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# ARTICLE

## Quantitative Determination of Cation-π Interaction between Metal Ions and Aromatic Groups in Aqueous Media by A Hydrogel Donnan Potential Method

Hailong Fan,[1] Honglei Guo,[2] Takayuki Kurokawa[2] and Jian Ping Gong[1,2*]

Cation−π interaction in aqueous media is known to play critical roles in various biological activities. However, quantitative experimental information, such as the binding ratio of metal ions to aromatic groups, is hardly available due to the lack of a suitable test system and method. Herein, we proposed a hydrogel Donnan potential method to determine the binding ratio of metal ions to aromatic groups on polymer networks in aqueous media. In this method, we adopted recently developed poly(cation−π) hydrogels with a rich adjacent sequence of the cationic group and aromatic group on the polymer network. A microelectrode technique (MET) is used to measure the Donnan potential of the poly(cation−π) hydrogels. From the Donnan potential, the binding ratios of various metal ions to the aromatic groups are quantitatively determined for the first time.

## 1. Introduction

Cation−π interaction is a noncovalent molecular interaction between the face of an electron-rich π system and an adjacent cation, known to exist widely in biological systems and play critical roles in various physiological activities, such as molecular recognition, protein folding, and enzyme catalysis, among others.[1-5] For instance, metal ions can interact with the aromatic residues of proteins through cation−π interactions. Understanding these interactions in various aqueous environments is a prerequisite for elucidating the physical mechanism of their biological function. The interaction of metal ions with biomolecules is not only necessary for normal biological functions, but it can also introduce physiological lesions.[6, 7] For example, barium is a competitive potassium channel antagonist that blocks the passive efflux of intracellular potassium, leading to a shift of potassium from extracellular to intracellular compartments resulting hypokalemia.[8]

Studying cation−π interactions between metal ions and aromatics in aqueous media are difficult.[9-14] The majority of molecules with π−electrons are water-insoluble, which limits the choice for potential research systems.[15] Hydrophilic modifications, as reported for water-soluble aromatic systems such as tryptophan (Trp), p-sulfonatocalix[4]arene, and peptides, bring forth the complexity of structures. The presence of diverse interactions in these systems, such as coordinate bonds and ionic bonds, makes it challenging to identify the specific associations by cation−π interaction.[10, 12, 13] Furthermore, the hydration effect usually weakens the cation−π interactions, which leads to weak signals when using routine

spectroscopic techniques, especially for the metal ions with a large hydration radius, e.g., Li+.[3, 15, 16] Moreover, previous studies in solution provide little information on the binding ratios between cations and aromatic species.[9, 13, 17-22]

Hydrogels are polymer networks that contain a large amount of water, similar to biological tissues.[23] Recently, we fabricated a series of hydrogels having an abundant of adjacently located cationic/aromatic residues, named poly(cation−*adj*−π) hydrogel (adj is short for adjacent and π stands for aromatic monomer).[24, 25] Such specific sequence prevents hydrophobic phenyl groups from aggregating in water, which provides a suitable system to study the cation-π interactions between small cations and aromatic side groups of polymer network in water. When small cations bind to aromatic groups on a hydrogel network, the same amount of oppositely charged small ions (counterions) are localized inside the network by the requirement of electroneutrality.[26] Such Donnan effect of ion binding has been considered recently. For example, a Donnan model has been proposed to predict metal binding onto bacterial surfaces.[27] Nonideal competitive adsorption (NICA)-Donnan model provides a physicochemically realistic description of the electrostatic contribution to metal ion binding to humic acid nanoparticles.[28]

Since the binding of ions to the aromatic group enhances the asymmetric distribution of small ions between inside and outside of the hydrogel, it causes a change in the Donnan potential of the hydrogel. By measuring the Donnan potential of the hydrogel, the binding ratio of metal ions to aromatic groups can be quantitatively determined.[26] In principle, the Donnan potential of a hydrogel in relative to the surrounding salt solution can be measured by their electric potential difference using two electrodes; one is in hydrogel and the other in the salt solution. However, accurately measuring the Donnan potential of hydrogels, especially the polyelectrolyte hydrogels, is a challenge, because it is difficult to make good contact of the electrode to the hydrogels.[29-32] Recently, we

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developed a microelectrode technique (MET) to detect the Donnan potential of brittle polyelectrolyte hydrogels using an extremely thin capillary electrode.[33] By measuring the Donnan potential of poly(cation−adj−π) hydrogel using a MET, we found that the small sodium cation can bind to phenyl groups in the hydrogels, competing with macrocations on the polymer networks.[26]

