

Efficiency of Solute Release from Thermoresponsive Poly(*N*-isopropylacrylamide) Gels: Electrochemical Studies

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An electrochemical method for the simultaneous determination of the diffusion coefficient and efficiency of release of probe species from thermoresponsive gels due to their volume phase transition is presented. The method combines steady-state voltammetry at microelectrodes and conductometry, and it is designed for charged redox species. This method might be modified for uncharged systems; in this case instead of the conductometric measurement an additional independent voltammetric experiment in the solution is required. The approach presented here has been examined for positively and negatively charged and uncharged ferrocene derivatives as probes in the poly(*N*-isopropylacrylamide) hydrogel. The release coefficient, θ , defined as the ratio of the concentrations of the probe in the expelled solution and the swollen gel, and determined for the charged ferrocene-based probes, is greater by approximately 25% than that found for the uncharged ferrocene derivative. The larger release efficiency for the charged probes is explained in terms of substantial dehydration of polymeric chains during the gel phase transition. The experiments were performed under the conditions of excess supporting electrolyte. No influence of the identity and concentration (up to 0.05 mol/L) of supporting electrolytes (i.e., either LiClO₄ or KCl) on the release coefficient was observed. The average values of release coefficients were determined to be 0.80 ± 0.02 , 1.03 ± 0.16 , and 1.07 ± 0.14 for 1,1'-ferrocenedimethanol, sodium ferroceneacetate, and ferrocenylmethyltrimethylammonium hexafluorophosphate, respectively.

Introduction

Polymeric hydrogels based on polyacrylamide and poly(acrylic acid) are known to exhibit either discontinuous or continuous volume phase transition.¹ Therefore, they can exist in two different states, swollen and collapsed (shrunken). This interesting feature makes polymeric gels attractive systems in numerous applications, including drug delivery systems, separation techniques, and construction of sensors.^{2–8} In such applications the knowledge of diffusion coefficients of ions and molecules is of great importance, since they are fundamental measures of molecular mobility. Recently, we have shown that steady-state voltammetry at microelectrodes is extremely convenient for the determination of some important parameters characterizing the transport properties of gels.^{9–13} These include diffusivities of probe molecules, local gel viscosity, and activation energy of transport.

In the optimization of the applications mentioned above (especially drug delivery and therapeutic applications) in addition to the transport characteristics of the gel matrixes, it is critical to understand and describe the efficiency of both loading the gel with various probe molecules and their release due to the gel volume phase transition. Quantitatively, these tasks may be achieved by determination of the concentration distribution of probe molecules in the gel and the external solution before and after the volume phase transition.

The partition of some organic and inorganic substances between the swollen gel and the external solution in contact with the gel has been studied by several groups.^{14–16} These studies provide valuable information on the loading capabilities

of the gel materials. However, they tell nothing or little about another important characteristic of the gel, i.e., the efficiency of substance release from the gel structure due to the phase transition. The release efficiency can be expressed quantitatively in terms of the ratio of the concentrations (amounts) of probe species in the expelled solution and the swollen gel; we call this ratio a release coefficient. An attempt to determine this quantity has been presented by Kawasaki et al.¹⁴ Their work, however, is limited to the various inorganic salts, and the presented method requires the use of the calibration curve.

In this work we present the methodology that allows simultaneous determination of the release coefficient and diffusivity of electroactive probe molecules. The method combines steady-state voltammetry at microelectrodes and conductometric measurements. This combination can be applied for any charged redox system at a wide range of ionic strength. It allows one to obtain these valuable data for one particular gel sample, without necessity of using any additional gel standards or synthetic solutions. For uncharged systems, however, instead of conductometry additional voltammetric experiments in the solution are required. The proposed procedure is relatively fast, and the instrumentation is inexpensive. The method is examined for uncharged and charged electroactive probes for temperature-sensitive poly(*N*-isopropylacrylamide) gels.

