Cation Dependent Surface Charge Regulation in Gated Nanofluidic Devices

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ABSTRACT: Surface charge governs nanoscale aqueous electrolyte transport, both in engineered analytical systems and in biological entities such as ion channels and ion pumps as a function of ion type and concentration. Embedded electrodes in a nanofluidic channel, isolated from the fluid in the channel by a dielectric layer, act as active, tunable gates to systematically modify local surface charge density at the interface between the nanochannel surface and the aqueous electrolyte solution, causing significant changes in measured nanochannel conductance. A systematic comparison of transport of monovalent electrolytes [potassium chloride (KCl), sodium chloride (NaCl)], 2:1 electrolytes [magnesium chloride (MgCl2), calcium chloride (CaCl2)], and electrolyte mixtures (KCl + CaCl2) through a gated nanofluidic device was performed. Ion—surface interactions between divalent Ca2+ and Mg2+ ions and the nanochannel walls reduced the native surface charge density by up to ~4–5 times compared to the monovalent cations. In electrolyte mixtures, Ca2+ was the dominating cation with nanochannel conductance independent of KCl concentration. Systematic changes in local electrostatic surface state induced by the gate electrode are impacted by the divalent cation—surface interactions, limiting modulation of the local surface potential by the gate electrode and resulting in cation dependent nanoscale ion transport as seen through conductance measurements and numerical models.

Surface charge is a fundamental parameter that governs nanoscale aqueous electrolyte transport in engineered systems for applications in energy conversion,1,2 fluid-analogs of solid-state electronics,3–5 biosensing,6,7 and in ion channels and ion pumps for precise control over ion and small molecule transport.8 Divalent ions play a critical role in regulating the opening, selectivity, and conductance of both cation and anion biological ion channels with direct implications for physiological processes such as neuronal excitability, epithelial fluid secretion, cancer cell proliferation, and blood pressure regulation.9–11 In ion channels and ion pumps, the nanochannel structure, conformation, subunits with local binding sites, relative hydrophobicity characteristics, local electrostatic domains at channel entrances and within ion channels, and most importantly, surface charge have been identified as important parameters governing ion flux, selectivity, and levels of ion conductance and rectification.10,12–14 Yet, engineered systems such as lab-on-chip (LoC) or micrototal analysis systems (μ-TAS) that attempt to mimic many of these ideal biological functions for the variety of applications listed above suffer from incomplete understanding of surface charge regulation15–18 in contrast to biological systems, especially with multivalent ions and electrolyte mixtures. Specifically, for gated LoC nanofluidic devices, the effect of local variation of electrostatic properties on transport of multivalent electrolytes and electrolyte mixtures, which underlie most practical applications, remains poorly understood with minimal reporting in the existing peer-reviewed literature.

Nanoscale architectures built with insulating materials such as glass, oxides, polymers, or a combination of these materials are commonly used substrates for numerous LoC devices for characterizing and manipulating nanoscale flows over the past decade.1,3,4,6,19 While it is well-known that oxide and polymer surfaces in contact with electrolyte solutions develop a net surface charge that can be passively controlled by regulating the electrolyte pH,23–25 active control over surface charge has been desired for real-time control over ionic transport for analytical operations in engineered nanoscale conduits. Active control can be achieved through embedded electrodes in the walls of nanofluidic channels that act as tunable gates to systematically modify local surface potential and/or surface charge density at the dielectric—fluid interface.4,14 The gate potential thus influences the electric field throughout the nanochannel depth,4,19 allowing direct electrostatic manipulation of ions and molecules in the fluid volume.1,26,27 However, systematically evaluating the efficacy of electrostatic gating toward engineering transport of multivalent and multicomponent electrolyte solutions is critical toward...
advancing nanofluidics for highly functional LoC or μ-TAS devices. Basic transport phenomena in gated or field-effect nanofluidic devices remain an open area of research. Consequently, nearly all reports to date on gated nanofluidic devices have focused on transport of potassium chloride (KCl) with limited evaluation of hydrochloric acid (HCl) and glycine based buffers. In the case of multi- or polyvalent electrolyte solutions, including mixtures, fundamental research for ungated nanofluidic devices shows that ion−surface and/or ion−ion interactions must be considered depending on the electrolyte type and composition along with ion concentration and surface charge density. Systematic comparison of gated transport for monovalent, 2:1 electrolytes, and simple electrolyte mixtures is further complicated by device to device variation, specifically by observed inconsistency of the surface charge density across fabricated devices.

In this report, a systematic comparison of transport of monovalent electrolytes [KCl, sodium chloride (NaCl)], 2:1 electrolytes [magnesium chloride (MgCl2), calcium chloride (CaCl2)], and electrolyte mixtures (KCl + CaCl2) through a gated nanofluidic device is demonstrated for the first time. Ion−surface interactions regulate the nanochannel surface charge density as a function of cation type, resulting in distinct cation dependent gating behavior. The glass-polydimethylsiloxane (PDMS) based devices here are cation selective under conditions of interacting electric double layers (EDLs); therefore, the cation was varied across electrolyte solutions for a fixed anion.

