The process of ion adsorption and associate with surface and selective separations.

ABSTRACT: Ion adsorption processes, known as “charge regulation”, is ion-specific and is dependent on the extent of confinement when the electric double layers (EDLs) between two charged surfaces overlap. A fundamental understanding of the mechanisms behind charge regulation remains lacking. Herein, we study the thermodynamics of charge regulation reactions in 20 nm SiO2 channels via conductance measurements at various concentrations and temperatures. The effective activation energies (Ea) for ion conductance at low concentrations (strong EDL overlap) are ~2-fold higher than at high concentrations (no EDL overlap) for the electrolytes studied here: LiCl, NaCl, KCl, and CsCl. We find that Ea values measured at high concentrations result from the temperature dependence of viscosity and its influence on ion mobility, whereas Ea values measured at low concentrations result from the combined effects of ion mobility and the enthalpy of cation adsorption to the charged surface. Notably, the Ea for surface reactions increases from 7.03 kJ mol−1 for NaCl to 16.72 ± 0.48 kJ mol−1 for KCl, corresponding to a difference in surface charge of −8.2 to −0.8 mC m−2, respectively. We construct a charge regulation model to rationalize the cation-specific charge regulation behavior based on an adsorption equilibrium. Our findings show that temperature- and concentration-dependent conductance measurements can help indirectly probe the ion–surface interactions that govern transport and colloidal interactions at the nanoscale—representing a critical step forward in our understanding of charge regulation and adsorption phenomena under nanoconfinement.

KEYWORDS: charge regulation, silica nanochannels, electric double layer, activation energy, surface reactions, selective ion transport

Interactions between aqueous ions and charged surfaces govern nanoscale ion transport in engineered systems and processes central to the water–energy nexus, such as energy conversion,1,2 nanofluidic circuitry,3–5 biosensing,6,7 and selective separations.8–10 Electrostatic potentials formed at the solid–fluid interface by the dissociation of ionizable surface moieties or adsorption of ions from the bulk solution give rise to an electric double-layer (EDL).11 The distribution and behavior of ions within the EDL can deviate significantly from the bulk solution—especially when confined to the nanoscale—and have drastic implications for the underlying transport mechanisms in micro- and nanofluidic systems.12,13

Biological channels, such as aquaporins and the potassium (K+) channel, exploit surface interactions with aqueous electrolytes, among other interactions, to achieve highly selective separations.14,15 Divalent ions in solution play a particularly critical role in regulating the surface charge and, consequently, the selectivity of these biological channels.16,17 The process of ion adsorption and association with surface groups, which alters the surface properties of the nanopore, is known as “charge regulation.”18 This phenomenon is a critical function for physiological processes such as neuron firing, muscle contractions, and blood pressure regulation.19 The ability of an ion to regulate surface charge depends on its physicochemical characteristics and its concentration in solution or, more importantly, near the channel surface.20 Charge regulation is exacerbated under confinement when the EDLs between two charged surfaces overlap. In this limit, the transport properties of the nanopore depend strongly on charge regulation, which controls the number of mobile ions...
RESULTS AND DISCUSSION

Ion Selectivity in Solid-State Nanochannels. The solid-state nanofluidic devices, illustrated in Figure 1A, are created using standard semiconductor fabrication techniques (see Materials and Methods). The nanochannels are defined by photolithographically patterning chromium nanowires with 20 nm height (H), 4 μm width (W), and 20 μm length (L) dimensions on an SiO$_2$ substrate. The wires are insulated in SiO$_2$, which possess silanol surface functionalities that deprotonate into a negative charge, and then sacrificially etched after bonding with microfluidic inputs and outputs (Supporting Information, Figure S1). Silver–silver chloride (Ag/AgCl) electrodes are placed in the bulk cis and trans reservoirs, connected by the etched nanochannels. A parallel array of ten identical nanochannels are used to enable detectable conductance measurements (O ~ 10$^{-11}$ S). Electrolyte solutions are exchanged in the cis and trans reservoirs using syringe pumps.

Contact between a solid surface and a polarizable electrolyte solution induces surface ionization. The resulting electrostatic forces, which attract counterions and repel co-ions in the electrolyte to maintain electroneutrality, produce an EDL at equilibrium. The extent of the EDL can be described by a characteristic length scale that quantifies the thickness of the diffuse layer, the Debye length ($\lambda_D$) where $\epsilon$ is the dielectric constant of the liquid, $\epsilon_0$ is the permittivity of free space, R is the ideal gas constant, T is the absolute temperature, F is Faraday’s constant, and C is the molar salt concentration in the bulk solution.

$$\lambda_D = \sqrt{\frac{\epsilon \epsilon_0 RT}{2F^2C}}$$

At high salt concentrations $\lambda_D$ is small, allowing cations and anions to simultaneously permeate the nanochannel (Figure 1B). Conversely, $\lambda_D$ can grow to lengths commensurate with the size of the nanochannel at low salt concentrations. When two EDLs are brought into close proximity to each other, the overlap of the EDLs modifies their charge profile. The overlap of EDLs between two interacting surfaces (e.g., parallel nanochannel walls) results in a so-called exclusion-enrichment effect, where the enrichment of counterions and exclusion of co-ions in the nanochannel induces permeselectivity. In the case of negatively charged surfaces like the silanol-based chemistry studied here, the negative potential developed within the nanochannels results in cation-selective transport (Figure 1B).

