Additivity of ionic currents in mixed electrolyte solutions and confined geometries

Jose J. Perez-Grau,[1] Javier Cervera,[2] Saima Nasir,[3,4] Mubarak Ali,[3,4] Wolfgang Ensinger,[3] Patricio Ramirez,[1,]* Salvador Mafe[2]

[1]Departament de Física Aplicada, Universitat Politècnica de València, E-46022 Valencia, Spain,

[2]Departament de Física de la Terra i Termodinàmica, Universitat de València, E-46100 Burjassot, Spain, E-mail: Salvador.Mafe@uv.es

[3]Department of Material- and Geo-Sciences, Materials Analysis, Technische Universität Darmstadt, Alarich-Weiss-Str. 02, D-64287 Darmstadt, Germany

[4]Materials Research Department, GSI Helmholtzzentrum für Schwerionenforschung, Planckstrasse 1, D-64291, Darmstadt, Germany

* Corresponding author E-mail: patraho@fis.upv.es

Electrolyte mixtures in aqueous solutions are central to biophysical chemistry and chemical engineering. Also, ions are usually confined to nanoscale volumes with surface electrical charges. Here, we analyze experimentally the additivity of ionic currents across negatively charged conical nanopores in mixed electrolyte solutions. These pores show an asymmetric axial distribution of carboxylic acid groups on the pore surface, which gives rectified current (I)-voltage (V) curves when a single-pore membrane is bathed by two symmetrical aqueous solutions at neutral pH values. We consider KCl, LiCl, NaCl, CsCl, CaCl$_2$, and K$_2$SO$_4$ pure electrolytes as well as the mixed electrolyte systems LiCl + KCl, NaCl + KCl, CsCl + KCl, CaCl$_2$ + KCl, and K$_2$SO$_4$ + KCl for concentrations ranging from 2 to 500 mM and applied voltages between –2 V and 2 V. The difference between the sum of the pure electrolyte currents and the mixed electrolyte current is studied in terms of the electrolyte concentration, the sign of the applied voltage in the current-voltage curves, and the mixed electrolyte type.

Keywords: conical nanopore, mixed electrolytes, lithium ion, calcium ion, current additivity

Graphical abstract
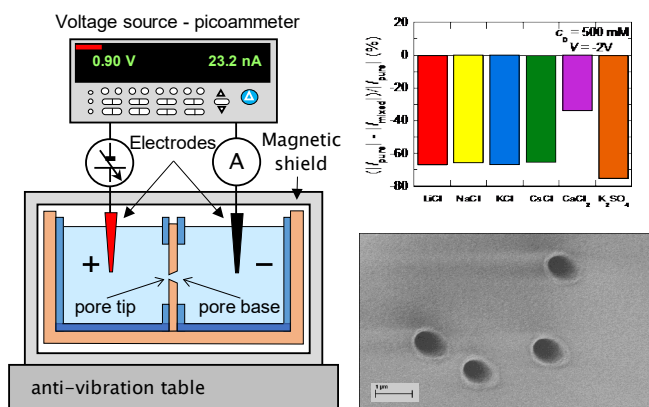
Electrical currents, mixed electrolyte solutions, and conical nanopores

1. Introduction

Solutions of electrolyte mixtures are central to both fundamental and applied science. The electrical interactions between the different ions in solution constitute a complex problem in biotechnology, analytical chemistry, and chemical engineering. This complexity increases further when the ions are confined in nanoscale volumes that incorporate surface charges, such as the ion channel proteins in the cell membrane, nanoporous ion-exchange membranes, and nanopores functionalized with fixed-charge moieties [1–7]. In these cases, because of the high surface-to-volume ratios of the nanostructures, the interaction between the mobile ions in solution and the pore surface charges regulate the ionic transport [8,9]. In particular, mixtures of electrolytes involving potassium and calcium cations are common in biological solutions [1] and carboxylic acid groups are bound to the pore surface of ion channel proteins [10,11]. Mixed electrolytes with monovalent and divalent ions are also characteristic of transport processes in ion-exchange [12] and solid-state [13] membranes.

In addition, the confinement of ionic species within charged asymmetric membranes is relevant to bipolar membranes [14], membranes with pH-dependent fixed charges [15], the ionic selectivity of artificial nanopores [16–21], and the conductance regulation of the ion channel proteins involved in a variety of cellular processes [1,22].

We propose here to analyze the effects of electrolyte concentration and current rectification on the additivity of the ionic currents in mixed electrolyte solutions and negatively charged conical nanopores. The nanostructures are functionalized with an asymmetric axial distribution of carboxylic acid groups on the pore surface that adds a new variable to the inherent problem complexity. The resulting single-pore membrane shows rectified current (I)-voltage (V) curves when bathed by two symmetrical aqueous solutions at neutral pH values. We consider KCl, LiCl, NaCl, CsCl, $CaCl_2$, and K_2SO_4 as pure electrolytes and the mixed electrolyte systems LiCl + KCl, NaCl + KCl, CsCl + KCl, $CaCl_2$ + KCl, and K_2SO_4 + KCl.

Wide ranges of electrolyte concentrations and voltages V are used. In all cases, we discuss the difference between the sum of the pure electrolyte currents and the mixed electrolyte current in terms of the concentration c_0, the sign of the applied voltage V, and the mixed electrolyte type. Also, we give a qualitative description of the transport phenomena that result from the interaction of the mobile ions in solution with the charged groups on the pore surface.

