m^2 , the medium trivalent near -0.10 C/m^2 , and the large trivalent near -0.05 C/m^2 . The small cation experiences a total conductance that is approximately 3 times larger than the large cation and twice as large as the medium cation.

While the absolute value of the total conductance at each position is of interest, another important consideration is the conductance relative to the bulk value; that is, how does the total conductance of a nanochannel differ from that of a microchannel. In Figure 3 we divide each total conductance by the corresponding bulk value of Eq. (18). We only show the small monovalent cation, because its behavior was similar to all the other cations. In Figure 3 we see that total conductance exceeds the bath value by ~ 4 orders of magnitude at very low concentration (10^{-6} M). As concentration increases, the relative total conductance falls quickly, exceeding bulk by only ~ 1 order of magnitude at a concentration of 10^{-3} M and reaching the bulk value at $\sim 10^{-1} \text{ M}$. Unlike many of the trends observed above, this qualitative result is very similar for all of the different cations.

Streaming Conductance

Next we consider the behavior of the streaming conductance (Eq. (15)) over the same parameter space. Generally, streaming conductance tends to increase as surface charge increases and as concentration decreases (Fig. 4). As we saw in the total conductances, most trends are not easily generalized and are more easily broken down by cation size and valence.

For monovalent cations, the increase in streaming conductance is initially rapid as the surface charge increases from zero or as the bath concentration decreases from 1 M . The rate of change decreases as one approaches the streaming conductance maximum in either surface charge or concentration. This is shown in Figure 4 (row 1) by the decrease in proximity of the contours as one moves into the high-surface-charge/low-concentration regime.

Another general trend is that increasing the valence of the cation results in a considerable drop in streaming conductance and can even cause the streaming conductance to become negative (Fig. 4). For example, where streaming conductance is the greatest among all the cations (the large monovalent cation in the high-surface-charge/low-concentration regime), the streaming conductance is $\sim 9 \text{ pS/bar}$. In the corresponding region for the large divalent cation, the streaming conductance is only $\sim 2 \text{ pS/bar}$. Streaming conductance also decreases with decreasing cation size, although the effects are less significant than those due to valence.

The change of sign in the streaming conductance for the di- and trivalents is related to charge inversion. In a nanofluidic device, the effect of charge inversion on current can be explained as follows. At large surface charges, more cations accumulate in the first layer of ions than necessary to neutralize the negative surface charge, and this cation surplus attracts anions into the second layer of ions. If enough anions accumulate, the sign of the electrostatic potential changes. If even more anions accumulate, the anions can dominate the current, changing it from positive (cation-dominated) to negative. In this second layer, the cation concentration is depleted relative to bulk, whereas the anion concentration can be much greater than bulk (see Discussion). Charge inversion typically occurs only with multivalent cations. Consistent with that, the streaming conductances are positive for all of the monovalents, while all of the di- and trivalent cations have negative conductances in parts of the parameter space we tested.

The surface charge that produces a negative streaming conductance varies slightly based on cation size. For the 0.15 and 0.3 nm divalent cations, a large surface charge is needed to produce a negative streaming conductance (greater than approximately -0.10 C/m^2). However, for a large divalent cation a negative streaming conductance is experienced for surface charges from 0 up to approximately -0.20 C/m^2 in the high concentration regime. Interestingly, where the small and medium divalent cations showed the largest negative streaming conductances, the large divalent cation has a positive streaming conductance.

The trivalent cations also produce charge inversion. These cations have even larger negative streaming conductances than the divalents, by approximately a factor of 3 where the streaming conductance is the most negative. For all three trivalent cation sizes, the region of negative streaming conductances occurs in the same part of parameter space, namely at very high surface charge and high concentration, parameters that promote charge inversion.

Power Conversion Efficiency

We now consider at how the maximum pressure-to-voltage power conversion efficiency (Eq. (21)) varies over our parameter space (Fig. 5). Under different conditions and with different ions, the power conversion efficiency varies considerably. To understand how different parameters affect the efficiency is of considerable interest in the development of new devices. Like the two forms of conductance we looked at, relatively few trends can easily be generalized over all 9 of the cations.

For the most part, as surface charge and concentration decrease toward 0, the maximum power conversion efficiency increases (Fig. 5). With a small surface charge and the low concentration there is a wide double layer that results in the exclusion of co-ions. As previously described by others³ (see also Discussion), the best way to maximize power conversion efficiency is to minimize the number of co-ions. Increasing the surface charge results in narrowing of the double layer and increasing of co-ion levels in the channel, reducing power conversion efficiencies. Consistent with that, for all 9 cations the region with near-zero surface charge and low ion concentration produces the greatest levels of power conversion efficiency. On the other hand, the high concentration region always produces power conversion efficiencies of less than 1%.

Another important phenomenon is that power conversion efficiency changes dramatically with valence and cation size. Increasing valence significantly decreases the level of maximum power conversion efficiency, in some regions by a factor of ~ 3 . More specifically, our calculations show that large monovalents produce the greatest power conversion efficiency levels, almost 20% for the channels we consider (Fig. 5, row 1). For the di- and trivalent cations, the maximum conversion efficiency was just over 5%, although most of the conditions produced efficiencies of less than 1% (Fig. 5, rows 2 and 3). Increasing the cation

diameter has a similar, but less significant, effect; it expands the concentration and surface charge range for which the efficiency is large (Fig. 5). In Figure 5 this can most easily be seen for the monovalent ions. For the large monovalent cations (0.90 nm in diameter), at low concentrations the 10% power conversion efficiency contour is nearly horizontal at a surface charge of -0.20 C/m^2 . However, as the cation diameter decreases from 0.90 nm to 0.30 nm, the 10% contour moves to a surface charge of -0.07 C/m^2 . While the qualitative picture is the same, increasing the cation size expands the regions of greater power conversion efficiency levels.