The decay of $\lambda_D$ with respect to increasing salt concentration, evidenced in eq 1 by the relationship between $\lambda_D$ and C ($\lambda_D \propto C^{-1/2}$), is shown in Figure 1C. The salt concentration where $\lambda_D$ is equivalent to the half-height of the nanochannel ($\lambda_D = 0.5H$) is referred to as the critical salt concentration ($C_{\text{critical}}$), marks the point of EDL overlap in the nanochannels. However, we note that eq 1 represents all ions as point charges, making $C_{\text{critical}}$ independent of specific ion identity when comparing 1:1 monovalent salts. This has recently been contradicted experimentally as $C_{\text{critical}}$ was found to vary over 10-fold when comparing the Nernstian behavior of 1:1 monovalent salts in negatively charged polycarbonate membranes. $C_{\text{critical}}$ presented in this study should therefore only be considered a rough approximation for the point of EDL overlap.

Ion conductance ($G$) across nanochannels is the superposition of the bulk conductance and conductance in the porosity of the pore. Its relevance in systems featuring nanoscale channels is therefore substantial.

Despite the importance of charge regulation in nanoporous systems, we lack a holistic understanding of the fundamental mechanisms behind charge regulation behavior that is needed to mimic biological functions. In industrially relevant polymer-based systems where the regulation of surface and internal charge is prevalent (e.g., membranes used for desalination), the sensitivity of polymeric matrices to their environment makes it difficult to deconvolute highly coupled transport phenomena and extract useful insight. Conversely, solid-state devices offer well-defined and precisely controlled platforms for studying nanofluidic ion transport. Surface charge inversion and channel asymmetry-induced current rectification are notable phenomena involving charge regulation that were experimentally observed in solid-state nanochannels. Furthermore, charge regulation can determine the surface interaction energies when fluids are nanoconfined between two surfaces. Free energy contributions from van der Waals and diffuse layer interactions can be approximated on the basis of the classical Derjaguin, Landau, Verwey, and Overbeek (DLVO) theory. However, these DLVO contributions are often inadequate in explaining experimental data and require a short-range non-DLVO contribution as a fitting parameter or incorporation of charge regulation modifications into DLVO theory.

Previous work suggests that surface charge reactions are critical to the temperature sensitivity of potassium chloride (KCl) conductance across 35 nm silicon dioxide (SiO$_2$) nanochannels, but the thermodynamics of the system were never assessed. Rather, the enthalpic ($\Delta H$) and entropic ($\Delta S$) change of the surface reactions were assumed to be constant over the temperature and concentration ranges studied. This assumption, which may be considered to be fine for very small temperature ranges, masks potentially important mechanisms like ion-specific interactions. Typical approaches for measuring the thermodynamics of surface reactions, such as calorimetry, are challenging when the surfaces are confined to the nanoscale. Employing temperature-controlled nanofluidic devices thus remains promising for further fundamental analysis of ion transport at the nanoscale.

Here, we report the use of solid-state nanofluidic devices to elucidate the thermodynamics of charge regulation reactions in nanochannels. We assess monovalent electrolyte transport through 20 nm SiO$_2$ nanochannels under surface charge-dominated (i.e., EDL overlap) and bulk solution-dominated regimes. By controlling the device temperature, we observe an Arrhenius-type activation behavior for ion transport that is governed by cation-specific charge regulation of the channel surfaces at low concentrations. We construct a charge regulation model where the surface charge is in equilibrium with the cation concentration to physically interpret the ordering of the cation-dependent surface regulation. Additionally, we provide mechanistic discussion on the charge regulation behavior of specific cations by their ability to saturate the SiO$_2$ surface, potentially owing to steric, dielectric, or viscous effects. This work measures the cation-specific thermodynamics of charge regulation reactions in nanoscale channels and represents a critical step toward an improved understanding of charge regulation phenomena and adsorption processes under nanoconfinement.
EDLs. For a simple 1:1 monovalent salt, the nanochannel conductance can be approximated by \(^{35,40}\)

\[
G = \frac{e(\mu_+ + \mu_-)CN_{WH}}{L} + \frac{2\mu_+ \sigma W}{L}
\]  

(2)

The first term on the right side of eq 2 displays the bulk conductance (\(G_{\text{bulk}}\)), which depends on the area and length of the nanochannel, bulk salt concentration, and electrophoretic mobilities of the cation (\(\mu_+\)) and anion (\(\mu_-\)). Here, \(e\) is the elementary charge and \(N_A\) is Avogadro’s constant. The mobility of ion \(i\), \(\mu_i\), is related to the diffusion coefficient of that ion, \(D_i\), by the Einstein relation, \(\mu_i = D_i e/k_BT\), where \(k_B\) is the Boltzmann constant. The final term on the right side of eq 2 captures the surface-governed conductance (\(G_{\text{surface}}\)) in the EDLs. For negatively charged surfaces, \(G_{\text{surface}}\) depends only on the channel surface charge (\(\sigma\)), \(\mu_+\), \(\mu_-\), and \(L\) of the channels. While EDL overlap is generally indicative of the importance of the final term of eq 2 relative to the first term, and consequently \(G_{\text{surface}}\) over \(G_{\text{bulk}}\), we highlight the evident importance of the nanochannel surface charge to the \(G_{\text{surface}}\).

