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SYNTHESIS AND CHARACTERIZATION OF FAST RESPONSIVE POLY(N-ISOPROPYLACRYLAMIDE) HYDROGELS

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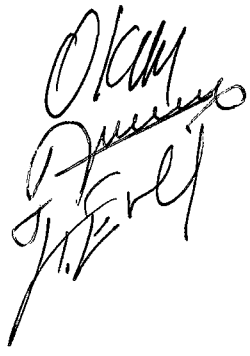

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LIST OF ABBREVIATIONS

NIPA	:	N-isopropylacrylamide
PEG	:	Poly(ethylene glycol)
DMSO	:	Dimethylsulfoxide
AAc	:	Acrylic acid
AAm	:	Acrylamide
NDMA	:	N,N'-dimethylacrylamide
LCST	:	Lower Critical Solution Temperature
NaCl	:	Sodium Chloride
BAAm	:	N,N'-methylenebisacrylamide
FCC	:	Free-Radical Crosslinking Copolymerization
APS	:	Ammonium persulfate
TEMED	:	N,N,N',N'- tetramethylethylenediamine

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LIST OF SYMBOLS

N_1 : Number of sites occupied by the solvent molecules in the lattice
V_1 : Molar volume of solvent molecules
N_2 : Number of sites occupied by the polymer chains in the lattice
V_2 : Molar volume of solvent molecules
x : Number of segments per a polymer chain
N_o : The total number of lattice sites
ν : The total number of possible conformations of the polymer molecule in the lattice
I : Number of polymer chains added to the lattice
z : The coordination number of the lattice or the number of cells
ΔS_m : Entropy change of mixing
Ω : The total number of distinguishable ways of placing the chains in the lattice
ν_1 : Volume fraction of solvent molecules ν_1
ν_2 : Volume fraction of polymer chain
w_{ij} : Energy of the formation of a contact between a pair of segments of molecules i and j
ΔH_m : Enthalpy change of mixing
χ_1 : Polymer-solvent interaction parameter
k : Boltzman's constant
T : Absolute temperature
ΔG_m : Free energy change of mixing
ΔG_{el} : Free energy change during deformation
ΔG_i : Free energy of electrostatic interactions
ΔG : Free energy change during swelling
n_i : The moles of the species i
ν_{i+1} : Volume fraction of the species $i + 1$
χ_{ij} : The interaction parameter between the species i and j
N : The average number of segments in the network chains
α : Deformation ratio (deformed length / initial length)
α_x : Macroscopic deformation ratio in x direction
α_y : Macroscopic deformation ratio in y direction
α_z : Macroscopic deformation ratio in z direction
ν_2 : Volume fractions of the crosslinked polymer in the gel
ν_2^o : Volume fractions of the polymer network after the gel preparation
$\Delta\mu_1$: Excess chemical potential
π : The osmotic pressure
ν_2' : The first coexisting polymer concentration
ν_2 : The second coexisting polymer concentration
F : Electrostatic force
q_1 : Charge of atom 1

q_2 : Charge of atom 2
r : Distance between two atoms
ε : Dielectric constant of surroundings
D_o : The diameters of the gel rods after preparation
D : The diameters of the gel rods after swelling
V_o : Gel volumes after the gel preparation
V : Gel volumes after swelling
m_o : The weights of the gel rods after preparation
m_{sw} : The weights of the gel rods after swelling
m_{rel} : The relative mass which is a parameter defining water retention
m_t : The mass of the gel sample at time t
ℓ_o : The initial undeformed length
ℓ : The deformed length
F : Gravitational force during uniaxial deformation
m : The value of weight read from the balance during uniaxial deformation
g : The gravitational acceleration
A : Cross-sectional area of the gel sample
f : The gravitational force per unit area
G_o : Elastic modulus after preparation

SYNTHESIS AND CHARACTERIZATION OF FAST-RESPONSIVE POLY(N-ISOPROPYLACRYLAMIDE) HYDROGELS

SUMMARY

In the present work, a series of poly(N-isopropylacrylamide) (PNIPA) hydrogels was prepared by free-radical crosslinking of N-isopropylacrylamide (NIPA) and N,N'-methylenebisacrylamide (BAAm) in aqueous solutions of poly(ethylene glycol) of molecular weight 300 g/mol (PEG-300). PEG-300 was used as a pore-forming agent during the hydrogel preparation.

Two sets of experiments were carried out. In the first set the crosslinker (BAAm) content was fixed at 1.2 mol % while the amount of PEG-300 was varied. The effect of the gel preparation temperature (T_{prep}) on the hydrogel properties was also investigated by carrying out the gelation experiments at both below and above the lower critical solution temperature of PNIPA. In the second set, the PEG-300 content of the PEG/water mixture was fixed at 70 v/v % while the crosslinker content was varied over a wide range. The hydrogels thus obtained were characterized by the swelling and elasticity tests as well as by the measurements of the deswelling-reswelling kinetics of the hydrogels in response to a temperature change between 25 °C and 48 °C.