Herein, we systematically studied the cation−π interactions of a series of metal cations and the aromatic groups in the network of poly(cation−adj−π) hydrogels by Donnan potential measurement (Fig. 1a,b). Specifically, we have selected twelve chloride salts from Group I (M$^+$ = Li$^+$, Na$^+$, K$^+$, Rb$^+$, Cs$^+$), Group II (M$^{2+}$ = Mg$^{2+}$, Ca$^{2+}$, Sr$^{2+}$, Ba$^{2+}$), and the transition metals (M$^{2+}$ = Co$^{2+}$, Ni$^{2+}$, Cu$^{2+}$) in the periodic table of elements (Fig. 1c) to study the cation−π interactions. By measuring the Donnan potential of the poly(cation−adj−π) hydrogels equilibrated in aqueous solutions of various salts, the binding ratio of the metal cations to the aromatic groups in the polymer was quantitatively determined. MET used in this work provides the stoichiometry of direct binding of metal cations to aromatic groups, due to the high sensitivity of the electric potential signal.
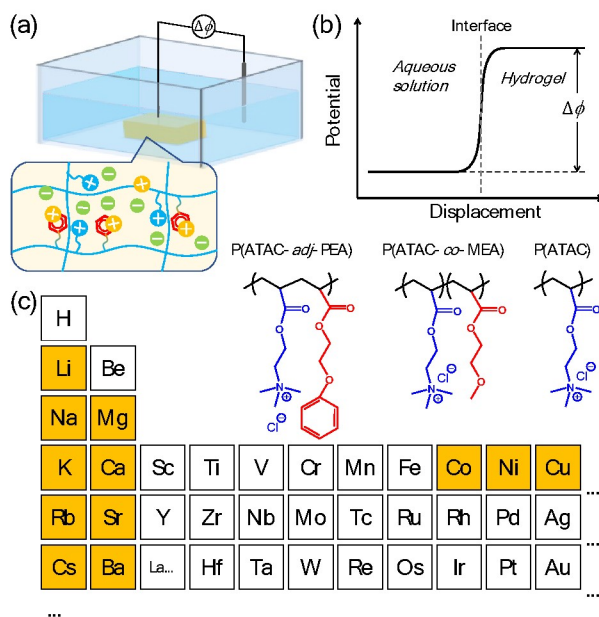


**Fig. 1** (a) Schematic illustration of the microelectrode technique and the mobile ion distribution inside a poly(cation−adj−π) hydrogel and the surrounding bath solution. (b) Illustration of a depth profile of the Donnan potential of a hydrogel in the bath solution. (c) Chemical structures of the polymers and metal elements (highlighted in orange) that their chloride salts used in this work.

## 2. Theoretical principle

### 2.1. Donnan potential

When a polyelectrolyte hydrogel is immersed in an aqueous salt solution, an electric potential difference is generated across the interface of gel and solution due to asymmetric mobile ion

distribution. At the equilibrium state, this potential, known as Donnan potential $\Delta\phi$, is related to the asymmetric mobile ion distribution as follows:[34]

$$\Delta\varphi = \varphi_g - \varphi_s = \frac{RT}{zF}ln\frac{a_s}{a_g} \qquad (1)$$

Here, $a$ is the activity of mobile ions, $z$ is the valency of the mobile ions being considered, $R$ is the gas constant, $T$ is the absolute temperature, and $F$ is the Faraday constant. The subscripts $g$ and $s$ denote the quantities in gel and solution, respectively. Equation 1 is valid for any mobile ions in the system. Generally, the activity of mobile ion $a$ is related to its concentration $C$ through the activity coefficient $\gamma$ by $a = \gamma C$. In this work, the activity of ions in the bath solution are known quantities. For polycationic hydrogels immersed in chloride salt solutions, metal cations are co-ions, and anionic chloride ions are counterions. Hereafter, we denote the ion species in the superscript of various quantities. We denote $M^{n+}$ for metal ions of n valence (n = 1, and 2). From Donnan potential $\Delta\varphi$, $a_g^{ion}$ could be determined for co-ions ($M^{n+}$) and counterions (Cl$^-$) by using Equation 1.

### 2.2. Definition of the activity coefficient of ions in hydrogel

Since the Donnan potential only gives the activity of the ions in the gel, we define the activity coefficient of Cl$^-$ in hydrogels $\gamma_g^{Cl}$ as the ratio of the activity $a_g^{Cl}$ estimated from Donnan potential to the concentration of Cl$^-$ ions in the absence of any interaction or ion binding, $C_{g,i}^{Cl}$, then we have:

$$\Delta\varphi = \frac{RT}{z_{Cl}F}ln\frac{a_s^{Cl}}{a_g^{Cl}} = \frac{RT}{z_{Cl}F}ln\frac{C_s^{Cl}\cdot\gamma_s^{Cl}}{C_{g,i}^{Cl}\cdot\gamma_g^{Cl}} \qquad ($$

Where $C_s^{Cl}$ and $\gamma_s^{Cl}$ are the concentration and activity coefficient of Cl$^-$ in the salt solution, respectively. The subscript $i$ refers to an ideal case in the hydrogel.