2. Experimental

The experimental setup, together with the solution and pore characteristics, is shown in Fig. 1a − d. The single-pore membrane is fabricated from a 12 μm thick polyimide (PI) foil (Kapton50 HN, DuPont) which is irradiated using heavy ions at the *UNILAC* linear accelerator (GSI, Darmstadt). The nanopore is obtained by exposing the resulting ion tracks to chemical etching using strong inorganic etchant (NaOCl with 13% active chlorine content) at 50 °C and asymmetric conditions (Fig. 1(d)), i.e. with the etchant on one side only in order to obtain the conical shape [23,24]. To allow an appropriate comparison between the different pure and mixed electrolyte systems (Fig. 1(c)), all experiments are conducted with the same single-pore membrane. The significance and reproducibility of the data is demonstrated by the consistency of the experimental trends observed with distinct electrolytes. In the measurements, the solution pH values are in the range 6.5 – 7.0, which are higher than the typical pKa values of the –COOH groups on the pore surface, so that these groups are in the ionized form –COO⁻ and the pore surface charges are negative [25,26]. Typical diameters of the approximately conical pores are shown to be in the ranges 200 – 1000 nm for the base and 20 – 80 nm for the tip, as evaluated from SEM images of the nanopore fracture, gold replicas of the nanopores, and electrical conductance data; additional details can be found elsewhere [25,27]. In our experiments, the base and tip diameters of the pore used are approximately 700 nm and 20 nm, respectively, as

inferred from the comparison of the experimental *I-V* curves from a Poisson-Nernst-Planck model previously developed [25].

Figs. 1(a) and 1(b) show the experimental system and the electrochemical cell. To measure the *I-V* curves, the Ag|AgCl electrodes with 2 M KCl solution salt bridges at the sides of a two-compartment cell are connected to the voltage-source picoammeter (Keithley Instruments, Cleveland, Ohio). The use of a double-layered magnetic shield (Amuneal Manufacturing, Philadelphia, PA) together with the supporting anti-vibration table (Technical Manufacturing Corporation, Peabody, Massachusetts) allows to effectively isolate the cell from electrostatic and mechanical environmental perturbations. Fig. 1(c) shows the different mixed electrolyte solutions used for pure electrolyte concentrations in the range $c_0 = 2 - 500$ mM and neutral solution pH values. For the sake of data reproducibility, the membrane is allowed to equilibrate with the appropriate solution before the electrical measurements. In order to check the stability of the sample, the *I-V* curve at the reference concentration 100 mM KCl is measured after each set of measurements. The differences between the successive *I-V* curves measured here are typically lower than 5%. Additional details can be found elsewhere [8,27].
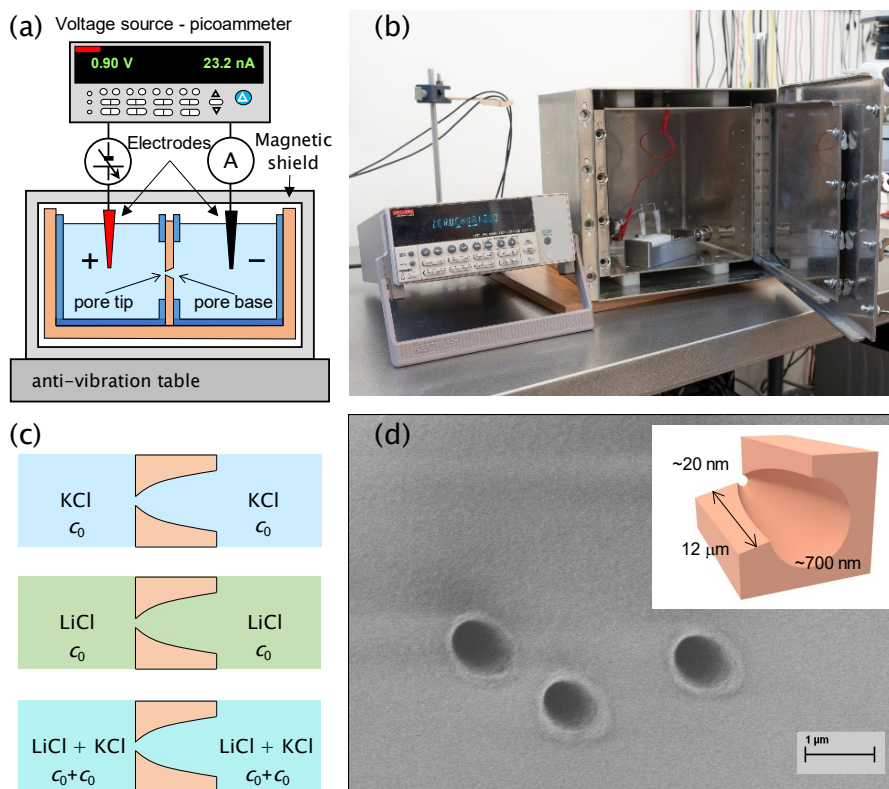
Fig. 1. (a) Experimental setup. During the measurements, the electrochemical cell is situated within a double-layer magnetic shield placed on an anti-vibration table in order to avoid external perturbations. The current (I)-voltage (V) curves of a membrane sample containing a single nanopore are obtained for voltages between $V = -2$ V and 2 V that are applied at the cone tip side of the conical nanopore. (b) The electrochemical cell within a double-layered magnetic shield is located on an anti-vibration table. (c) Schematic of the experimental system for the cases of pure KCl, pure LiCl, and mixed LiCl + KCl electrolyte solutions. The membrane is immersed in two identical aqueous solutions at neutral pH values. The concentrations are in the range $c_0 = 2 - 500$ mM for the pure electrolyte, with the total concentration c_0 (first electrolyte) + c_0 (second electrolyte) for the mixed electrolyte solution. (d) Scanning electron microscopy image of an asymmetric track-etched PI membrane with pore density 10^7 cm^{-2} fabricated together with the single pore-membrane.