Differences Due to Geometry and Stern Layer

For the results shown so far, we chose to define the Stern layer height as the diameter of the counterion, a definition that reproduced experiments in the past.¹⁷ For completeness, we repeated all calculations with a zero Stern layer height (i.e., zero velocity at the wall). Remakes of Figures 2–5 using a zero Stern layer height are available online in the Supplementary Material as Figs. S1–S4. Almost all of the major qualitative trends held. Overall, the magnitudes of the streaming and total conductances are larger with a zero Stern layer height, due to the increased amount of charge with a finite velocity. The only notable exception to the general trends that we outlined above is in the total conductance: with a zero Stern layer, total conductance tends to increase—rather than decrease—as valence increases (Fig. S1). Other changes included that the local maxima in the total conductances disappeared entirely with a zero Stern layer height (Fig. S1). The streaming conductances still showed similar nonmonotonic behavior, but the change in magnitude resulted in the loss of many of the local minima previously observed (Fig. S3). In the power conversion efficiencies, the local minima in the multivalent ions disappeared with a zero Stern layer height (Fig. S4). However, for the large divalent cation a minimum appeared at low concentration and large surface charge (Fig. S4).

By changing the Stern layer height, one changes the amount of charge that is moving. This results in an increased amount of charge with a finite velocity in the first layer of counterions near the wall (where concentration is high) and therefore cation conductance went up. When charge inversion occurred, the streaming conductances dipped below zero much less frequently because of this. Note, however, the amount of charge inversion (i.e., the height of the anion bump seen in Fig. 7B) is independent of Stern layer definition; the Stern layer height only defines the velocity of the ions, not their wall-to-wall concentration profile.

Lastly, we note that our calculations were performed with 50 nm channels. We also performed the same calculations with a 100 nm channel height and found no qualitative differences (data not shown).

DISCUSSION

In this section, we attempt to understand the causes for the trends in Figs. 2–5, especially how nonlinear phenomena like charge inversion and ion layering affect the qualitative picture.

Streaming Conductance

First, we attempt to understand the molecular effects causing the trends in the streaming conductance results. The dominant trend in the streaming conductance results (Fig. 4) is that as concentration decreases and surface charge increases, streaming conductance increases. To understand what is happening, it is easiest to look at how streaming conductance is defined. Streaming conductance is given by the integral of the product of the pressure-driven

velocity (Eq. (13)) and the total charge density profiles (Eq. (15)). This velocity function is solely geometry-dependent and therefore independent of ion species parameters. Thus, where the net charge concentration profile is nonzero farthest from the wall dominates the streaming conductance. One way to achieve this is having a wide double layer at low concentrations with high surface charge.

Another way is with ion layering producing a bump in the cation concentration profile in the second layer of ions. For the monovalent cations (Fig. 4, row 1), ion layering has a very significant role for the qualitative picture. As shown in Figure 6, the largest cation experiences a rise in concentration after the initial spike near the wall. However, due to the increased velocity further from the wall, the slight rise in concentration can result in very large streaming conductances. This is shown in the low concentration regions for the monovalent cations (Fig 4, row 1), especially when the surface charge is large to promote layering (Fig. 6).

The behavior for multivalent cations is different than for the monovalents. When we analyze the concentration profiles for the di- and trivalent cations (Fig. 7), ion layering is not as apparent. Instead, for the di- and trivalent cations, charge inversion has a considerable effect on the qualitative picture, while this was not present for the monovalents. To see how charge inversion affects the behavior of the multivalent counterions, it is easiest to look at profiles.

Figure 7A shows net charge as a function of slit position for a small trivalent cation at four different concentrations (10^{-6} M, 10^{-3} M, 10^{-2} M, and 10^{-1} M). For all cations, the behavior as x increases is the same. There is no net charge until the distance is an ion radius from the wall, and then there is a huge spike, in all four cases going to ~ 70 M. Because the magnitude of the initial spike is almost independent of concentration, differences in streaming conductance are dominated by the differences in behavior after the initial spike. The large initial jump in concentration is due to the negative surface charge of the wall attracting a large number of cations. After the initial layer of cations, the different net charge profiles separate from one another. For the two smallest concentrations (10^{-6} M and 10^{-3} M, black and red curves in Fig. 7A, respectively) the net charge profiles are almost identical. The net charge hardly dips below zero for either concentration. This is because there are too few anions to significantly overcome the positive net charge brought about by the large concentration of cations. However, for higher concentrations the net charge profile changes sign.

Figure 7B shows the anion concentration profile normalized to the bulk concentration (so that everything would fit on the same scale). The behavior is not monotonic, with the anion concentration rising and then falling. In all cases, the maximum is above the bath concentration, indicating charge inversion.