The purpose of this paper is to demonstrate that systematic changes in local electrostatic surface state induced by a gate electrode are impacted by ion−surface interactions leading to surface charge regulation, and consequently, the resulting nanoscale ion transport is strongly affected by cation type in gated nanofluidic devices. In particular, divalent cation−surface interactions reduce the surface charge density and limit the current modulation under some of the tested gating conditions. A multi-species numerical model confirmed that ion−surface interactions had a significant impact on the surface charge density at pH ≥ 6 for CaCl2. Ion−surface interactions between the charged walls and the divalent cations in the electrolyte regulate the surface charge density and consequently limit the ability of the gate electrode to alter the net surface charge density and modulate nanochannel conductance.

**EXPERIMENTAL PROCEDURES**

The gated nanofluidic device consisted of two microfluidic channels (8 μm deep × 50 μm wide × 3 cm long) which served as fluidic reservoirs to a bank of three nanochannels (16 nm deep × 30 μm wide × 2.5 mm long). Four individually addressable gold (Au) gate electrodes were embedded in the roof of the nanofluidic channels and separated from the electrolyte in the nanochannel by a polydimethylsiloxane (PDMS) dielectric layer (PDMS thickness ~0.7 μm). Only one active gate electrode was used for this work. The nanofluidic nanochannel network was patterned on a borosilicate glass substrate using UV lithography and wet etching techniques. Individually addressable Au gate electrodes were patterned onto a second glass substrate. A PDMS dielectric layer was spun onto the glass cover containing the electrode array. The cover with embedded electrodes and the glass substrate with the patterned channel network were bonded via O2 plasma bonding to form sealed channels. Details on device fabrication and basic device operation and characterization have been reported previously.

The device testing setup included two power supplies (Keithley 3390 function generators) used to supply independent axial (Vg) and gate (Vf) potentials. Axial potential used here was Vg = 3 V and Vf = 5 V, as discussed below, and the gate potential was in the range of −3 V ≤ Vf ≤ 3 V. Current (I) through the nanochannels was monitored using a Keithley 6485 picoammeter (Figure 1b). Devices were first tested with the gate electrodes floating at each respective concentration, pH, or electrolyte composition in order to measure the intrinsic (i.e., Vf = 0 V) nanochannel conductance. All electrical measurements were conducted in an earth-grounded Faraday cage. Dedicated devices for each type of electrolyte were used to avoid contamination, with the obvious exception of devices used for electrolyte mixtures. Electrolyte solutions were fabricated devices.4,41

![Figure 1. Device layout along with scanning electron microscope (SEM) images. (a) Schematic showing the different functional layers of the nanofluidic device. Two microchannels (8 μm deep × 50 μm wide × 3 cm long) served as reservoirs to a bank of three nanochannels (16 nm deep × 30 μm wide × 2.5 mm long). The micro- and nanochannel network was fabricated on a borosilicate glass substrate with individually addressable gold (Au) gate electrodes patterned on the glass cover. A polydimethylsiloxane (PDMS) dielectric layer supported on the glass cover isolated the gate electrodes from the aqueous electrolytes in the nanochannels. (b) Side-view schematic of the nanochannel, showing the active gate electrode for the data reported. Electrical connections are shown with yellow lines. (c) Scanning electron microscope (SEM) image of an open nanochannel cross section. The slit-like channel cross section lies between the arrows. The dashed red lines denote the locations on the physical device where the SEMs were taken. The channel height was ∼16 nm, as expected from previous reports on device fabrication and characterization. (d) SEM image of PDMS bonded to glass in regions where no channel is expected.](Image)
prepared for concentrations ranging from 0.01 to 100 mM at pH 7 ± 0.2. Each device was initially tested with deionized water (18 MΩ, 10⁻⁷ M salt) to provide the same baseline for comparison between devices. Only devices with an initial deionized (DI) conductance within 4.4 ± 0.5 pS were used for comparison of results across devices as a function of cation type. The gate was located at \( L_g = 0.43 \pm 0.02 \text{L} \) for all devices, where \( L \) is the length of the nanochannel, as dependence of device operation on gate location has been reported previously.¹⁹

After initial conductance measurements with deionized water, electrolyte concentrations were tested in ascending order of concentration. After the electrolyte concentration was increased, the device was thoroughly rinsed with the next highest concentration, similar to previously reported procedures.⁴³ Monovalent electrolytes (KCl and NaCl) were tested at 6 concentrations including DI water and concentrations ranging from 0.01 to 100 mM in order of magnitude increments. Divalent electrolytes (CaCl₂ and MgCl₂) were tested at those concentrations with the addition of 0.33 and 3.33 mM, respectively. Overall data trends were verified over multiple devices with data for each experimental condition comprising several data runs over multiple days.