For co-ions, we also define the activity coefficient of M$^+$ in hydrogels $\gamma_g^M$ as the ratio of the activity $a_g^M$ measured from Donnan potential to the concentration of M$^+$ ions in the absence of any interaction or ion binding, $C_{g,i}^M$,

$$\Delta\varphi = \frac{RT}{z_MF}ln\frac{a_s^M}{a_g^M} = \frac{RT}{z_MF}ln\frac{C_s^M\cdot\gamma_s^M}{C_{g,i}^M\cdot\gamma_g^M}$$

Next, we derive $C_{g,i}^{Cl}$ and $C_{g,i}^M$ thus defined. They can be theoretically estimated from the Donnan equilibrium. For salt with monovalent metal ions (for example, NaCl):

$$\Delta\varphi_i = \frac{RT}{z_{Cl}F}ln\frac{C_s^{Cl}\gamma_s^{Cl}}{C_{g,i}^{Cl}} = \frac{RT}{z_{Na}F}ln\frac{C_s^{Na}\gamma_s^{Na}}{C_{g,i}^{Na}} \qquad (4)$$

Here $\Delta\varphi_i$ is the Donnan potential for the ideal case. So

$$C_{g,i}^{Cl}\cdot C_{g,i}^{Na} = \gamma_s^{Na}\gamma_s^{Cl}C_s^{Cl}\cdot C_s^{Na} = \gamma_s^{Na}\gamma_s^{Cl}C_s^2 \qquad (5)$$

Here $C_s$ is the salt concentration in the bath solution. From the electric neutrality condition:

$$C_{g,i}^{Cl} = C_p^+ + C_{g,i}^{Na} \qquad (6)$$

Here $C_p^+$ is the polycation concentration of the gel.

From equations (5) and (6), we can get:

$$C_{g,i}^{Cl} = C_p^+ + \frac{\gamma_s^{Na}\gamma_s^{Cl}C_s^2}{C_{g,i}^{Cl}} \qquad (7)$$

$$C_{g,i}^{Cl} = \left[C_p^+ + \sqrt{C_p^{+2} + 4\gamma_s^{Na}\gamma_s^{Cl}C_s^2}\right]/2 \qquad (8)$$

For chloride salt with a divalent metal ion (for example, CaCl$_2$),

$$\Delta\varphi_i = \frac{RT}{z_{Cl}F}ln\frac{C_s^{Cl}\gamma_s^{Cl}}{C_{g,i}^{Cl}} = \frac{RT}{z_{Ca}F}ln\frac{C_s^{Ca}\gamma_s^{Ca}}{C_{g,i}^{Ca}} \qquad (9)$$

So

$$C_{g,i}^{Cl\,2} \cdot C_{g,i}^{Ca} = \left(\gamma_s^{Cl} C_s^{Cl}\right)^2 \cdot \gamma_s^{Ca} C_s^{Ca} \tag{10}$$

where

$$C_s^{Ca} = \frac{1}{2} C_s^{Cl} = C_s \tag{11}$$

from the electric neutrality condition:

$$C_{g,i}^{Cl} = C_p^+ + 2 \times C_{g,i}^{Ca} \tag{12}$$

Based on equations (10) and (11), we can get:

$$C_{g,i}^{Ca} = \frac{4\gamma_s^{Cl2}\gamma_s^{Ca}\,C_s^{\,3}}{C_{g,i}^{Cl\,2}} \tag{13}$$

From equations (12) and (13), we obtained

$$C_{g,i}^{Cl} = C_p^+ + 2 \times \frac{4\gamma_s^{Cl2}\gamma_s^{Ca}\,C_s^{\,3}}{C_{g,i}^{Cl\,2}} \tag{14}$$

So

$$C_{g,i}^{Cl\,3} - C_p^+ \times C_{g,i}^{Cl\,2} - 8\gamma_s^{Cl2}\gamma_s^{Ca} C_s^{\,3} = 0 \tag{15}$$

Therefore

$$C_{g,i}^{Cl} = \frac{C_p^+ - \sqrt[3]{Y_1} - \sqrt[3]{Y_2}}{3} \tag{16}$$

Where

$$Y_{1,2} = -C_p^{+\,3} + \frac{3}{2}[-72 \times \gamma_s^{Cl2}\gamma_s^{Ca}C_s^{\,3} \pm \sqrt{5148 \times \gamma_s^{Cl4}\gamma_s^{Ca2}C_s^{\,6}} +$$