We use eq 2 with concentration-dependent ion mobilities to fit measured data for KCl conductance across the nanochannels shown in Figure 1D. Data were measured at 22 °C. The model was fit to the data using \(\sigma\) as the fitting parameter. At high concentrations (\(C \geq 10^{-2}\) mol L\(^{-1}\)), KCl conductance follows \(G_{\text{bulk}}\) due to the negligible scale of the EDLs. KCl conductance behavior begins to transition from bulk-dominated transport to surface-dominated transport when \(C\) decreases below \(10^{-2}\) mol L\(^{-1}\) as \(\lambda_0\) grows (\(\lambda_0 \propto C^{-1/2}\)) and \(G_{\text{bulk}}\) weakens (\(G_{\text{bulk}} \propto C\)). Fully surface-governed transport is established when \(C \leq 10^{-4}\) mol L\(^{-1}\) and the EDLs strongly overlap between the interacting SiO\(_2\) surfaces, resulting in completely cation-selective transport across the nanochannels.

**Probing the Thermodynamics of Salt Transport in Nanochannels.** We control the temperature of our nano-fluidic device by modulating the current supplied to a thermoelectric heater (Figure 2A). We use a Keithley 2400 Sourcemeter to concurrently measure the temperature from a calibrated thermistor (Figure S2) adhered to a SiO\(_2\) chip of the same thickness as the device base. The nano-fluidic device is separated from the heater by a 5 mm bar of copper to ensure uniform heating. Thermally conductive tape (8810, 3M) is used for the connections between the SiO\(_2\) substrates, copper bar, and heater, whereas thermally conductive epoxy (BondaTherm, Wakefield-Vette) is applied to adhere the thermistor to the surface of the SiO\(_2\) chip.

We perform voltage sweeps from -0.5 to +0.5 V, at 0.1 V increments, to assess the \(I-V\) characteristics of 1 mol L\(^{-1}\) KCl transport across the nanochannels at various temperatures (Figure 2B). KCl conductance increases from 127 to 171 nS when increasing the temperature from 25 to 55 °C, respectively. From eq 2, the increasing conductance with respect to temperature at this high concentration (i.e., bulk-dominated transport regime) stems from the temperature dependence of the cation and anion mobilities.\(^{32,41-43}\) Salt conductance can be related to salt permeability (\(P_s\)) by \(^{44}\)

\[
P_s = \frac{RL}{(WH)^2C} GT = \alpha GT
\]  

(3)
where \( \alpha \) is a temperature-independent parameter. In this form, the thermodynamics of salt transport are readily probed using the linearized form of an Arrhenius-type equation \(^5,45,46\)

\[
\ln(P_{\text{KCl}}) = \ln(P_0) - \left( \frac{E_a - RT}{RT} \right) \tag{4}
\]

where \( P_0 \) is a pre-exponential factor and \( E_a \) is the activation energy for salt conductance. We fit the temperature-dependent transport data of 1 mol L\(^{-1}\) KCl to eq 4 (Figure 2C). The strong correlation \( R^2 = 0.99 \) indicates that KCl transport across the nanochannels follows typical activation behavior, allowing us to measure an \( E_a \) of 10.6 kJ mol\(^{-1}\) from the slope of the curve.

We extend our analysis of \( E_a \) over a wider range of KCl concentrations (\( 10^{-5} \) to 1 mol L\(^{-1}\)), displayed in Figure 3. Concentrations below \( 10^{-5} \) mol L\(^{-1}\) were not considered due to the likelihood of competitive association between cations and protons for negatively charged surface sites (\( C_{\text{H+}} = 10^{-5.8} \) mol L\(^{-1}\)). \(^{37}\) Further, experimental triplicates were run simultaneously to improve confidence in the data, requiring semiautomation of the experimental procedure and additional data processing (details in SI, Figure S3). At high KCl concentrations (\( C \geq 10^{-2} \) mol L\(^{-1}\)), when the EDLs are small relative to the channel size, \( E_{\text{KCl}} \) remains constant at roughly 10.6 kJ mol\(^{-1}\). This value reasonably agrees with previous measurements of the activation energy of KCl conductance in water \(^48\) and is attributed to the temperature dependence of solvent viscosity or ion diffusivity via the Einstein relation. \(^31,42\)

We observe an exponential increase in \( E_{\text{KCl}} \) over the transition region between bulk-dominated and surface-dominated transport regimes (\( 10^{-4} < C < 10^{-2} \)) before plateauing at \( \sim 27 \) kJ mol\(^{-1}\) when \( C \leq 10^{-4} \) and strong EDL overlap occurs (\( H < \lambda_B = 30.4 \) nm). This observation suggests that the physics governing \( E_a \) transition from the temperature dependence of electrophoretic mobility to a mechanism, or some amalgamation of mechanisms, highly correlated with \( \sigma \) (eq 2). At \( C_{\text{critical}} \) when EDL overlap first occurs—\( E_{\text{KCl}} = 19.9 \pm 2.5 \) kJ mol\(^{-1}\)—the error of \( E_{\text{KCl}} \) at this concentration is large relative to the other concentrations studied (\( >2 \)-fold higher) and could indicate subtle fabrication differences between the separately examined devices. In particular, the effective height of the nanochannels can vary between individual devices up to 1 nm due to possible differences in the number of locally accessible surface sites for precursor chemisorption and nucleation during atomic layer deposition of the nanowires. \(^{49}\) It is therefore possible that not all three nanofluidic devices experienced EDL overlap exactly at \( C_{\text{critical}} \). This further supports the idea that \( E_a \) is driven by overlapping EDLs when not in the bulk-dominated transport regime.