### RESULTS AND DISCUSSION

Three nanofluidic channels with one active embedded gate electrode connect two microchannel reservoirs (Figure 1). The axial potential, \( V_a \), drives ionic transport through the nanochannel. An independently controlled potential applied to the gate electrode, \( V_g \), modified the local surface charge density (and electric field) at the dielectric–electrolyte interface enabling field-effect control over ionic transport, quantified by changes in the measured current.

**Cation Dependence.** The intrinsic nanochannel device conductance \( (G_i = 1/V_a) \) was first measured with \( V_a = 0 \text{ V} \) as a function of cation type (Figure 2a,b) at pH = 7 ± 0.2. In agreement with previous results for KCl and NaCl, and anomalous transport of NaCl with respect to KCl,⁴³ the two monovalent cations showed similar intrinsic (\( V_a = 0 \text{ V} \)) conductance \( (G_i) \). \( G_i \) for both KCl and NaCl followed known surface charge governed (SCG) transport at \( c_{bulk} < \sim 1 \text{ mM} \) and had a linear dependence on concentration at \( c_{bulk} > \sim 1 \text{ mM} \) indicating bulk transport behavior.

To satisfy electroneutrality, the total space charge within the nanochannel volume must balance the total surface charge on the nanochannel walls. \( G_s \) is thus the summation of the surface charge governed and the bulk conductance,¹⁶,⁴⁴

\[
G_s = G_{SCG} + G_{bulk} = \frac{2\pi \mu_l |\sigma|}{L} + \frac{F \sigma}{L} \sum_{i=1}^{m} \mu_i L^2 q_i
\]

where \( \sigma \) is the surface charge density (negative for both PDMS and glass) on the nanochannel walls, \( \mu_l \) is the mobility of species \( i, \sigma_{bulk} \) is the bulk electrolyte concentration, and \( \mu_i, L, h \) are the channel width, length, and height, respectively.²⁸ The dominant term in eq 1 \((G_{SCG} \text{ or } G_{bulk})\) depends on the bulk electrolyte concentration.⁷,⁸ At the transition concentration, \( c_p \) the bulk and SCG conductances are similar.

Three of the nanochannel walls in our device are borosilicate glass, and one is PDMS supported on borosilicate glass. It is worth noting that the surface charge governed transport of KCl demonstrated in our PDMS–glass device has been reported for a wide variety of nanofluidic devices,²⁴⁴-⁴⁶ showing that the baseline data trends for the most commonly studied electrolyte for these types of devices match those reported previously.

In contrast to NaCl and KCl, CaCl₂ and MgCl₂ showed cation dependent intrinsic conductance behavior as a function of electrolyte concentration that deviated from the well-known KCl intrinsic conductance profile. \( G_s \) for CaCl₂ and MgCl₂ (Figure 2b) was independent of bulk concentration at \( c_{bulk} \leq \sim 0.1 \text{ mM} \), also suggesting SCG transport for divalent cations. Intrinsic conductance of MgCl₂ showed a marked decrease from 4.5 pS at \( c_{bulk} = 0.1 \text{ mM} \) to 1.2 pS at \( c_{bulk} = 1 \text{ mM} \). CaCl₂ conductance decreased from 4.0 pS for \( c_{bulk} = 1 \text{ mM} \) to 0.8 pS for \( c_{bulk} = 3.33 \text{ mM} \) showing a change in conductance per unit concentration of 1.37 pS/mM for CaCl₂ and 3.67 pS/mM for MgCl₂ before transitioning to linear concentration dependence in the bulk transport regime.

Since, \( G_s \) is proportional to \( \sigma \) for dilute electrolyte solutions (i.e., in the surface charge governed regime), the decrease in \( G_s \) for divalent ions corresponds to \( \sim 3.75 \times \) reduction in \( \sigma \) for MgCl₂ between \( c_{bulk} = 0.1 \text{ mM} \) and \( c_{bulk} = 1 \text{ mM} \) and \( \sim 5 \times \) reduction in \( \sigma \) for CaCl₂ between \( c_{bulk} = 1 \text{ mM} \) and \( c_{bulk} = 3.33 \text{ mM} \). As shown in Figure 2b, two distinct transition concentrations were observed for intrinsic conductance of divalent cations: (i) sharp reduction in intrinsic conductance at concentrations that would typically correspond to SCG behavior for monovalent cations with \( c_i \approx 0.1 \text{ mM} \) for MgCl₂ and \( c_i \approx 1 \text{ mM} \) for CaCl₂ is caused by a decrease in the magnitude of the surface charge density, due to ion–surface interactions between divalent cations and the negatively charged walls as discussed in the main text. The dashed lines are intended as eye-guides.

