ELSEVIER

Polymer 40 (1999) 2969–2974

polymer

Determination of average molecular weight between cross-links ($\overline{M}_c$) from swelling behaviours of diprotic acid-containing hydrogels

Murat Şen*, Arzu Yakar, Olgun Güven

Hacettepe University, Department of Chemistry, 06532 Beytepe, Ankara, Turkey

Received 15 September 1997; revised 16 March 1998; accepted 16 March 1998

Abstract

Determination of average molecular weight between cross-links ($\overline{M}_c$) of itaconic acid-containing poly(vinyl pyrrolidone) and maleic acid-containing poly(acrylamide) hydrogels sensitive to pH changes of the swelling medium was investigated. Poly-electrolyte hydrogels with varying compositions were prepared in the form of rods from ternary mixtures of *N*-vinyl 2-pyrrolidone/itaconic acid/water and acrylamide/maleic acid/water. Gelation was achieved by irradiating the system with γ rays at ambient temperature. The equation modified by the authors recently for the determination of $\overline{M}_c$ is observed to describe very well the swelling behaviour of charged polymeric networks. In addition to the evaluation of $\overline{M}_c$ from swelling data, the same equation also provides the simultaneous measurement of polymer–solvent interaction parameter of the systems investigated.

Keywords: Hydrogel; Molecular weight between cross-links; *N*-Vinyl 2-pyrrolidone/itaconic acid copolymer

---

1. Introduction

Poly-electrolytes are polymers which contain relatively ionizable groups at levels ranging from a few mol% to 100 of the repeating units. Poly-electrolytes may be anionic, cationic or amphophilic, and may be synthetic or naturally occurring. Examples of common poly-electrolytes include polymeric acids, such as poly(acrylic acid) [1–3], poly(methacrylic acid) [4,5], poly(acrylamide-co-itaconic acid) [6,7], poly(acrylamide-co-maleic acid) [8,9] and polymeric bases such as poly(vinyl amine) [10], poly(4-vinyl pyridine) [11] and salts of the polymeric acids mentioned above.

Much attention has been directed in recent years to poly-electrolyte-type hydrogels that undergo controllable volume changes in response to small variation in solution conditions [12]. Temperature and pH have been the solution variables in typical physiological, biological and chemical systems [13,14]. Temperature- and pH-sensitive gels have been suggested for use in a variety of novel applications, including controlled drug delivery [10,14,15], immobilized enzyme systems [16,17] and separation processes [18,19].

One of the basic parameters that describes the structure of an electrolyte and non-electrolyte-type hydrogels is the molecular weight between cross-links ($\overline{M}_c$). This describes the average molecular weight of polymer chains between two consecutive junctions. These junctions may be chemical cross-links, physical entanglements, crystalline regions, or even polymer complexes [20]. Several theories have been proposed to calculate the molecular weight between cross-links in polymeric networks. The earliest theory to describe the equilibrium swelling characteristics of networks was developed by Flory and Rehner [21–23] for a cross-linked polymer system where the polymer chains are reacted in the solid state, and the macromolecular chains exhibit a Gaussian distribution. This theory deals with neutral polymer chains and tetra-functional cross-linking within the polymer gel.

A similar equation which is applicable to systems where solvent was present during the cross-linking process of the macromolecular chains was presented by Peppas and Merrill [24], where an additional term representing the polymer volume fraction in the relaxed state was introduced.

During the last decade, the molecular treatment of rubber-like elasticity has been improved by Flory and Erman [25,26] including detailed swelling–structure relationship [27–30]. These relationships, theories and the results are reviewed by Queslel and Mark [31,32] and Mark and Erman [33], for the characterization of model and randomly cross-linked networks. In the following discussion a brief

---

* Corresponding author.

0032-3861/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0032-3861(98)00251-1

description of most favourable approaches developed for the determination of $\overline{M}_c$ is given together with our recent modification made to cover the hydrogels containing diprotic acid segments. The molecular weight between cross-links ($\overline{M}_c$) for non-ionic networks is suggested to be expressed by Eq. (1) [33].

$$\overline{M}_c = -\frac{(1-2/\phi)V_1\nu_{2r}^{2/3}\nu_{2m}^{1/3}}{\bar{v}[\ln(1-\nu_{2m})+\nu_{2m}+\chi\nu_{2m}^2]} \qquad (1)$$

where $\overline{M}_c$ is the average molecular weight between cross-links, $\bar{v}$ is the specific volume of the polymer, V_1 is the molar volume of the swelling agent, ν_{2m} is the polymer volume fraction in the equilibrium-swollen system, ν_{2r} is the polymer volume fraction in the relaxed state, i.e. after cross-linking but before swelling, ϕ, is the number branches originating from a cross-linking site and χ is the Flory polymer–solvent interaction parameter.