Several physical parameters associated with ion conductance in nanochannels exhibit enhanced temperature sensitivity when conductance is surface dominated. Hence, there are several possible mechanistic explanations for the increase in \( E_{\text{KCl}} \) at low KCl concentrations. It was previously suggested that the acid–base equilibrium of SiO\(_2\) or the reduced cation mobility within the EDLs may explain the temperature sensitivity of \( G_{\text{surface}} \). \(^{32}\) Albeit plausible, previous atomistic simulations also showed the (de)protonation of isolated
silanols to be an activationless process (i.e., no significant activation energy). Further, $E_{a,KCl}$ values measured at $C \leq 10^{-4}$ mol L$^{-1}$ are over 2-fold higher than the $E_a$ values associated with electrophoretic mobility. It is thus more likely that the $E_{a,KCl}$ values measured at low concentrations correspond to the enthalpy change of some nonproton surface reaction. We hypothesize this is the thermodynamic signature for K$^+$ regulation of the charged silanol groups.

**Ion-Specific Charge Regulation.** We further investigate surface charge regulation as the thermodynamic signature at low concentrations by assessing the conductance of three other 1:1 monovalent salts, namely, lithium chloride (LiCl), sodium chloride (NaCl), and cesium chloride (CsCl). Salt conductance was measured at 22 °C and fit by eq 2, as depicted in Figure 4A. Similar to data in Figure 1D, the conductance models for each salt were fit to the data by solving for $\sigma$. We find $\sigma$ follows the order $\sigma_{\text{LiCl}} > \sigma_{\text{NaCl}} > \sigma_{\text{CsCl}}$, where $\sigma$ can differ substantially between salts. For example, $\sigma_{\text{NaCl}}$ ($-8.20$ mC m$^{-2}$) is over an order of magnitude greater than $\sigma_{\text{KCl}}$ ($-0.80$ mC m$^{-2}$). The ordering of $\sigma$ with respect to salt type is direct evidence of cation-specific charge regulation when in the surface-dominated transport regime ($C \leq 10^{-4}$ mol L$^{-1}$).

We probe the thermodynamics of LiCl, NaCl, and CsCl transport across the nanochannels for comparison with KCl (Figure 4B). The activation behavior of the three new salts largely mirrors the trends observed in Figure 3. The value of $E_a$ at the plateau regions, where transport is either bulk-dominant ($C \geq 10^{-2}$ mol L$^{-1}$) or surface-dominant ($C \leq 10^{-4}$ mol L$^{-1}$), do not settle upon the same value for each salt. At $C = 1$ mol L$^{-1}$, we observe a linear relationship between $E_a$ and the electrolyte’s absolute viscosity $B$-coefficient, $|B_j|$ (Figure 4C). $|B_j|$ is an additive property that measures the kosmotropic/chaotropic tendencies of an ion or electrolyte. In other words, $|B_j|$ describes the concentration-dependent influence of electrolytes on solution viscosity based on their ability to “make” or “break” the structure of water through hydrogen bonding interactions. The strong correlation between $|B_j|$ and $E_a$ at $C = 1$ mol L$^{-1}$ ($R^2 = 0.99$) suggests that this thermodynamic signature is from the temperature dependency of viscous-based electrophoretic drag on the ion. This corroborates our physical understanding of $E_a$ measured at high concentrations, where ion mobility is intrinsically related to the solution viscosity ($\eta$) by $\mu = e/6\pi\eta$ for monovalent ions.

We note that this finding differs from previous studies, suggesting that the activation behavior of electrolyte conductance should mirror the solvent viscosity, with higher $E_a$ corresponding to higher viscosity and vice versa. Instead, we find that an increased disruption of the water hydrogen bonding network by electrolytes with higher $|B_j|$ increases the $E_a$ of the transport process at a rate of $\partial E_a/\partial |B_j| = 68.4$ kJ L$^{-1}$—regardless of whether that disruption affects the viscosity positively or negatively. The intercept of the linear fit depicted in Figure 4C ($E_a = 9.6$ kJ mol$^{-1}$) represents the activation behavior for ion conduction in pure water. We expect the ion conduction of pure water to be governed by protons at the pH used in this study ($pH = 5.8$); notably, this value reasonably agrees with $E_a$ values calculated for proton mobility from pure water viscosity data ($E_a \approx 11$ kJ mol$^{-1}$).