Therefore, $C_{g,i}^{Cl}$ for ideal mobile ions can be calculated from the cation concentration of the gel $C_p^+$, salt concentration $C_s$, activity coefficient of cation $\gamma_s^M$ and anion $\gamma_s^{Cl}$ in salt solution using Equation (8) and (16) for monovalent and divalent metal ions, respectively. Then we can calculate the activity coefficient of Cl⁻ in hydrogel ($\gamma_g^{Cl}$) from the Donnan potential $\Delta\varphi$ measured by MET based on Equation 2. From $C_{g,i}^{Cl}$, the concentration of ideal co-ion in hydrogel ($C_{g,i}^M$) can be obtained by using Equation (6) and (12) for monovalent and divalent metal ions, respectively. Then we can also calculate the activity coefficient of Mⁿ⁺ in hydrogel ($\gamma_g^M$) by using Equation (3).

### 2.3. Derivation of binding ratio of metal ions to the aromatic groups

When the metal ions bind to aromatic groups of P(ATAC-adj-PEA) hydrogels through cation-π interaction, the Cl⁻ ions in the hydrogel is balanced by three cations by the electric neutrality requirement: cation on polymer ($C_p^+$), mobile metal cations in gel ($C_g^{M^{n+}}$), and metal ions bound to the aromatic groups of the polymer ($C_{g,b}^{M^{n+}}$).

$$C_g^{Cl} = C_p^+ + nC_g^{M^{n+}} + nC_{g,b}^{M^{n+}} \tag{17}$$

If we ignore the effect from ion-ion interaction, then $C_{g,i}^{M^{n+}} = C_g^{M^{n+}}$ and $C_g^{Cl} = a_g^{Cl}$. From equations (6) or (12)

$$a_g^{Cl} = C_p^+ + nC_{g,i}^{M^{n+}} + nC_{g,b}^{M^{n+}} = C_{g,i}^{Cl} + nC_{g,b}^{M^{n+}} \tag{18}$$

So, the concentration of n-valency metal ion Mⁿ⁺ absorbed to aromatic groups of polymer in hydrogels by cation-π interaction can be calculated:

$$C_{g,b}^{M^{n+}} = (a_g^{Cl} - C_{g,i}^{Cl})/n \tag{19}$$

Therefore, the binding ratio $R$ of metal ion to the aromatic group can be calculated as:

$$R = \frac{C_{g,b}^{M^{n+}}}{C_p^\pi} \tag{20}$$

Here $C_p^\pi$ is the molar concentration of aromatic groups in the swollen gels. Since the ion binding effect and ion-ion repulsion effect cancel with each other to some extent, the binding ratio thus estimated might be slightly lower than the true value.

From the volume swelling ratio $Q$ of the hydrogels in salt solution relative to their as-prepared states, $C_p^+ = C_{p,0}^+/Q$ and $C_p^\pi = C_{p,0}^\pi/Q$ can be estimated from the initial cationic monomer concentration $C_{p,0}^+$ and aromatic monomer concentration $C_{p,0}^\pi$ at synthesis.

## 3. Materials and methods

### 3.1. Materials

The monomers 2-(acryloyloxy)ethyl trimethyl ammonium chloride (ATAC, 79.4% in water), 2-phenoxyethyl acrylate (PEA), and 2-methoxyethyl acrylate (MEA) were obtained by Osaka Organic Chemical Co., Ltd., Japan. N,N'-methylenebis(acrylamide) (MBAA), 2-oxoglutaric acid, chloride salts, and dimethyl sulfoxide (DMSO) were obtained from Wako Pure Chemical Industries, Ltd., Japan. All these reagents were used as received. All solutions were prepared using Millipore water.

### 3.2. Synthesis of polymer hydrogels

The hydrogels were fabricated by using the free-radical copolymerization of the prescribed monomers in DMSO, according to our previous work.[26] To synthesize P(ATAC–adj–PEA) hydrogel, ATAC and PEA monomers (2.4 M in total concentration, at 1:1 molar ratio), 0.25-mol% UV initiator (2-oxoglutaric acid, 6.0 mM) and chemical crosslinker (MBAA, 2.4 mM) were first dissolved in DMSO, and then the resulting mixture was poured into a reaction cell consisting of a pair of glass plates with a 1-mm spacing and irradiated with a 365-nm UV light (4 mW cm⁻²) for 11 h. After the polymerization, the as-prepared gel was immersed in a large amount of aqueous salt solution with an ionic strength of 0.01 mol kg⁻¹ to wash away the DMSO solvent and residual chemicals. The saltwater was exchanged every 12 h for more than two weeks until the samples reach equilibrium. Before the test, the hydrogels were stored in salt solutions. As control samples, a pure polycation hydrogel, P(ATAC), and a copolymer hydrogel, P(ATAC–co–MEA), from cationic ATAC and a non-aromatic monomer (MEA), in equal molar ratios, were also prepared. These hydrogels were synthesized at the same concentrations of monomer, crosslinker, and initiator with those of the P(ATAC–adj–PEA) hydrogel in DMSO (Fig. 1c).