In an attempt to predict the swelling behaviour of hydrogels with monoprotic acid moieties, Brannon-Peppas and Peppas derived the following expression [34].

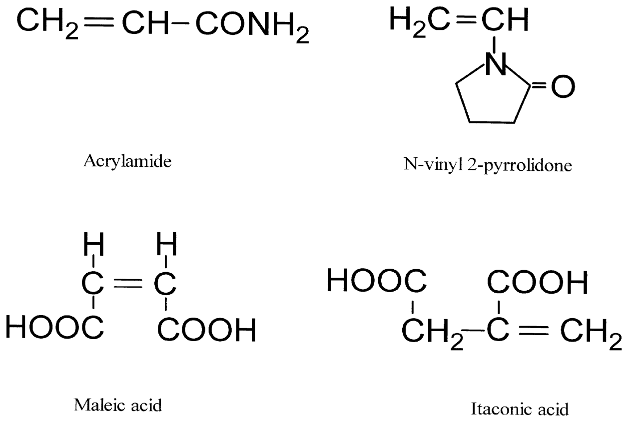
$$\frac{V_1}{4I}\left(\frac{K_a}{10^{-\mathrm{pH}}+K_a}\right)^2\left(\frac{\nu_{2m}}{\bar{v}}\right)^2 = \left[\ln(1-\nu_{2m})+\nu_{2m}+\chi\nu_{2m}^2\right] + \left(\frac{V_1}{\bar{v}\overline{M}_c}\right)\left(1-\frac{2\overline{M}_c}{\overline{M}_n}\right)\nu_{2r}\left[\left(\frac{\nu_{2m}}{\nu_{2r}}\right)^{1/3}-\left(\frac{\nu_{2m}}{2\nu_{2r}}\right)\right] \qquad (2)$$

where, K_a is the dissociation constant of polyacid, I is the ionic strength of the swelling medium, and $\overline{M}_n$ is the number average molecular weight of starting polymer. By combining the approaches of Mark and Erman considering a phantom model for the network and that of Peppas et al. we have obtained a modified expression from which the $\overline{M}_c$ and χ could be determined simultaneously for a hydrogel with diprotic acid segments [35].

$$\left(\frac{\left[2K_{a1}K_{a2}+10^{-\mathrm{pH}}K_{a1}\right]}{2\left[(10^{-\mathrm{pH}})^2+10^{-\mathrm{pH}}K_{a1}+K_{a1}K_{a2}\right]}\right)^2\left(\frac{V_1\nu_{2m}^2X^2}{4I\bar{v}^2}\right) = \ln(1-\nu_{2m})+\nu_{2m}+\chi\nu_{2m}^2+\frac{(1-2/\phi)V_1\nu_{2r}^{2/3}\nu_{2m}^{1/3}}{\bar{v}\overline{M}_c} \qquad (3)$$

where, K_{a1} and K_{a2} are the first and second dissociation constants of diprotic acid and X is the weight fraction of ionizable polymer in the gel system.

In this expression the mixing, elastic-retractive and ionic contributions to the chemical potential of a diprotic acid containing hydrogel in equilibrium-swollen state have been incorporated into the phantom model of network structure. In the highly swollen state, the constrained junction theory indicates that a real network exhibits properties closer to those of the phantom network model. Consequently Eq. (3) is a more realistic representation for equilibrium swelling, thus it is used to estimate the average chain length ($\overline{M}_c$) between cross-links of highly swollen hydrogels [35]. The equation derived has been used to determine simultaneously the $\overline{M}_c$ and χ parameters for the hydrogels prepared from N-vinyl 2-pyrrolidone/itocanic acid and acrylamide/maleic acid copolymers.



Scheme 1.