It was found that the equilibrium swelling capacity of PNIPA hydrogels increases with decreasing crosslinker ratio, or with increasing amount of PEG-300 used in the hydrogel preparation. Increasing amount of PEG-300 also increased the deswelling rate of swollen PNIPA hydrogels in water at 48 °C. The results were explained with the formation of pores ("water channels") in the skin layer of the hydrogels. The higher the amount of PEG-300 in the gel formation system, the larger the water channels at the gel surface, so that water molecules can easily diffuse out of the gel phase. However, the reswelling rate of the collapsed hydrogels at 25 °C decreased on rising PEG-300 content. It was also shown that the gel preparation temperature T_{prep} also affects the swelling behaviour of the hydrogels, if the PEG-300 content in the reaction solution is less than 20 v/v %. Experiments carried out at various crosslinker contents showed that the deswelling rate decreases while the reswelling rate increases as the crosslinker content is increased due to the simultaneous decrease of the mesh size of PNIPA hydrogels.

HIZLI TEPKİ VEREN POLİ(N-İZOPROPİLAKRİLAMİD) HİDROJELLERİN SENTEZ VE KARAKTERİZASYONU

ÖZET

Bu çalışmada, N-izopropilakrilamid (NIPA) ve N,N'-metilenbisakrilamid'in (BAAm), 300 g/mol molekül ağırlıklı poly(etilen glikol)'ün (PEG) sulu çözeltilerinde serbest radikal çapraz bağlanma reaksiyonu ile oluşan poly(N-izopropilakrilamid) (PNIPA) hidrojellerinin bir serisi hazırlanmıştır. Hidrojel sentezi sırasında PEG-300 gözenek oluşturucu madde olarak kullanılmıştır.

Deneyler iki grup halinde yapılmıştır. Birinci grup denemede, PEG-300 miktarı değiştirilirken çapraz bağlayıcı içeriği sabitlenmiştir. PNIPA'nın en düşük kritik çözelti sıcaklığı (LCST) değerinin üstünde ve altında olmak üzere iki farklı sıcaklıkta sentezlenerek, jel sentez sıcaklığının (T_{prep}) hidrojellerin özellikleri üzerindeki etkisi incelenmiştir. İkinci grup denemede, çapraz bağlayıcı içeriği geniş bir aralıkta değiştirilirken, PEG/su karışımının PEG-300 içeriği % 70 v/v olarak sabitlenmiştir. Elde edilen hidrojeller, şişme ve elastisite testleri ile olduğu kadar hidrojellerin 25 °C ve 48 °C' deki sıcaklık değişimine gösterdikleri tepki nedeniyle büzülme ve şişme kinetikleri de ölçülerek karakterize edilmiştir.

PNIPA hidrojellerinin denge şişme kapasitelerinin, çapraz bağlayıcı oranının azalmasıyla veya jel sentezi sırasında kullanılan PEG-300 miktarının artışıyla, arttığı gözlenmiştir. PEG-300 miktarındaki artış, şişmiş PNIPA hidrojellerinin suyun içinde 48 °C'deki büzülme kinetiğini arttırmıştır. Bu sonuçlar, hidrojellerin kabuk tabakasında porların ("su kanalları") oluştuğunu açıklamaktadır. Jel oluşum sistemindeki daha yüksek PEG-300 miktarı, jel yüzeyinde daha geniş su kanalları oluşturur. Bu yüzden su molekülleri jel fazından kolaylıkla dışarı çıkabilir. Bununla birlikte büzülmüş olan jellerin, 25 °C'deki şişme hızı PEG-300 içeriğinin artışına bağlı olarak azalmaktadır. Reaksiyon çözeltisindeki PEG-300 içeriğinin % 20 v/v'den düşük olduğu durumda, jel sentez sıcaklığının (T_{prep}) hidrojellerin şişme davranışını etkilediği görülmüştür. Çeşitli çapraz bağlayıcı içeriklerinde uygulanan deneyler, çapraz bağlayıcı içeriğindeki artışın büzülme hızında düşüşe, şişme hızında ise artışa neden olduğunu göstermiştir. Bunun sebebi PNIPA hidrojellerinin ağ büyüklüğündeki azalmadır.

1. INTRODUCTION

A gel is a form of matter intermediate between a solid and a liquid [1]. Thus, it has both liquid and solid-like properties. The liquid-like properties result from the fact that the major constituent of gels is usually a liquid. The properties of the gel depend strongly on the interaction of its two components, which are the solvent and the polymer network. The liquid prevents the polymer network from collapsing into a compact mass; the network prevents the liquid from flowing away. A gel consists of monomer units that are polymerized into linear chains and crosslinked into a nonlinear three-dimensional network [2].

A gel can be viewed as a container of solvent since the solvent molecules are comprised by the network. Another aspect of gels is that a gel is a single polymer molecule. It means that all the monomer units in one piece of gel are connected to each other and form one big molecule on a macroscopic scale [3, 4].

Polymer gels are known to exist in two distinct phases, swollen and collapsed. In dried state, a gel is a solid material whereas it swells until it reaches the equilibrium state. Fig.1.1 shows schematically the two states of gels: collapsed and swollen states.