3. Results and discussion

The conical nanopore I–V curves (Figs. 2 and 3) are characterized by a low resistance (large currents) when the current enters the cone tip at $V > 0$ and a high resistance when the

current enters the cone basis at $V < 0$ [25], as shown by Figs. 2a (KCl, first measurement run) and 2b (LiCl) together with Figs. 3a (KCl, second measurement run for checking pore recovering and data reproducibility) and 3b (CaCl$_2$) for pure electrolytes; see also Figs. 2c (LiCl + KCl) and 3c (CaCl$_2$ + KCl) for the case of mixed electrolytes. The differences between the sum of pure electrolyte currents (I_{pure}) and the mixed electrolyte current (I_{mixed}) at positive and negative voltages are shown (Figs. 2d and 3d) parametrically in the concentration c_0. Note that in order to analyze the effect of pore rectification on the current additivity, we consider the same individual electrolyte concentration c_0 both in the pure and mixed case.
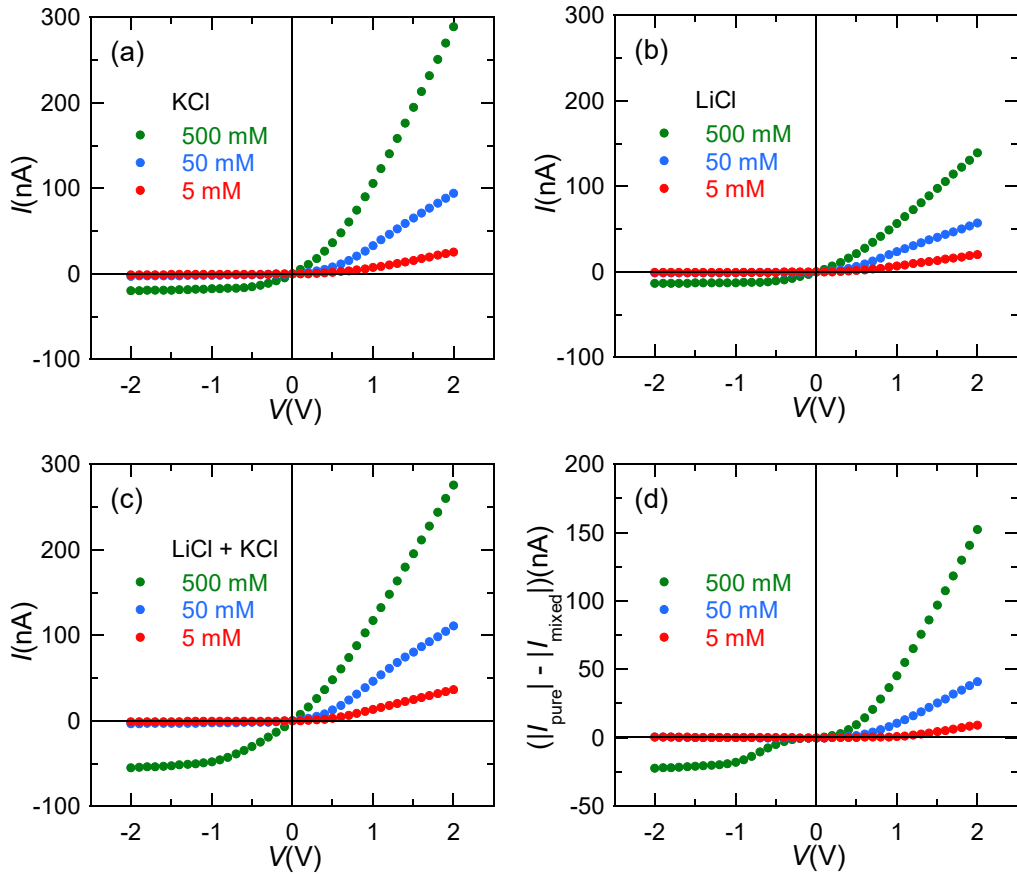

Fig. 2 (a) I–V curves for the KCl concentrations $c_0 = 5$, 50, and 500 mM (first experimental run). (b) I–V curves for the LiCl electrolyte at the above concentrations. (c) I–V curves for the LiCl + KCl mixed electrolyte at concentrations 5 + 5, 50 + 50, and 500 + 500 mM. (d) The