2. Experimental

2.1. Chemicals

The four monomers used in this study, namely, N-vinyl 2-pyrrolidone (VP) and itaconic acid (IA), maleic acid (MA), acrylamide (AAm) were obtained from Fluka and BDH, respectively. The chemical formulae of these monomers are shown in Scheme 1. KH_2PO_4, K_2HPO_4 and H_3PO_4 used to prepare phosphate buffers were obtained from BDH.

2.2. Preparation of hydrogels

Three components were used in the preparation of VP/IA hydrogels: VP, IA and water. Aqueous solutions of monomers of 2 ml VP and 60, 120 and 180 mg IA were prepared in 1 ml of pure water in different compositions (VP/IA mole ratios, 97.6:2.4, 95.3:4.7, 93.2:6.8). Three components were used in the preparation of AAm/MA hydrogels: AAm, MA and water. Aqueous solutions of monomers of 1 g AAm and 20, 40 and 60 mg MA were prepared in 1 ml of pure water in different compositions (AAm/MA mole ratios, 98.8:1.2, 97.6:2.4, 96.5:0.35). Monomer solutions thus prepared were placed in the PVC straws of 4 mm diameter and irradiated to 25 kGy in air at ambient temperature in Gammacell 220 type γ irradiator at a fixed dose rate of 0.44 kGy/h. Hydrogels obtained in long cylindrical shapes were cut into pieces of 3–4 mm long and stored for later evaluations.

2.3. Composition of gels

Irradiated mixtures were dried in a vacuum oven at 315 K to constant weight and subjected to Soxhlet extraction with water as solvent. Uncrosslinked polymer and/or residual monomer were removed with this extraction from the gel structure. Extracted gels were dried again in vacuum oven at 315 K to constant weight. Percentage gelation, i.e. percentage conversion of monomers into insoluble network, was based on the total weight of diprotic acid and monomer in the initial mixture. The amount of IA and MA in monomer, polymer and/or copolymer form was determined by titration of extract against NaOH (0.05 M) to phenolphthalein end point. No titrate was consumed for AAm/MA sol fractions, and 100% gelation was achieved for all AAm/MA mixtures after 25 kGy irradiation. The mole percentages of monomers in the initial mixtures and in the hydrogel systems are given in Table 1.

2.4. Swelling studies

Dried hydrogels (3–4 mm thickness, 4 mm diameter) were left to swell in a solution of desired pH (2–9), ionic strength $I = 0.1$ M, and temperature 25°C. Swollen gels removed from the water at regular intervals were dried superficially with filter paper weighed and placed in the same bath. The measurements were continued until a constant weight was reacted for each sample. This weight was used to calculate the volume fraction ν_{2m} and equilibrium degree of swelling (EDS), Q, of polymer in a given gel sample swollen to equilibrium in water.

$$Q = [1 + \rho/\rho_w(w^{-1} - 1)] \tag{4}$$

where ρ and ρ_w are the densities of swollen gel and water; w is the weight fraction of polymer in swollen gel. For the determination of ν_{2r} weight fraction of polymer in freshly synthesized sample was used for w in Eq. (4). The equilibrium degree of swelling (EDS) was defined as $Q = 1/\nu_{2m}$.

The specific volume of hydrogel systems $\bar{v}$ (cm^3 g^{-1}) was calculated by using densities of hydrogels and the numerical values are given in Table 2. The densities of hydrogels was determined by a pycnometer.

3. Results and discussion

3.1. Composition of hydrogels

When pure *N*-vinyl 2-pyrrolidone and acrylamide monomers have been irradiated with gamma rays, polymerization and cross-linking reactions take place simultaneously. Total dose required for the onset of gelation was determined to be 3 kGy for pure VP and the sensitising effect of water for the gelation of VP was very well demonstrated in our previous study [36]. Total dose required for 100% gelation of AAm/MA hydrogels has been found to be 7 kGy when MA was used in the range of 0.0–3.5 mol% in the initial mixture [37]. In this study for the preparation of mechanically stable hydrogels, the ternary mixtures of VP/IA/H_2O and AAm/MA/H_2O were irradiated to 25 kGy with gamma rays. Mole percentages of monomers in the initial mixtures and in the copolymeric gels and percentage gelation are summarized in Table 1.