Drastic changes in the state of the gel can be brought about by infinitesimal changes in the external conditions. Continuous, discontinuous and reentrant volume phase transitions occur between the states in response to chemical and physical stimuli, such as temperature, solvent composition, pH, ionic composition, electric field, light and particular molecules [3, 5]. For example, when the temperature is lowered, the polymer network loses its elasticity and therefore becomes increasingly compressible. When a certain critical temperature is reached, the elasticity falls zero and the compressibility becomes infinite. For a gel to undergo the phase transition, it is necessary that the network chains interact with each other through both repulsive and attractive interactions and the balance of competing interactions has to be

modified by various stimuli. Therefore, the phase behavior of a gel crucially depends on the nature of interactions between polymers [1].

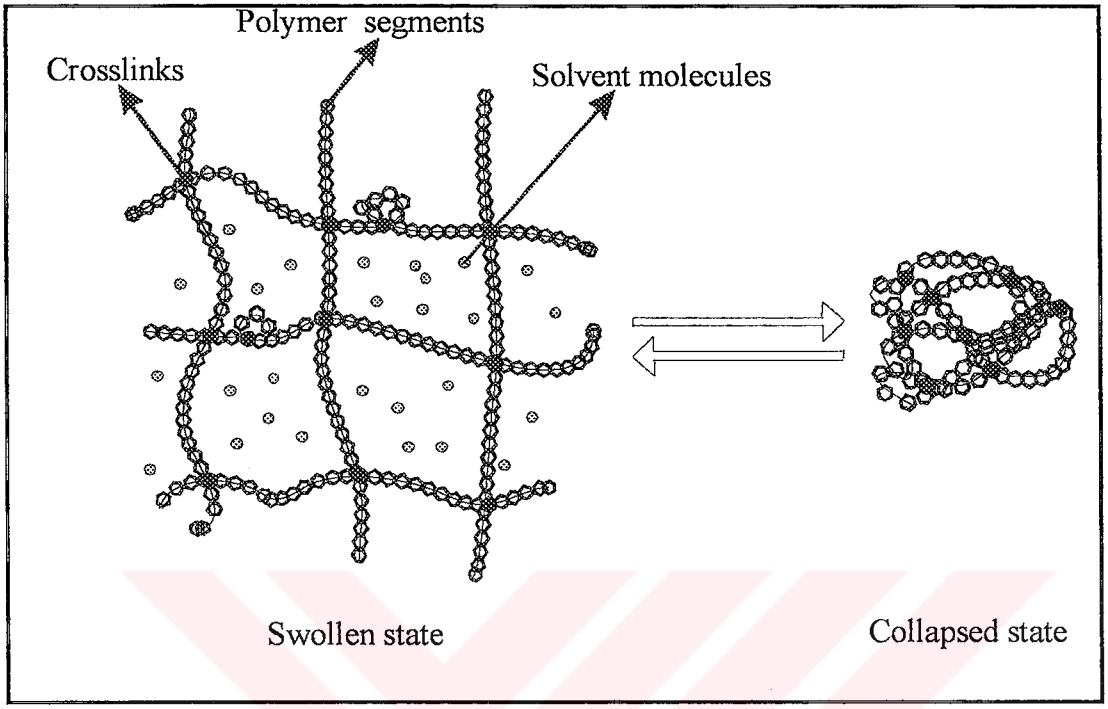


Figure. 1.1: The two states of gels: collapsed and swollen states. Hydrogels can undergo large discontinuous volume phase transitions in response to small changes in ambient conditions.

The physical characteristics of hydrogel phase transitions are universally shared by large number of other materials. The swelling transition illustrated in Fig. 1.1 is analogous to the gas-to-liquid phase transition and has been observed in synthetic hydrogels and, hydrogels made of natural polymers such as DNA, polysaccharides, and polypeptides. Some of original concepts first proposed by van der Waals for understanding the liquid-to-gas phase transformation provide a conceptual foundation for understanding the liquid-to-gas phase transformations [2].

The physical chemistry of various gels has been studied intensively since 1940's [1]. The first mean-field treatment of the gel network system was given independently by Flory [6] and Huggins [7]. In 1968, based on Flory-Huggins theory, Dusek and Patterson predicted a volume phase transition of the network system between dense phase and dilute phase [8]. Tanaka observed the volume phase transition in slightly ionized poly(acrylamide) gels immersed in an acetone-water mixture [1]. The observation of the coil-globule transition in a single polystyrene chain in

cyclohexane was reported by Tanaka and Swislow [9]. At the same year, Horkay and Zrinyi studied the mechanical and swelling behavior of chemically crosslinked poly(vinyl acetate) gels [10]. At the end of 1980's, studies on the swelling behavior and phase transitions in temperature-sensitive poly(N-isopropylacrylamide) (PNIPA) gels immersed in aqueous solutions of poly(ethylene glycols) (PEGs) of various molecular weights [11, 12], water-DMSO [5, 13], water-methanol, or water-ethanol mixtures [14] were reported.