The $E_a$ for salt transport across the nanochannels appears to follow some pseudexponential relationship with $\sigma$ when the EDLs are strongly overlapped at $C = 10^{-4}$ mol L$^{-1}$ (Figure 5A). We note that the relationship between $E_a$ and $\sigma$ was assessed at $C = 10^{-4}$ mol L$^{-1}$, rather than $C = 10^{-3}$ mol L$^{-1}$, to avoid potentially significant proton effects. The observed increase in $E_a$ when transitioning to the low concentration limit (Figure
4B) suggests added effects from surface charge regulation on the measured thermodynamic signatures. We isolate the effective $E_a$ for surface reactions ($E_{a,surf}$) by taking the difference in $E_a$ values measured at $C = 10^{-3}$ mol L$^{-1}$ and $C = 0.1$ mol L$^{-1}$ (Figure 4D). We find $E_{a,surf}$ increases from 7.03 kJ mol$^{-1}$ for NaCl ($\sigma_{NaCl} = -8.20$ mC m$^{-2}$) to 16.72 ± 0.48 kJ mol$^{-1}$ for KCl ($\sigma_{KCl} = -0.8$ mC m$^{-2}$). The decision on where to evaluate the difference in $E_a$ values between the low concentration and high concentration limits influences the relative magnitude of $E_{a,surf}$ for each ion, but it does not alter the overall trend or the resulting insights (Figure S5).

The trends in Figure 4D indicate that stronger surface charge regulation (i.e., larger fraction of the surface charge neutralized by the cation) generally increases $E_{a,surf}$ and confirm that the activation behavior observed in Figure 4B, when $C \leq 10^{-4}$ mol L$^{-1}$, is due to cation-specific charge regulation. We note that the non-monotonic relationship between $E_{a,surf}$ and $\sigma$ suggests that entropic processes are also an important component to surface charge regulation not captured in $E_{a,surf}$ which describes only enthalpy.\(^{35,58}\) Considering the transition-state theory of rate processes, we posit that the thermodynamics of surface-dominated transport can be explained by an equilibrium between the cations in the overlapped EDLs and the negatively charged SiO$_2$ surface, as illustrated in the inset of Figure 4D.

**Adsorption Equilibrium Explains Ion-Specific Charge Regulation Behavior.** To rationalize the cation-dependent surface charge density from the conductance measurements (Figure 4A), we construct a charge regulation model (see Materials and Methods), assuming strong EDL overlap of nearly uniform potential with the Donnan approxima-

\[ S^- + M^+ \rightleftharpoons SM \]  

where $S^-$ is a negatively charged site, $M^+$ is the cation, and SM is the cation adsorbed to the site. We neglect any local shifts in the pH that would shift the silanol acid/base equilibrium. The local proton concentration can change as a function of the salt ionic strength, and the protons may regulate the surface charge themselves through competitive adsorption in an ionic strength dependent manner.\(^{20,66}\) We will return to assess the validity of this assumption as we analyze the model results, but for now, we choose to neglect these reactions so as to construct the simplest model that captures the experimental data. From the reaction displayed in eq S, we can define an equilibrium constant, $K$, with units of concentration

\[ K = \frac{C_a (\Gamma - \Gamma_{ad})}{\Gamma_{ad}} \]  

where $C_a$ is the concentration of cations in the nanochannel, $\Gamma$ is the total number density of negatively charged adsorption sites, and $\Gamma_{ad}$ is the number density of the subset of sites which have cations adsorbed to them.

For strong EDL overlap at low concentrations, the transport is dominated by the cation (see Materials and Methods), so we can approximate the conductance as

\[ G \approx \frac{H W \mu \kappa e}{L} \sqrt{\frac{21K}{H}} \]  

Here, $G$ plateaus to a constant at low concentration. Adsorption equilibria are typically framed in terms of bulk ion concentrations; however, this plateau is independent of the bulk concentration if the cation of interest is present. The plateau is a consequence of the equilibrium set by the screening cation concentration in the nanochannel, which far exceeds the low bulk ion concentration. The magnitude of the plateau scales with the square root of $K$ since the concentration of charge carriers is the geometric mean between the volumetric density of surface charges in the pore and $K$. At high concentrations, the surface sites are completely neutralized, and the conductance can be approximated by the first term on the right side of eq 2. For the purposes of the charge regulation model, we assume that the cation and anion mobility are independent of concentration and equal to the mobility at infinite dilution. While this assumption is inaccurate for the highest concentrations tested, it is sufficient for the low concentration region where the charge regulation adsorption reactions are influential.

Fitting the charge regulation model to the data (Figure 5A), we find that the model can reproduce the cation-specific conductance curves with cation-specific adsorption equilibrium constants. The fitted values are $K_{Li} = 7.9$ µM, $K_{Na} = 352$ µM, $K_{Ca} = 5.5$ µM, and $K_{Cs} = 10.4$ µM. As seen in Figure 5A, the fitted model is able to capture the correct plateau and inflection of the conductance curves for each electrolyte. As expected from eq 7, larger values of $K$ correspond to higher $G$ at low concentrations. Figure 5B demonstrates how the concentration of cations within the nanochannel far exceeds the bulk in the low concentration limit, and the concentration within the nanochannel is approximately equal to the bulk in the high concentration limit. Consequently, the nanochannel surface charge plateaus at low concentrations and decreases at high concentrations as more cations neutralize the surface sites (Figure 5C). The fitted values of $K$ depend strongly on the magnitude of the surface sites, which we have currently
Figure 5. Nanochannel charge regulation based on adsorption equilibrium. (A) Ion conductance across nanochannels with respect to bulk concentration at 22 °C. Data are taken from Figure 4A and fit by eq 7 assuming $\Gamma = 0.1$ C m$^{-2}$. (B) Fraction of surface charge sites neutralized by Na$^+$ with respect to concentration. The dotted blue line marks the adsorption equilibrium constant for NaCl ($K_{NaCl} = 7.49$ mM). The dotted blue line represents the concentration of Na$^+$ within the channel ($C_e$) when the bulk concentration, $C_{bulk}$ (solid blue line), is equal to $10^{-5}$ M. Here, $\Gamma = 0.01$ C m$^{-2}$ for visualization purposes. (C) Surface charge of the nanochannels with respect to concentration in equilibrium with NaCl, CsCl, LiCl, and KCl, ordered from top to bottom assuming $\Gamma = 0.1$ C m$^{-2}$. Cation adsorption equilibrium constants are indicated as insets of the panels. (D) Surface charge of the nanochannels, on a log-scale, relative to the dielectric saturation ratio, $d/a$, of the charge-regulating cation. Charge regulation by cations with $d/a < 1$ is limited by steric saturation, whereas regulation by cations with $d/a > 1$ is limited by dielectrophoretic saturation. (E) Illustration of sterically limited (left) and dielectrically limited (right) charge regulation. Cations in the red-shaded region contacting the negatively charged surface are adsorbed and considered fully immobilized. Beyond the adsorbed layer, cations remain mobile. The light blue circles surrounding the cations represent their hydration shell. Black arrows correspond to the alignment of water dipoles.