For understanding conductance trends, however, it is the *absolute* anion concentration that matters. Since that increases with bath concentration, at lower cation concentrations there are less anions than there are at larger cation concentrations. In Figure 7A we see that as concentration increases, the net charge dips drops below zero by a greater amount. The rise in anion concentration in the diffuse layer results in decreased net charge. The streaming conductance is negative (Fig. 7C), indicating that the number of anions in the second layer has become so large as to dominate the current. (Note that well before the anions dominate the current that there is charge inversion; only when the layer of anions has become large enough to counteract the large cation current does the current change sign.) Figure 7C summarizes this, showing the streaming conductance at the different concentrations (10^{-6} M, 10^{-3} M, 10^{-2} M, and 10^{-1} M). The streaming conductance is mildly positive at the

lowest concentration (10^{-6} M) and dips below zero for the other three concentrations (10^{-3} M, 10^{-2} M, and 10^{-1} M).

Lastly, to look at the effects of ion-ion and ion-wall correlations in a different way, in Fig. 8 we compare the DFT results with the two PB systems described in Theory and Methods. Specifically, the figure shows how the conductances change with the cation diameter for the three methods. A range of Stern layer heights are shown, with the upper bound of the conductances from zero Stern layer height and the lower bound from the cation diameter as the Stern layer height. Figs. 8A and 8B show the streaming conductance with a monovalent and divalent cation, respectively. (The corresponding total conductances in Figs. 8C and 8D are discussed in the next section.) The DCA-PB model tends to track the DFT results fairly well, while the PB0 model tends to differ significantly and therefore we do not discuss it further.

For the monovalent system, the DFT conductance becomes superlinear at large diameters because ion layering (which starts to occur at a diameter of ~ 0.6 nm) significantly increases the streaming conductance, as described above. At a diameter of ~ 0.6 nm is also where the DCA-PB starts to deviate from the DFT, as one would expect since they have the same distance of closest approach for the ions and are otherwise very similar when strong correlations are absent. For the divalent system, the absence of the screening correlations (Eq. (8)) in both PB models produces differences between these models and DFT, even at small diameters. The DFT and DCA-PB models give similar streaming conductances at large diameters, but this is merely a coincidence. Since both the upper and lower bounds of the DFT conductance increase with diameter while the lower DCA-PB bound actually decreases, the intersection of the two conductance regions is mathematically inevitable (two lines with oppositely signed slopes must intersect) and not due to the DCA-PB model having the correct physics; as described above, at this high surface charge (-0.3 C/m²), charge inversion plays a role and the DCA-PB model does not have this at all.

Total Conductance

We now examine the molecular level phenomena that result in the different trends observed in Figure 2. We again begin with the definition of total conductance and build from there. Total conductance is defined as the integral of the sum of the advection current density and the electromigration current density. The advection current density is a function of the electro-osmotic flow (EOF) velocity. Unlike the geometry-dependent PDF velocity, the EOF velocity is a function of local electrostatic potential (Eq. (14)). The electromigration velocity depends on $D_i z_i^2$ (Eq. (9)).

As before, it is easiest to begin with the monovalent cations. At high concentrations (over approximately 10^{-2} M), near bulk properties tend to dominate the qualitative picture (Fig. 3). For the monovalent cations, as one increases surface charge, total conductance increases (Fig. 2, row 1) because, as surface charge increases, more cations will be attracted to the area near the wall.

For multivalent cations, it is more complicated. In Fig. 9 we plot both the advective (Fig. 9A) and the electromigration (Fig. 9B) current densities for the medium trivalent cation at 10^{-5} M. For each curve, the area under it is the current. Except at very low surface charge (e.g., -0.01 C/m²), the advective term is approximately an order of magnitude smaller than the electromigration term. This means that the electromigration term tends to dominate the voltage-driven current and so we focus on it for surface charges ranging from -0.05 C/m² to -0.25 C/m².

The electromigration current density is determined by the ion concentration profiles across the slit, weighted by the diffusion coefficients and square of the valences (Eq. (9)). These concentration profiles tend to narrow as surface charge increases and this is reflected in the current density profiles (Fig. 9B). In our case, the -0.25 C/m^2 and the -0.1 C/m^2 current densities have the same maximum, but because of the different decays away from the wall, the -0.1 C/m^2 case has more area (current) than the -0.25 C/m^2 case. As surface charge decreases to -0.05 C/m^2 , the current density profile broadens, but the maximum decreases compared to -0.1 C/m^2 and they have almost the same current (Fig. 9C); the total conductance versus surface charge reaches a maximum at -0.1 C/m^2 (Fig. 9C).

After -0.1 C/m^2 , the conductance decreases again. This occurs because, as the surface charge decreases below -0.1 C/m^2 , the electromigration term no longer dominates the current; the advective term becomes comparable. At low surface charges, the concentration of the ions near the wall becomes more bulk-like. In this case, the bulk concentration is very small (10^{-5} M) and so the net total conductance is very small.

It is important to note that the local maximum that is observed at an intermediate surface charge (Fig. 9C) is not a robust result, as discussed at the end of Results. When we changed the Stern layer to be at the device wall, the local maximum went away and the streaming conductances increased with increasing surface charge and concentration (see online Supplementary Material Fig. S3).