### 3.3. Swelling measurement

The swelling ratio $Q$ was defined as the ratio of the sample volume $V$ in salt solution with an ionic strength of 0.01 mol kg⁻¹ to that in the as-prepared state $V_0$, $Q = V/V_0$. Since the swelling is isotropic, we measured the thickness of gel at as-prepared state $d_0$ and at swelling equilibrium $d$, and calculated the swelling ratio using relation $Q = \left(\frac{d}{d_0}\right)^3$.

### 3.4. Donnan potential measurement

A salt solution with an ionic strength of 0.01 mol kg⁻¹ is chosen as the reference solution. The corresponding salt concentrations $C_s$ for monovalent metal ions and divalent metal ions were 0.01 M and 0.0033 M, respectively. At this concentration, the signal-to-noise ratio of the Donnan potential is high enough to measure.[26] The Donnan potentials $\Delta\phi$ of the samples in different salt solutions were measured by MET according to our previous reports.[26, 28] Briefly, microelectrodes were prepared by placing a reversible silver/silver chloride electrode into a glass capillary filled with a 3 M KCl solution. Glass capillaries with tip diameter of 170–200 nm were prepared by pulling a borosilicate glass tube (outer diameter of 1.00

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mm and inner diameter of 0.78 mm) using a horizontal automatic micropipette puller (P-2000, Sutter). The electrode was connected to the inputs of a high-impedance intracellular preamplifier (Model 8700 Cell Explorer, Dagan), and a carbon electrode placed in the bath solution was used as the reference electrode. A glass microelectrode, controlled using a micromanipulator (DMA-1511, Narishige), was inserted into the hydrogel at a constant speed of 8 $\mu$m s$^{-1}$. The output signals were recorded using an oscilloscope (Iwatsu, DS-4264) in real-time mode, and electrical potential signals were recorded at 100 samplings per second. All the measurements were conducted at 25 °C.

## 4. Results and discussions

The swelling volume ratio ($Q$) of the hydrogels in relative to their as-prepared state in these aqueous salt solutions of ionic strength 0.01 mol kg$^{-1}$ are shown in Table 1. The P(ATAC) hydrogels showed almost the same swelling ratio, independent of the ion species and charge valence. This result confirms that there is no specific interaction between the polyelectrolyte network and small ions, so the swelling ratio is only related to the ionic strength of the salt solutions that was kept the same in this study. However, for the P(ATAC–*adj*–PEA) hydrogels, the swelling ratios in salt solutions of divalent metal ions are systematically higher than those in monovalent metal cation solutions. This result suggests metal ion binding to the aromatic groups on the polymer network by cation-$\pi$ interaction.

**Table 1.** Volume swelling ratio (Q) of the hydrogels relative to their as-prepared state in aqueous salt solution with an ionic strength of 0.01 mol kg$^{-1}$. Error ranges are the standard deviation of n = 3.