difference between the sum of pure electrolyte currents $I_{pure} = I_{LiCl} + I_{KCl}$ and the mixed electrolyte current $I_{mixed} = I_{LiCl + KCl}$ parametrically in the concentration c_0.
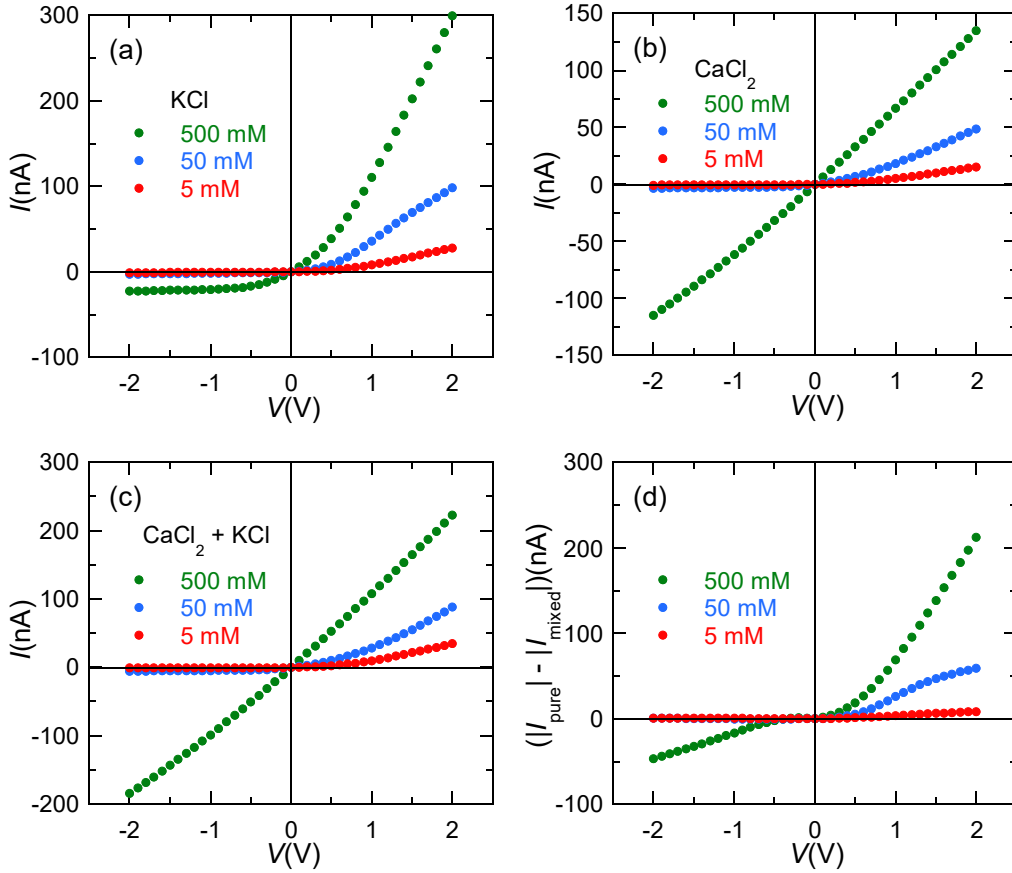

Fig. 3. (a) I–V curves for KCl concentrations $c_0 = 5$, 50, and 500 mM for a second experimental run, different to that of Fig. 2(a), conducted in order to check the pore stability and data reproducibility. (b) I–V curves for the CaCl$_2$ electrolyte at the above concentrations. (c) I–V curves for the CaCl$_2$ + KCl mixture at concentrations 5 + 5, 50 + 50, and 500 + 500 mM. (d) The difference between the sum of pure electrolyte currents $I_{pure} = I_{CaCl_2} + I_{KCl}$ and the mixed electrolyte current $I_{mixed} = I_{CaCl_2 + KCl}$ parametrically in the concentration c_0.

Fig. 4 shows the relative difference, expressed as percentage in %, between the absolute values of the pure and mixed electrolyte currents of Fig. 2 (LiCl + KCl) and Fig. 3 (CaCl$_2$ + KCl) over the whole range of applied voltages for three values characteristic of the low (5 mM), intermediate (50 mM), and (500 mM) high concentration range. As it could be expected from

the concentration-dependent interaction between the cations and anions in free aqueous solutions, the sum of the two pure electrolyte currents is higher than the mixed electrolyte current over most of the concentration and voltage ranges. However, the combined effect of the pore surface charges and nanostructure asymmetry leads to the opposite result at negative voltages ($V = -2$ V) and high enough concentrations ($c_0 > 100$ mM), both for the monovalent and the divalent cations.
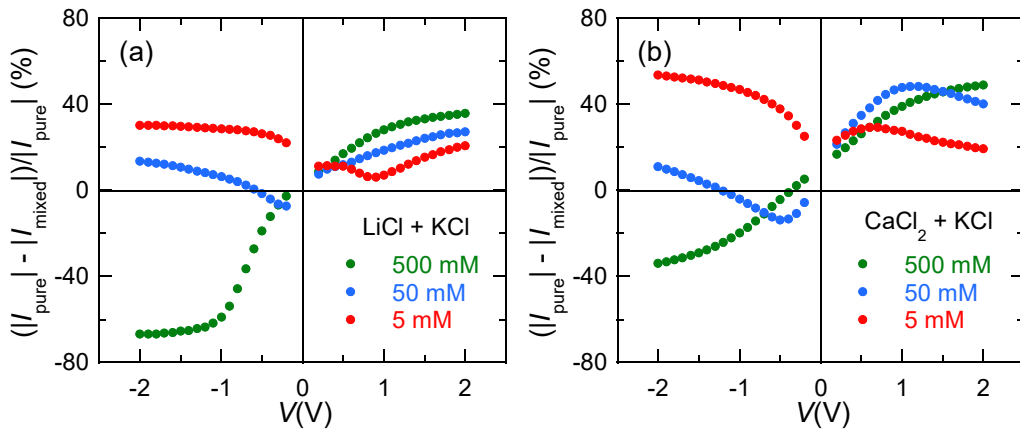

Fig. 4. (a) The relative difference, expressed in %, between the absolute values of the pure and mixed electrolyte currents of Fig. 2 for the LiCl + KCl case as a function of the applied voltage parametrically at $c_0 = 5$, 50, and 500 mM. (b) The difference between the absolute values of the pure and mixed electrolyte currents of Fig. 3 for the $CaCl_2$ + KCl case as a function of the applied voltage parametrically in the above concentrations.