The ability to alter the physical response of the hydrogels by varying their compositions makes them extremely important in many technological and scientific applications [2]. Because they have the capacity to contain a large volume of solvent in their swollen state, they have been used in a variety of super absorbent materials. Separation and filtration devices specific for small ions or for large-molecular weight macromolecules have also been successfully fabricated from these materials.

Hydrogels made of hydrophobically modified monomers such as the PNIPA hydrogels that undergo phase transitions at about 34 °C have been employed as drug delivery devices, materials for tissue reconstruction, materials for preventing surgical adhesions [2, 15]. This type of gels has also been used for the separation of a range of materials such as proteins, yeasts and bacteria from aqueous solutions [16, 17]. In addition, hydrogel phase transitions driven by enzymatic reactions have been used in some controlled drug delivery strategies [18]. Porous hydrogels have been prepared for three-dimensional scaffoldings, soft contact lenses and artificial lenses [19, 20]. The application of these materials in medicine, agriculture, food preparation, and several other industries continues to grow. In these applications, a fast response rate of the hydrogels to the external stimuli is needed. To increase the response rate of the hydrogels, various techniques have been proposed recently.

The aim of this study is to prepare fast-responsive PNIPA hydrogels by use of PEG of molecular weight 300 g/mol as a pore-forming agent during the gel formation process. PNIPA hydrogels were synthesized by free-radical crosslinking polymerization of NIPA in the presence of BAAm as crosslinker. Water/PEG mixtures of various compositions were used as the polymerization solvent. In the first set of experiments, both the crosslinker ratio (the mole ratio of crosslinker to monomer) and the initial monomer concentration were fixed at 1/85 and 7.92 w/v %, respectively, while PEG content in the solution was varied between 0 and 70 %. In

the second set, the crosslinker content was varied from 1.16 to 15 mol % while the initial monomer concentration and PEG content of the solvent mixture were fixed at 7.92 w/v % and 70 %, respectively.

2. SWELLING OF HYDROGELS

2.1. Entropy of Mixing in Polymer Solutions

Polymer solutions show deviation from the ideal solution behavior due to the fact that the molecular sizes of both polymer and solvent differ from each other. A special restriction on the arrangement of the two components in space resulted from the connectivity of polymeric chain segments. Flory [6, 21] and Huggins [7] expressed the total number of configurations of a mixture from N_1 solvent molecules with a molar volume V_1 and N_2 polymer chains with a molar volume V_2. In Fig. 2.1 lattice theory suggested by Flory-Huggins is illustrated. Polymer chains are represented as consisting of x segments, each occupies one lattice site as the solvent molecule, i.e.,

$$x = V_2 / V_1 \tag{2.1}$$

The total number of lattice sites can be given as:

$$N_0 = N_1 + xN_2 \tag{2.2}$$

According to this theory N_2 polymer molecules are added one-by-one to the lattice before adding the solvent molecules. When adding a polymer, the first segment of the chain can be placed in any empty cell. However, for the connectivity required to represent a polymer molecule, each successive segment of remaining x-1 segment must be placed in any empty cell adjacent to the previously-placed segment. The individual numbers of possible placements are calculated for each segment of the chain and, by multiplying these numbers together, the total number (ν) of possible conformations of the polymer molecule in the lattice is obtained [22]. If i chains have already been inserted into the lattice, the number of possible conformations for the (i+1)th polymer molecule (ν_{i+1}) is given by:

$$\nu_{i+1} = \left\{ \frac{(N_0 - xi)!}{[N_0 - x(i+1)]!} \right\} \left[\frac{z-1}{N_0} \right]^{x-1} \tag{2.3}$$

where z is the coordination number of the lattice or the number of cells that are first neighbour to a given cell. The total number of distinguishable ways of placing the N_2 chains on $N_1 + xN_2$ sites is;

$$\Omega = \frac{1}{N_2!} \prod^{N_2-1} \prod \nu_{i+1} \tag{2.4}$$

The number of ways Ω_2 by which chains can be placed on xN_2 sites is obtained by setting $N_1 = 0$ in Equation (2.4). The configurational entropy of mixing is;

$$\Delta S_m = k \ln \frac{\Omega}{\Omega_2} = -k[N_1 \ln \nu_1 + N_2 \ln \nu_2] \tag{2.5}$$

where ν_1 and ν_2 are the volume fractions of solvent and polymer defined as

$$\nu_1 = \frac{N_1}{N_1 + xN_2} \quad , \quad \nu_2 = \frac{xN_2}{N_1 + xN_2} \tag{2.6}$$

