Correlation between crosslinking efficiency and spatial inhomogeneity in poly(acrylamide) hydrogels

Nermin Orakdogen and Oguz Okay (✉)

Istanbul Technical University, Department of Chemistry, 34469 Maslak, Istanbul, Turkey
E-mail: okayo@itu.edu.tr; Fax: 0212-2856386

Summary

Elasticity and light scattering measurements were carried out on poly(acrylamide) (PAAm) hydrogels prepared from acrylamide (AAm) and N,N'-methylenebisacrylamide (BAAm) monomers under various reaction conditions. Elasticity tests showed that the crosslinking efficiency of BAAm ε_{xl}, that is the fraction of BAAm forming effective crosslinks decreases as the initial monomer concentration C_o is decreased. At $C_o = 3$ %, ε_{xl} was found to be $10^{-2} - 10^{-3}$, indicating that 99 to 99.9 % of BAAm used in the hydrogel preparation are wasted in elastically ineffective links. Debye-Bueche analysis of the light scattering data showed that, irrespective of the gel synthesis conditions, the correlation length ξ, that is, the extension of inhomogeneities in the hydrogels is 10^1 nm. The extent of frozen concentration fluctuations in the hydrogels represented by $\langle \eta^2 \rangle$ decreases with increasing crosslinking efficiency of BAAm. The combination of the light scattering and the elasticity data of gels shows a direct correlation between the fraction of wasted crosslinker molecules during gelation and the spatial gel inhomogeneity.

Introduction

Free-radical crosslinking copolymerization of acrylamide (AAm) and N,N'-methylenebisacrylamide (BAAm) has been widely used to synthesize polymer hydrogels. As is well known, gelation during polymerization reactions occurs non-randomly due to the existence of various non-idealities such as the conversion and structure dependent reactivities of the functional groups, association tendency of poorly soluble crosslinker molecules in the reaction system, cyclization and multiple crosslinking reactions [1-3]. These non-idealities during gelation necessarily result in the formation of polymer gels with a large number of network defects, affecting their physical properties such as swelling, elasticity, transparency, and permeability. One of the network defects is the inhomogeneous crosslink density distribution, known as the spatial gel inhomogeneity [4,5]. Since the gel inhomogeneity is closely connected to the spatial concentration fluctuations, scattering methods have been employed to investigate the spatial inhomogeneities [6-11]. It was shown that the scattering light intensity from gels is always larger than that from the polymer solution. The excess scattering over the scattering from polymer solution is related to the degree of the

inhomogeneities in gels. It should be noted that, although extensive work has been reported in the literature for the spatial inhomogeneity in PAAm gels, a direct correlation between the extent of spatial gel inhomogeneity and the number of elastically ineffective crosslinks has not been reported before.

Here we present elasticity and light scattering measurements on poly(acrylamide) (PAAm) hydrogels which will enable us to correlate the extent of the spatial gel inhomogeneity with the magnitude of non-idealities in AAm – BAAm copolymerization. For this purpose, several sets of gels with varying amounts of the crosslinker BAAm were prepared at various initial monomer concentrations. The effective crosslink densities of the hydrogels were determined by the elasticity tests. Light scattering data were analyzed within the framework of the Debye-Bueche theory to calculate the correlation lengths as well as the frozen concentration fluctuations in the hydrogels. As will be seen below, a direct experimental evidence was obtained showing that the concentration fluctuations in PAAm gels originate from the BAAm molecules forming elastically ineffective links.

Experimental

Materials

Acrylamide (AAm, Merck), N,N'-methylenebisacrylamide (BAAm, Merck), ammonium persulfate (APS, Merck), and N,N,N',N'-tetramethylethylenediamine (TEMED) were used as received. Distilled and deionized water (HPLC-grade) was used throughout this study. The stock solutions of the monomers and the initiator system in water were prepared using the following concentrations: AAm (10g / 50 mL), BAAm (0.3 g / 50 mL), APS (0.060 g / 10 mL), and TEMED (0.75 mL / 20 mL).