Fig. 5 shows the relative difference between the absolute values of the pure and mixed electrolyte currents for all solutions at voltages $V = -2$ V and 2 V and fixed electrolyte concentrations $c_0 = 50$ mM (Figs. 5a and 5b) and 500 mM (Fig. 5(c) and 5(d)). For all systems studied here, the sum of the two pure electrolyte currents is consistently higher than the mixed electrolyte current except for the case of the negative voltage at high concentrations. Clearly, this fact suggests that the nanoscale effect due to the pore charge asymmetry is significant. Because no rectification is observed in the nanopore $I-V$ curves for acidic pH values higher

than the pKa of the carboxylic groups, no difference between the negative and positive voltage cases is possible for the neutral pore [28].
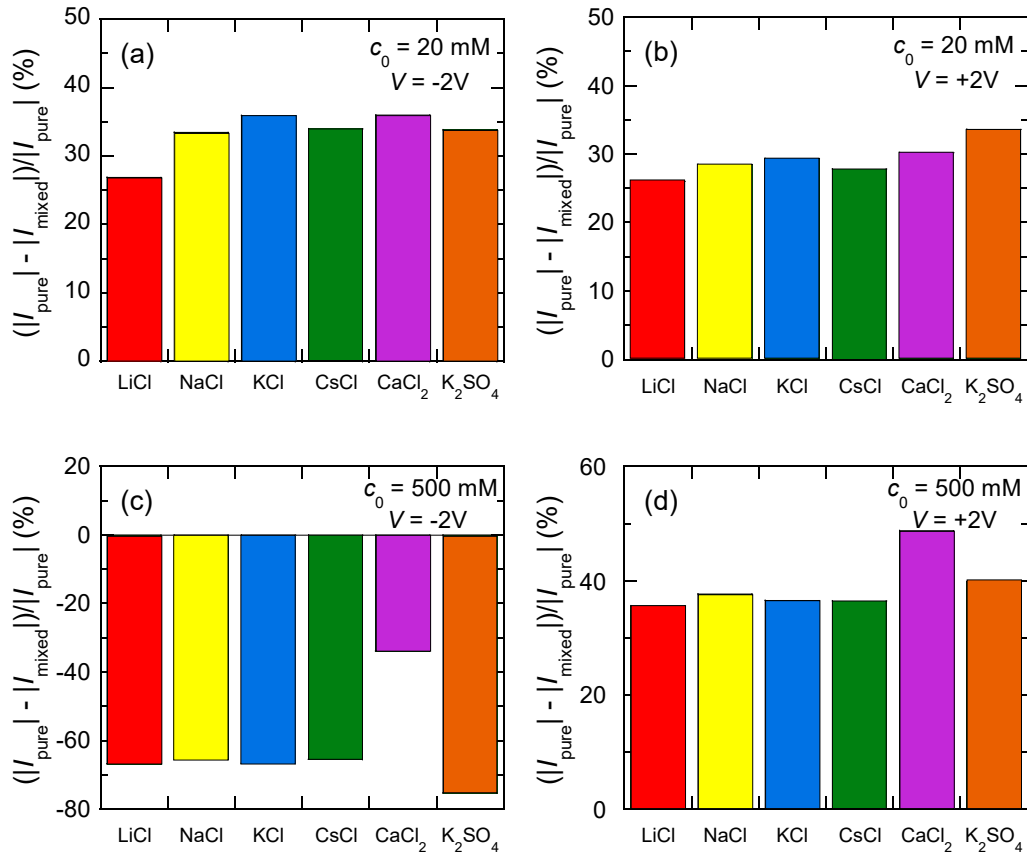

Fig. 5. (a) The relative difference, expressed in percentage (%), between the absolute values of the pure and mixed electrolyte currents for the LiCl + KCl, NaCl + KCl, CsCl + KCl, $CaCl_2$ + KCl, and K_2SO_4 + KCl systems at voltage $V = -2$ V and concentration $c_0 = 50$ mM. (b) $V = 2$ V and $c_0 = 50$ mM. (c) $V = -2$ V and $c_0 = 500$ mM. (d) $V = 2$ V and $c_0 = 500$ mM.