Another phenomenon seen in Fig. 2 is that, for the monovalent cations (and to a lesser extent for the divalent cations), changing cation size produces unexpected results in the total conductance. Moving from the smallest cation (0.15 nm) to the medium cation (0.30 nm), the total conductance values decrease. However, as one further increases the cation size to 0.90 nm , the total conductance increases sharply. To see this, consider that the 200 pS contour in Fig. 2 is nearly vertical for all of the cations except the large monovalent. For the 8 cations that show the near vertical contour, this means that in the high concentration regime, surface charge has very little effect on the total conductance. However, for the large monovalent cation the 200 pS contour deviates from the pattern and suggests an influence from the large surface charges. This results from ion layering for the large monovalent cation (Fig. 6). The counterion concentration profile oscillates in the low-concentration/high-surface-charge regime if the ion is large enough. A rise in counterion concentration in the higher velocity regime after the initial jump near the wall results in a more significant net charge in the second (and potentially third and fourth) ion layer than in the non-oscillating cases. The rise in conductance as cation size increases is much less apparent for the di- and trivalent cations because they do not tend to have layering (Fig. 7).

We now turn to the results in Figure 3, where each total conductance was divided by the bulk value. The results show that when the total conductance is divided by the bulk value, the relative total conductance at low concentration can be very large and that as concentration increases, the total conductance approaches the bulk value. The very large values, relative to bulk, can be attributed to the fact that at very low concentrations the double layers are so wide that they overlap and ions never reach their bulk concentration in the center; the Debye length is long in relation to the dimensions of nanochannel. This essentially expels the anions from the nanofluidic channel, resulting in a large space charge that is not present in the microchannel. For the discussion of power conversion efficiency below, it is again important to note that while the *relative* total conductance is greatest at low concentration, the *absolute* total conductance at low concentration is quite small compared to the near-bulk total conductances at high concentration (Fig. 2).

Lastly, we compare the DFT results for total conductance to PB results in Figs. 8C and 8D. Like for the streaming conductance with the monovalent cation, the DFT and the DCA-PB results start to diverge when ion layering becomes important (at a diameter of ~ 0.6 nm) and increases the total conductance superlinearly. The divalent case is more subtle. At first glance, the DFT and DCA-PB results seem to give the same answers and for the zero Stern layer height they do. But, for the wide Stern layer (the lower bound of the conductance), they differ by a very large percentage, something this obscured by the large range on the y -axis for the plot. Since the underlying physics and the resulting ion concentration and electrostatic potential profiles are very different (especially when there is charge inversion), any similarity in conductance is a coincidence rather than a validation of PB models.

Power Conversion Efficiency

Maximum power conversion efficiency (Eq. (21)) depends on the dimensionless parameter

$$\alpha = \frac{S_{\text{str}}^2}{q_{\text{ch}} g_{\text{ch}}} \quad (22)$$

where S_{str} is the streaming conductance, q_{ch} is the pressure conductance in the channel, and g_{ch} is the total conductance in the channel (see Theory and Methods). The maximum possible power conversion efficiency occurs when α is 1, resulting in 100% efficiency. α is inversely proportional to total conductance and proportional to the square of the streaming conductance. Thus, α (and power conversion) can be maximized when the streaming conductance is maximized while total conductance is minimized.

As previously described by others,³ this kind of balance is difficult when co-ions are in the channel. In a channel, pressure driven flow causes both co- and counterions to move in the same direction, so the co-ion and counterion currents tend to cancel each other. On the other hand, voltage driven flow causes the co- and counterions to move in opposite directions, so their currents enhance the total current. Thus, as the concentration of co-ions decreases, the streaming conductance increases and the total voltage conductance decreases, maximizing efficiency.⁶ The number of co-ions in the device is the smallest at small surface charges and when the double layer is the widest (i.e., at low ion concentrations). In Figure 5, one can see that a power conversion efficiency maximum occurs for all 9 cations in the low-concentration/low-surface-charge regime. As surface charge increases, the double layer narrows and power conversion efficiency falls.

Monovalents have the highest efficiency because their double layers are the widest. In addition, monovalents tend to undergo layering that increases their streaming conductance (Figs. 4 and 6). Ion layering of monovalents has, in fact, recently been suggested as a way to dramatically increase power conversion efficiency.⁶ Multivalent cations, on the other hand, have none of these favorable properties. They have narrower double layers compared to monovalents and they do not layer easily (Fig. 7). Also, multivalent ions tend to undergo charge inversion (Fig. 7), which reduces the streaming conductance—sometimes even to 0—which disproportionately reduces efficiency (Eq. (22)).

CONCLUSION

There are many different ways to model nanofluidic devices. Poisson-Boltzmann-based theories describing the behavior inside nanofluidic devices were an essential starting point, but they trade off accuracy for computational efficiency. DFT is more computationally intensive, but does a better job at including the ion-ion and ion-wall correlations^{15,16} that we showed here can dominate nanofluidic device behavior over large parts of parameter space.

We have shown that in large regions of surface charge and concentration parameter space ion profiles are nonmonotonic and that those nonmonotonic profiles result in unexpected, complicated device properties. By performing calculations over such a wide parameter space, we have shown how nanoscale phenomena like ion layering and charge inversion affect the global picture. In the future, it may be possible to use these nanoscale correlations to increase power conversion efficiency⁶ or in other, novel nanochannel applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by NIH grant R01-AR054098 (Michael Fill, PI).