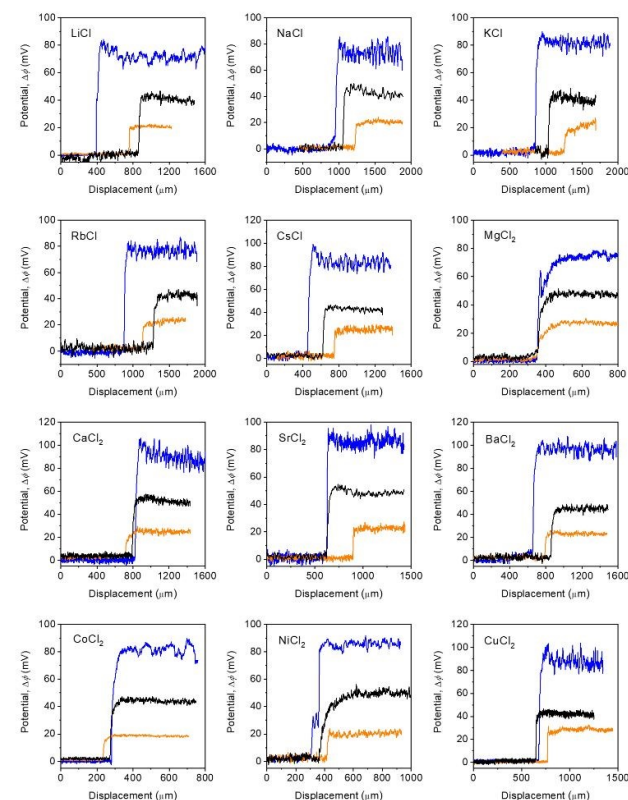|  | P(ATAC-adj-PEA) | P(ATAC-co-MEA) | P(ATAC) |
|---|---|---|---|
| LiCl | 15.4 ± 1.2 | 62.4 ± 2.1 | 50.6 ± 1.9 |
| NaCl | 15.6 ± 0.9 | 64.0 ± 1.9 | 52.7 ± 2.1 |
| KCl | 13.8 ± 1.1 | 63.1 ± 2.2 | 49.1 ± 1.8 |
| RbCl | 14.5 ± 0.9 | 58.4 ± 1.8 | 53.5 ± 1.9 |
| CsCl | 15.3 ± 1.1 | 59.5 ± 2.0 | 52.7 ± 2.1 |
| MgCl$_2$ | 21.9 ± 1.4 | 76.8 ± 2.6 | 55.3 ± 1.9 |
| CaCl$_2$ | 21.3 ± 1.3 | 76.2 ± 2.1 | 54.0 ± 1.8 |
| SrCl$_2$ | 19.7 ± 1.2 | 71.9 ± 1.9 | 54.8 ± 2.0 |
| BaCl$_2$ | 18.2 ± 1.1 | 73.2 ± 2.4 | 57.3 ± 1.9 |
| CoCl$_2$ | 19.7 ± 1.2 | 75.1 ± 2.2 | 58.4 ± 2.2 |
| NiCl$_2$ | 20.1 ± 1.1 | 78.2 ± 1.9 | 54.4 ± 2.1 |
| CuCl$_2$ | 17.6 ± 1.3 | 76.1 ± 1.9 | 56.6 ± 2.4 |

The depth profiles of the electric potential of the three kinds of hydrogels in these aqueous salt solutions of ionic strength 0.01 mol kg$^{-1}$, as measured by MET, are shown in Figure 2. In the bulk solution, the potential value is almost constant with the displacement of the microelectrode. When the microelectrode is initially inserted into the hydrogels, the potential suddenly increases. Inside the hydrogels, the potential value plateaus at positive values. The potential difference between the bulk hydrogel and the solution corresponds to the Donnan potential of the hydrogel. It should be mentioned that the abrupt potential increase

corresponds to the contact of the microelectrode to the hydrogel surface, and the displacement position of the potential jump varies from measurement to measurement, depending on the initial distance between the microelectrode and the gel surface. As shown in Figure 2, P(ATAC–*adj*–PEA) hydrogels showed much higher Donnan potential values than P(ATAC–*co*–MEA) and P(ATAC) hydrogels. It should be mentioned that the large fluctuations in the potentials of the hydrogels are due to the strong adhesion of P(ATAC–*adj*–PEA) to the glass capillary of the electrode.[24]