Table 1
Mole percentages of diprotic acids in the feed compositions, in the gel systems and % gelation achieved

Gel name	Diprotic acid (mol%)		% gelation
	In feed	In gel	
VP/IA-1	2.4	2.0	87.7
VP/IA-2	4.7	3.0	85.4
VP/IA-3	6.8	3.2	82.7
AAm/MA-1	1.2	1.2	100.0
AAm/MA-2	2.4	2.4	100.0
AAm/MA-3	3.5	3.5	100.0

The considerations for selecting the particular feed compositions are firstly the solubility of diprotic acids in aqueous monomer solution and the shape stability of swollen hydrogels. The maximum solubility of IA and MA was found to be 240 and 90 mg in 2 ml VP/1 ml water and 1 g AAm/1 ml water mixture, respectively. However, the hydrogels prepared from these initial compositions were not mechanically stable and disintegrated into small parts during swelling. So only hydrogels with three compositions could be investigated in this study.

As shown in Table 1, increasing mole percentage of IA in the initial mixture increases the amount of IA in the gel system but causes a decrease in the extent of gelation from monomer to gel. These results indicate that IA acts as an effective chain transfer agent in the copolymerization of VP. On the other hand 100% gelation was observed for AAm/MA mixtures after 25 kGy irradiation.

3.2. Equilibrium swelling of hydrogels

Figs 1 and 2 represent the equilibrium degree of swelling (EDS) of VP/IA and AAm/MA hydrogels at 25°C in phosphate buffer solution from pH 2 to 9 at fixed ionic strength of $I = 0.1$ M. Consistent with poly-electrolytic behaviour, swelling of hydrogels was found to increase with pH. The solid curves in these figures represent the theoretical swelling curves of hydrogels. The construction of theoretical swelling curves are explained in detail in our previous work [35]. The experimental data points and theoretical curves are in very good accordance, as can be seen from these figures. In all compositions maximum extents of swelling were reached at pH 7, this being due to the complete dissociation of acidic groups of itaconic acid and maleic acid at this pH value. The first and second dissociation constants of IA and MA are $pK_{a1} = 3.85$, $pK_{a2} = 5.44$ and $pK_{a1} = 1.85$, $pK_{a2} = 6.06$, respectively [38]. Since the two dissociation constants for IA are rather close, the consecutive swellings at around these pH values overlap and only single-step swelling versus pH curves are observed in Fig. 1. For MA-containing hydrogels, however, due to large difference in pK_a values, swelling takes place in a stepwise manner, as shown in Fig. 2. The swelling shows

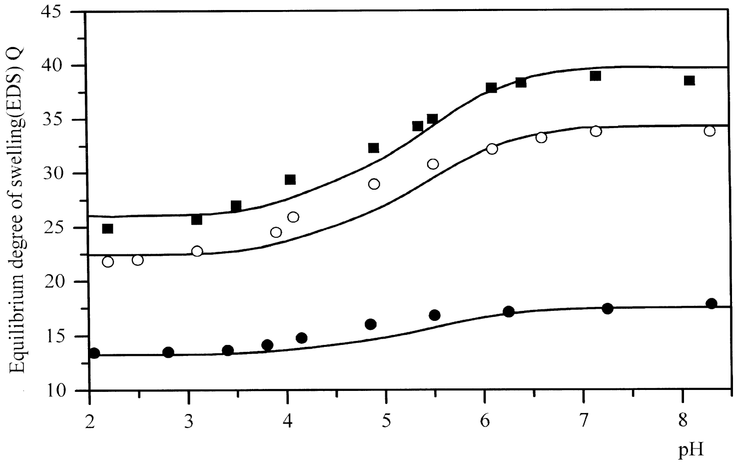


Fig. 1. Effect of pH on the equilibrium swelling of VP/IA copolymeric hydrogels: (●) VP/IA-1; (○) VP/IA-2; (■) VP/IA-3. Solid curves are theoretical predictions drawn according to Eq. (3).

sudden increases at the pH values around corresponding pK_a values.

The change in equilibrium degree of swelling with pH has also been evaluated for the determination of average molecular weight between cross-links and the polymer–solvent interaction parameter.