Hydrogel preparation

Free-radical crosslinking copolymerization reactions of AAm and BAAm were carried out in aqueous solutions at 21^0C in the presence of 2.63 mM APS and 24.9 mM (0.375 v/v %) TEMED as the redox initiator system. Several sets of experiments were carried out. The gel synthesis parameters varied were the initial monomer concentration denoted by C_o (mass of AAm + BAAm in 100 mL reaction solution) and the crosslinker (BAAm) content of the monomer mixture. The reactions were carried out in glass tubes as well as in the light scattering vials.

To illustrate the synthetic procedure in glass tubes, we give details for the preparation of a PAAm gel at C_o = 4 w/v % and 1 mol % BAAm: Stock solutions of AAm (1.96 mL), BAAm (1.43 mL), APS (1.00 mL), and water (4.61 mL) were mixed in a 10 mL graduated flask. After cooling in ice-water bath and bubbling nitrogen for 15 min, TEMED stock solution (1.0 ml) was added to the mixture. The solution was then poured into several glass tubes of 4.5 - 5 mm internal diameters and about 100 mm long. The glass tubes were sealed and the polymerization was conducted at 21^0C for one day. The gel samples thus obtained were subjected to the swelling and mechanical tests, as will be described below.

For the light scattering measurements, PAAm gels were prepared in the light scattering cuvettes. All glassware was kept dustfree by rinsing in hot acetone prior

using. The solutions were filtered through membrane filters (pore size = 0.2 μm) directly into the cuvettes. This process was carried out in a dustfree glovebox. All the gels subjected to light scattering measurements were clear and appeared homogeneous to the eye. For calculation of excess scattering from gels, all the crosslinking polymerizations were repeated under the same experimental conditions except that the crosslinker BAAm was not used [9].

Light scattering measurements

The light scattering measurements were carried out at 21^0C using a commercial multi-angle light scattering DAWN EOS (Wyatt Technologies Corporation) equipped with a vertically polarized 30mW Gallium-arsenide laser operating at $\lambda = 690$ nm and 18 simultaneously detected scattering angles. The light scattering system was calibrated against a toluene standard (Rayleigh ratio at 690 nm = 9.7801×10^{-6} cm^{-1}, DAWN EOS software). The scattered light intensities were recorded from angles $\theta = 14.5^0$ to 163.3^0 which correspond to the scattering vector q range $3.1 \times 10^{-4} - 2.4 \times 10^{-3}$ A^{o-1}, where $q = (4\pi n / \lambda)\sin(\theta / 2)$, n is the refractive index of the medium. To obtain the ensemble averaged light scattering intensity of gels, eight cycles of measurements with a small rotation of the vial between each cycle were averaged.

Swelling measurements

For the equilibrium swelling measurements, PAAm gels after preparation in the form of rods of about 4.5-5 mm in diameter were cut into samples of about 15 mm length. Then, each sample was placed in an excess of water at 21 ± 0.5^oC. In order to reach swelling equilibrium, the gel samples were immersed in water for at least two weeks replacing the water every other day. The swelling equilibrium was tested by weighing the gel samples. Then, they were dried at 40^oC under vacuum to constant weight. The equilibrium weight swelling ratio q_w was calculated as $q_w = (m / m_{dry})$, where m and m_{dry} are the weight of gel after equilibrium swelling in water and after drying, respectively.

Mechanical Measurements

All the mechanical measurements were conducted at 21 ± 0.5 ^{0}C. Uniaxial compression measurements were performed on gel samples prepared in glass tubes at the state of gel preparation. For this purpose, the gels in the form of rods of 4.5 - 5 mm in diameter were cut into samples of about 10 mm length. Then, each cylindrical gel sample was placed on a digital balance [12]. A load was transmitted vertically to the gel through a rod fitted with a PTFE end-plate. The force acting on the gel was calculated from the reading of the balance m as $F = m\ g$, where g is the gravitational acceleration. The resulting deformation $\Delta l = l_0 - l$, where l_0 and l are the initial undeformed and deformed lengths, respectively, was measured using a digital comparator (IDC type Digimatic Indicator 543-262, Mitutoyo Co.), which was sensitive to displacements of 10^{-3} mm. The force and the resulting deformation were recorded after 20 s of relaxation. Note that the deformation ratio of the gel samples under the applied force remained constant after about 10 s, indicating that the 20 s of relaxation time for the network chains was sufficient for the present gels. The measurements were conducted up to about 20 % compression. The deformation ratio