**Table 2.** Activity coefficients of ions at the ionic strength of 0.01 mol kg$^{-1}$ (25 °C).[35]

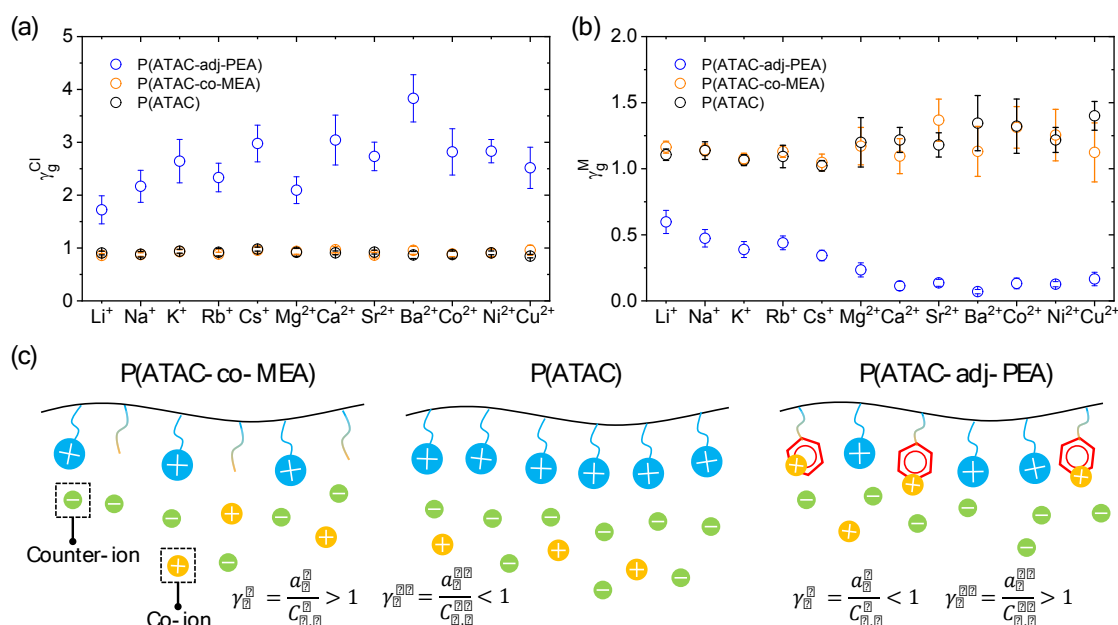| Ion | Activity coefficient |
|---|---|
| Li$^+$ | 0.907 |
| Na$^+$ | 0.902 |
| K$^+$ | 0.899 |
| Rb$^+$, Cs$^+$ | 0.898 |
| Mg$^{2+}$ | 0.69 |
| Ca$^{2+}$, Co$^{2+}$, Ni$^{2+}$, Cu$^{2+}$ | 0.675 |
| Sr$^{2+}$, Ba$^{2+}$ | 0.67 |
| Cl$^-$ | 0.899 |



**Fig. 2** Depth profiles of the electric potential of hydrogels in aqueous chloride salt solutions. The blue line is P(ATAC-adj-PEA) hydrogels, the orange line is P(ATAC-co-MEA) hydrogels, and the black line is P(ATAC) hydrogels. The ionic strength is 0.01 mol kg$^{-1}$ in all solutions, and the corresponding salt concentrations $C_s$ for monovalent metal ions and divalent metal ions are 0.01 M and 0.0033 M, respectively.

Based on the Donnan potential, we calculated the activity coefficients of counterion ($\gamma_g^{Cl}$) and co-ion ($\gamma_g^{M}$) in the hydrogels (Fig. 3). The activity coefficients of cations ($\gamma_s^{M}$) and anion ($\gamma_s^{Cl}$) in bath solutions (ionic strength of 0.01 mol kg$^{-1}$ at 25 °C) were from literature and are shown in Table 2.[35] For the counterions, the effective concentration of Cl$^-$ ($a_g^{Cl}$, calculated by Donnan potential, Equation 2) in the P(ATAC-co-MEA) and P(ATAC) hydrogels are slightly lower than the concentration of the ideal system $C_{g,i}^{Cl}$, resulting in the $\gamma_g^{Cl}$ values that are less than 1, which indicates that attraction between the polycations and counterions in the absence of other interactions between metal cations and polymers, for example, coordinate bond. In contrast, $\gamma_g^{Cl}$ in the P(ATAC-adj-PEA)

hydrogels showed large values ($\gamma_g^{Cl} > 1$), which implies a large number of extra salt ions absorbed in the hydrogels.

For the co-ions, the effective mobile ion concentration of M$^{n+}$ ($a_g^{M}$, calculated by Donnan potential, Equation 3) in the P(ATAC-co-MEA) and P(ATAC) hydrogels are slightly higher than that in the ideal system $C_{g,i}^{M}$, resulting in the $\gamma_g^{M}$ values larger than 1, which indicates the repulsion between the polycations and the co-ions. Whereas, the effective mobile ion concentrations of M$^{n+}$ in the P(ATAC-adj-PEA) hydrogels are much lower than 1, which implies that a large number of co-ions are in a non-free state and cannot contribute to the Donnan potential in the hydrogel, indicating they are bonded to the aromatic groups on the polymer chains by cation-π interaction.