APPENDIX: ION CONCENTRATIONS AT A SURFACE CHARGE

Large surface charges necessarily require large counterion concentrations near the wall. For example, the cation concentrations at contact for the net charge profiles in Fig. 7A is ~ 23 M for a surface charge of -0.3 C/m². In other cases, Monte Carlo simulations give contact concentrations of ~ 70 M¹⁵ for a surface charge of -0.5 C/m² and >100 M for even larger surface charges.¹⁶ It is important to note that these are Monte Carlo simulation results, not DFT results, and therefore are the best available solutions to these double layer problems with charged, hard spheres near a smooth, hard, charged wall. (That the DFT agrees with these simulations speaks to the accuracy of the DFT, but the existence of these large concentrations comes from the simulations.^{15,16})

A simple way to understand how the contact concentrations of an electrolyte depends on the surface charge is the contact theorem of statistical mechanics.⁵³⁻⁵⁵ This mathematically-exact thermodynamic sum rule relates the contact concentrations of ions, $\rho_i(R_i)$ (i.e., their concentration at their distance of closest approach, which is the radius for our hard-sphere ions) to the surface charge σ on a smooth, hard wall and the pressure P_{ions} of the ions in the bulk. Specifically,⁵³⁻⁵⁵

$$\sum_i \rho_i(R_i) = \frac{\sigma^2}{2kT\epsilon\epsilon_0} + \frac{P_{\text{ions}}}{kT} \quad (23)$$

where the other symbols are the same as in Theory and Methods.

The importance of this theorem is at least twofold. First, it may be used as check of thermodynamic self-consistency for any approximate theory like DFT or PB and its variants. DFT consistently does a very good job of approximately satisfying the theorem.¹⁵ Second, it shows how the contact concentrations change with surface charge. Specifically, in the case of only one cation and one anion species and in the limit of large surface charge, Eq. (23) gives that the density of the counterions (with radius R) is

$$\rho_{\text{counter}}(R) \approx \frac{\sigma^2}{2kT\epsilon\epsilon_0} \quad (24)$$

where we have assumed that the pressure and co-ion concentration are negligible.

Eq. (24) shows that for ions near a smooth, hard, charged wall, the counterion contact density grows as the *square* of the surface charge and is *not* inherently bounded, as is

assumed by theories like Bikerman's.⁴⁵ This counterintuitive result is the result of a number of intertwined effects. In the Bikerman theory, packing fraction is the quantity that is used to penalize the accumulation high concentrations of ions. However, packing fraction is not a local concept; it implicitly assumes a uniform concentration and therefore that there are ions at the same concentration in the immediate neighborhood of the ions. This is not true, however, as the ion concentrations near a surface charge decay exponentially with distance. In fact, Rosenfeld³⁵ showed that the true local packing fraction that cannot exceed 1 is defined as a local average of the concentrations, specifically the n_3 term in Eq. (6), and that this definition is thermodynamically self-consistent (verified numerically by Roth and Dietrich²⁷).

For ions, large contact concentrations are possible because of two competing effects. It is true that large local concentrations do produce large positive (repulsive) energies through the $\mu_i^{\text{HS}}(y)$ term. However, the electrostatic terms produce large counteracting negative terms. This is especially true for the screening term $\mu_i^{\text{SC}}(y)$, which many times is as large or larger than the other terms.^{16,19,56,57} Importantly, this term is generally not included in the PB theory variants.

REFERENCES

1. Napoli MT, Pennathur S, Eijkel JCT. Nanofluidic technology for biomolecule applications: a critical review. *Lab Chip*. 2010; 10:957–985. [PubMed: 20358103]
2. Daiguji H, Yang P, Szeri AJ, Majumdar A. Electrochemomechanical energy conversion in nanofluidic channels. *Nano Lett*. 2004; 4:2315–2321.
3. van der Heyden FHJ, Bonthuis DJ, Stein D, Meyer C, Dekker C. Electrokinetic energy conversion efficiency in nanofluidic channels. *Nano Lett*. 2006; 6:2232–2237. [PubMed: 17034089]
4. van der Heyden FHJ, Bonthuis DJ, Stein D, Meyer C, Dekker C. Power generation by pressure-driven transport of ions in nanofluidic channels. *Nano Lett*. 2007; 7:1022–1025. [PubMed: 17352506]
5. Pennathur S, Eijkel JCT, van den Berg A. Energy conversion in microsystems: Is there a role for micro/nanofluidics? *Lab Chip*. 2007; 7:1234–1237. [PubMed: 17896005]
6. Gillespie D. High energy conversion efficiency in nanofluidic channels. *Nano Lett*. 2012; 12:1410–1416. [PubMed: 22300476]
7. van der Heyden FHJ, Stein D, Besteman K, Lemay SG, Dekker C. Charge inversion at high ionic strength studied by streaming currents. *Phys. Rev. Lett*. 2006; 96:224502. [PubMed: 16803311]
8. He Y, Gillespie D, Boda D, Vlassiouk I, Eisenberg RS, Siwy ZS. Tuning transport properties of nanofluidic devices with local charge inversion. *J. Am. Chem. Soc*. 2009; 131:5194–5202. [PubMed: 19317490]
9. Bazant MZ, Kilic MS, Storey BD, Ajdari A. Towards an understanding of induced-charge electrokinetics at large applied voltages in concentrated solutions. *Adv. Colloid Interface Sci*. 2009; 152:48–88. [PubMed: 19879552]
10. Torrie GM, Valleau JP. Electrical double layers. I. Monte Carlo study of a uniformly charged surface. *J. Chem. Phys*. 1980; 73:5807–5816.
11. Torrie GM, Valleau JP. Electrical double layers. 4. Limitations of the Gouy-Chapman theory. *J. Chem. Phys*. 1982; 86:3251–3257.
12. Nielaba P, Forstmann F. Packing of ions near an electrolyte-electrode interface in the HNC/LMSA approximation to the RPM model. *Chem. Phys. Lett*. 1985; 117:46–48.
13. Nilson RH, Griffiths SK. Influence of atomistic physics on electro-osmotic flow: An analysis based on density functional theory. *J. Chem. Phys*. 2006; 125:164510. [PubMed: 17092108]
14. Messina R, González-Tovar E, Lozada-Cassou M, Holm C. Overcharging: The crucial role of excluded volume. *Europhys. Lett*. 2002; 60:383.
15. Gillespie D, Valiskó M, Boda D. Density functional theory of the electrical double layer: the RFD functional. *J. Phys.: Condens. Matter*. 2005; 17:6609–6626.

