**Feature Article**

# Effect of the Volume Phase Transition on Diffusion and Concentration of Molecular Species in Temperature-Responsive Gels: Electroanalytical Studies

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**Abstract**

Effect of the volume phase transition on the diffusion and concentration of molecular probes was studied in temperature-responsive polymeric hydrogels. Results were compared for two gels, poly(*N*-isopropylacrylamide), NIPA, and poly(*N*-isopropylacrylamide-*co*-acrylic acid), NIPA-AA. These gels undergo discontinuous, reversible volume phase transition as a response to temperature changes; this transition results in release of approximately 40% and 90% of the solution/solvent from NIPA-AA and NIPA gel phases, respectively. 1,1′-Ferrocenedimethanol, $Fc(MeOH)_2$, served as an electroactive and spectroscopic probe. Diffusion of $Fc(MeOH)_2$ was investigated using voltammetry and chronoamperometry with platinum disk electrodes, while UV-vis supported electroanalytical techniques to determine the concentration of that probe in the gel. The diffusion coefficient of $Fc(MeOH)_2$ was inversely proportional to the concentration of the polymer in both NIPA and NIPA-AA swollen gels for temperatures below the volume phase transition, and differed from that in an aqueous solution. The diffusion coefficient was 16 and 46% smaller than that in an aqueous solution for 3% NIPA and NIPA-AA gels at 25 °C, respectively. As a result of the volume phase transition, after the gel collapses, no significant changes in the diffusion coefficient values were observed for NIPA-AA gels. However, for NIPA gels, the diffusion coefficient of a probe decreases approximately two orders of magnitude. The volume phase transition also resulted in a change of the concentration of a probe in the collapsed gel phase. The concentration of $Fc(MeOH)_2$ in collapsed NIPA gel was as much as 4.5 times higher than that in the original swollen gel, while for NIPA-AA gel that increase in concentration was only 20%.

Keywords: Temperature-responsive gels, Volume phase transition, Transport, Voltammetry, Microelectrodes

## 1. Introduction

The last two decades have witnessed a remarkable progress in research on polymeric gels. The reason for this is the 1973 discovery by Toyoichi Tanaka of the phase transition of gels [1]. Polymeric gels may exist in two distinct phases, swollen and collapsed states. In the collapsed state, the volume of gels can decrease as much as 1000 times. Volume transition of gels occurs when the gels are stimulated by change of chemical or physical factors such as temperature [2], solvent composition [3], pH [4], and electric field [5].

The ability of gels to undergo such significant but reversible changes in volume in response to a precisely programmed stimulus allows unique new systems to be made. The number of applications based on volume phase transitions of polymeric gel increases continuously. Applications include temperature-sensitive gels and glucose-sensitive gels for controlled delivery insulin systems [6], light triggered optical shutter [7], chemical sensors [8], and even an artificial pancreas [9]. In such application, the knowledge of the diffusion coefficient of ions and molecules as a fundamental measure of molecular mobility and electrostatic interactions is of great importance.

Two types of temperature responsive polymeric gels, poly(*N*-isopropylacrylamide), NIPA, and poly(*N*-isopropylacrylamide-*co*-acrylic acid), NIPA-AA, were investigated and compared in this work. These gels undergo discontinuous, reversible volume phase transitions as a response to temperature changes. They swell at low temperature and shrink at high temperature. The phase transition temperature for NIPA and NIPA-AA hydrogel is 32 °C and 45 °C, respectively [10]. The volume phase transition of NIPA and NIPA-AA hydrogels results in the release of approximately 90% and 40% of solvent, respectively. The NIPA is one of the most important and well-described intelligent gels discovered so far. It is not only a temperature responsive gel but it undergoes volume phase transition as a response to changes in solvent composition, ionic strength, and pH.

In this work transport and concentration of molecular probes in NIPA and NIPA-AA temperature-responsive hydrogels were studied. The main goal was to compare results for both gels in their swollen state, and as effected by the volume phase transition. Diffusion coefficients and activation energy of diffusion of an electroactive probe, $Fc(MeOH)_2$, in swollen NIPA gels as well as distribution of $Fc(MeOH)_2$ between a collapsed gel phase and released

liquid have been studied by us and reported in [11]. In this work, a new improved procedure was used to determine diffusion coefficients in collapsed NIPA gels, and as a result, new improved transport data were obtained and reproducibility of experimental results was significantly improved.