Fig. 6 shows the relative difference between the pure and mixed electrolytes currents for the KCl + KCl and LiCl + KCl systems, over all the range of concentrations, at positive and negative voltages. The enhanced interaction of the negative pore charges with divalent rather monovalent anions is also of interest [29,30], and Fig. 7 considers thus the case of the $CaCl_2$+ KCl + and K_2SO_4 + KCl systems for the sake of comparison. The effects of the divalent cations and anions on the surface charge regulation of the nanopore conductance have been studied in detail previously [8,16].
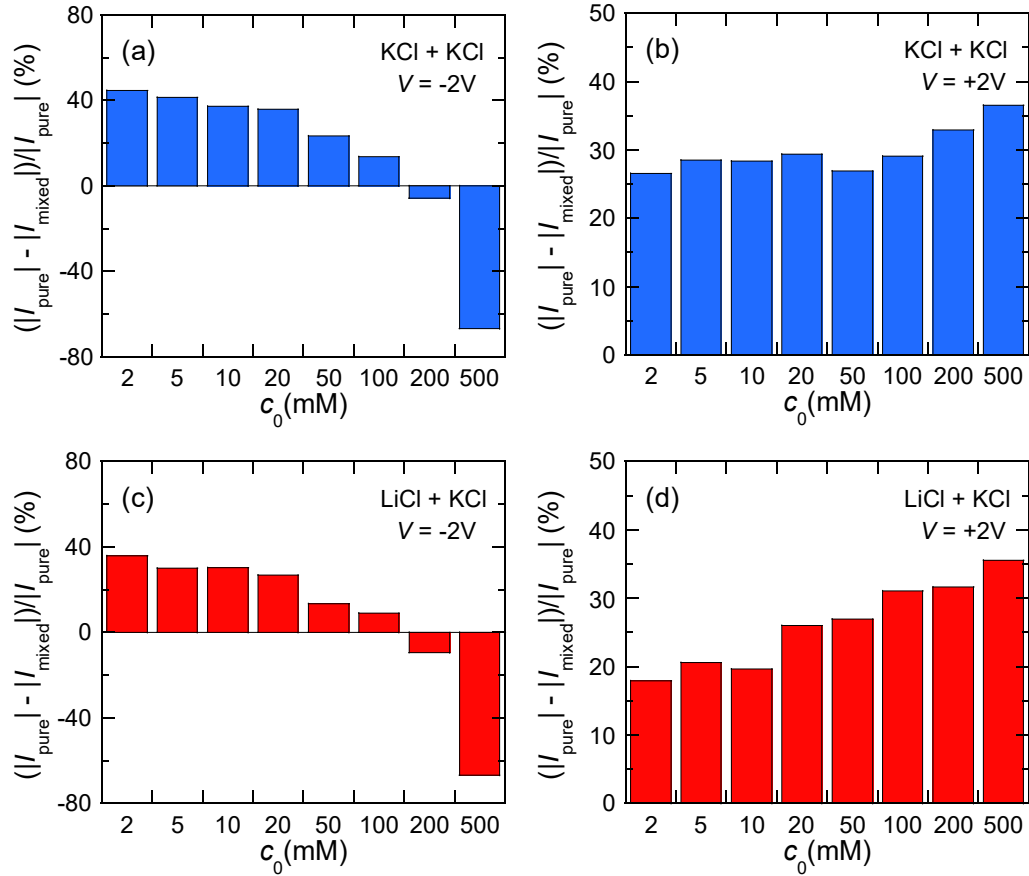
Fig. 6. (a) The relative difference (%) between the pure and mixed electrolytes currents for the KCl + KCl system and concentrations in the range 2 – 500 mM at voltages $V = -2$ V (*left*) and $V = 2$ V (*right*). (b) The LiCl + KCl system at the same concentration range and voltages $V = -2$ V (*left*) and $V = 2$ V (*right*).
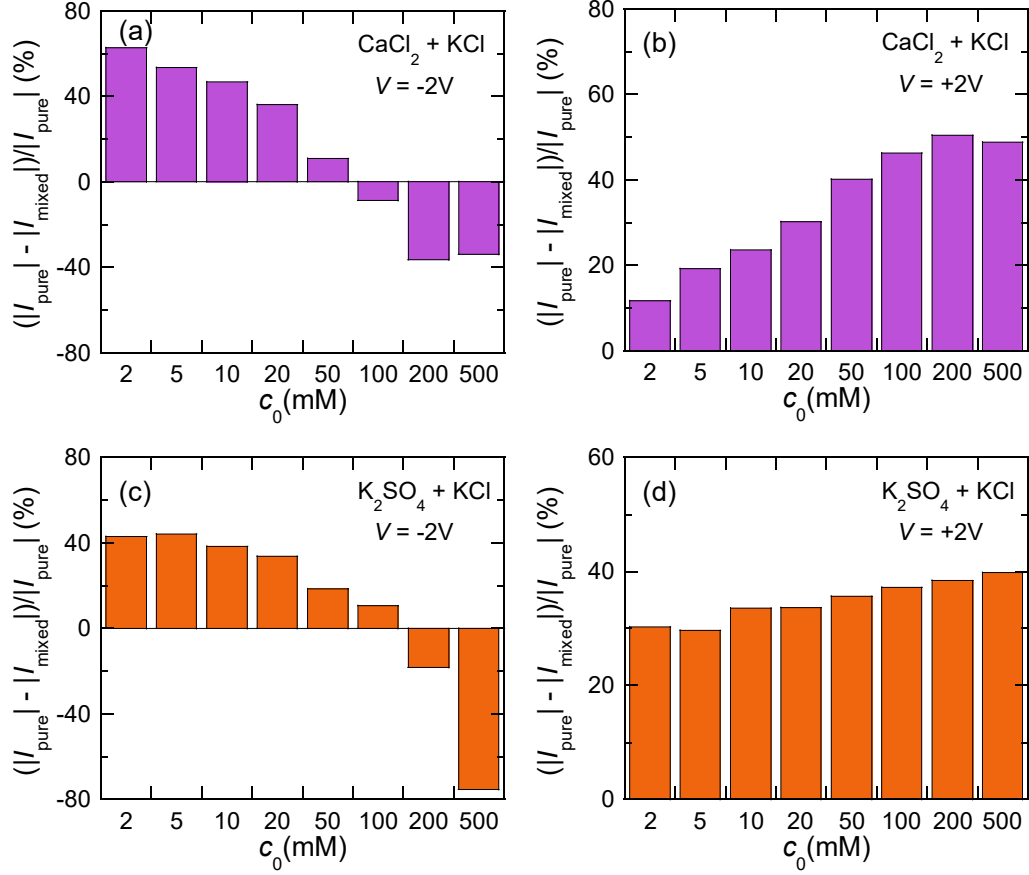
Fig. 7. (a) The relative difference (%) between the pure and mixed electrolytes currents for the CaCl$_2$ + KCl system and concentrations in the range 2 − 500 mM at voltages $V = -2$ V (*left*) and $V = 2$ V (*right*). (b) The K$_2$SO$_4$ + KCl system at the same concentration range and voltages $V = -2$ V (*left*) and $V = 2$ V (*right*).

We attempt to give a now qualitative explanation of the above results, observed for all systems studied. In particular, we will focus on the experimental fact that the sum of the pure electrolyte currents is significantly higher than the mixed electrolyte current except for high concentrations at negative voltage (Figs. 6 and 7).