16. Valiskó M, Boda D, Gillespie D. Selective adsorption of ions with different diameter and valence at highly-charged interfaces. *J. Phys. Chem. C*. 2007; 111:15575–15585.
17. Gillespie D, Khair AS, Bardhan JP, Pennathur S. Efficiently accounting for ion correlations in electrokinetic nanofluidic devices using density functional theory. *J. Colloid Interface Sci.* 2011; 359:520–529. [PubMed: 21531429]
18. Gillespie D, Xu L, Wang Y, Meissner G. (De)constructing the ryanodine receptor: Modeling ion permeation and selectivity of the calcium release channel. *J. Phys. Chem. B*. 2005; 109:15598–15610. [PubMed: 16852978]
19. Gillespie D. Energetics of divalent selectivity in a calcium channel: The ryanodine receptor case study. *Biophys. J.* 2008; 94:1169–1184. [PubMed: 17951303]
20. Gillespie D, Fill M. Intracellular calcium release channels mediate their own countercurrent: The ryanodine receptor case study. *Biophys. J.* 2008; 95:3706–3714. [PubMed: 18621826]
21. Gillespie D, Giri J, Fill M. Reinterpreting the anomalous mole fraction effect: The ryanodine receptor case study. *Biophys. J.* 2009; 97:2212–2221. [PubMed: 19843453]
22. Gillespie D, Xu L, Meissner G. Selecting ions by size in a calcium channel: The ryanodine receptor case study. *Biophys. J.* 2010; 98:332a.
23. Gillespie D, Chen H, Fill M. Is ryanodine receptor a calcium or magnesium channel? Roles of K^+ and Mg^{2+} during Ca^{2+} release. *Cell Calcium*. 2012; 51:427–433. [PubMed: 22387011]
24. Rosenfeld Y. Free energy model for inhomogeneous fluid mixtures: Yukawa-charged hard spheres, general interactions, and plasmas. *J. Chem. Phys.* 1993; 98:8126–8148.
25. Mier-y-Teran L, Suh SH, White HS, Davis HT. A nonlocal free-energy density-functional approximation for the electrical double layer. *J. Chem. Phys.* 1990; 92:5087–5098.
26. Yu Y-X, Wu J. Density functional theory for inhomogeneous mixtures of polymeric fluids. *J. Chem. Phys.* 2002; 117:2368–2376.
27. Roth R, Dietrich S. Binary hard-sphere fluids near a hard wall. *Phys. Rev. E*. 2000; 62:6926–6936.
28. Roth R, Kroll KM. Capillary evaporation in pores. *J. Phys.: Condens. Matter*. 2006; 18:6517–6530. [PubMed: 21690851]
29. Kierlik E, Rosinberg ML. Free-energy density functional for the inhomogeneous hard-sphere fluid: Application to interfacial adsorption. *Phys. Rev. A*. 1990; 42:3382–3387. [PubMed: 9904418]
30. van der Wouden, EJ.; Bommer, J.; Pennathur, S.; Eijkel, JCT.; van den Berg, A. Fabrication of a Nanofluidic Field Effect Transistor for Controlled Cavitation in Nanochannels.. XXII ICTAM; Adelaide, Australia. August 25th -29th, 2008; 2008.
31. Lenzi A, Viola F, Bonotto F, Frey J, Napoli M, Pennathur S. Method to determine the effective ζ potential in a microchannel with an embedded gate electrode. *Electrophoresis*. 2011; 32:3295–3304. [PubMed: 22025198]
32. Vincze J, Valiskó M, Boda D. The nonmonotonic concentration dependence of the mean activity coefficient of electrolytes is a result of a balance between solvation and ion-ion correlations. *J. Chem. Phys.* 2010; 133:154507. [PubMed: 20969403]
33. Gillespie D, Boda D, He Y, Apel P, Siwy ZS. Synthetic nanopores as a test case for ion channel theories: The anomalous mole fraction effect without single filing. *Biophys. J.* 2008; 95:609–619. [PubMed: 18390596]
34. Evans R. Nature of the liquid-vapor interface and other topics in the statistical mechanics of non-uniform, classical fluids. *Adv. Phys.* 1979; 28:143–200.
35. Rosenfeld Y. Free-energy model for the inhomogeneous hard-sphere fluid mixture and density-functional theory of freezing. *Phys. Rev. Lett.* 1989; 63:980–983. [PubMed: 10041238]
36. Rosenfeld Y, Schmidt M, Löwen H, Tarazona P. Fundamental-measure free-energy density functional for hard spheres: Dimensional crossover and freezing. *Phys. Rev. E*. 1997; 55:4245–4263.
37. Roth R. Fundamental measure theory for hard-sphere mixtures: A review. *J. Phys.: Condens. Matter*. 2010; 22:063102. [PubMed: 21389360]
38. Gillespie D, Nonner W, Eisenberg RS. Coupling Poisson-Nernst-Planck and density functional theory to calculate ion flux. *J. Phys.: Condens. Matter*. 2002; 14:12129–12145.