Experimental Section

Chemicals. The polymer constituents *N*-isopropylacrylamide (NIPA; 97%), *N,N'*-methylenebisacrylamide (BIS; 99%), ammonium persulfate (APS; 99.99%), and *N,N,N',N'*-tetramethylethylenediamine (TEMED; 99.5%) were purchased from Aldrich. 1,1'-Ferrocenedimethanol (Fe(C₅H₄)₂(CH₂OH)₂ or Fc(MeOH)₂; 98%) was purchased from Aldrich, and sodium ferroceneacetate (Fe(C₅H₅)(C₅H₄)(CH₂COO)Na or FcAc⁻) and ferro-

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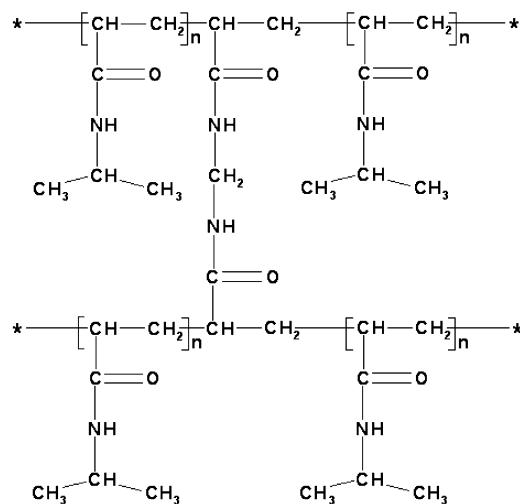


Figure 1. Schematic structure of *N*-isopropylacrylamide polymer cross-linked with *N,N'*-methylenebisacrylamide.

cenylmethyltrimethylammonium hexafluorophosphate ($\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4)(\text{CH}_2\text{N}(\text{CH}_3)_3)\text{PF}_6$ or FcTMA^+) were prepared in our laboratory according to the procedures available in the literature. High-purity lithium perchlorate (LiClO_4 ; 99%, Fluka) and potassium chloride (KCl ; 99.99%, Aldrich) were chosen as supporting electrolytes. All chemicals were used as received except for NIPA, which was recrystallized twice from a benzene/hexane mixture (90:10, v/v).

NIPA polymer cross-linked with BIS was synthesized and purified according to the previously described procedure.¹¹ The mole fraction of each monomer was 0.99:0.01 for NIPA and BIS, respectively. The schematic structure of the cross-linked NIPA polymer is shown in Figure 1.

Voltammetric Measurements. Electrochemical measurements were performed using an AutoLab model PGSTAT 30 potentiostat, controlled via software by a PC. All experiments were carried out in a three-electrode system. A platinum counter electrode and a platinum quasi-reference electrode,¹⁷ to eliminate a possible leak of electrolyte from the bridge, were used. The latter is especially vital for the systems containing no supporting electrolyte.¹⁸ A $10.5 \pm 0.2 \mu\text{m}$ radius platinum disk microelectrode (nLab, Warsaw, Poland) was used as the working electrode. The electrode system was placed in a water-jacketed glass cell. The temperature of that cell was controlled using a refrigerated circulator (Polystat, Cole Parmer). Before each experiment, the microelectrode was polished with aluminum oxide powder of various sizes (down to $0.05 \mu\text{m}$) on a wet pad, rinsed with water, and then dried with ethanol. The surface of the microelectrode was inspected optically with an Olympus model PME 3 microscope.

Steady-state voltammetry experiments were performed at 25 °C with a scan rate of 10 mV/s. Six replicates of voltammograms were taken for each redox probe.

Conductivity Measurements. The conductance was measured using a conductance meter, Radiometer model CDM230, with a CDC241-9 conductivity cell. The cell constant was determined using conductivity standard solutions purchased from Fluka. Its average value was $1.10 \pm 0.01 \text{ cm}^{-1}$ ($k \pm s(k)$). All measurements were performed at 25 °C, and for each system 10 replicates of conductance measurements were taken.