The main experimental approach in this work is voltammetry and chronoamperometry at microelectrode. Those electroanalytical methods are supported by spectroscopic studies. Diffusion coefficient of an electroactive probe, $Fc(MeOH)_2$, was determined from electroanalytical measurements. The following equation shows the relationship between the diffusion coefficient, $D$, and the steady-state current, $I_s$, at a disk microelectrode:

$$D = I_s/4nFcr_d \tag{1}$$

where $n$ is number of electrons transferred, $F$ is the Faraday constant, $c$ is the concentration of an electroactive probe, and $r_d$ is the radius of a disk. This method requires a knowledge of the concentration of an electroactive probe.

Chronoamperometry with microelectrodes can be used for determination of the diffusion coefficient value when the concentration of a probe is not known [12]. The diffusion coefficient of the electroactive species can be determined from the slope of the linear dependence of $I_t/I_s$ on $t^{-1/2}$:

$$\frac{I_t}{I_s} = 1 + \left(\frac{2r_d}{\pi\sqrt{\pi Dt}}\right) \tag{2}$$

where $I_t$ is the time dependent current.

## 2. Experimental

### 2.1. Reagents

*N*-isopropylacrylamide, NIPA, *N,N'*-methylenebisacrylamide, BIS, acrylic acid, AA, *N,N,N',N'*-tetramethylethylenediamine, TMED, ammonium persulfate and lithium perchlorate were purchased from Aldrich. 1,1'-Ferrocenedimethanol, $Fc(MeOH)_2$ was purchased from Fluka. All chemicals except acrylic acid, AA, were used as received. Acrylic acid was purified by vacuum distillation (21 mm Hg, 52 °C) and stored in a refrigerator. All solutions were prepared using high purity water obtained from Milli-Q (Millipore Model RG) purification system.

### 2.2. Gel Preparation

The synthesis of NIPA and NIPA-AA gels was a free radical polymerization procedure [10]. Purification of these gels was developed by us and described in [13]. This procedure can be compared to squeezing (gel collapses at high temperature) and refilling (gel swells at low temperature) of a sponge. Once the purification was complete, the collapsed gel was placed in an oven and dried for 3 days at

80 °C. This step results in a hard transparent to translucent dry polymer or co-polymer. To introduce electroactive probes, a known mass or volume of a known concentration electroactive probe solution was added to a specific weighed amount of dry NIPA or NIPA-AA polymer. After sitting overnight or up to 3 days at room temperature, a gel was formed with a well-defined concentration of the electroactive probe [13].

### 2.3. Voltammetry and Chronoamperometry

Staircase voltammetry and chronoamperometry were applied with Ametek PARC Model 283 potentiostat/galvanostat. Voltammetric measurements were carried out in a jacketed glass cell with a three-electrode system consisting of a Pt pseudo reference electrode, a Pt wire counter electrode, and Pt microdisk working electrodes (Project Ltd., Warsaw, Poland). A refrigerated circulator (Isotemp model 1016P, Fisher Scientific) controlled the temperature of the cell.

Working Pt microdisk electrodes were 5.0 μm and 12.0 μm radius. They were polished before use with Microcloth polishing cloth (Buehler) and a water-based 0.1 μm diamond suspension polishing solution (Buehler). Optical inspection of the electrode surface was accomplished with an inverted microscope for reflected light (Nikon, Model Epiphot-200).

## 3. Results and Discussion

The diffusion coefficient of 1,1'-ferrocenedimethanol, $Fc(MeOH)_2$, in aqueous solutions and swollen NIPA and NIPA-AA hydrogels was determined using steady-state voltammetry with Pt microdisk electrodes according to Equation 1. One-electron voltammetric waves of the oxidation of $Fc(MeOH)_2$ were very well defined and reproducible, with the relative standard deviation not greater than 5% for aqueous solutions and both gels. This indicates that the presence of the polymeric matrix does not compromise our ability to measure the steady-state voltammetric response. The diffusion coefficient of $Fc(MeOH)_2$ determined in swollen NIPA and NIPA-AA gels was smaller than that obtained in an aqueous solution of the same concentration of a probe and supporting electrolyte, $LiClO_4$. For example, the $D$-value for $Fc(MeOH)_2$ at 25 °C in 1% and 3% NIPA-AA gels was 20 and 46% smaller than that in an aqueous solution, respectively, while for 1% and 3% NIPA gels it was 10 and 16% smaller than that in an aqueous solution, respectively. It should be added here, that diffusion coefficients of $Fc(MeOH)_2$ in NIPA and NIPA-AA swollen gels determined from steady-state voltammograms obtained using two different sizes of microelectrodes, 5.0 and 12.0 μm is radius, were identical within experimental error.