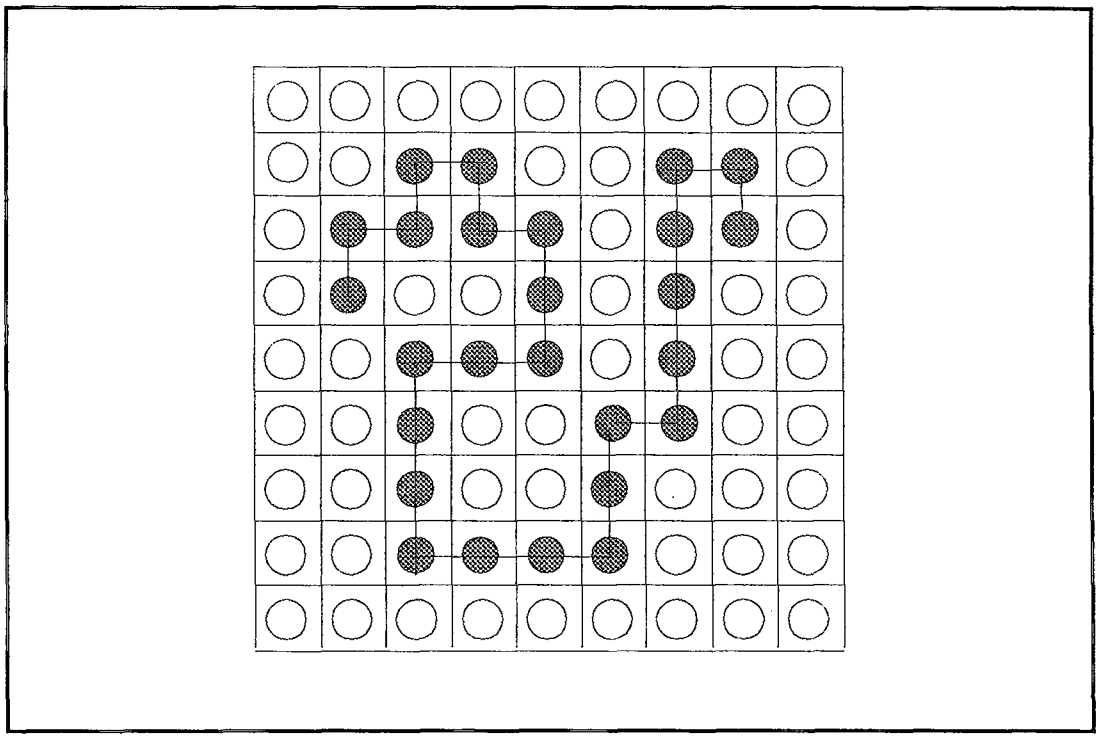


Figure. 2.1: Lattice Theory suggested by Flory-Huggins. A part of the lattice consisting of a polymer chain is represented by the filled symbols is seen in the Figure. Open symbols represent solvent molecules [22].

2.2. Enthalpy and Free Energy of Mixing in Polymer Solutions

Solvent-solvent, segment-solvent and segment-segment interactions are possible within the same chain. The energies of these three types of interactions are represented by w_{11}, w_{12}, w_{22} respectively. The change in the internal energy for the formation of an unlike molecular pair is given by:

$$\Delta w = w_{12} - \frac{1}{2}(w_{11} + w_{22}) \tag{2.7}$$

and the expression for the enthalpy of mixing is given as:

$$\Delta H_m = zN_1 v_2 \Delta w_{12} \tag{2.8}$$

To eliminate z and Δw_{12}, a parameter called Flory (or polymer-solvent) interaction parameter (χ_1) was introduced;

$$\chi_1 = \frac{z\Delta w_{12}}{kT} \tag{2.9}$$

The expression for the enthalpy of mixing was then rewritten by combining Equations (2.8) and (2.9):

$$\Delta H_m = kT\chi_1 N_1 \nu_2 \tag{2.10}$$

The quantity $kT\chi_1$ represents merely the difference in energy of a solvent molecule immersed in the pure polymer $(\nu_2 \cong 1)$ compared with one surrounded by molecules of its own kind, i.e., in the pure solvent.

The free energy of mixing can simply be obtained by combining equations (2.5) and (2.10):

$$\Delta G_m = kT[N_1 \ln \nu_1 + N_2 \ln \nu_2 + N_1 \chi_1 \nu_2] \tag{2.11}$$

2.3. Swelling of Polymer Networks

Swelling is one of the characteristic features of polymer networks. The ability to absorb good solvents arises from the spontaneity of the mixing processes (Equation 2.5), while their resistance to dissolution arises from crosslinks between the network chains. As the network is swollen by absorption of solvent, the chains between network junctions are required to assume elongated configurations. As a consequence, a force akin to the elastic refractive force develops. As swelling proceeds, this force increases and the diluting force decreases. Ultimately, a state of equilibrium swelling is reached in which these two forces are in balance. A close analogy exists between the swelling equilibrium and the osmotic equilibrium. The elastic reaction of the network structure may be interpreted as a pressure acting on the solution, or swollen gel. In the equilibrium state this pressure is sufficient to increase the chemical potential of the solvent in the solution, so that it equals that of the excess solvent surrounding the swollen gel. Swelling of polymer networks is a thermodynamic phenomenon, and it gives a measure of the amount of solvent absorbed by the polymer under equilibrium conditions. In case of swelling in solvent mixtures, it additionally gives a measure of the distribution of solvent components between the gel and solution phases. At constant temperature, the equilibrium swelling in solvent mixtures can be classified into three general types:

First, the solvent composition inside the polymer network (gel) is proportional to the external solvent composition. Such a case can be considered as an ideal system

where the sorption of solvent in polymers is comparable to the Henry's law. For ideal systems, the sorption isotherm is assumed to be linear, i.e., the solvent concentration inside the gel is proportional to that outside.