Sample Preparation and Experimental Approach. A known amount of dry, ground NIPA polymer was placed into a certain volume of a solution (10 mL in this work) with a known concentration of an electroactive probe and, optionally,

supporting electrolyte. The solution with the dry polymer was left overnight at room temperature in a graduated cylinder. After this period of time the swelling process was complete (the entire solution was absorbed by the dry polymer), and as a result, a swollen gel was formed with a very well defined polymer-to-solution ratio, concentration of electroactive probe, and, optionally, supporting electrolyte. In other words, after the solution was left overnight, only one phase (i.e., the gel phase) was present in the cylinder and the volume of the swollen gel was equal to the initial volume of the solution used. Gels loaded with both ionic and neutral probes swell to the same extent. The change of the total volume of the newly prepared swollen gel compared to the initial volume of the solution was less than 1%. During the swelling process the gels retained the shape of the container used. No gas bubbles and empty spaces were formed, and the surface level was flat. Therefore, measurements of volume similar to those performed for liquids (by using a graduated cylinder) were employed. This procedure was developed in our group and is well documented in several papers.^{10–13} It was tested for NIPA and NIPA-AA gels in various media (including nonaqueous solvents) with polymer concentration in the range between 2% and 5% (w/v).

Determination of the release coefficient consisted of the following steps. First, the gel sample containing both the electroactive probe and supporting electrolyte was heated to 40–45 °C, which is well above the gel volume phase transition temperature of 34 °C.¹⁹ The two phases, collapsed gel and the solution expelled from the gel, were carefully separated. Additionally, the expelled solution was centrifuged to remove small pieces of the polymer. The clear solution was then cooled to 25 °C. At this temperature the conductivity measurements followed by the steady-state voltammetry were performed. Before voltammograms were recorded, an additional amount of a supporting electrolyte was added to the solution. Since an unknown amount of the supporting electrolyte remains in the collapsed gel, the addition of the electrolyte is needed to maintain the excess supporting electrolyte and, consequently, to eliminate migrational contribution to the transport of charged species in the expelled solution. It should be emphasized here that the method does not require the presence of supporting electrolyte in a gel sample. This electrolyte must be added to the expelled solution to ensure the purely diffusional conditions in the voltammetric experiment. The concentration of supporting electrolyte should not be higher than 0.05 M to avoid a significant increase in the solution viscosity and correspondingly a decrease in the diffusion coefficients, while the ratio of the concentrations of supporting electrolyte and electrode process substrate should not be less than 20.

It should be mentioned here that there is no need to add any amount of supporting electrolyte for conductance measurements. If supporting electrolyte is added to the swollen gel (and then part of it is released from the gel due to the phase transition), its concentration should not exceed the concentration of the probe by 2 orders of magnitude. Otherwise, the conductivity of the expelled solution would be dominated by the presence of supporting electrolyte; this would result in a drastic decrease in the precision and accuracy of the determination of the ionic probe contribution to the total conductivity of the solution. On the other hand, the lower limit of the concentration of the ionic probe is determined by the quantification limit of the cell used for the experiment.

The same steps of the procedure described above were applied to the blank samples of the gel (i.e., the gel swollen by an aqueous solution of supporting electrolyte). This allowed us to

obtain background signals, and to determine quantitatively the volume of the expelled solution. The latter was measured in a calibrated cylinder at 25 °C, and for five measurements was estimated to be 8.2 ± 0.1 mL ($V \pm s(V)$) for a 10 mL swollen gel sample. The magnitude of the expelled solution volume is not affected by the presence of both redox probes and supporting electrolytes at the concentrations used in the experiments.

All experiments presented in this paper were performed for 4% NIPA gels under the conditions of approximately 25-fold excess supporting electrolyte with respect to the concentration of electroactive species (approximately 2 mM). Two supporting electrolytes were used in the experiments, LiClO₄ and KCl.

Theoretical Section

In the concept of release coefficient two values of the probe concentration are essential. The first one refers to the probe concentration in the swollen gel, which is fixed and is known precisely by applying our experimental method for preparing a swollen gel, while the second one corresponds to the released solution and is unknown. To determine the latter, we employ the combination of conductometric and steady-state voltammetric measurements. Both the conductivity and steady-state current at microelectrodes are, by definition, directly proportional to the probe concentration and its diffusivity.

The conductivity of a solution expelled from the gel due to the volume phase transition, κ_{expl} , can be represented as a sum of two contributions:

$$\kappa_{\text{expl}} = \kappa_{\text{el}} + \kappa_{\text{b}} \quad (1)$$

where κ_{el} represents the contribution of ions of an electroactive electrolyte, while κ_{b} refers to the contribution of ionic impurities and ions of supporting electrolyte, if present. By “electroactive electrolyte” we mean the electrolyte containing either a cation or an anion that can be either electrooxidized or electroreduced.