The activation energy of diffusion, $E_a$, for $Fc(MeOH)_2$ that reflects the local microscopic viscosity of the solvent in which that species diffuses [14], can be calculated from the

Table 1. Diffusion coefficient, $D$, and activation energy of diffusion, $E_a$, of Fc(MeOH)$_2$ in various media, and macroscopic viscosity, $\eta$, of those media; 0.1 M LiClO$_4$.

| Medium | $D$ (cm²/s @ 25°C) | $E_a$ (kJ/mol) | $\eta$ (cP) |
|---|---|---|---|
| Aqueous solution | $6.4 \times 10^{-6} \pm 3.9 \times 10^{-7}$ | $18.9 \pm 0.23$ | $9.4 \times 10^{-1}$ |
| 2.4% NIPA gel | $5.5 \times 10^{-6} \pm 1.7 \times 10^{-7}$ | $18.6 \pm 0.29$ | $1.5 \times 10^{5}$ |
| 2.0% NIPA-AA gel | $4.4 \times 10^{-6} \pm 5.6 \times 10^{-8}$ | $19.2 \pm 0.18$ | $2.0 \times 10^{5}$ |

temperature dependence of the diffusion coefficient value according to the Arrhenius-like equation [11, 15]:

$$D = Ae^{-E_a/RT} \tag{3}$$

where $A$ is the preexponetial factor, $R$ is the gas constant, and $T$ denotes absolute temperature.

Table 1 summarizes the diffusion coefficients, $D$, and activation energy of diffusion, $E_a$, of Fc(MeOH)$_2$ in aqueous solutions, NIPA and NIPA-AA gels from voltammetric experiments. Additionally, macroscopic viscosity values, $\eta$, of aqueous solutions, NIPA and NIPA-AA gels [11, 15] are given in that Table. Transport data of Table 1 suggest that even if there are some differences between NIPA and NIPA-AA gels, the local microscopic viscosity of a solution immobilized in NIPA and NIPA-AA swollen networks is very similar to that in an aqueous solution. The identical (within experimental error) $E_a$-values for both gels and an aqueous solution also support this conclusion.

A decrease of the diffusion coefficient of a probe in swollen gels can be explained by "obstruction effect" and "hydration effect" [16]. According to a model proposed by us for swollen gels [15], the diffusion coefficient of a probe in swollen gels, $D'$, can be described by the following equation:

$$D'/D^0 = -1.667\,H\varphi + 1 \tag{4}$$

where $-1.667$ is a coefficient related to a geometry of polymeric segments as described by "obstruction effect", $D^0$ is the diffusion coefficient of a probe in an aqueous solution without polymeric network, $\varphi$ is the total volume fraction occupied by the polymer. The $H$-value is the hydration coefficient; it indicates the strength of interactions between polymeric segments and water/solvent. This model has been tested for several probes [11, 15], and the diffusion coefficient of 4-hydroxy-tempo, TEMPO, in NIPA-AA gels was successfully predicated based on that model using the $H$-value for NIPA-AA polymer, $D$-value of TEMPO in an aqueous solution, and the volume fraction of NIPA-AA polymer in that gel [15].

The normalized diffusion coefficient of Fc(MeOH)$_2$, $D'/D^0$, as a function of the concentration of a polymer in NIPA and NIPA-AA gels is presented in Figure 1. The hydration coefficients, $H$, were calculated from the slopes of the dependence $D'/D^0$ vs. $\varphi$. The $H$-values are 3.22 and 8.77 for NIPA and NIPA-AA hydrogels, respectively. This difference indicates much stronger interactions between NIPA-AA polymer and water than those between water and NIPA.
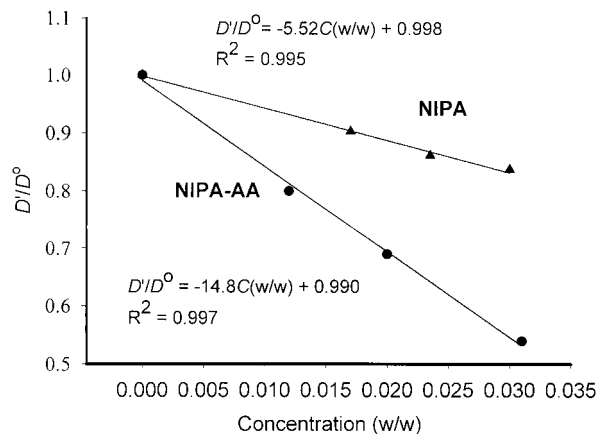


Fig. 1. Dependence of the normalized diffusion coefficient, $D'/D^0$, of Fc(MeOH)$_2$ on the concentration of the polymer in a swollen gel: (▲) NIPA, and (●) NIPA-AA; 25°C, 0.1 M LiClO$_4$.