Consider first the case of dilute electrolyte concentrations in the range $c_0 = 0.002 − 0.1$ M, which are lower than the pore fixed charge concentration $X = 0.1 − 1$ M [25]. In this *low concentration regime*, the Donnan exclusion dominates the ionic transport [2,25]. Thus, the coion (Cl$^-$) is virtually excluded from the negatively charged pore and the counterions (the cations here) are the only mobile electrical carriers available for conduction. In pure

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electrolytes, the negative charge concentration X of the pore should be compensated by the counterion (e.g., K^+ or Li^+) concentration of the respective pure electrolyte, i.e., $X = c_{K+}$ and $X = c_{Li+}$ separately. On the contrary, the sum of the two counterions concentrations is bound to X in the mixed electrolyte case, $X = c_{K+} + c_{Li+}$. As a consequence, in the low concentration regime where the counterion is dominant over the coion conduction, the sum of the pure electrolyte currents should be higher than the mixed electrolyte current, both at $V > 0$ and $V < 0$. Qualitatively similar arguments apply to the other electrolyte systems.

Consider now the case of concentrated electrolyte solutions in the range $c_0 = 0.1 - 1$ M, which is typical of the negative pore charge concentration X. In this *high concentration regime*, the Donnan exclusion no longer dominates the ionic transport and thus not only the counterions (e.g., K^+ and Li^+) but also the coion (Cl^-) can contribute to conduction [2,25]. However, because of the current rectification shown in Figs. 2 and 3, the coion contribution to the total current depends on the axial asymmetry of the pore charges [25,28]. For voltages $V > 0$, Cl^- enters the conical pore from the basis side (Fig. 1) characterized by the low charge concentration $X_{basis} = 2\sigma/FR_{basis}$, where σ is the pore surface charge density, F is Faraday's constant, and R_{basis} is the basis radius [2,25]. Thus, the ionic conduction resembles that of a free electrolyte solution where the sum of the currents obtained from the two pure electrolytes is higher than that of the mixed electrolyte.

On the contrary, for sufficiently high voltages $V < 0$, the Cl^- ion enters the pore from the tip side (Fig. 1) where the charge concentration $X_{tip} = 2\sigma/FR_{tip}$ is now significant because $R_{tip} << R_{basis}$ [25,27]. In this case, the relatively high electrolyte concentration $2c_0$ characteristic of the mixed electrolyte is more effective than the pure electrolyte concentration c_0 for the Debye screening [2,25] of the pore charges. Thus, the coion Cl^- enters the pore more easily, thus contributing to conduction, for the mixed electrolyte case than for the pure electrolyte case (see Figs. 4 and 5 of Reference 25). As a consequence, the absolute value of the mixed

electrolyte current is higher than the sum of the pure electrolyte currents when c_0 attains high enough values and $V < 0$.

In agreement with the qualitative explanation concerning the role of the coion Cl^- in conduction, the transition from positive to negative current differences is shifted to lower pure electrolyte concentrations c_0 for the $CaCl_2 + KCl$ system (Fig. 7(a)) compared with the cases of the $LiCl + KCl$ (Fig. 6(a)) and $LiCl + KCl$ (Fig. 6(c)) systems. Note that in the first case the Cl^- external concentration is $3c_0$ while it is only $2c_0$ in the second cases.

As to theoretical modeling, the fact is that we have not developed complete models for the electrolyte mixtures studied here. However, we suspect from the experimental results obtained that specific effects other than ionic diffusion coefficients are significant for the case of the calcium ion. This fact opens the door for future theoretical models. For instance, previous theoretical work on electric double layers and nanopore rectification with multivalent ions at high concentrations have emphasized the role of anion leakage and the strong correlations between anions and multivalent cations [31,32]. In particular, the divalent and trivalent cations may bring the strongly correlated anions with them into the negative zones that otherwise would repulse the anions [31,32].

In a different experimental context, we check finally the pure electrolyte currents identity $I_{KCl} + I_{NaA} = I_{NaCl} + I_{KA}$, where A^- is an anion other than Cl^-, in the low concentration regime of $c_0 = 5$, 20, and 50 mM (Figure 8). Note that this case allows to compare the currents between solutions with the same total electrolyte concentration, thus extending the previous results. The above mentioned current identity can also be written as $I_{KCl} - I_{NaCl} = I_{KA} - I_{NaA}$ that resembles loosely Kohlrausch's law of independent ionic migration [33]. This law establishes that the molar conductivity can be decomposed into contributions of the individual ions in dilute solutions. Similar regularities are approximately valid for two electrolytes with a common anion and two cations [34]. In our case, the currents should be proportional to the ionic conductivities

because the pore geometry factors characteristic of the conductance are the same for all electrolytes.