3.3. Determination of $\overline{M}_c$ and χ values of hydrogels

Eq. (3) which is derived for the prediction and understanding of swelling behaviour of a hydrogel containing diprotic acid units has been rearranged into the following form:

$$\left(\frac{[2K_{a1}K_{a2}+10^{-\mathrm{pH}}K_{a1}]}{2[(10^{-\mathrm{pH}})^2+10^{-\mathrm{pH}}K_{a1}+K_{a1}K_{a2}]}\right)^2\left(\frac{V_1X^2}{4I\bar{v}^2}\right) - \ln(1-\nu_{2m})\nu_{2m}^{-2}-\nu_{2m}^{-1}=\chi+\frac{(1-2/\phi)V_1\nu_{2r}^{2/3}\nu_{2m}^{-5/3}}{\bar{v}\overline{M}_c} \quad (5)$$

If the swelling data of a gel is used to plot the left-hand side of Eq. (5), (A) against the coefficient of $1/\overline{M}_c$ on the right-hand side, (B) a linear relation must be obtained with χ and $\overline{M}_c$ values as the intercept and inverse slope, respectively;

$$A=\chi+B/\overline{M}_c \quad (6)$$

Some of the information about the structural properties of hydrogels necessary for the construction of these plots are collected in Table 2. The other relevant experimental parameters to be used with Eq. (5) are as follows: ionic strength, $I=0.1$ M, molar volume of the solvent, $V_1=18$ g cm^{-3} and the number branches originating from a crosslinking site, $\phi=3$.

In the preparation of hydrogels, no cross-linking agents were used in this work. Cross-linking has been achieved by high energy radiation. It has been determined and known for sometime that the radiation-induced cross-links produced are either H or Y types [39]. In either case there are three branches originating from a cross-linking site. By using the

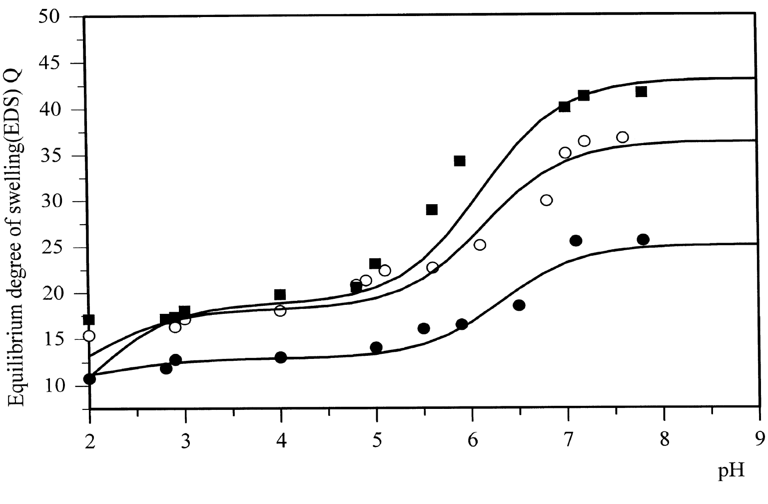


Fig. 2. Effect of pH on the equilibrium swelling of AAm/MA copolymeric hydrogels: (●) AAm/MA-1; (○) AAm/MA-2; (■) AAm/MA-3. Solid curves are theoretical predictions drawn according to Eq. (3).

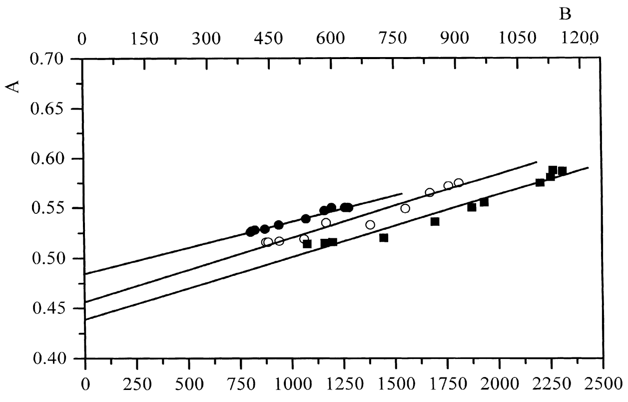


Fig. 3. Determination of χ and $\overline{M}_c$ values of VP/IA hydrogels from swelling data. Please see the text for the explanation of A and B: (●) VP/IA-1; (○) VP/IA-2; (■) VP/IA-3.

experimentally measured polymer volume fraction, ν_{2m} of the gels in their equilibrium-swollen state and the above-mentioned data, Figs 3 and 4 are constructed. $\overline{M}_c$ and χ values were determined via linear regression analysis of the lines given in Figs 3 and 4. The calculated values are listed in Table 3.