For a diluted electrolytic system the conductivity can be expressed by the following general formula:

$$\kappa = \frac{F^2}{RT} \sum_i z_i^2 D_i c_i \quad (2)$$

where z_i , D_i , and c_i are the charge number, diffusion coefficient, and concentration of the i th ion, respectively, F , R , and T have their usual meanings, and the summation covers all ionic species.

For the expelled solution of an electrolyte $S\nu_S X\nu_X$, eq 2 can be written as

$$\kappa_{\text{el}} = \frac{F^2}{RT} (z_S^2 \nu_S D_S + z_X^2 \nu_X D_X) c_{\text{expl}} \quad (3)$$

where S and X denote the substrate of an electrode process and its counterion, respectively, ν_S and ν_X are their stoichiometric coefficients, and c_{expl} is the concentration of electroactive electrolyte in the expelled solution (equal to $n_{\text{expl}}/V_{\text{expl}}$, where n_{expl} and V_{expl} refer to the number of moles of electrolyte in the expelled solution and the volume of the expelled solution, respectively).

Combination of eqs 1 and 3 results in the following expression for the conductivity of the expelled solution:

$$\kappa_{\text{expl}} - \kappa_{\text{b}} = \frac{F^2}{RT} (z_S^2 \nu_S D_S + z_X^2 \nu_X D_X) c_{\text{expl}} \quad (4)$$

This equation contains three unknowns: D_S , D_X , and c_{expl} . Usually the electroactive substrate is accompanied by simple ions

such as Na⁺, K⁺, Cl⁻, PF₆⁻, etc., which are well characterized in terms of their transport properties in aqueous systems. This fact reduces the number of unknowns in eq 4 to two, i.e., D_S and c_{expl} . To determine them, an additional relation containing both variables is needed. We found that steady-state voltammetry at microelectrodes may serve this purpose. The steady-state diffusional current, I_{ss} , at microelectrodes is given by

$$I_{\text{ss}} = gnFr_e D_S c_S^{\text{b}} \quad (5)$$

where g is the microelectrode geometry factor (for a microdisk it equals 4), n is the number of electrons exchanged per molecule, r_e denotes the microelectrode radius, and c_S^{b} is the bulk concentration of the substrate (electroactive ion) equal to $\nu_S c_{\text{expl}}$ (i.e., $\nu_S n_{\text{expl}}/V_{\text{expl}}$).

Combination of eqs 4 and 5 yields the following expression for c_{expl} :

$$c_{\text{expl}} = \frac{RT}{z_X^2 \nu_X D_X F^2} (\kappa_{\text{expl}} - \kappa_{\text{b}}) - \frac{z_S^2 I_{\text{ss}}}{gnFr_e z_X^2 \nu_X D_X} \quad (6)$$

It is seen that the c_{expl} parameter depends linearly on the quantities measured, i.e., κ_{expl} , κ_{b} , and I_{ss} . Therefore, according to the rules of the random errors propagation, the uncertainty in the determination of this parameter, expressed in terms of the variance ($s^2(c_{\text{expl}})$, where s denotes standard deviation) is a simple linear combination of the uncertainties in the measured quantities. This conclusion assumes an insignificantly small error in the determination of T , D_X , and r_e . The expression for $s^2(c_{\text{expl}})$ can be represented as

$$s^2(c_{\text{expl}}) \cong \left(\frac{RT}{z_X^2 \nu_X D_X F^2} \right)^2 [s^2(\kappa_{\text{expl}}) + s^2(\kappa_{\text{b}})] + \left(\frac{z_S^2}{gnFr_e z_X^2 \nu_X D_X} \right)^2 s^2(I_{\text{ss}}) \quad (7)$$

Although the primary task of this approach is focused on the c_{expl} determination, as was mentioned earlier, the model also allows one to calculate the diffusion coefficient of the probe in the expelled solution, D_S . The expression for D_S can be found by linking eqs 5 and 6. The resulting formula is not linear with respect to the parameters measured, and therefore, the uncertainty in the determination of this quantity will be poorer than that for c_{expl} .