Fig. 8 shows that the above currents identity is approximately verified –most differences $\Delta I \equiv 100 \left| \left[(I_{KCl} + I_{NaA}) - (I_{NaCl} + I_{KA}) \right] / \left[(I_{KCl} + I_{NaA}) + (I_{NaCl} + I_{KA}) \right] \right|$ are of the order of 1%. Interestingly, the physical reason behind this experimental fact is not that of a free electrolyte solution (Kohlrausch's law). Indeed, in the low concentration regime of Fig. 8, the anions Cl^- and A^- of the pure electrolyte solutions are virtually excluded from the negatively charged pore so that only the cations K^+ and Na^+ are the electrical carriers responsible for ionic conduction, as explained above. Thus, the current difference identity $I_{KCl} - I_{NaCl} = I_{KA} - I_{NaA}$ arises from the negative pore charges excluding the electrolyte anions rather than from Kohlrausch's law of independent ionic migration in free electrolyte solutions.
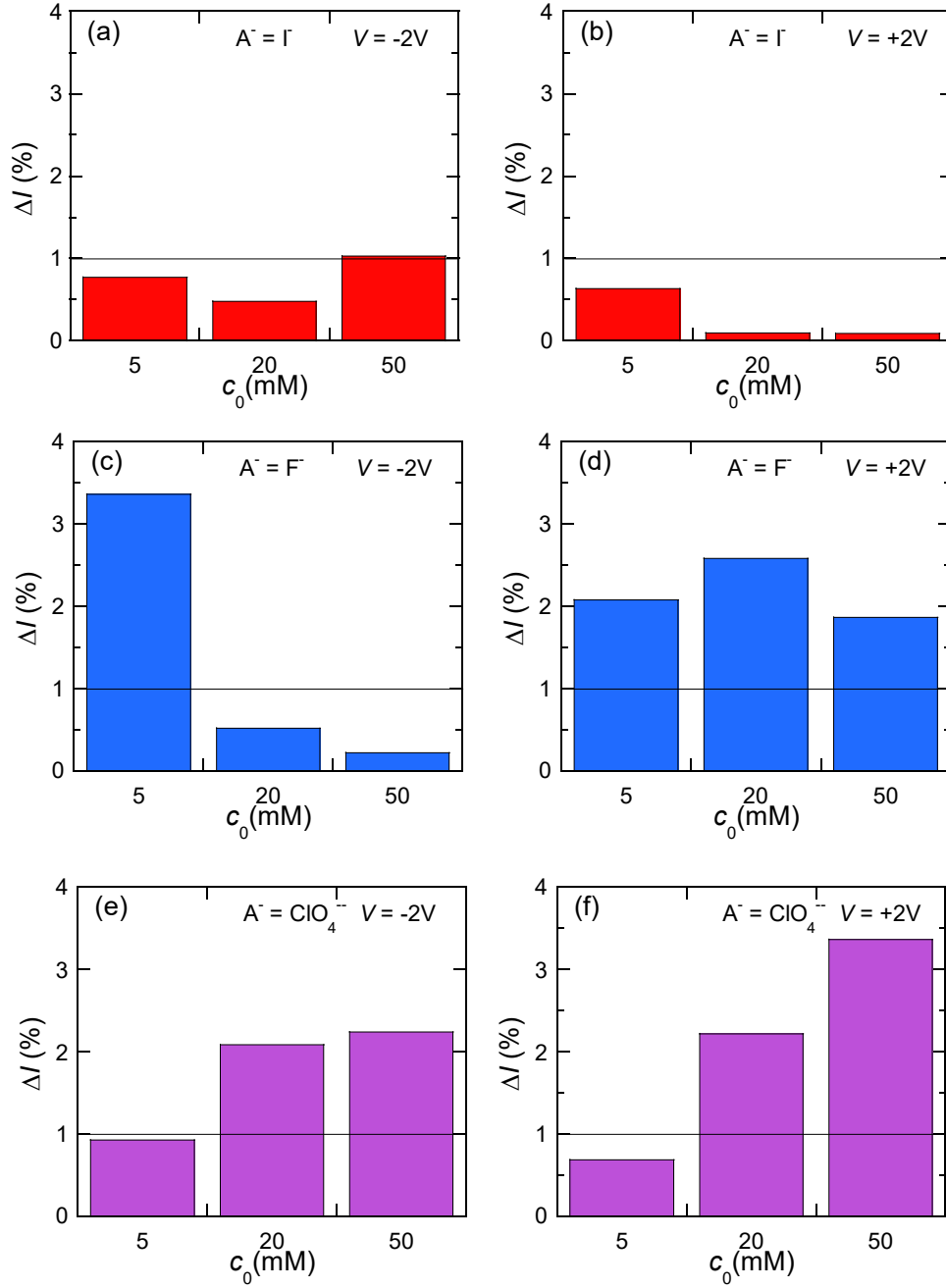
Fig. 8. (a – f) The absolute value of the currents ratio $\Delta I \equiv 100 \; |[(I_{KCl} + I_{NaA}) - (I_{NaCl} + I_{KA})]$ $/[(I_{KCl} + I_{NaA}) + (I_{NaCl} + I_{KA})]|$, expressed in %, for the anions $A^- = I^-$ (a, b), F^- (c, d), and ClO_4^- (e, f). In this case, the low concentration regime of $c_0 = 5$, 20, and 50 mM is considered for the voltages $V = 2$ V and -2 V.

4. Conclusions

In conclusion, we have studied experimentally the additivity of ionic currents for the case of electrolyte mixtures in aqueous solutions confined to nanoscale volumes with surface electrical charges. Because of the asymmetric axial distribution of carboxylic acid groups on the pore surface, significant rectification effects on the current additivity are shown for two symmetrical aqueous solutions at neutral pH values. Different monovalent and multivalent ions over a wide range of concentrations and applied voltages are considered. Also, we have checked that the currents identity $I_{KCl} + I_{NaA} = I_{NaCl} + I_{KA}$, where A^- is an anion other than Cl^-, is approximately verified in the low concentration regime $c_0 = 5 - 50$ mM. We have attempted a qualitative description of the results obtained in terms of basic physical chemistry concepts.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. There are no conflicts of interest to declare.

CRediT authorship contribution statement

Jose J. Perez-Grau: Investigation, Methodology, Formal analysis. **Javier Cervera:** Formal analysis, Supervision, Project administration, Funding acquisition. **Saima Nasir:** Investigation, Methodology, Formal analysis. **Mubarak Ali:** Investigation, Methodology, Formal analysis, Writing–review & editing. **Wolfgang Ensinger:** Methodology, Writing–review & editing, Supervision, Project administration, Funding acquisition **Salvador Mafe:** Conceptualization, Methodology, Formal analysis, Writing –original draft. **Patricio Ramirez:** Investigation, Methodology, Formal analysis, Writing–review & editing, Funding acquisition.

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