Table 2
Structural characteristics VP/IA networks

Gel name	Weight fraction of diprotic acid in the gel (X)	$\bar{v}$ (cm^3 g^{-1})	v_{2r}
VP/IA-1	0.025	0.95	0.76
VP/IA-2	0.035	0.90	0.68
VP/IA-3	0.037	0.87	0.65
AAm/MA-1	0.019	0.72	0.76
AAm/MA-2	0.038	0.53	0.70
AAm/MA-3	0.057	0.45	0.66

Table 3
$\overline{M}_c$ and χ values of hydrogels

Gel name	$\overline{M}_c$	χ
VP/IA-1	9100 ± 1000	0.48 ± 0.01
VP/IA-2	15 500 ± 2900	0.46 ± 0.02
VP/IA-3	16 200 ± 2550	0.44 ± 0.02
AAm/MA-1	90 700 ± 17 000	0.53 ± 0.01
AAm/MA-2	14 500 ± 3800	0.50 ± 0.04
AAm/MA-3	7700 ± 1150	0.52 ± 0.06

The effect of presence of diprotic acid on the network properties and polymer–solvent (water) interaction parameter is obvious from these results. With increasing amount of IA in the copolymer structure the average $\overline{M}_c$ values increase, whereas χ values slightly decrease. The former effect indicates that IA does not act as a cross-linking agent; furthermore, it shows chain transfer agent properties, as seen from Table 1. The conversion to gel decreases with increasing IA amount. The χ parameter of cross-linked pure PVP has been found to be 0.49 [36]. The χ values at pH interval 2–9 given in Table 3 are in very good accordance with this reported value of interaction parameter. A value of 0.48 was obtained for VP/IA gel with an IA content of 2.0 mol%. On the other hand, with increasing amount of MA in the copolymer structure, the average $\overline{M}_c$ value decreased, which can be interpreted as MA being effective in the cross-linking process, whereas χ values changed between 0.50 and 0.53 which are very close to the χ parameter of pure poly(acrylamide). The χ parameter of cross-linked pure poly(acrylamide) has been reported to be 0.494 [40]. However, it is very difficult to assert a correlation between MA content and χ value from these three data.

4. Conclusion

In this study a new equation has been used for the determination of average molecular weight between consequent

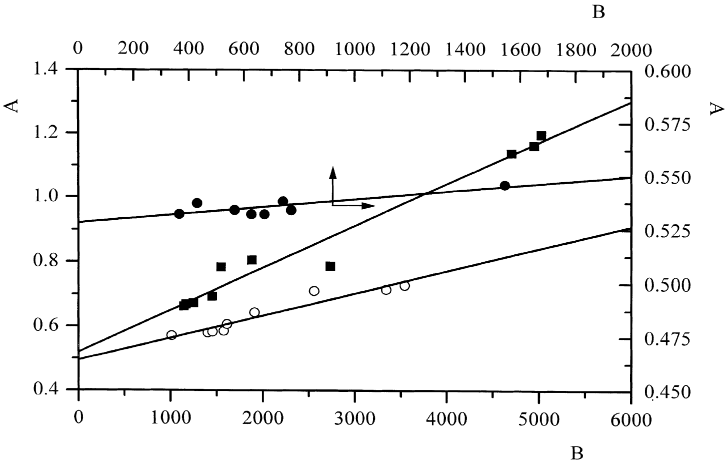


Fig. 4. Determination of χ and $\overline{M}_c$ values of AAm/MA hydrogels from swelling data. Please see the text for the explanation of A and B: (●) AAm/MA-1; (○) AAm/MA-2; (■) AAm/MA-3.

cross-links of diprotic acid-containing copolymeric hydrogels. The equation is applied to swelling data of *N*-vinyl 2-pyrrolidone/itaconic acid and acrylamide/maleic acid hydrogels. Hydrogels were prepared in water and swollen to equilibrium in phosphate buffer solutions at pH interval 2–9. Equilibrium swelling values at each pH value were used for the determination of $\overline{M}_c$. The experimentally determined equilibrium swelling behaviour of hydrogels are observed to obey very closely the model prediction. Further to the determination of $\overline{M}_c$ values from a linearized form of swelling equation, it is also possible to calculate the polymer–solvent interaction parameter from the same analysis.