α (deformed length/initial length) was calculated as $\alpha = 1 - \Delta l/l_0$. The corresponding stress f was calculated as $f = F / A$, where A is the cross-sectional area of the specimen, $A = \pi r_0^2$, where r_o is its initial radius. The elastic modulus G_o of gels just after their preparation was determined from the slope of linear dependence

$$f = G_0 \left(\alpha - \alpha^{-2} \right) \qquad (1)$$

Typical stress-strain data correlated according to Eq. (1) are shown in Fig. 1 for gels prepared at an initial monomer concentration $C_o = 5$ % but with varying crosslinker (BAAm) contents. For a network of Gaussian chains, the elastic modulus G_0 of gels just after their preparation is related to the effective crosslink density ν_e by [13,14]:

$$G_0 = A \nu_e RT \nu_2^0 \qquad (2)$$

where the front factor A equals to 1 for an affine network and 1- 2 / ϕ for a phantom network, where ϕ is the functionality of the crosslinks, ν_2^0 is the volume fraction of crosslinked polymer after the gel preparation, R and T are in their usual meanings.
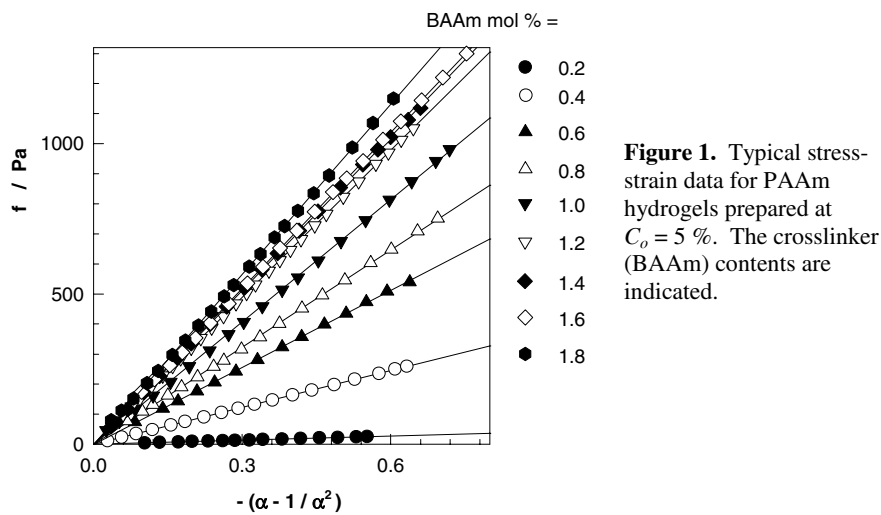

Figure 1. Typical stress-strain data for PAAm hydrogels prepared at $C_o = 5$ %. The crosslinker (BAAm) contents are indicated.

Results and Discussion

Eight different sets of PAAm hydrogels were prepared. In each set, the initial monomer concentration C_o was fixed while the crosslinker (BAAm) content was varied over a wide range. In Fig. 2, the modulus of elasticity G_o and the equilibrium swelling ratio q_w of the hydrogels are plotted against the crosslinker content for three series of gels prepared at $C_o = 3$, 5, and 7 %. As expected, G_0 increases while q_w decreases with the crosslinker concentration. Further, the elastic modulus G_0 also increases when the monomer concentration C_o is increased at a fixed BAAm content. The initial period of the G_o versus BAAm % plots was used to estimate the lower limit of the crosslinker concentration required for the onset of gelation. These plots are shown in Fig. 3. The best-fit curves through the G_0 versus BAAm % data intersect