The ratio of the concentrations of an electrolyte in the expelled solution and the swollen phase of the gel defines a quantity that we call the release coefficient:

$$\theta = c_{\text{expl}}/c_{\text{swol}} \quad (8)$$

The parameter c_{swol} is unified with the electrolyte total concentration in the swollen gel and is equal to $n_{\text{swol}}/V_{\text{swol}}$ (where n_{swol} and V_{swol} refer to the number of moles of electrolyte in the swollen gel and volume of the swollen gel, respectively).

It should be noted that in some cases the value of θ can be greater than one. The concentration of the solute in the released solution may be larger than that in the swollen gel because of the difference between the volumes of the swollen gel and the expelled solution (if the molar solubility of the solute is not exceeded). Knowing the volume of the released solution, one is able to derive the molar ratio of the electrolyte distributed between either the swollen or collapsed gel and the expelled solution (θ_n and $\bar{\theta}_n$, respectively). Using the parameter defined

by eq 8 and the obvious equality $n_{\text{swol}} = n_{\text{expl}} + n_{\text{coll}}$, the molar ratios have the following forms:

$$\theta_n = \frac{n_{\text{expl}}}{n_{\text{swol}}} = \theta \frac{V_{\text{expl}}}{V_{\text{swol}}} \quad (9)$$

and

$$\bar{\theta}_n = \frac{n_{\text{expl}}}{n_{\text{coll}}} = \frac{\theta V_{\text{expl}}}{V_{\text{swol}} - \theta V_{\text{expl}}} \quad (10)$$

where n_{coll} refers to the number of moles of electrolyte in the collapsed gel.

Analysis of the definitions given by eqs 9 and 10 reveals the following regularities: (1) the θ_n quantity provides the fraction of the total amount of the loaded substance that has been released from the gel due to the volume phase transition, (2) the value $1 - \theta_n$ refers to the fraction that remains in the collapsed state of the gel after the phase transition, and (3) the parameters θ_n and $\bar{\theta}_n$ are linked by the following relation: $1/\theta_n - 1/\bar{\theta}_n = 1$.

It should be pointed out that θ_n and $\bar{\theta}_n$ are more convenient quantities to interpret than θ , since they directly provide information on the fraction of a substance being partitioned between two phases.

The concept of the release coefficient is not free of some limitations. These limitations arise from the fact that the concentration of the probe in the expelled solution may be affected by the polymer content in the gel (assuming that the initial volume and the amount of the probe in the swollen gel are known precisely prior to the determination of the release coefficient). According to our previous studies, the volume of the released solution is practically independent of the polymer content in the NIPA gel in the range 2–5% (w/v).^{20,21} However, the amount and, as a consequence, the concentration of the probe released from the gel may vary with polymer concentration. This fact narrows the fundamental nature of the release coefficient.

Results and Discussion

All electroactive species ($\text{Fc}(\text{MeOH})_2$, FcAc^- , and FcTMA^+) used in our experiments give one-electron, reversible anodic responses at Pt microelectrodes in aqueous solutions.²² These species are of different charge numbers, and their molecular sizes are similar. Voltammograms for the oxidation of these molecules/ions recorded in gel and liquid media were well reproducible with the coefficient of variation less than 3%. The height of the voltammograms did not depart from the steady-state value by more than 4%. As was mentioned in the Experimental Section the voltammetric experiments were repeated several times. Each time a microelectrode was immersed in a gel sample at random locations. No statistically significant differences in microelectrode responses at different locations of the swollen gel were observed. This indicates that the gels were homogeneous or close to homogeneous, and that there was homogeneous distribution of the probe species and the solvent throughout the gel structure. An optical inspection of the gel samples illuminated with light confirmed the homogeneity of the gels obtained. The representative voltammograms for all probe systems obtained in the swollen gel and the expelled solutions with excess supporting electrolyte are shown in Figure 2. For small contents of polymer in the swollen gel (2–5%) the differences in diffusion coefficients of probe species in neutral polymeric gels and aqueous solutions are relatively