assumed to be $\Gamma = 0.1$ C m$^{-2}$. In the surface-dominated transport regime, a shift in the assumed $\Gamma$ corresponds to an inverse shift in the fitted equilibrium constant (eq 6). Even so, similar trends and behavior are evident even if the number of surface sites are assumed to be different when fitting the equilibrium constants (Figures S6).

The low concentration scaling of $\sigma$ for direct cation adsorption differs significantly from the hydroxide adsorption assumed for carbon nanotubes (CNTs). For strongly confined transport in CNTs, the overlap in EDLs has been associated with a concentration dependent surface charge that depends on local hydroxide adsorption equilibrium. This leads to a deviation from a conductance plateau at low concentration. The hydroxide ions determine the surface charge in these CNT systems, but their contribution to the current through the pore is marginal. In contrast, the cations that carry the current through the nanochannels in our study also determine the channel surface charge density at low bulk concentration through an adsorption equilibrium. Although the local cation concentration within the nanochannel regulates the surface charge, the system of equations predicts a plateau at low concentration rather than a departure from the plateau. This feature of the model agrees with the experimental conductance data for each ion (Figure 5A).

The role of proton/hydroxide charge regulation impacting the surface charge density at low concentration cannot be entirely ruled out, but the plateau in conductance signifies that the adsorbing species is the primary current carrier. Deviations from a plateau at low concentrations have been rationalized by a breakdown in neutrality within 1D conduits or by slip-induced convection. In our measurements, the 2D confinement of the electrolyte in 20 nm SiO$_2$ channels more strongly upholds electroneutrality and would have negligible influence from slip flow. The ability of the model to capture the plateau behavior in the data further supports our assumptions of (i) negligible acid/base equilibria and (ii) electroneutrality in the nanochannel domain.

Cation saturation at charged SiO$_2$ surfaces is frequently explained by steric packing based on the bare ionic or hydrated size of the cation. However, we find that the ordering of $K$ ($K_{Na} > K_{Cs} > K_{Li} > K_{K}$) does not follow a purely steric framework (Table S1). This suggests other cation-specific effects are important to the surface adsorption of cations under strong EDL overlap. A second possible source of cation saturation may be caused by the cation’s dielectric decrement to the solution close to the surface, called dielectrophoretic saturation. Dielectrophoretic saturation arises from the presence of ion solvation shells as well as the dielectric hole created by the ion. The dominant mechanism for cation saturation at the surface can be determined by comparing the cation’s “dielectric diameter, $d'$, to its hydrated diameter, $a$ (additional discussion in Table S1). For cations with $d/a > 1$, dielectrophoretic saturation dominates, whereas cations with $d/a < 1$ are saturated by steric packing.
We find that cation ordering by $d/a$ follows the same ordering of the fitted $K$ values (Figure 5D). Notably, Na$^+$ ($d/a = 0.97$), the cation with the largest $K$ value, is the only cation saturated by steric effects. This suggests that poor steric packing of Na$^+$ may require a much larger concentration of Na$^+$ in the nanochannel to neutralize the surface charge (Figure 5E). However, $d/a$ differs between Na$^+$ and K$^+$ by only $\sim 8\%$, despite an order-of-magnitude difference in $\sigma$. It is therefore evident that other factors that we cannot accurately account for within the scope of this study may also influence cation packing at the surface, such as hydrogen-bonding by the cation near the surface, chemical ion–surface interactions, or partial ion dehydration. These phenomena merit further future investigation.

**Thermodynamic Characteristics of Adsorption Reactions in Nanochannels.** One consequence of conductance scaling at low concentration is that the temperature dependence of $G$ can arise from two physical phenomena. First, a shift in the temperature can change the effective ion mobility, either by the Einstein relation or through intrinsic dependence of the processes.