Due to the presence of ionic acrylate groups, the NIPA-AA network has a much larger degree of hydration than the nonionic NIPA polymer. Note that the molar ratio of the two monomers in the NIPA-AA gel, NIPA to AA, was 94 to 5. Therefore, one can conclude that relatively small amount of acrylic acid in the NIPA-AA polymer has a very significant effect on properties of NIPA-AA gels, including phase transition temperature and a fraction of the solvent released from the gel phase during that transition. Volume phase transition temperature is 45°C and 32°C for NIPA-AA and NIPA gels, receptively. NIPA-AA gels release approximately 40% of the solvent from the polymeric phase, while NIPA gels release more than 90% of the solvent. Consequently, swelling ratio of the collapsed gel is approximately 2 and 30 for NIPA and NIPA-AA, respectively. An open structure for diffusion exists in NIPA-AA gels even when collapsed, but it is considerably restricted for the collapsed NIPA gels.

After NIPA and NIPA-AA gels collapse and release fraction of the solvent, oxidation of Fc(MeOH)$_2$ at Pt microelectrodes still results in well defined steady-state voltammograms, see Figure 2. However, the reproducibility of results is not as good as for swollen gels, with the relative standard deviation not greater than 13% and 27% for NIPA-AA and NIPA gels, respectively. Figure 3 shows the variation of the diffusion coefficient of Fc(MeOH)$_2$ in NIPA and NIPA-AA gels with temperature. As one can see, there is a distinct difference in behavior of NIPA and NIPA-AA gels after the volume phase transition occurs. The diffusion coefficient of Fc(MeOH)$_2$ in collapsed gels decreases dramatically, and in 3% NIPA collapsed gel it
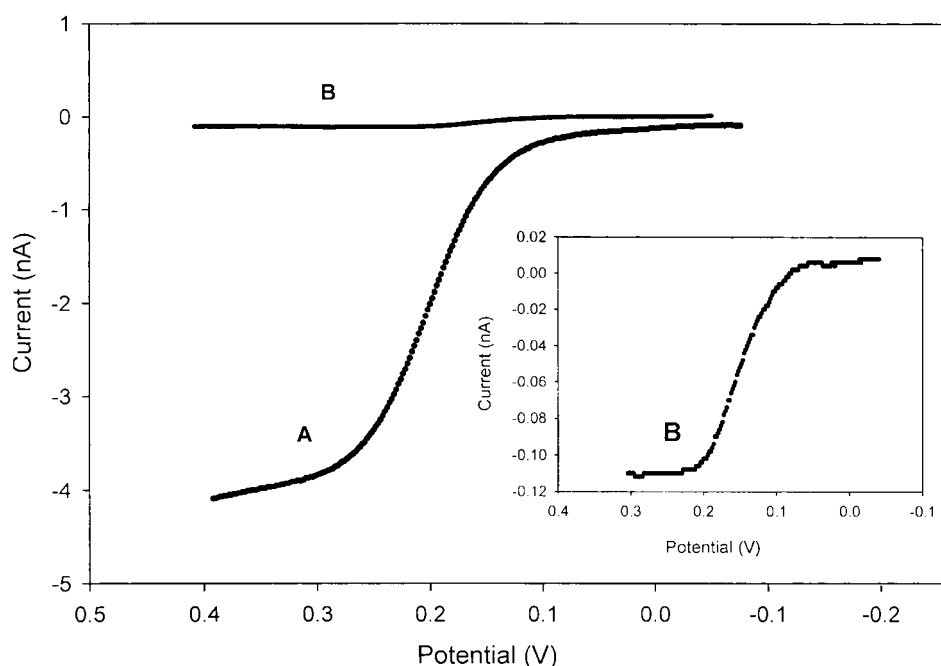
Fig. 2. Steady-state voltammogram of the oxidation of (A) 2.0 mM Fc(MeOH)$_2$ in collapsed 2.0% NIPA-AA gel, (B) 4.0 mM Fc(MeOH)$_2$ in collapsed 3.0% NIPA gel; 0.1 M LiClO$_4$, Pt microdisk, $r_d = 5$ μm, 55 °C.
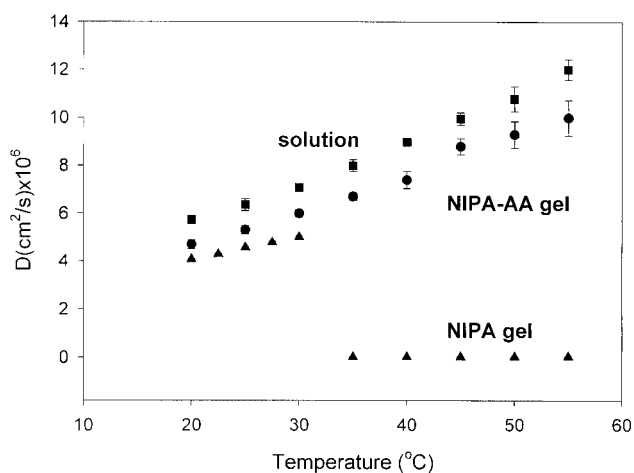