Figure 2. Cation dependent intrinsic nanochannel conductance, measured with the gate electrode floating \( (V_g = 0 \text{ V}) \). (a) The two monovalent cations showed similar intrinsic conductance in agreement with previous results for anomalous transport of NaCl with respect to KCl.¹⁵ (b) The decrease in conductance from expected surface charge governed behavior at \( c_i \approx 0.1 \text{ mM} \) for MgCl₂ and \( c_i \approx 1 \text{ mM} \) for CaCl₂ is caused by a decrease in the magnitude of the surface charge density, due to ion–surface interactions between divalent cations and the negatively charged walls as discussed in the main text. The dashed lines are intended as eye-guides.

**Conductance of Gated Nanochannels.** Changes in the local surface charge density and electric field were induced by the gate electrode to modulate ionic transport and, therefore, the measured current.³³,³⁴,³₂,³³ To our knowledge, this is the first systematic comparison of gating across electrolyte types and, further, the first presentation of gating data for NaCl, MgCl₂, and CaCl₂. It is worth noting that gating of ionic transport is essential to numerous analytical applications as discussed in the introduction. The current was monitored at electrolyte...
concentrations between 0.01 and 100 mM for +3 V ≤ \( V_g \) ≤ −3 V at a fixed axial potential (\( V_a \)). A representative plot of measured current as a function of gate voltage for various cations is shown in Figure S1.

Following previously reported analysis for gated devices,\(^5,37\) the total measured current arises from two components and can be written as \( I = G_c V_a + G_g V_g \). Here, \( G_c \) is the intrinsic nanochannel conductance (\( V_a = 0 \)) and \( G_g \) is the transconductance (\( dI/dV_g \)). To further verify that the two components of the current were independent, transconductance data was taken at \( V_a = 3 \) V and \( V_a = 5 \) V for all data sets.

The dimensionless conductance ratio, \( G_g/G_c \), compares the transconductance to the intrinsic nanochannel conductance (Figure 3). For the monovalent cations, the maximum value of \( G_g \) was observed at the transition concentration, \( c_r \approx 1 \) mM (i.e., the transition between surface charge governed and bulk transport). Limited gating was observed for KCl and NaCl at concentrations that correspond to bulk intrinsic conductance (that is, 10 and 100 mM here). The data trends reported here for \( G_g/G_c \) (and for \( G_c \) as noted above) for KCl are consistent with previously reported results for KCl in TiO\(_2\) nanopores and HCl in silica nanopores.\(^5,37\) Similar to the intrinsic conductance (Figure 2), no significant cation dependence was observed between KCl and NaCl within experimental error as shown in Figure 3a. Our results show that NaCl follows the same concentration dependent gating behavior as the other monovalent symmetric electrolytes reported previously,\(^5,37\) with the maximum conductance ratio (\( G_g/G_c \)) at the transition concentration to bulk electrolyte transport.

As with intrinsic conductance, cation dependent behavior was observed for \( G_g/G_c \) for CaCl\(_2\) and MgCl\(_2\). For MgCl\(_2\), \( G_g/G_c \) at \( c_{bulk} = 0.1 \) mM was 0.2 compared to ~0.6 for monovalent ions even though KCl, NaCl, and MgCl\(_2\) have comparable \( G_c \) at 0.1 mM. Starting at 0.1 mM, gate modulation increased with concentration for MgCl\(_2\), with the maximum value of \( G_g/G_c \) at 1 mM, which is the transition concentration to bulk transport behavior for MgCl\(_2\).

For CaCl\(_2\), \( G_g/G_c \) showed a local maxima at 3.33 mM, which is the transition concentration to bulk transport behavior. \( G_g/G_c \) for Ca\(^{2+}\) decreased from 0.9 at 0.33 mM to ~0.3 at 1 mM (which was transition from SCG to the reduced conductance, \( c_r \)). Consequently, the gate electrode showed reduced modulation for both divalent ions at their respective values of \( c_r \) (0.1 mM for MgCl\(_2\) and 1 mM for CaCl\(_2\)). Near this concentration (\( c_r \)), ion–surface interactions reduce the surface charge density, as discussed above, and appear to limit the current modulation under gating conditions (Figure 3b).

In contrast to Mg\(^{2+}\), a second maxima was observed for CaCl\(_2\) at 0.33 mM. This second maxima was observed for CaCl\(_2\) and not MgCl\(_2\), likely since all concentrations used in the gating experiments fall within the concentration range where ion–surface interactions regulate the surface charge density for MgCl\(_2\) (\( c_r = 0.1 \) mM for MgCl\(_2\)) but not for CaCl\(_2\) (\( c_r = 1 \) mM for CaCl\(_2\)). At concentrations \( c > c_r \), bulk transport behavior is known to dominate; thus, modulation of the surface charge density will have a limited impact on nanochannel conductance, and ion–surface interactions are expected to effect the magnitude of \( G_g/G_c \) in the range of \( c_r/c_r \).