The temperature resolved measurements of conductance in this work allow us to indirectly access the thermodynamic characteristics of the adsorption reactions. The equilibrium constant can be related to an enthalpy and entropy of reaction, $\Delta H$ and $\Delta S$, respectively, relative to a 1 mol L$^{-1}$ standard state, $K_0$:

$$K = K_0 \exp \left( \frac{\Delta S}{R} - \frac{\Delta H}{RT} \right)$$  (8)

If we account for the ionic mobility temperature dependence, $\mu = \mu_0 \exp(-E_{a,\mu}/RT)$, then the conductance has the following proportionality to the temperature at low concentration

$$G = \frac{H \sigma q}{} \exp \left( \frac{\Delta S}{2R} - \frac{(E_{a,\mu} + \Delta H/2)}{RT} \right)$$  (9)

where $E_{a,\mu}$ characterizes the activation energy for the mobility of the ions. $E_{a,\mu}$ is assumed constant for both ions at all concentrations considered here. At high concentration, the temperature dependence becomes a function of only $E_{a,\mu}$ as discussed earlier (Figure 4C). Assuming that the $E_i$ for the anion and cation diffusion are equal to $E_{a,\mu}$, the conductance can then be written as

$$G = \frac{H \sigma q}{} \mu_0 \exp \left( \frac{E_{a,\mu}}{RT} \right)$$  (10)

We thus find $E_i - RT \approx E_{a,\mu} + \Delta H/2$ at low concentrations and $E_i - RT \approx E_{a,\mu}$ at high concentrations. This relies on the assumption that $E_{a,\mu}$ is independent of concentration; however, data from Figure 4B show that the effective value of $E_i$ can depend on concentration to some extent. In reality, each of these quantities may have some additional concentration dependence not accounted for in our model. We neglect these complicated dependencies for the sake of preliminary analysis. Using the effective values of $E_i$ measured in the high ($C = 0.1$ mol L$^{-1}$) and low ($C = 10^{-4}$ mol L$^{-1}$) concentration regions from Figure 4B, we can approximate the standard enthalpy and entropy of the cation adsorption reactions relative to the standard state (Table 1).

<table>
<thead>
<tr>
<th>Cation</th>
<th>Adsorption Enthalpy, $\Delta H$ (kJ mol$^{-1}$)</th>
<th>Adsorption Entropy, $\Delta S$ (J K$^{-1}$ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li$^+$</td>
<td>15</td>
<td>$-44$</td>
</tr>
<tr>
<td>Na$^+$</td>
<td>14</td>
<td>$-12$</td>
</tr>
<tr>
<td>K$^+$</td>
<td>33</td>
<td>$+13$</td>
</tr>
<tr>
<td>Cs$^+$</td>
<td>19</td>
<td>$-34$</td>
</tr>
</tbody>
</table>

*Note: Values calculated assuming a standard state, $K_0$, of 1 mol L$^{-1}$.

The values in Table 1 can only be taken as estimates since the choice of where to evaluate the approximation can shift their values. Nevertheless, we show that the low $\sigma$ of the nanochannels when regulated by K$^+$ can be related to its high enthalpy of adsorption relative to the other cations. This high enthalpy allows K$^+$ to overcome its relatively high adsorption entropy to achieve a small K value. Conversely, the large $\sigma$ for Na$^+$ is explained by a relatively low enthalpy of adsorption paired with a relatively high entropy of adsorption, both contributing to its larger K value. This is generally consistent with the picture of steric vs dielectrophoretic saturation illustrated in Figure 5E. When surface adsorption is dictated by the dielectric decrement of the ion, the lower permittivity at the nanochannel surface will lead to higher adsorption enthalpies and free energies.

**CONCLUSION**

We employed solid-state nanofluidic devices with precise temperature control to assess the temperature dependence of monovalent electrolyte conductance across 20 nm SiO$_2$ channels. The measured activation energy, $E_{a,\mu}$, of transport in the bulk-dominated transport regime ($C \geq 10^{-2}$ mol L$^{-1}$) arises from the temperature dependence of the electrophoretic mobility of the ions. In particular, we find good agreement between the measured $E_a$ and the chaotropic/kosmotropic tendencies of the cations, suggesting that the temperature dependence arises from viscosity effects. Conversely, when the EDLs of the nanochannel walls strongly overlap ($C \leq 10^{-4}$ mol L$^{-1}$), the $E_i$ measured for ion transport increases significantly. This $E_i$ follows a pseudoexponential relationship with the surface charge, $\sigma$, and indicates that the activation behavior observed during strong EDL overlap is due to cation-specific charge regulation of the nanochannel surface.

We attribute the increased $E_i$ of surface-dominated transport ($C \leq 10^{-4}$ mol L$^{-1}$) to the temperature dependence of an adsorption equilibrium between the cations in the overlapped EDLs and the negatively charged SiO$_2$ surface. Ultimately, we have shown that the regulation of surface charge within the nanochannels is essential for describing the surface-dominated...
conductance of nanometric pores. By taking temperature- and concentration-dependent transport measurements, we can estimate the cation-specific parameters controlling cation adsorption reactions on the pore wall. Therefore, conductance measurements may be used to indirectly probe the ion-surface interactions that determine ionic transport and colloidal interactions at the nanoscale. While temperature-dependent analysis can safely neglect the influence of the double layers and surface adsorption reactions at high ionic concentrations, the specific surface-ion interactions can have a non-negligible contribution to the observed temperature dependence at low concentrations. These findings motivate future studies of surface adsorption with varying surface chemistries, extent of confinement, solution pH, ionic valencies, or even competitive adsorption with mixtures of salts by carefully controlling the electrolyte composition and the temperature. The present study therefore represents an important step forward in our understanding of charge regulation and adsorption phenomena under nanoconfinement.