with the positive abscissa at 0.03, 0.19, and 0.55 mol % BAAm for C_o = 7, 5, and 3 %, respectively. Thus, the larger the dilution degree of the reaction system, the higher is the threshold concentration of BAAm for the formation of an infinite network. Furthermore, the upper limit of the crosslinker content for the formation of transparent gels was found to be 1.6 mol % BAAm for $C_o \geq 5$ %. PAAm gels prepared at 1.8 mol % BAAm or above became first translucent and then opaque during the gelation reactions. It is obvious that these gels have heterogeneities in a spatial scale of submicrometer to micrometer. Therefore, only gel samples with less than or equal to 1.8 % BAAm were subjected to light scattering measurements.
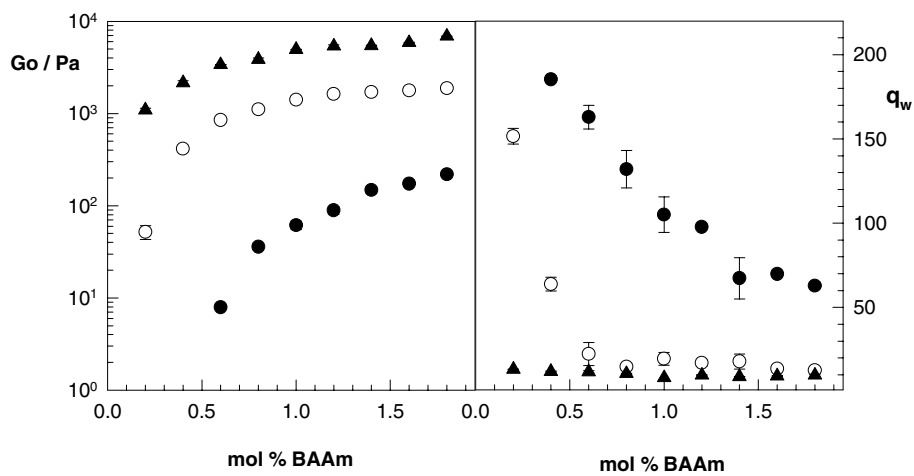

Figure 2. The elastic modulus of gels after preparation G_0 and the weight swelling ratio of the equilibrium swollen gels in water q_w shown as a function of BAAm concentration. C_0 = 3 (●), 5 (○), and 7 w/v % (▲).
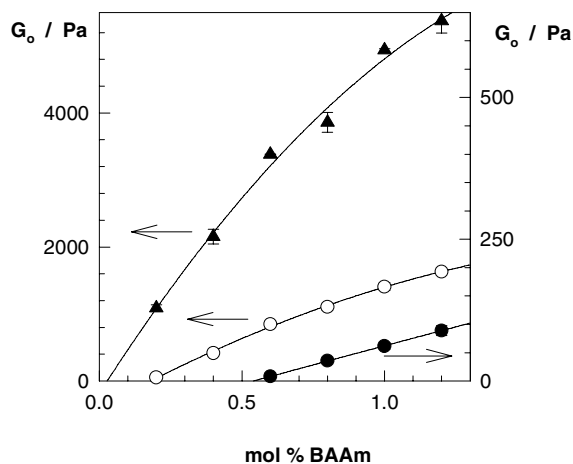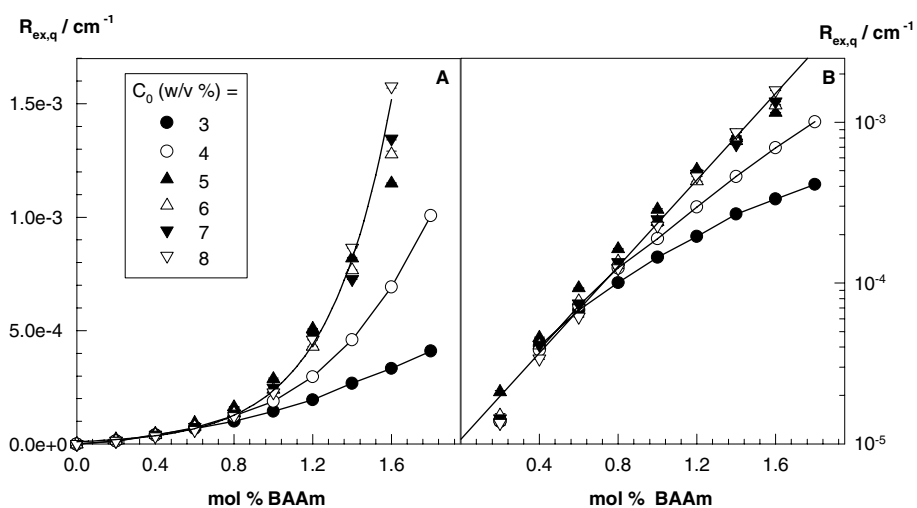

Figure 3. The initial period of G_0 versus BAAm % plots for gels prepared at C_0 = 3 (●), 5 (○), and 7 w/v % (▲). The best fit curves to the experimental data are shown in the Figure.