Fig. 3. Diffusion coefficient of 1,1′-ferrocenedimethanol, Fc(MeOH)$_2$, as a function of temperature: (■) aqueous solution, (●) 2% NIPA-AA gel, and (▲) 3% NIPA gel; 0.1 M LiClO$_4$ in all samples.

was $1.5 \times 10^{-8}$, and $2.1 \times 10^{-8}$ cm$^2$/s at 50 and 55 °C, respectively. These values are approximately 2 orders of magnitude smaller than those observed in swollen gels, for example $5.4 \times 10^{-6}$ cm$^2$/s at 25 °C [11]. This significant decrease is due to the small swelling ratio of the NIPA polymer in the collapsed state, where liquid channels are considerably restricted for molecular/solvent transport. The diffusion coefficients of Fc(MeOH)$_2$ in 3% NIPA-AA collapsed gels were, $9.3 \times 10^{-6}$, and $10.0 \times 10^{-6}$ cm$^2$/s at 50 and 55 °C, respectively, and did not differ significantly from those for swollen NIPA-AA gels, for example $5.5 \times 10^{-6}$ cm$^2$/s

at 25 °C. Since an open structure still exists in the collapsed NIPA-AA gel phase, no significant changes of Fc(MeOH)$_2$ diffusion coefficients are observed as a result of the volume phase transition. It should be added here, that diffusion coefficients in collapsed gels were determined from chronoamperometric experiments, according to Equation 2. The slope of the linear dependence of $I_t/I_s$ on $t^{-1/2}$ was determined using a least square fitting routine. The volume phase transition of temperature responsive gels may result in a change of the concentration of species in a gel phase. Since chronoamperometry with microelectrodes does not require knowledge of the concentration of electroactive species for determination of the diffusion coefficient, it is a very useful technique for transport studies in collapsed gels.

Investigations of the distribution of Fc(MeOH)$_2$ probe between the collapsed gel phase and released aqueous solution and possible changes in the concentration of that probe as a result of the volume phase transition have been performed using UV/vis, and results are presented in Table 2. Fc(MeOH)$_2$ has a maximum absorbance wavelength of 430 nm [15]. For 3.0% NIPA gels with 2 mM Fc(MeOH)$_2$ in the swollen state, the concentration of the Fc(MeOH)$_2$ in the solution released during the volume phase transition is 1.5 mM. This indicates that the collapsed polymeric phase retains a higher fraction of the original concentration of Fc(MeOH)$_2$. This can be attributed to hydrophobic interactions and/or van der Waals interactions between Fc(MeOH)$_2$ and the NIPA polymeric network. Based on the volume and the mass of the released solution and the mass of the collapsed gel, with the assumption that density of polymeric phase is close to that of aqueous solution, we can estimate the concentration of Fc(MeOH)$_2$

Table 2. Concentration of Fc(MeOH)$_2$ in 3% swollen gels, collapsed gels and expelled solutions.