Second, if the attractions between solvent molecules are stronger than the attractions between the solvent molecule and the polymer, then adding one solvent to the other actually decreases the chance of the solvent molecules partition within the polymer network, and lowers the total swelling. Because the total swelling is lowered, this behavior is termed negative deviation.

Third, the total swelling is above the swelling of either pure constituents. In this case, unlike solvent molecules may interact with one another less than the solvent molecule and the polymer do. Because the total swelling is increased relative to the ideal behavior, this behavior is termed positive definition [23].

2.4 Theory of Swelling

The Flory-Rehner phenomenological theory has been most widely used to describe the change in the Gibbs free energy (ΔG) during the swelling process[21, 24]. This theory assumes that ΔG of swelling equals to the sum of the individual free energy terms, i.e., the changes in the free energy of mixing (ΔG_m), in the free energy of elastic deformation (ΔG_{el}), and in case of ionic network, in the free energy of electrostatic interactions (ΔG_i);

$$\Delta G = \Delta G_m + \Delta G_{el} + \Delta G_i \tag{2.12}$$

If the network is made up only of neutral monomers, ΔG_m and ΔG_{el} sum up to generate the total Gibbs free energy of the system, i.e.,

$$\Delta G = \Delta G_m + \Delta G_{el} \tag{2.13}$$

The derivation of ΔG_m within the framework of Flory-Huggins theory was already given in Section 2.2. For multicomponent systems, Equation (2.11) can be written as;

$$\Delta G_m = RT\left(\sum_i n_i \ln \nu_i + \sum_{i<j} n_i \nu_j \chi_{ij}\right) \tag{2.14}$$

where n_i is the moles of the species i, v_i is its volume fraction, χ_{ij} is the interaction parameter between the species i and j.

For the free energy of elastic deformation (ΔG_{el}) several theories are available [21, 25, 26]. The simplest affine network model in which the junction points are assumed to be embedded in the network is widely used to describe qualitatively the elasticity of networks. As a result of this assumption, components of each chain vector transforms linearly with macroscopic deformation. The change in the free energy of elastic deformation of the affine network is given by [27];

$$\Delta G_{el} = (1/2)(RT/NV_1)\left(\alpha_X^2 + \alpha_Y^2 + \alpha_Z^2 - 3 - \ln(\alpha_X \alpha_Y \alpha_Z)\right) \tag{2.15}$$

where N is the average number of segments in the network chains, and V_1 is the molar volume of solvent and,

$$\alpha_X^2 = \frac{\langle x^2 \rangle}{\langle x^2 \rangle_0}, \qquad \alpha_Y^2 = \frac{\langle y^2 \rangle}{\langle y^2 \rangle_0}, \qquad \alpha_Z^2 = \frac{\langle z^2 \rangle}{\langle z^2 \rangle_0}, \tag{2.16}$$

where x, y and z are the components of chain end-to-end distance, the subscript o indicates relaxed state. If α represents the linear deformation factor, then by the condition of isotropy we have $\alpha = \alpha_X = \alpha_Y = \alpha_Z$. The linear deformation factor α is related to equilibrium swelling ratio by the following equation;

$$\alpha = \left(\frac{v_2^0}{v_2}\right)^{1/3} \tag{2.17}$$

where v_2 and v_2^0 are the volume fractions of the polymer network at equilibrium degree of swelling and after the gel preparation, respectively. If the polymer network is prepared by crosslinking of polymer chains without solvent, as was considered in Flory's original theory [21], v_2^0 must be equal to 1. Equation (2.15) can now be given in terms of α as;

$$\Delta G_{el} = (3/2)(RT/NV_1)\left(\alpha^2 - 1 - \ln\alpha\right) \tag{2.18}$$

Substituting Equation (2.17) into Equation (2.18) leads to;

$$\Delta G_{el} = (3/2)(RT/NV_1)\left((v_2^0/v_2)^{2/3} - 1 - \ln(v_2^0/v_2)^{1/3}\right) \tag{2.19}$$

Substitution of Equations (2.14) and (2.19) into Equation (2.13) gives the free energy equation of swelling for non-ionic (uncharged) networks;

$$\Delta G = RT\left(\sum_i n_i \ln v_i + \sum_{i<j} n_i v_j \chi_{ij} + \frac{3}{2}\frac{1}{NV_1}\left((v_2^0/v_2)^{2/3} - 1 - \ln(v_2^0/v_2)^{1/3}\right)\right) \tag{2.20}$$

ΔG decreases as the gel swells, i.e., as the solvent molecules move from outside to the inside of the gel phase. At the swelling equilibrium, ΔG reaches to its minimum value. Thus the partial derivative of ΔG with respect to the number of solvent molecules, defined as the excess chemical potential $\Delta\mu_1$, becomes zero at the equilibrium swelling condition:

$$\Delta\mu_1 = \left(\frac{\partial \Delta G}{\partial \Delta n_1}\right)_{T,P,n_2} = RT\left[\ln(1-v_2) + v_2 + \chi v_2^2 + N^{-1} v_2^{1/3} v_2^{o2/3}\right] = 0 \tag{2.21}$$

The osmotic pressure π, which relates to the excess chemical potential by the equation:

$$\pi = -\frac{\Delta\mu_1}{V_1} \tag{2.22}$$

becomes also zero at the swelling equilibrium.