Figs. 4A-4F show the Rayleigh ratio $R(q)$ versus the scattering vector q plots for the eight different sets of PAAm hydrogels. $R(q)$ versus q plots for PAAm solutions are

also shown in the Figures by the open circles. In accord with the results reported earlier [4-11], the gels scatter much more light than the corresponding polymer solution of the same concentration. Even the presence of a small amount of the crosslinker BAAm results in increased scattered light intensities from the gel samples.
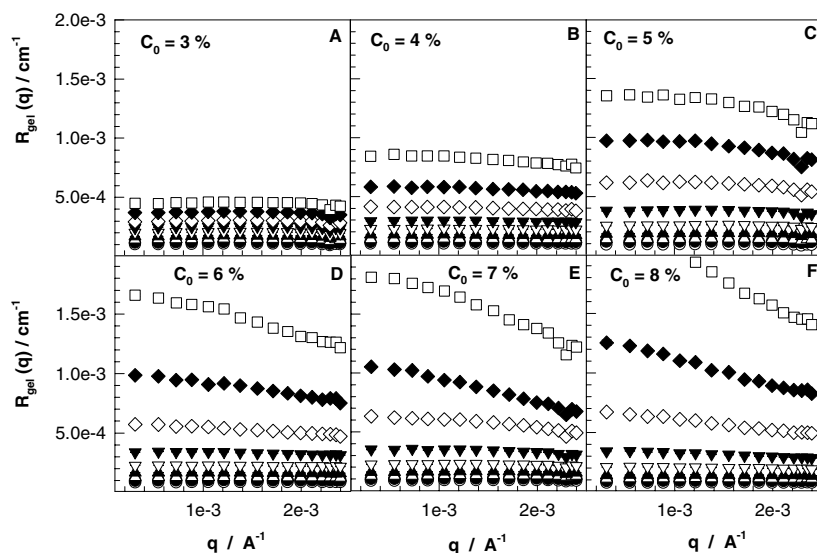
Figure 4. Rayleigh ratio $R_{gel}(q)$ versus scattering vector q plots for PAAm gels formed at various initial monomer concentrations C_0 indicated in the Figures. BAAm mol % = 0 ($\bigcirc$), 0.2 ($\bullet$), 0.4 ($\triangle$), 0.6 ($\blacktriangle$), 0.8 ($\triangledown$), 1.0 ($\blacktriangledown$), 1.2 ($\diamondsuit$), 1.4 ($\blacklozenge$), and 1.6 ($\square$).

Figure 5. The excess scattering $R_{ex,q}$ measured at $\theta = 90°$ shown as a function of BAAm % for PAAm gels formed at various initial monomer concentrations C_0 indicated in the Figure. Figure B shows the same data in a semi-logarithmic plot.

Comparison of the Figures also shows that, for a given crosslinker content, the scattered light intensity increases with the monomer concentration C_o. Furthermore, at low BAAm content, the scattered light intensity is nearly q-independent but for higher BAAm content, the q dependence becomes more pronounced.

Excess scattering intensities from gels, $R_{ex}(q)$, were calculated as $R_{ex}(q) = R_{gel}(q) - R_{sol}(q)$, where $R_{gel}(q)$ and $R_{sol}(q)$ are the Rayleigh ratios for gel and polymer solution, respectively. To compare the excess scattering of different gels, we will focus on the scattering intensity measured at a fixed scattering angle $\theta = 90^o$. Fig. 5A shows the excess scattering at $\theta = 90^o$ ($R_{ex,q}$) plotted as a function of BAAm %. $R_{ex,q}$ increases first slightly up to about 1 mol% BAAm but then rapidly increases with a further increase in BAAm concentration, suggesting approaching partial phase separation. As shown in Figure 5B, a good linear behavior was obtained if the data points for $C_o \geq 5$ % are redrawn in a semi-logarithmic plot, indicating an exponential law between $R_{ex,q}$ and BAAm %. This suggests the occurrence of a macroscopic phase separation in the gel samples formed at $C_o \geq 5$ as the crosslinker content is increased.
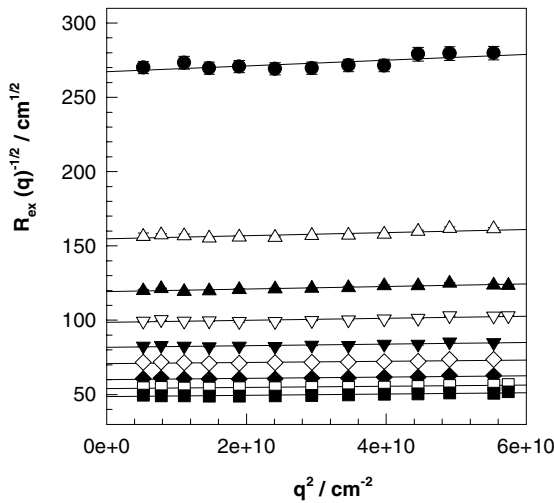