39. Gillespie D, Nonner W, Eisenberg RS. Density functional theory of charged, hard-sphere fluids. *Phys. Rev. E*. 2003; 68:031503.
40. Barthel, JMG.; Krienke, H.; Kunz, W. *Physical Chemistry of Electrolyte Solutions: Modern Aspects*. Springer; New York: 1998.
41. Boda D, Gillespie D. Steady state electrodiffusion from the Nernst-Planck equation coupled to local equilibrium Monte Carlo simulations. *J. Chem. Theory Comput.* 2012; 8:824–829.
42. Jiang X, Qiao R. Electrokinetic transport in room-temperature ionic liquids: Amplification by short-wavelength hydrodynamics. *J. Phys. Chem. C*. 2011; 116:1133–1138.
43. Travis KP, Todd BD, Evans DJ. Departure from Navier-Stokes hydrodynamics in confined liquids. *Phys. Rev. E*. 1997; 55:4288–4295.
44. Qiao R, Aluru NR. Ion concentrations and velocity profiles in nanochannel electroosmotic flows. *J. Chem. Phys.* 2003; 118:4692–4701.
45. Bikerman JJ. Structure and capacity of electrical double layer. *Philosophical Magazine Series 7*. 1942; 33:384–397.
46. Boda D, Valiskó M, Henderson D, Eisenberg B, Gillespie D, Nonner W. Ionic selectivity in L-type calcium channels by electrostatics and hard-core repulsion. *J. Gen. Physiol.* 2009; 133:497–509. [PubMed: 19398776]
47. Gillespie D, Boda D. The anomalous mole fraction effect in calcium channels: A measure of preferential selectivity. *Biophys. J.* 2008; 95:2658–2672. [PubMed: 18515379]
48. Csányi É, Boda D, Gillespie D, Kristóf T. Current and selectivity in a model sodium channel under physiological conditions: Dynamic Monte Carlo simulations. *Biochim. Biophys. Acta Biomembr.* 2012; 1818:592–600.
49. Andersen MB, Frey J, Pennathur S, Bruus H. Wall deprotonation during capillary filling of silica nanochannels coated with hydrophilic 3-cyanopropyltrimethylchlorosilane. *J. Colloid Interface Sci.* 2011; 353:301–310. [PubMed: 20943229]
50. Jensen KL, Kristensen JT, Crumrine AM, Andersen MB, Bruus H, Pennathur S. Hydronium-dominated ion transport in carbon-dioxide-saturated electrolytes at low salt concentrations in nanochannels. *Phys. Rev. E*. 2011; 83:056307.
51. Laanait N, Mihaylov M, Hou B, Yu H, Vanýsek P, Meron M, Lin B, Benjamin I, Schlossman ML. Tuning ion correlations at an electrified soft interface. *Proc. Natl. Acad. Sci.* 2012; 109:20326–20331. [PubMed: 23175787]
52. Stein D, Kruithof M, Dekker C. Surface-charge-governed ion transport in nanofluidic channels. *Phys. Rev. Lett.* 2004; 93:035901. [PubMed: 15323836]
53. Henderson D, Blum L. Some exact results and the application of the mean spherical approximation to charged hard spheres near a charged hard wall. *J. Chem. Phys.* 1978; 69:5441–5449.
54. Henderson D, Blum L, Lebowitz JL. An exact formula for the contact value of the density profile of a system of charged hard spheres near a charged wall. *Journal of Electroanalytical Chemistry and Interfacial Electrochemistry*. 1979; 102:315–319.
55. Martin PA. Sum rules in charged fluids. *Rev. Mod. Phys.* 1988; 60:1075–1127.
56. Boda D, Giri J, Henderson D, Eisenberg RS, Gillespie D. Analyzing the components of the free energy landscape in a calcium selective ion channel by Widom's particle insertion method. *J. Chem. Phys.* 2011; 134:055102. [PubMed: 21303162]
57. Gillespie D. Analytic theory for dilute colloids in a charged slit. *J. Phys. Chem. B*. 2010; 114:4302–4309. [PubMed: 20210321]

1. Comparison of DFT and PB to experiments. The bare silica nanochannel used by van der Heyden et al.⁷ was 490 nm deep, 50 μm wide, and 4.5 mm long with a surface charge of -0.15 C/m^2 . In all panels, the symbols are the experimental data and the lines are the calculations using DFT (solid line), DCA-PB (dashed line), and PB0 (dotted line). (A) The streaming conductance as a function of CoSep concentration. (B) The competition of CoSep with K^+ . The streaming conductance versus varying concentrations of K^+ is shown in the presence of 0.1 mM CoSep (black) and 1 mM CoSep (red). In both the experiments⁷ and the DFT calculations, the result with 1 mM K^+ was not appreciably different than with no K^+ . Therefore, the results at the arrows labeled with circled 1 and 2 closely correspond to the same experiment. The arrows show that in the presence of K^+ , the DFT results are as good or better as they are for the pure CoSep case.

2.