2.5. Phase Separation Phenomena

Phase separation phenomena in polymer solutions are brought about by variations in temperature, pressure, ionic concentration of the network, pH and solvent activity. A network-solvent system may also exhibit phase separation where three phases of different concentrations may exist in equilibrium inside the swollen network. One of the phases is pure solvent $(v_2 = 0)$. The remaining two phases are a less swollen and a highly swollen phase. Such a state is referred to as triphasic equilibrium, described by the equations;

$$\Delta\mu_1(\nu_2') = \Delta\mu_1(\nu_2'') \tag{2.23}$$

where ν_2' and ν_2'' represent the two coexisting polymer concentrations. This state may be reached by varying the temperature. Phase diagram shown in Fig. 2.2 is constructed by calculating the osmotic pressure for many combinations of volume and either temperature or solvent concentration.

In the upper diagram this information is presented as a series of isotherms, which are curves that specify all possible combinations of pressure and volume at a given temperature. The lower diagram was derived from the upper, but it gives the volume of the gel as a function of temperature or solvent concentration.

The complete phase diagram for the gel has three regions. Below the swelling curve the gel has a negative osmotic pressure and is always unstable; it will expel solvent and shrink until it reaches the zero-pressure swelling curve. Another region represents states with a positive osmotic pressure, which are stable only if there is no excess solvent, the gel could absorbs in order to expand. Between these realms is the domain of dual stability, where some part of the gel shrinks and another part swells. The boundary of this region is the coexistence curve for the two phases. The difference in volume between the two phases is greatest along the swelling curve, and it decreases steadily at higher temperature. Ultimately the coexistence curve reaches a maximum temperature where the two phases are identical where they cease to exist as distinguishable phases. That is the critical point of the gel [28].