**Electrolyte Mixtures.** Most practical applications and real biological systems contain electrolyte solutions comprising multiple ionic species. However, systematic study of transconductance for electrolyte mixtures has not yet been reported. KCl and CaCl\(_2\) were selected for comparison given the broader set of knowledge existing for these two electrolytes and the vital role of calcium ions in many biological systems with nanoscale critical length scales.\(^16,47,48\) Electrolyte mixtures of KCl and CaCl\(_2\) were evaluated at pH = 7 ± 0.2 at a fixed ionic strength to ensure a consistent Debye length across experiments. The relative composition of the electrolyte solution was altered from 0% CaCl\(_2\) (i.e., 1 mM KCl) to 100% CaCl\(_2\) (0.33 mM CaCl\(_2\)) with a complete summary of the prepared electrolyte compositions in Table S1. The highest measured \( G_c \) (Figure 4a) was at 0% CaCl\(_2\). As CaCl\(_2\) percentage was increased from 0%

![Figure 3. Conductance ratio as a function of cation type for (a) monovalent cations and (b) divalent cations. The conductance ratio \( G_g/G_c \) is a nondimensional parameter that compares the transconductance, \( G_g \) to the intrinsic nanochannel conductance, \( G_c \). The dashed lines are intended as an eye-guide.](image)

![Figure 4. Intrinsic nanochannel conductance and deduced surface charge density for electrolyte mixtures. (a) The measured intrinsic nanochannel conductance as a function of electrolyte composition for a fixed ionic strength of 1 mM. The estimated values for intrinsic conductance were calculated using 0% CaCl\(_2\) as a baseline case and assuming a constant surface charge density. (b) The deduced surface charge density as a function of electrolyte composition calculated from the measured intrinsic nanochannel conductance at each electrolyte composition and eqs S3, S5, S6, and S8. The surface charge density for each electrolyte composition (\( \sigma_{EC} \)) is shown relative to the surface charge density for the 0% CaCl\(_2\), or 1 mM KCl case (\( \sigma_0 \)).](image)
shown in Figure 4a, indicating that one or both of the main assumptions (i.e., constant surface charge density across electrolyte compositions or the relative concentrations of K+ to Ca2+ in the nanochannel match the relative concentration in the bulk) may be problematic for matching theoretical estimates to the experimental measurements. The difference between the measured and estimated values is not explained by the ratio of K+ to Ca2+ in the nanochannel alone, as the estimated and measured intrinsic conductances for 100% CaCl2 also did not match. Therefore, the constant surface charge density and, consequently, the constant space charge density assumption fails for Gg in the case of KCl + CaCl2 mixtures.

Instead, using the measured Gg at each electrolyte composition, the surface charge density was estimated as a function of electrolyte composition relative to the 0% CaCl2 case (Supporting Information). The estimated relative σ (Table S2) showed that the magnitude of σ decreased by more than 1/2 as CaCl2 composition goes from 0% to 25% (Figure 4b). As the relative concentration was increased beyond 25% CaCl2, σ remained constant indicating Ca2+ is the dominating ion in the mixture and regulates the surface charge.

Similar to the trends in Figure 4a, introduction of Ca2+ suppressed transconductance (Gg) (Figure 5a). The highest Gg was observed at 0% CaCl2 with approximately equivalent transconductance for electrolyte compositions greater than 25% CaCl2. The decrease in Gg between 0% CaCl2 and 25% CaCl2 was 43% compared to 68% for Gg. Considering Gg/Gs (Figure 5b) and the above observations about the ability of the gate to modulate conductance, it is likely that the effect of the gate electrode is reduced at electrolyte compositions greater than 25% CaCl2 because the gate is unable to manipulate the surface potential due to interactions between Ca2+ and the charged wall. Electrostatic gating is known to alter the surface potential, which influences the local electrostatic and chemical interactions (including ion adsorption), and thus the net surface charge density in the gated region.

**Electrolyte pH Manipulation.** In addition to local control over the surface charge density enabled by the gate electrode, it is well-known that σ can be manipulated by altering the electrolyte pH. In order to further evaluate the surface charge regulation hypothesis, the intrinsic nanochannel conductance was measured as a function of pH for a representative 1 mM KCl and 0.33 mM CaCl2.

A detailed, multi-species numerical model was developed and implemented using COMSOL Multiphysics for each electrolyte solution to estimate the surface charge density from the measured conductance of the nanochannels as a function of pH. The Poisson-Nernst-Planck equations for nanofluidic transport of four ions (H+, OH−, K+, Cl− or H+, OH−, Ca2+, Cl−) were solved, where σ was the fit parameter used to match the experimentally measured and simulated intrinsic conductances. A complete description of the modeling methodology, which is consistent with several previous reports, is given in the Supporting Information.