MATERIALS AND METHODS

Device Fabrication. The initial development of the device fabrication can be found elsewhere. In brief, we deposit a sacrificial layer of chromium (Cr) with a height (H) of 20 nm on SiO$_2$ which is patterned into nanowire structures via photolithography. We apply plasma-enhanced chemical vapor deposition (PECVD) to cover the Cr wires in SiO$_2$ and then bond a polydimethylsiloxane (PDMS) cover patterned with microfluidic channels to the SiO$_2$ surface. Cr etchant is pumped through the microfluidic channels for 24 h, leaving behind geometrically well-defined nanochannels that connect the cis and trans reservoirs of the device. The fabrication procedure and resulting nanofluidic device are pictured in Figure S1. After etching is complete, the system is rinsed with DI water for 48 h to remove residual etchant. Successful etching is validated by a change in the color of the channels observed under a microscope and KCl conductance measurements.

Bubble Prevention and Mitigation. The formation of unwanted gas bubbles in liquid-perfused microchannels commonly hinders the use of micro- and nanofluidic devices. Bubbles can block ion transport across the nanochannel and disrupt the local electric field, thereby altering conductance measurements. To prevent bubble formation in the cis and trans reservoirs, we pump DI water through the PDMS-covered microfluidic channels immediately after PDMS bonding to exploit the temporary increased hydrophilicity of the SiO$_2$ surface. Nevertheless, air bubbles can still be introduced into the system during solution changes. We therefore use an inline bubble trap (PreciGenome, San Jose, CA) to degas the solution prior to it entering the cis and trans reservoirs (Figure S7).

Conductance Measurements. After rinsing the system with DI water for 48 h, salt solutions with concentrations ranging from 10^{-6} to 1 mol L^{-1} were pumped into the cis and trans reservoirs. Chloride-based salts (purity ≥99.9%) used for conductance measurements were purchased from Sigma-Aldrich (St. Louis, MO). Conductance measurements are enabled by inserting Ag/AgCl electrodes into the microchannels of the PDMS layer that connect to the cis and trans reservoirs. The current between these electrodes, which are separated by the nanochannels, is measured by an electrometer Keithley 6514. Current and temperature measurements are based on the average of 200 sampled data points. The conductance of the nanochannels under various conditions are determined by the slope of the I−V curve over voltage sweeps from −0.5 to 0.5 V (step size = 0.1 V). A Keithley 230 is used as the voltage source. All measurements were taken at pH = 5.8 with the nanofluidic device in a Faraday cage.

Modeling Surface Charge Regulation. We construct a charge regulation model using the Donnan approximation. The Donnan approximation neglects the details of the spatial variations of ion concentrations and potentials within the pore and has been used to model capacitive deionization and electrolyte transport across charged membranes. Despite its simplicity, the approximation is most accurate in the low bulk ion concentration limit, which is the region in the conductance measurements where the EDLs play the most important role in determining the transport characteristics. From this, we can define the local surface charge density, $\sigma$, of our nanochannels as

$$\sigma = -e(\Gamma - \Gamma_{ad}) = -\frac{e\Gamma}{1 + C_K^{-1}}$$

(11)

Here $\epsilon$ and $\Gamma$ are again the elementary charge and the total number density of negatively charged adsorption sites, respectively. We emphasize that the adsorption equilibrium is set by the local concentration of cations within the nanochannel, which is elevated due to the net-negatively charged channel walls. When $K$ is large relative to the local cation concentration, there is a stronger propensity for the ions to remain desorbed and for the surface to maintain its negative charge. In the Donnan approximation, assuming Boltzmann-distributed anions and cations (i.e., neglecting concentrated solution effects), the electroneutrality condition gives a relationship between $\sigma$ and the uniform potential within the nanochannel, $\phi$

$$\hat{\sigma} = \frac{\sigma}{\varepsilon HC} = \sinh \left( \frac{\phi \varepsilon}{RT} \right)$$

(12)

where $\hat{\sigma}$ is the dimensionless surface charge density. The ionic densities of the cations and the anions within the nanochannel are given by

$$C_i = C(\sqrt{\hat{\sigma}^2 + 1 + \hat{\sigma}})^{-1}$$

(13a)

$$C_a = C(\sqrt{\hat{\sigma}^2 + 1 + \hat{\sigma}})^{-1}$$

(13b)

From eqs 11 and 13a, we arrive at an implicit formula for $\hat{\sigma}$

$$\hat{\sigma} = \frac{\hat{\sigma}_{max}}{1 + \frac{1}{CK^{-1}}(\sqrt{\hat{\sigma}^2 + 1 + \hat{\sigma}})^{-1}}$$

(14)

where $\hat{\sigma}_{max}$ is the dimensionless maximum charge density with no cation adsorption. Equation 14 describes the regulation of $\sigma$ with respect to $C$ and $K$. Note that $\hat{\sigma}$ and $\hat{\sigma}_{max}$ take on negative values in our analysis.

ASSOCIATED CONTENT

$\dagger$ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsnano.2c06633.

Details for data processing of semiautomated measurements; dielectric diameter calculations; pictured nanofluidic device; thermistor calibration; surface charge correlation to activation energy and calculated surface reaction energy; adsorption equilibrium with respect to surface site magnitude; bubble prevention and mitigation in nanofluidic device (PDF)

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greatly influenced the outcome of this work. May he rest peacefully.

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