Figure 6. Debye - Bueche plots for PAAm gels prepared at $C_0 = 3$ w/v %. BAAm mol % = 0.2, (●), 0.4 (△), 0.6 (▲), 0.8 (▽), 1.0 (▼), 1.2 (◇), 1.4 (◆), 1.6 (□), and 1.8 (■).

Since the thermal concentration fluctuations in gels are eliminated in $R_{ex,q}$, excess scattering is a measure of the degree of spatial inhomogeneities. Thus, the results demonstrate that the extent of the inhomogeneities in PAAm gels is strongly increased when the crosslinker content is increased. To interpret the light scattering results from gels, several Lorentzian and Gaussian scattering functions have been proposed empirically. For example, the excess scattering $R_{ex}(q)$ was given by the Debye-Bueche (DB) function as [15-18]:

$$R_{ex}(q) = \frac{4\pi K \xi^3 \langle \eta^2 \rangle}{\left(1 + q^2 \xi^2\right)^2} \tag{3}$$

where K being the optical constant, $K = 8 \pi^2 n^2 \lambda^{-4}$, ξ is the correlation length of the scatterers, and $\langle \eta^2 \rangle$ is the mean square fluctuation of the refractive index. Note that the correlation length ξ of DB theory is a characteristic length scale in the gel

and, it is a measure of the spatial extent of the fluctuations. According to eq. (3), the slope and the intercept of $R_{ex}(q)^{-1/2}$ vs q^2 plot (DB plot) give ξ and $\langle \eta^2 \rangle$ of a gel sample. In Fig. 6, the data points shown in Fig. 4A for gels with $C_o = 3\%$ are replotted in the form of DB plots. It is seen that straight lines are obtained in this analysis, indicating that the DB function works well. Similar DB plots were also obtained for the other series of gels. Calculated values of ξ and $\langle \eta^2 \rangle$ for all the gel samples from DB analysis are shown in Fig. 7 as a function of BAAm %. The correlation length of the scatterers ξ is about 10^1 nm and slightly increasing function of the BAAm concentration. The mean square fluctuations $\langle \eta^2 \rangle$ are in the range $10^{-7} - 10^{-5}$ and they increase with the BAAm content. The increase in $\langle \eta^2 \rangle$ with BAAm % is first rapid in the range 0.2 - 1 % but then slight at higher BAAm contents.
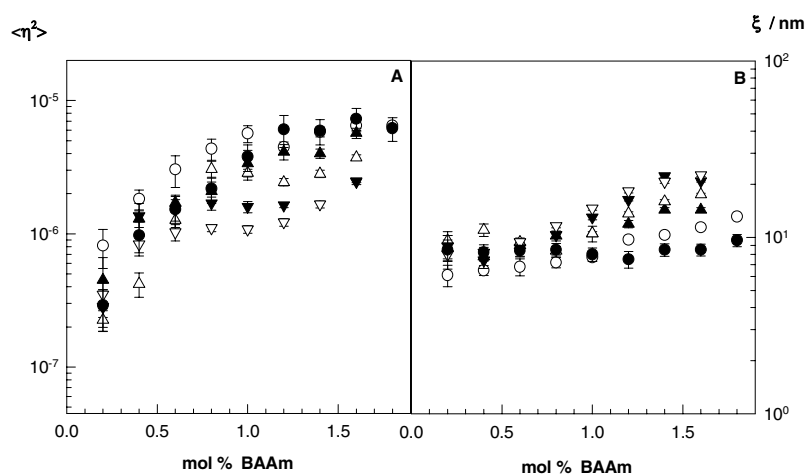
Figure 7. The mean square fluctuation of the refractive index $\langle \eta^2 \rangle$ (A) and the correlation length ξ (B) in PAAm gels shown as a function of the BAAm concentration. $C_0 = 3$ (●), 4 (○), 5 (▲), 6 (△), 7 (▼), and 8 w/v % (▽).
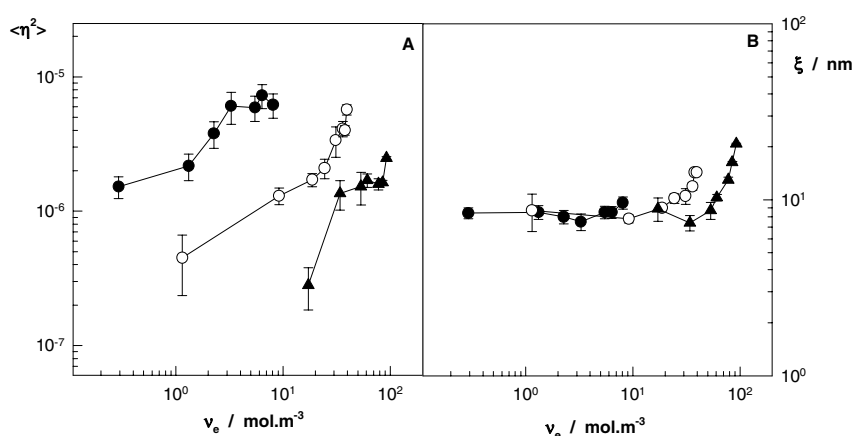