As noted above, the nanofluidic device here comprises three glass and one PDMS wall. Given that nanoscale transport is directly controlled by surface charge, especially at dilute electrolyte concentrations (larger Debye lengths) in the surface charge governed regime, it is reasonable to expect that different nanochannel walls could add another layer of complexity to nanofluidic transport. Moreover, it is known that the electroosmotic velocity is different for PDMS microchannels compared to glass microchannels. Capillary electrophoresis experiments in microchannels have shown that the magnitude of the zeta (ζ) potential for PDMS is between 0.25× and 0.75× the magnitude of the ζ potential for glass. For the experimental conditions here, this difference in the magnitude of the ζ potential corresponds to a ~0.25−0.75× difference in the magnitude of the surface charge density. On the other hand, some other previous reports have indicated that silica and PDMS have similar pK values and thus approximately the same change in surface charge density as a function of pH.

Therefore, we systematically evaluate the effect of heterogeneous wall charge on intrinsic nanochannel conductance through a detailed, parametric numerical calculation.

Two numerical models were implemented using COMSOL for each electrolyte as a function of pH to determine the effect of likely unequal surface charge density of PDMS and glass. The first COMSOL model considered a homogeneous surface charge distribution (σPDMS = σglass) and the second considered the most extreme expected difference in surface charge density between the top and bottom walls, with a 4× higher surface charge density on the bottom (glass) wall compared to the surface charge density of the top (PDMS) wall (4σPDMS = σglass). For both cases, the total surface charge was held constant as a function of pH (i.e., (wL)σPDMS + (wL)σglass = constant). In agreement with past results, the transport mechanism of ions in the present system was dominated by electromigration, with convection contributing to less than 7% of the total conductance. As a result, the impact on measured conductance due to induced variation in electroosmotic flow arising from the hybrid glass–PDMS system is likely negligible.

Notably, for a fixed total surface charge, the intrinsic conductance in the case of a homogeneous charge distribution and in the case of heterogeneous charge distribution between the top (PDMS) and bottom (glass) walls differed by less than 2% (Figure S4) showing that the intrinsic conductance is independent of likely unequal surface charge density on the top and bottom walls. The intrinsic conductance, therefore, is determined by the total surface charge of all nanochannel walls and the resulting space charge in the nanochannel volume as a function of pH. Our observation that experimentally measured Gg and Gg/Gs for KCl match previously reported trends for homogeneous nanochannels (discussed above) is supported by the modeling results which indicate that the transport is
governed by the total surface charge and the total change in surface charge.

More work is needed to develop a strong understanding of the impact of heterogeneous walls; however, the glass–PDMS heterogeneity does not appear to be a major factor for the intrinsic conductance reported here. Our data and models indicate that the transport is strongly (and as expected) dominated by the space charge in the nanochannel volume, which in turn is impacted by the total surface charge, i.e., an effective charge density from all four walls enclosing the fluid volume. In the case of transconductance, the gate electrode alters the local surface potential and/or surface charge density which influences both electrostatic and chemical ion–surface interactions. Ion–surface interactions in turn determine the effective surface charge density and subsequently the space charge in the nanochannel volume. Quantification of specific ion–surface interactions will require detailed information on surface reactions and is further complicated by the lack of explicitly known surface reactions between ions and PDMS or ions and borosilicate glass. Comprehensive studies evaluating influence of heterogeneous nanochannel walls on nanochannel transport are beyond the scope of this work and form topics for future investigations.

The experimentally measured intrinsic nanochannel conductance for 1 mM KCl and 0.33 mM CaCl₂ as a function of pH is plotted with the numerically computed intrinsic conductance in Figure 6a. The corresponding computed value of the effective surface charge density for all four walls at each pH is shown in Figure 6b. It is worth noting for practical applications that the average surface charge density reported here, which governs the nanoscale ion transport at dilute electrolyte concentrations, for PDMS–glass devices falls within the lower range for silica [~0.001 to −0.1 C/m²], which is known to vary based on fabrication methods. The experimentally measured intrinsic conductance was independent of pH for both electrolytes between pH 10 and pH 8 with similar intrinsic conductance measured for KCl at pH 10 and pH 8 and CaCl₂ at pH 10 and pH 8, consistent with experimental measurements for 1 mM KNO₃ in microchannels. The nearly constant intrinsic conductance corresponds to a nearly constant value of the surface charge density for each electrolyte. This is in contrast with the classical behavior (see Supporting Information), which predicts the surface charge density should decrease with pH for both silica and PDMS between pH 8 and pH 10 but does not consider ion–surface interactions. Notably, at pH 10, the computed value of the surface charge density for KCl filled nanochannels was ~2.8 times higher than the surface charge density for CaCl₂ filled nanochannels.