Total conductance in a 50 nm wide nanofluidic device for 9 different cations at concentrations from 10^{-6} M to 1 M and the surface charge ranging from 0 C/m² to -0.30 C/m². A rainbow color scale is used, with red representing the largest values and violet representing the smallest. The colors are constant between the different cations so a single color represents the same range of values in all 9 panels. Due to the large conductances at high concentrations compared to low concentrations, contours greater than 200 pS have been cutoff to allow for the resolution of finer details. The contour labels represent the conductance in pS. Moving from left to right, the cation diameter is increasing (0.15 nm, 0.30 nm, and 0.90 nm). Moving down, the valence is increasing (+1, +2, +3). In this and

other figures, the Stern layer height is defined as the counterion diameter. For comparison, a Stern layer height of 0 is shown in the Supplementary Material as Figs. S1–S4.

3.

The total conductance for the small monovalent cation (Fig. 1, top row, left) was divided by the corresponding bulk conductance. A rainbow color scale is used to demonstrate the relative total conductance, with red representing the highest values and violet representing the lowest values. In the high concentration regime, the total conductance was approximately the same as the bulk value, resulting in a ratio approximately equal to 1. As concentration decreases, the relative total conductance increases rapidly, reaching over 1000 times bulk at very low concentrations. This result holds qualitatively for all 9 cations.

4.

Streaming conductance in a 50 nm wide nanofluidic device for 9 different cations at concentrations from 10^{-6} M to 1 M and the surface charge ranging from 0 C/m² to -0.30 C/m². A rainbow color scale is used, with red representing the largest values and violet representing the smallest. The colors are constant between the different cations so a single color represents the same range of values in all 9 panels. The contour labels have units of pS/bar. Moving from left to right, the cation diameter is increasing (0.15 nm, 0.30 nm, and 0.90 nm). Moving down, the valence is increasing (+1, +2, +3).

5.

Pressure-to-voltage power conversion efficiencies in a 50 nm wide nanofluidic device for 9 different cations at concentrations from 10^{-6} M to 1 M and the surface charge ranging from 0 C/m^2 to -0.30 C/m^2 . A rainbow color scale is used, with red representing the highest values and violet representing the smallest values. The colors are constant between the different cations so a single color represents the same range of values in all 9 panels. The contour labels represent the maximum power conversion percentage. Moving from left to right, the cation diameter is increasing (0.15 nm, 0.30 nm, and 0.90 nm). Moving down, the valence is increasing (+1, +2, +3). In the very low surface charge regime, power conversion levels decrease suddenly. However, due to the difficulty in resolving the decrease we have omitted it from the panels.

6.

Monovalent cation concentration as a function of slit position. The three different colors represent three different cation sizes at a 10^{-5} M concentration and a surface charge of -0.025 C/m². The different peak positions result from the cations' different distances of closest approach. The largest cation (red) shows an oscillatory concentration profile due to ion layering. The anion concentration is less than 10^{-3} M for all three cation sizes, resulting in the net charge profile looking identical to the cation concentration profile.

7.

(A) Total charge moving away from the wall as a function of slit position for a small trivalent cation at -0.30 C/m^2 and four bulk concentrations. The four anion concentration profiles correspond to bulk cation concentrations of 10^{-1} M (blue), 10^{-2} M (green), 10^{-3} M (red), and 10^{-6} M (black). For all four bulk concentrations the net charge attained a nearly identical maximum of $\sim 70 \text{ M}$. (B) Anion concentration as a function of slit position for a small trivalent at -0.30 C/m^2 and the same four bulk concentrations. The concentrations shown are all relative to the bulk anion concentration. To aid the eye, a horizontal line at 1 has been added. (C) Total conductance as a function of concentration. The colored lines correspond to the value at each of the four different surface charges used.

8. Comparison of DFT with two PB models in calculations of the streaming and total conductances as cation diameter increases from 0.1 to 1 nm. The surface charge is -0.3 C/m^2 . In all systems, the bath cation concentration is 1 mM. The DFT results are the shaded region (red in panels A and C, green in panels B and D). DCA-PB results are in the region defined by the vertical black lines. PB0 results are between the two thick blue lines. The upper and lower bounds of these regions are the conductances calculated using a Stern layer height of 0 and the cation diameter, respectively. (A) The streaming conductance with a monovalent cation. (B) The streaming conductance with a divalent cation. (C) The total voltage conductance with a monovalent cation. (D) The total voltage conductance with a divalent cation. Note that while the DCA-PB conductances with zero Stern layer height are very similar to the DFT conductances, the wide Stern layer results are substantially different with large relative errors.

9.

(A) Advective current density as a function of slit position. All calculations were performed at a fixed concentration of 10^{-5} M with a medium size (0.30 nm diameter) trivalent cation (Fig. 1, bottom row, center). The four colored profiles represent different surface charges (black: -0.01 C/m^2 , red: -0.05 C/m^2 , green: -0.10 C/m^2 , and blue: -0.25 C/m^2). Total conductance is the sum of the area under corresponding curves in Figs. 9A and B. As the surface charge increases, the area under the curve first increases and later decreases. (B) Electromigration current density is given as a function of slit position for the same parameters as in Fig. 9A. All curves are labeled with the surface charge, except for the -0.01 C/m^2 profile (black). (C) The total conductance at a fixed concentration of 10^{-5} M as a

function of surface charge. The values at the surface charges corresponding to the profiles are indicated with vertical colored lines.