| Medium | Concentration of Fc(MeOH)$_2$ (mM) | | |
| --- | --- | --- | --- |
| | Swollen gel | Expelled solution | Collapsed gel |
| 3.0% NIPA-AA | 1.5 | 1.1 | 1.8 |
| 3.0% NIPA | 2.0 | 1.5 | 9 |

in the collapsed gel as 9 mM, 4.5 times higher than that in the original swollen gel and 6 times higher than that in released liquid. The same studies were performed for 3.0% NIPA-AA gel with 1.5 mM Fc(MeOH)$_2$. The collapsed NIPA-AA gel phase also retained higher concentration of Fc(MeOH)$_2$. However, this effect is much weaker than for NIPA gel. The solution released during the volume phase transition of the gel contained 1.1 mM Fc(MeOH)$_2$. The concentration of Fc(MeOH)$_2$ in the collapsed NIPA-AA gel is estimated as 1.8 mM, which is approximately 20% higher than that in original swollen gel.

## 4. Conclusions

Diffusion properties of two temperature responsive gels, NIPA and NIPA-AA gels were studied and compared. Before the volume phase transition, for swollen gels, a slight decrease of the diffusion coefficient of Fc(MeOH)$_2$ in both gels was detected. Identical activation energy of diffusion in both gels and aqueous solution suggests that the microscopic viscosity in a gel is similar to that of an aqueous solution, even if the macroscopic viscosity is very large. The diffusion coefficient of Fc(MeOH)$_2$ in NIPA gels decreases almost two orders of magnitude as a result of the volume phase transition, whereas no significant changes of the diffusion coefficient are observed in NIPA-AA gels. This striking difference can be attributed to a different swelling ratio of both polymeric gels in their collapsed state. For NIPA gels that release approximately 90% of a solvent as a result of the volume phase transition, liquid channels in a collapsed phase are considerably restricted for molecular/solvent transport. Relatively open structure exists in collapsed NIPA-AA gels, and therefore, transport of species is not influenced significantly by the volume phase transition.

The distribution of Fc(MeOH)$_2$ between polymeric phase and aqueous solution released form a gel was studied using UV-vis spectroscopy. The concentration of Fc(MeOH)$_2$ probe in collapsed NIPA gel is 4.5 times higher than that in a swollen gel, while in collapsed NIPA-AA gels it is only 20% higher that that in the swollen phase.

## 5. Acknowledgements

## 6. References

[1] R. Dagani, *Chemical and Engineering News*, **1997**, June 9.
[2] S. Hirotsu, Y. Hirokawa, T. Tanaka, *J. Chem. Phys.* **1984**, *81*, 1392.
[3] T. Tanaka, D. J. Fillmore, S. T. Sun, I. Nishio, G. Swislow, A. Shah, *Phys. Rev. Lett.* **1980**, *45*, 1636.
[4] J. Ricka, T. Tanaka, *Macromolecules* **1984**, *17*, 2916.
[5] Kurauchi, T. Shiga, Y. Hirase, A. Okade, Polymer Gels, p. 237, Plenum Press, New York **1991.**
[6] T. Tanaka, *Phase Transitions of Gels* in *Polyelectrolyte Gels. Properties, Preparation and Application*; R. S.Harland and R. K. Prud'homme, Eds.; ACS Symposium Series, Vol. 480; American Chemical Society: Washington, DC **1992.**
[7] I. Tasaki, *Physiology and Electrochemistry of Nerve Fibers*, Academic Press, New York **1982.**
[8] L. Geng, R. A. Reed, M. Longmire, R. W. Murray, *J. Phys. Chem.* **1987**, *91*, 2908.
[9] J. W. Shay, *Cell and Muscle Mobility*, Plenum Press, New York, **1984.**
[10] M. Shibayama, Y. Fujikawa, S. Nomura, *Macromolecules* **1996**, *29*, 6535.
[11] W. Zhang, I. Gaberman, M Ciszkowska, *Anal. Chem.* **2002**, *74*, 1343.
[12] G. Denuault, M. V. Mirkin, A. J. Bard, *J. Electroanaly. Chem.* **1991**, *308*, 27.
[13] S. Petrovic, W. Zhang, M. Ciszkowska, *Anal. Chem.* **2000**, *72*, 3449.
[14] S. R. Jacob, Q. Hong, B. A. Coles, R. G. Compton, *J. Phys. Chem. B* **1999**, *103*, 2963.
[15] W. Zhang, C. Ma, M. Ciszkowska, *J. Phys. Chem. B* **2001**, *105*, 3435.
[16] J. H. Wang, *J. Am. Chem. Soc.* **1954**, *76*, 4755.