**Fig. 3** (a) Activity coefficient $\gamma_g^{Cl}$ of P(ATAC-adj-PEA), P(ATAC-co-MEA), and P(ATAC) hydrogels calculated based on their Donnan potentials. (b) Activity coefficient $\gamma_g^{M}$ of P(ATAC-adj-PEA), P(ATAC-co-MEA), and P(ATAC) hydrogels calculated based on their Donnan potentials. The ionic strength was 0.01 mol kg$^{-1}$ for all the solutions; namely, the ionic concentration of monovalent metal salts was 0.01 M, and divalent metal salts was 0.0033 M. All the hydrogels were reached the equilibrium state in salt solutions. The error bars represent the standard deviation based on the Donnan potential values in hydrogels. (c) Schematic illustration of ions surrounding polymer chains in hydrogels.
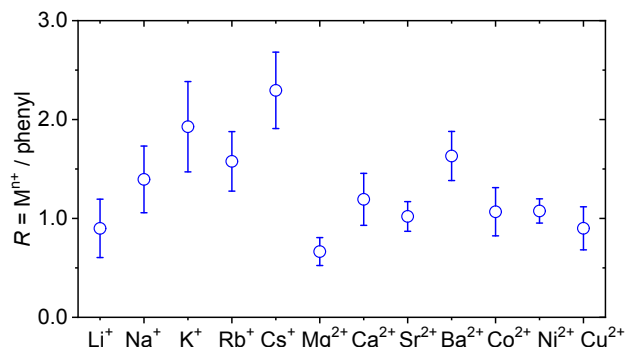


**Fig. 4** Molar ratio between metal ions bound to phenyl groups $R$ in hydrogel by cation–π interactions. The ionic strength was 0.01 mol kg$^{-1}$ for all solutions. The ionic concentration of monovalent metal

salts was 0.01 M, and the concentration of divalent metal salts was 0.0033 M. The error bars represent the standard deviation based on the Donnan potential values in hydrogels.

Then we calculated the molecular ratios $R$ of metal cations bind to the aromatic groups of the P(ATAC–*adj*–PEA) hydrogel. Figure 4 shows the molar ratio of metal cation binding to the phenyl groups. For monovalent metal cations (Group I), the molar binding ratio, which can be regard as a measure of interaction strength or affinity, follows the order of Cs$^+$ > K$^+$ > Rb$^+$ > Na$^+$ > Li$^+$. This sequence is consistent with the results of previous reports.[9, 16] Based on the electrostatic model proposed by Kumpf and Dougherty, the binding energy between K$^+$ and benzene is larger than that of Rb$^+$/benzene, and much larger than that of Na$^+$/benzene.[16] Cs$^+$ has the strongest

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cation−π interaction among the Group I metal cations. Zhu et al. indicated that non-electrostatic forces play an important role in this case due to the relatively high polarizability of $Cs^+$.[9] Our results give direct evidence, for the first time, that $Li^+$ can associate with the phenyl group in an approximately 1:1 ratio in aqueous solutions. Previous studies have found that carbon nanotube (CNT)-based Li batteries show superior high capacity, high cyclability, and high energy density.[36] This result may help us better understand the binding interaction between $Li^+$ and π-cloud of CNT.

For the divalent metal cations of Group II, the molar binding ratio follows the order of $Ba^{2+} > Ca^{2+} > Sr^{2+} > Mg^{2+}$. As for the transition metal cations, the binding ratios of $Co^{2+}$ and $Ni^{2+}$ to phenyl groups show no obvious differences but are notably slightly higher than the binding ratio of $Cu^{2+}$. Compared with $Ca^{2+}$, the transition metal cations $Co^{2+}$, $Ni^{2+}$, and $Cu^{2+}$ have a lower binding ratio. $Ca^{2+}$ lacks d-electrons and preferentially binds to the $sp^2$ clusters of phenyl through cation−π interactions.[37] It should be mentioned that the binding ratio between monovalent and divalent cations cannot be compared directly in this study due to the difference of metal cation concentrations.

Compared with reported techniques, which give the relative affinity of cations to aromatic species, MET, whose accuracy has been confirmed in previous study,[26] can further provide the detailed stoichiometric binding ratio between metal cations and aromatic groups, even for metal cations having a large hydration radius that form weak cation−π interactions.

## Conclusions

In summary, the poly(cation−*adj*−π) hydrogel is an ideal system for the study of cation−π interactions in aqueous media. Through the application of the microelectrode technique (MET) to the chemically cross-linked poly(cation−*adj*−π) hydrogels, the binding ratio $R$ of various cationic metal ions to aromatic groups by cation-π interaction can be quantitatively calculated. In a salt solution of relatively low ionic strength (0.01 mol $kg^{-1}$), each aromatic group on the polymer chains can adsorb one to two metal cations, depending on the type and valence of the metal ions. In this study, we observed, for the first time, the association between $Li^+$ and phenyl groups could be as high as ~1:1. This work provides new insights into the understanding of the binding process of cations in biological systems, as well as the impact of cation−π interactions on carbon nanotube (CNT)-based Li batteries. We believed that the MET method could be a powerful tool to study the cation-π interactions in future works, for example, the role of counter ion types, the type of aromatic and cationic groups on the polymer chains and so on.

## Conflicts of interest

There are no conflicts to declare.

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