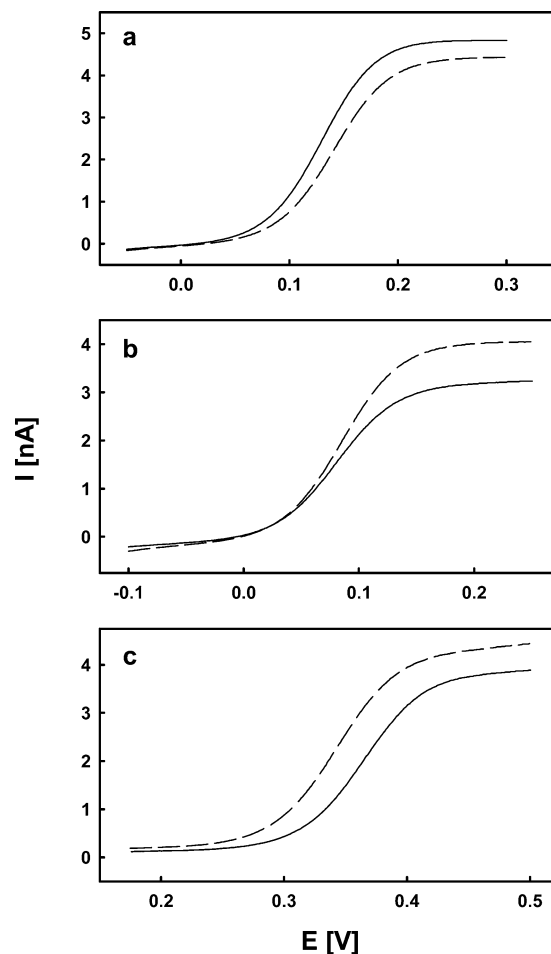


Figure 2. Steady-state voltammograms of (a) 1,1'-ferrocenedimethanol, (b) ferroceneacetate (sodium salt), and (c) ferrocenylmethyltrimethylammonium (PF_6^- salt) in swollen NIPA gels (solid lines) and expelled solution from the gel due to the volume phase transition (dashed lines). The concentration of all ferrocene derivatives in the swollen gel is approximately 2 mM, the supporting electrolyte is 46 mM KCl, and $T = 25^\circ\text{C}$.

small.^{11–13,20} Thus, the differences in the voltammetric wave heights observed in Figure 2 should be attributed primarily to the differences in the probe species concentrations and some differences in their diffusivities.

The combination of the voltammetric and conductometric data, as described in the Theoretical Section, allowed us to calculate the release coefficients for all redox systems studied. The obtained results (θ , θ_n) along with the diffusivities of the electroactive species (D_S) and parameters measured experimentally are listed in Table 1. The following diffusivities of counterions were used in the calculations: 1.33×10^{-10} and 1.52×10^{-10} m^2/s for Na^+ and PF_6^- , respectively.²³

It should be mentioned here that the procedure for the determination of the release coefficient, θ , for $\text{Fc}(\text{MeOH})_2$ was slightly simplified. Since $\text{Fc}(\text{MeOH})_2$ bears no net charge, it does not contribute to the total conductivity of the system. Therefore, c_{expl} for this probe was determined directly from the steady-state voltammetric current (eq 5) using its D value obtained from the independent voltammetric experiment.

An analysis of the data of Table 1 reveals two important regularities. First, the release efficiencies of the charged and uncharged ferrocene-based probes differ. Second, no significant influence of the supporting electrolyte was observed; the differences in results for LiClO_4 and KCl are within experimental error.