Figure 8. $\langle \eta^2 \rangle$ (A) and ξ (B) shown as a function of the effective crosslink density ν_e of PAAm hydrogels formed at $C_0 = 3$ (●), 5 (○), and 7 w/v % (▲).

For the interpretation of the light scattering results, not only the nominal crosslink density, that is the BAAm % used in the hydrogel preparation, but also, the effective crosslink density should be taken into account. Using the elastic moduli data of gels shown in Fig. 2 together with eq. (2), we calculated the effective crosslink densities ν_e of the hydrogels. For calculations, we assumed phantom network behavior ($\phi = 4$). It was also assumed that the gel fraction is unity, i.e., the polymer concentration after the gel preparation ν_2^0 was taken as equal to $C_o/(100\rho)$ where ρ is the polymer density (1.35 g/mL). In Fig. 8, ξ and $\langle \eta^2 \rangle$ values are replotted against the effective crosslink density ν_e of gels formed at three different initial monomer concentrations. Comparison of Figs. 7 and 8 shows that the light scattering data provide a much better correlation with the gel synthesis conditions, if ν_e is taken as the independent experimental parameter instead of BAAm %. Hence ν_e is more sensitive then BAAm % to capture the difference in the network microstructure. The correlation length ξ, i.e., the extension of the inhomogeneities is almost independent of the gel synthesis parameters up to the upper limit of the crosslinker content for each series of gels. The increase in ξ observed at high BAAm contents for each series of gels is due to the approaching of the reaction system to the phase separation limit. Fig. 8 also shows that the difference between the gels is due almost entirely to the extent in the concentration fluctuations $\langle \eta^2 \rangle$. The lower the initial monomer concentration C_o, the larger is the concentration fluctuations in gels. This is probably due to the increasing extent of the multiple crosslinking reactions in more diluted reaction systems, leading to the formation of clusters of crosslinks [1,2]. In order to quantify the extent of these non-idealities, we calculated the crosslinking efficiency of BAAm ε_{xl}, that is the fraction of BAAm forming effective crosslinks. Using the effective and nominal crosslink densities of the hydrogels, ε_{xl} was calculated as:

$$\varepsilon_{xl} = \frac{\nu_e}{\left(\dfrac{2\rho}{M_r} \right) X} \qquad (4)$$