References

[1] Harland RS, Prud'homme RK, editors. Polyelectrolyte gels. ACS Symposium Series 480. Washington, DC: American Chemical Society, 1992.

[2] Samsonov GV, Kuznetsova NP. Adv Polym Sci 1992;104:1.

[3] Kazanskii KS, Dudrovskii SA. Adv Polym Sci 1992;104:97.

[4] Eliassaf J. J Polym Sci 1965;23 (B):767.

[5] Malavasic T, Osredkar U, Anzur I, Vizovisek I. J Macromol Sci Chem. 1986;A23:853.

[6] Karadağ E, Saraydin D, Öztop HN, Güven O. Polym Adv Tech 1994;5:664.

[7] Karadağ E, Saraydin D, Çetinkaya S, Güven O. Biomaterials 1996;17:67.

[8] Saraydin D, Karadağ E, Öztop HN, Güven O Biomaterials 1994;15:917.

[9] Saraydin D, Karadağ E, Güven O. Polym Adv Tech 1994;6:719.

[10] Scranton AB, Rangarajan B, Klier J. Adv. Polym. Sci. 1995;122:3.

[11] Bartels T, Arends J. J Polym Sci Polym Chem 1981;19:128.

[12] Tanaka T. Gels. In: Encycl Polym Sci Eng, 2nd edn, vol. 7. 1987:514.

[13] Peppas NA, editor. Hydrogels in medicine and pharmacy. Boca Raton, FL: CRC Press, 1986.

[14] Kudela V. Hydrogels. In: Encycl Polym Sci Eng, 2nd edn., vol. 7. 1987:783.

[15] Şen M, Güven O. Radiat. Phys and Chem, in press.

[16] Putman P, Kopecek J. Adv Polym Sci 1995;122:55.

[17] Güven O, Şen M. Angew Makromol Chemie 1993;207:101.

[18] Karadağ E, Saraydin D, Güven O. Sep Sci Tech 1995;30:3747.

[19] Saraydin D, Karadağ E, Güven O. Sep Sci Tech 1995;30:3291.

[20] Peppas NA. J Bioact Compat Polym 1991;6:241.

[21] Flory PJ, Rehner J. J Chem Phys 1943;11:512.

[22] Flory PJ, Rehner J. J Chem Phys 1943;11:521.

[23] Flory PJ. Principles of polymer chemistry. Ithaca, NY: Cornell University, 1953.

[24] Peppas NA, Merrill EW. J Polym Sci Polym Chem Ed 1976;14:441.

[25] Flory PJ. J Chem Phys 1977;66:5720.

[26] Flory PJ, Erman B. Macromolecules 1982;15:800.

[27] Flory PJ. Macromolecules 1979;12:119.

[28] Brotzman BE, Eichinger BE. Macromolecules 1983;16:1131.

[29] Gottlieb M, Gaylord RJ. Macromolecules 1984;17:2024.

[30] Queslel JP, Mark JE. Polym Bull 1983;10:119.

[31] Queslel JP, Mark JE. Adv Polym Sci 1985;71:119.

[32] Queslel JP, Mark JE. In: Allen G, editor. Comprehensive polymer science. Oxford: Pergamon Press, 1988.

[33] Mark JE, Erman B, editors. Rubberlike elasticity a molecular primer. New York: Wiley, 1988.

[34] Brannon-Peppas L, Peppas NA. Chem Eng Sci 1991;46:715.

[35] Şen M, Güven O. Polymer 1998;39:1165.

[36] Güven O, Şen M. Polymer 1991;32:2491.

[37] Akkaş P. MS. Thesis, Hacettepe University, Ankara Turkey, 1996.

[38] Weast RC, editor. Handbook of chemistry and physics, 53rd edn. OH: The Chemical Rubber Co., 1972.

[39] Wilson JE. Radiation chemistry of monomers, polymers and plastics. New York: Marcel Dekker, 1974.

[40] Rosiak J, Burczak K, Zolozynzka T, Pekala W. Radiat. Phys. Chem. 1983;22:917.