Multi-valent and even monovalent ions in solution are known to reduce the magnitude of the surface charge density of un gated micro- and nanofluidic channels as a function of ion valence, electrolyte concentration, and the bare surface charge density (and thus pH). In the devices considered here, the magnitude of the bare surface charge density is highest at pH 10 and the magnitude of the surface charge density is likely regulated by cation–surface interactions for both the 2:1 and 1:1 electrolytes at pH 10, causing the experimentally observed plateau in the intrinsic conductance for KCl and CaCl₂ between pH 10 and pH 8.

As expected, the magnitude of the surface charge density (derived from the intrinsic conductance data) decreased for both KCl and CaCl₂ filled channels from pH 8 to pH 7 and from pH 7 to pH 6, but with a lower magnitude of the surface charge density for CaCl₂ filled nanochannels compared to KCl filled nanochannels. In contrast to KCl filled channels, the CaCl₂ filled nanochannels were isoelectric at pH 6, indicating divalent cation–surface interactions reduce the magnitude of the surface charge density for pH ≥ 6.

From the COMSOL model of the intrinsic conductance data, the nanochannel surface was isoelectric for both KCl and CaCl₂ filled channels at pH ≤ 4 consistent with previous reports which indicate the isoelectric point is pH 2–3 for glass and pH 2–4 for PDMS. However, at pH 2, the numerically modeled intrinsic conductance did not match the experimentally measured intrinsic nanochannel conductance. The increase in the computed conductance from the 4 species numerical model from pH 4 to pH 2 is due to the higher concentration of H⁺ ions and the significantly higher mobility of H⁺ compared to K⁺ and Ca²⁺ (μ_H⁺ ≈ 5μ_K⁺ or μ_H⁺ ≈ 12μ_Ca²⁺) since, at such low pH, bulk transport behavior for HCl is expected.

Interestingly, the increase in conductance due to H⁺ ions was observed experimentally for CaCl₂ but not for KCl, though the computed conductance for CaCl₂ at pH 2 was still ~2.4X the experimentally measured value. While the anomalous experimental result for KCl at pH 2 is in agreement with past observations of Duan and Majumdar, the discrepancy between theory and experiments was attributed to an active proton–cation exchange process and lack of incorporating size and layering effects in models for nanochannels with multiple ionic species. Given that this anomalous transport behavior for nanofluidic channels is a recent finding beginning with the work of Duan and Majumdar, the discrepancies between theory and experiments remains an active area of research with little consensus in existing literature.

The COMSOL model for the surface charge density confirmed that, at 0.33 mM CaCl₂ and pH ≥ 6, Ca²⁺ regulates the value of the surface charge density, as discussed above. In the case of multi-valent ions, interactions between counterions (i.e., those with opposite polarity to the wall charge) in the electrolyte with the charged wall and/or with each other are known to cause charge inversion or the reversal of the polarity of the effective surface charge density at sufficiently high electrolyte concentration. Charge inversion is generally attributed to either transverse correlations between ions and charged surface sites, including electrostatic interactions and chemical binding, or lateral ion–ion correlations (as in strongly
correlated liquid theory). Advanced numerical methods such as molecular dynamics simulations include effects of the discrete nature of charged surface sites, ions, water molecules, and size effects. However, no consensus exists with regard to the actual mechanism by which charge inversion occurs for divalent ions or the critical electrolyte concentration for charge inversion. Past reports for nanochannels indicate that the critical concentration for 2:1 electrolyte concentration for charge inversion. Past reports for nanochannels showed the highest measured electrolytes is 350 mM or higher while one recent work indicates that the critical concentration for 2:1 electrolyte concentration for charge inversion is 10 mM MgCl₂ in agreement with observed trends for intrinsic nanochannel conductance. The dashed lines are intended as eye-guides only.

As noted, the applicability of SCL theory is determined by the magnitude of ion–ion correlations, which is quantified by the interaction parameter. The interaction parameter depends on the magnitude of the bare surface charge density and the ion valence. Considering the value of the interaction parameter for the system reported here (see Supporting Information) and the concentration range used in this work (pH data for 0.33 mM CaCl₂ with relevant transitions observed well below even 10 mM), neither lateral correlations (i.e., ion–ion interactions) nor charge inversion are expected in our system and have therefore not been considered in the COMSOL model. The surface charge regulation at pH ≥ 6 evident from the pH dependent intrinsic conductance of CaCl₂ is therefore attributed to transverse ion–surface correlations.