TABLE 1: Parameters Measured Experimentally (Probe Concentrations in the Swollen Gel, Conductivities of Ionic Probes in the Released Solution, and Steady-State Currents of the Probe Species Oxidation in the Released Solution) and Concentration and Molar Release Coefficients (θ and θ_n)^a for Uncharged and Charged Ferrocene Derivatives^b

probe	C_{swol} (mM)	$\kappa_{expl} - \kappa_b$ (mS/cm)	I_{ss} (nA)	θ	θ_n	$D_S \times 10^{10}$ (m ² /s)
LiClO ₄						
Fc(MeOH) ₂	1.99 ± 0.01		4.45 ± 0.03	0.80 ± 0.02	0.66 ± 0.02	6.9 ± 0.1 ^{c,d}
FcAc ⁻ (Na ⁺ salt)	2.05 ± 0.01	0.146 ± 0.011	4.44 ± 0.09	1.02 ± 0.16	0.84 ± 0.13	5.3 ± 0.8
FcTMA ⁺ (PF ₆ ⁻ salt)	2.01 ± 0.01	0.157 ± 0.011	3.78 ± 0.05	1.06 ± 0.14	0.87 ± 0.11	4.4 ± 0.6
KCl						
Fc(MeOH) ₂	2.03 ± 0.01		4.48 ± 0.03	0.79 ± 0.02	0.65 ± 0.02	6.9 ± 0.1 ^c
FcAc ⁻ (Na ⁺ salt)	1.95 ± 0.01	0.140 ± 0.043	4.24 ± 0.08	1.04 ± 0.16	0.85 ± 0.13	5.2 ± 0.8
FcTMA ⁺ (PF ₆ ⁻ salt)	2.01 ± 0.01	0.162 ± 0.032	4.09 ± 0.06	1.08 ± 0.13	0.89 ± 0.11	4.7 ± 0.6

^a See eqs 8 and 9. ^b The last column contains their diffusion coefficients in the released aqueous solution at 25 °C. All results are accompanied by their standard deviations. ^c Determined from an independent steady-state voltammetric experiment. ^d Reported values at 25 °C in LiClO₄ aqueous solution are 7.3×10^{-10} and 6.4×10^{-10} m²/s (refs 9 and 12, respectively).

Although the model was verified with the gel samples containing initially 0.05 mol/L supporting electrolyte, the same results (within experimental error) were obtained for the total absence or smaller concentration of the supporting electrolyte in the gel sample. Therefore, the presence of the supporting electrolyte at a concentration of up to 0.05 mol/L in the swollen gel does not affect the results presented.

The θ and θ_n values for FcAc⁻ and FcTMA⁺ are larger by approximately 25% than those for Fc(MeOH)₂. In other words, uncharged molecules of Fc(MeOH)₂ are more effectively stored in the NIPA gel structure than the charged ferrocene derivatives. As a consequence, a smaller fraction of Fc(MeOH)₂ can be found in the solution released from the gel due to the phase transition. As has already been mentioned all ferrocene-based probes are of similar molecular sizes, so the differences in their release efficiencies must be attributed predominantly to specific interactions between the probe species and side groups of polymeric chains. The smaller content of uncharged Fc(MeOH)₂ in the expelled solution may suggest its accumulation on NIPA chains due to the possible formation of sufficiently strong hydrogen bonds between hydrogen atoms in -CH₂OH groups (attached to ferrocene aromatic rings) and carbonyl groups in polymeric chains.

It is also known that the volume phase transition of the NIPA polymeric gel is accompanied by the significant dehydration of NIPA chains.²⁴ The dehydrated polymeric chains determine the hydrophobic behavior of the collapsed gel. A decrease in the water content, thus a decrease in the polarity of the system, and an increase in the hydrophobicity of the polymeric chains above the volume phase transition temperature must result in a more effective removal of ionic species from the gel system. These effects may also explain the larger values of release parameters determined for the ionic probes.

Concluding Remarks

The electrochemical method for the simultaneous determination of the diffusion coefficient and the concentration of a substance released from the gel due to the gel phase transition described in this paper has been examined for a series of ferrocene derivatives. Although the procedure was designed for charged probes, it can also be applied to uncharged species. However, in this case additional independent experiments are needed to determine the probe species diffusivity.

We believe that the approach presented in this work can be employed for the probe systems that are of medical, pharmaceutical, or therapeutic significance. These organic species very often possess the redox properties and, thus, fulfill the main requirement imposed by this method. In addition to this, the method may allow one to determine the partitioning and the

release efficiency of many electrolytes containing metal cations. This requires a slight modification of the electrochemical setup, i.e., replacing the solid Pt microelectrode with a mercury film electrode, which enables reproducible reduction of many metal cations. These projects are now under way in our laboratories.

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