where M_r is the molecular weight of repeat unit (71 g/mol), and X is the crosslinker ratio in the comonomer feed (mole BAAm / mole AAm). Note that, if $\varepsilon_{xl} = 1$, all the crosslinker (BAAm) molecules used in the hydrogel synthesis participate in forming effective crosslinks; as ε_{xl} decreases, more and more BAAm molecules are wasted in elastically ineffective links. In Fig.9A, the crosslinking efficiency ε_{xl} is plotted against the BAAm % for the three series of gels. It is seen that the crosslinking efficiency of BAAm ε_{xl} rapidly decreases with decreasing monomer concentration. At $C_o = 3$ %, $\varepsilon_{xl} = 10^{-2} - 10^{-3}$, indicating that 99 to 99.9 % of BAAm used in the hydrogel preparation were wasted. In Fig. 9B, the concentration fluctuations $\langle \eta^2 \rangle$ in gels are plotted against the crosslinking efficiency ε_{xl}. The lines were drawn through the data points of gels having the same BAAm contents. The results demonstrate that the concentration fluctuations $\langle \eta^2 \rangle$ in PAAm hydrogels are reduced as the crosslinking efficiency is increased. Thus, we obtained direct experimental evidence that the frozen concentration fluctuations in gels originate from the crosslinker molecules forming elastically ineffective links. Moreover, for a given crosslinking efficiency, $\langle \eta^2 \rangle$ decreases further as the BAAm % is decreased. Since multiple crosslinking becomes less probable the smaller the number of pendant vinyl groups in the reaction system, decreasing BAAm concentration also decreases the number of multiple crosslinks so that $\langle \eta^2 \rangle$ decreases.
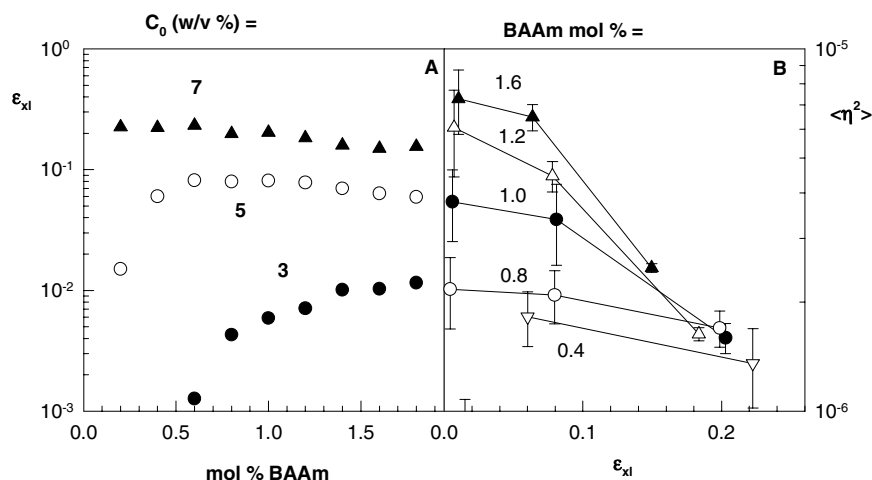
Figure 9. (A): The crosslinking efficiency of BAAm ε_{xl} shown as a function of the BAAm content of the hydrogels formed at $C_0 = 3$ (●), 5 (○), and 7 w/v % (▲). **(B):** The mean square fluctuation of the refractive index $\langle \eta^2 \rangle$ in PAAm hydrogels shown as a function of the crosslinking efficiency ε_{xl}. BAAm mol % = 0.4 (▽), 0.8 (○), 1.0 (●), 1.2 (△), and 1.6 (▲).

Conclusions

Elasticity and light scattering measurements were carried out on PAAm gels formed under various reaction conditions. Debye-Bueche analysis of the light scattering data indicates that, irrespective of the gel synthesis parameters, the correlation length ξ, i.e., the extension of inhomogeneities in the hydrogels is about 10^1 nm. The extent of the frozen concentration fluctuations in the hydrogels represented by $\langle \eta^2 \rangle$ decreases with increasing efficiency of the crosslinking reactions, i.e., with increasing monomer concentration during the hydrogel preparation. The combination of the light scattering and elasticity data thus shows a direct correlation between the fraction of wasted crosslinker molecules during gelation and the spatial gel inhomogeneity.

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