As noted in Figure 7, Ca²⁺ as a function of pH showed significantly different behavior than the monovalent K⁺ ion. Gₙ for K⁺ between pH 8 and pH 10 was nearly independent of pH (Figure 6a), with a similar trend for Ca²⁺ filled nanochannels. However, Gₙ for K⁺ filled channels increased from pH 6 to pH 8, before sharply decreasing at pH 10. Interestingly, as pH was increased from pH 6 to pH 10, the Ca²⁺ followed similar trends as K⁺ with the Gₙ CaCl₂ < Gₙ KCl at pH 8, further suggesting that Ca²⁺ limits modulation of the surface potential at the dielectric–fluid interface by the gate electrode. Ca²⁺ filled nanochannels showed the highest measured Gₙ at pH 2, in-line with Gₙ trends, which likely indicate increased concentration of H⁺ in the diffuse layer for CaCl₂ at pH 2. In contrast, Gₙ (and Gₙ) remains nearly unchanged between pH 2 and pH 6 for KCl.

Figure 7. Transconductance as a function of pH for 1 mM KCl and 0.33 mM CaCl₂ with relevant transitions observed well below even 10 mM, neither lateral correlations (i.e., ion–ion interactions) nor charge inversion are expected in our system and have therefore not been considered in the COMSOL model. The surface charge regulation at pH ≥ 6 evident from the pH dependent intrinsic conductance of CaCl₂ is therefore attributed to transverse ion–surface correlations.

Our summary is as follows:

- Notably, the applicability of SCL theory is determined by the magnitude of ion–ion correlations, which is quantified by the interaction parameter. The interaction parameter depends on the magnitude of the bare surface charge density and the ion valence. Considering the value of the interaction parameter for the system reported here (see Supporting Information) and the concentration range used in this work (pH data for 0.33 mM CaCl₂ with relevant transitions observed well below even 10 mM), neither lateral correlations (i.e., ion–ion interactions) nor charge inversion are expected in our system and have therefore not been considered in the COMSOL model. The surface charge regulation at pH ≥ 6 evident from the pH dependent intrinsic conductance of CaCl₂ is therefore attributed to transverse ion–surface correlations.

SUMMARY AND CONCLUSIONS

This paper presented for the first time a systematic comparison of cation dependent transconductance as a function of monovalent, divalent, and polyvalent mixtures for gated nanochannels, where local change in the surface potential at the dielectric–fluid interface was induced by an embedded gate electrode. A broad parametric study with 16 nm deep nanochannels for a large range of evaluated electrolyte concentrations (10⁻⁷−10⁻¹ M), one of the widest reported pH ranges (pH 2–10), and electrolyte mixtures, with first reported transconductance for NaCl, CaCl₂, and MgCl₂, demonstrated that systematic changes in local electrostatic surface state are impacted by ion–surface interactions for divalent cations at pH ≥ 6, and the resulting nanoscale ion transport is strongly affected by cation type in a gated nanofluidic device. Results for KCl were in agreement with previous reports on gated nanofluidic transport of KCl and HCl establishing a viable baseline for the devices reported here, yet several new and unexpected observations were noted along with critical implications for nanofluidic transport and subsequent use of these devices in analytical systems.

Conductance decreased for MgCl₂ and CaCl₂ at concentrations typically associated with surface charge governed transport for monovalent electrolytes, suggesting a decrease in the total surface charge density due to divergent cation–surface interactions. Consequently, addition of divalent ions can be used to regulate the effective surface charge density and thereby directly affect the nanochannel conductance.

A multi-species numerical model used to compute the surface charge density confirmed that ion–surface interactions had a significant impact on the surface charge density at pH ≥ 6 for CaCl₂. Data from KCl and CaCl₂ electrolyte mixtures clearly indicated that Ca²⁺ in the mixture is the dominating ion as determined by a decrease in surface charge density when CaCl₂ was added (between 0% CaCl₂ composition and 25% CaCl₂ composition) and a surface charge density that was independent of KCl concentration for % CaCl₂ > 25%. The transconductance data further suggests the surface charge regulation by Ca²⁺ at % CaCl₂ > 25% limits the ability of the gate electrode to modulate the potential at the dielectric–fluid interface. Ion–surface interactions between the charged walls and the divalent cations in the electrolyte regulate the surface charge density and consequently limit the ability of the gate electrode to alter the net surface charge density and modulate nanochannel conductance.

Our several new experimental observations, supporting models, and detailed discussion of data trends including matching with existing data show evidence of surface charge regulation by divergent cations for negatively charged nanochannel walls with potential significant impact on how such devices can be used to construct analytical devices performing logic operations at the nanoscale. Further quantification of specific ion–surface interactions will require detailed information on surface reactions and is further complicated by the lack of explicitly known surface reactions between ions and PDMS or ions and borosilicate glass. Therefore, conductance models of gated nanofluidic channels that include effects of both electrostatic and chemical ion–surface interactions continue to be a challenge.
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