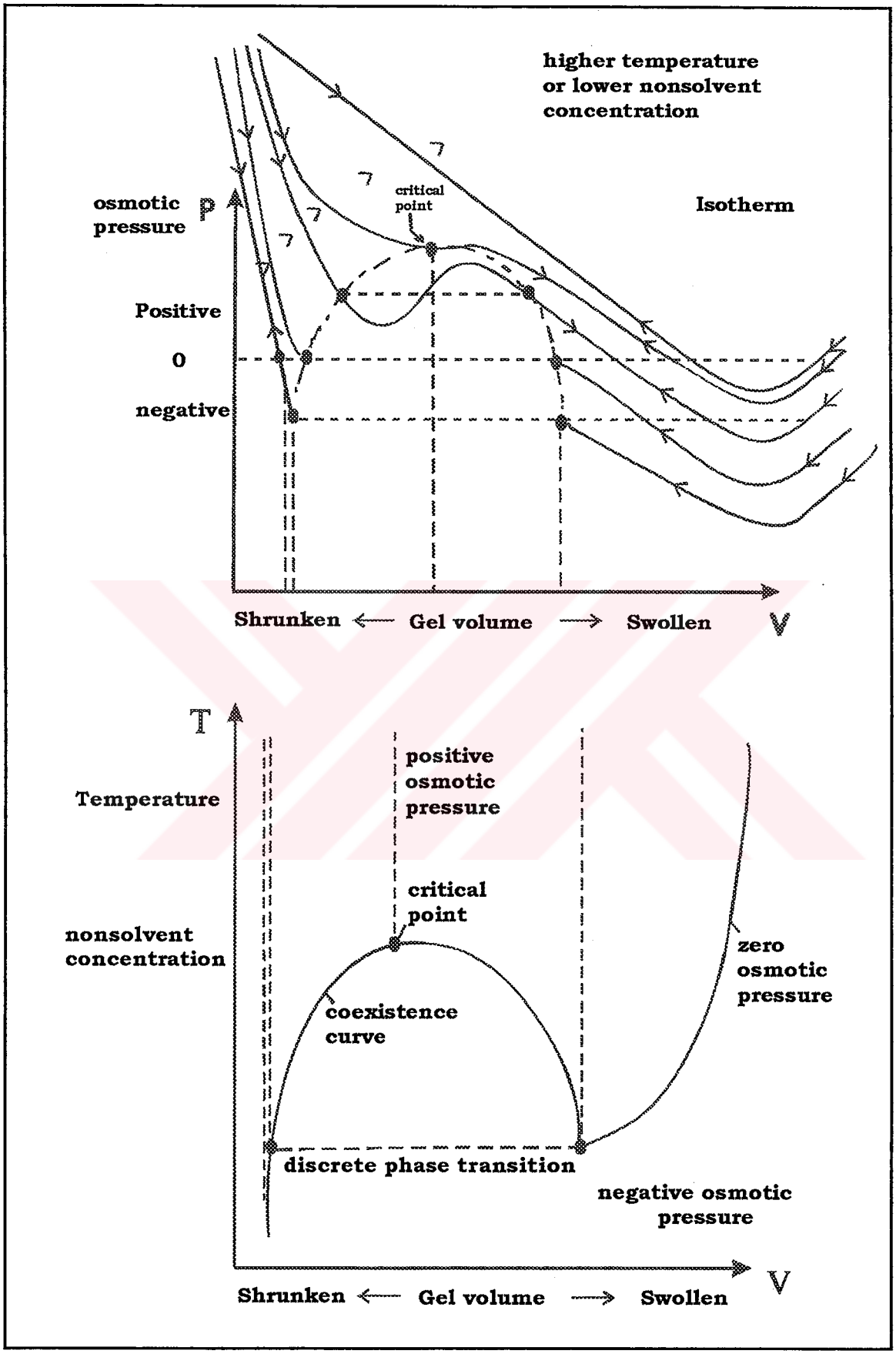


Figure. 2.2: The phase diagram of a gel

2.6 Fundemental Interactions and Gel Phase Transitions

2.6.1 Van der Waals Interaction

Van der Waals interaction is a non-specific attractive force. It arises when any two atoms are located in distance of 3 to 4 A°. The basis of van der Waals interaction is change in the distribution of electronic charge around an atom with time. At a moment, the charge distribution is not perfectly symmetric. This temporary asymmetry in electron distribution around an atom causes a similar asymmetry in that around its neighbouring atoms. This interaction between a pair of atoms increases as they come closer. At a short distance, very strong repulsive forces become dominant due to overlapping of the outer electron clouds. The van der Waals interaction energy of a pair of atoms is considerably weaker than hydrogen or electrostatic bonds [29].

A partially hydrolyzed poly(acrylamide) gel undergoes phase transition in acetone-water mixtures because of polymer-polymer affinity resulted from van der Waals interaction. It was necessary to add acetone, a nonpolar pure solvent compared to water, in order to increase the attraction to a sufficient large value to induce the transition. The transition is also observed when the temperature is varied while the solvent composition is fixed near the transition threshold at room temperature. The gel swells at higher temperature and shrinks at lower temperatures.

2.6.2 Hydrophobic Interactions

The hydrophobic groups which cannot interact with water molecules squeeze together to decrease their surfaces that is in contact with water.

Hydrophobic interaction depends strongly on temperature because of that it is based on entropy and enthalpy. Elevating temperature brings about a disorder structure among the water molecules around hydrophobic groups and then they attract each others forcefully. Contrary, hydrophobic interaction is decreased by reduced temperature.

Hydrophobic interaction is in contrast to van der Waals interactions depending on temperature. PNIPA gel is the best example for this expression. Hirokawa observed a volume phase transition at 33.2 °C in PNIPA gels, [30]. Although the gel is in

swollen state at lower temperature due to the hydrophobic interactions, it shrinks at higher temperature.

2.6.3 Electrostatic Interactions

Electrostatic interactions arise between charged atoms and their groups. Electrostatic force caused by electrostatic interactions is given below by Coulomb's Law:

$$F = q_1.q_2 / r^2\varepsilon \tag{2.24}$$

where q_1 and q_2 are charges of atom or atom groups, r is distance between them, ε is dielectric constant of surroundings. Electrostatic force is inversely proportional to the dielectric constant of surroundings. Less dielectric constant in a hydrophobic surroundings results in strong interaction [29]. As a result of it the groups with the same type of charge repel and then the groups with different charge attract each other. This rule is responsible for polymeric chains containing charged groups and polyelectrolyte gels produced by these chains. Repulsion forces occur among positively or negatively charged groups in the polymeric chains of network which forms the gel.

2.6.4 Hydrogen Bonding

Hydrogen bonding forms between two strongly polar molecules which one of them contains hydrogen atom. Partial negative end of one of these molecules is bonded to partial positive end of other by hydrogen bonding. Water molecules linking to each others by hydrogen bonding and protein molecules containing hydrogen bonds are shown as examples. The hydrogen bonds arised from side groups of the chain within the network bring about volume phase transition. For example one network is poly (acrylic acid) (PAAc) and the other is poly(acrylamide) (PAAm). The gel was originally designed and developed by Okano and his colleagues who found that the gel is shrunken at low temperatures in water and the volume increased as temperature rose. There was a sharp but a continuous volume change at about 30 °C [31]. Zhuo and his group indicated that the hydrogen bonds between water molecules and amide groups of polymer chains inside PNIPA gel prepared at -18 °C arranges regularly and exhibits a spiral structure [32].

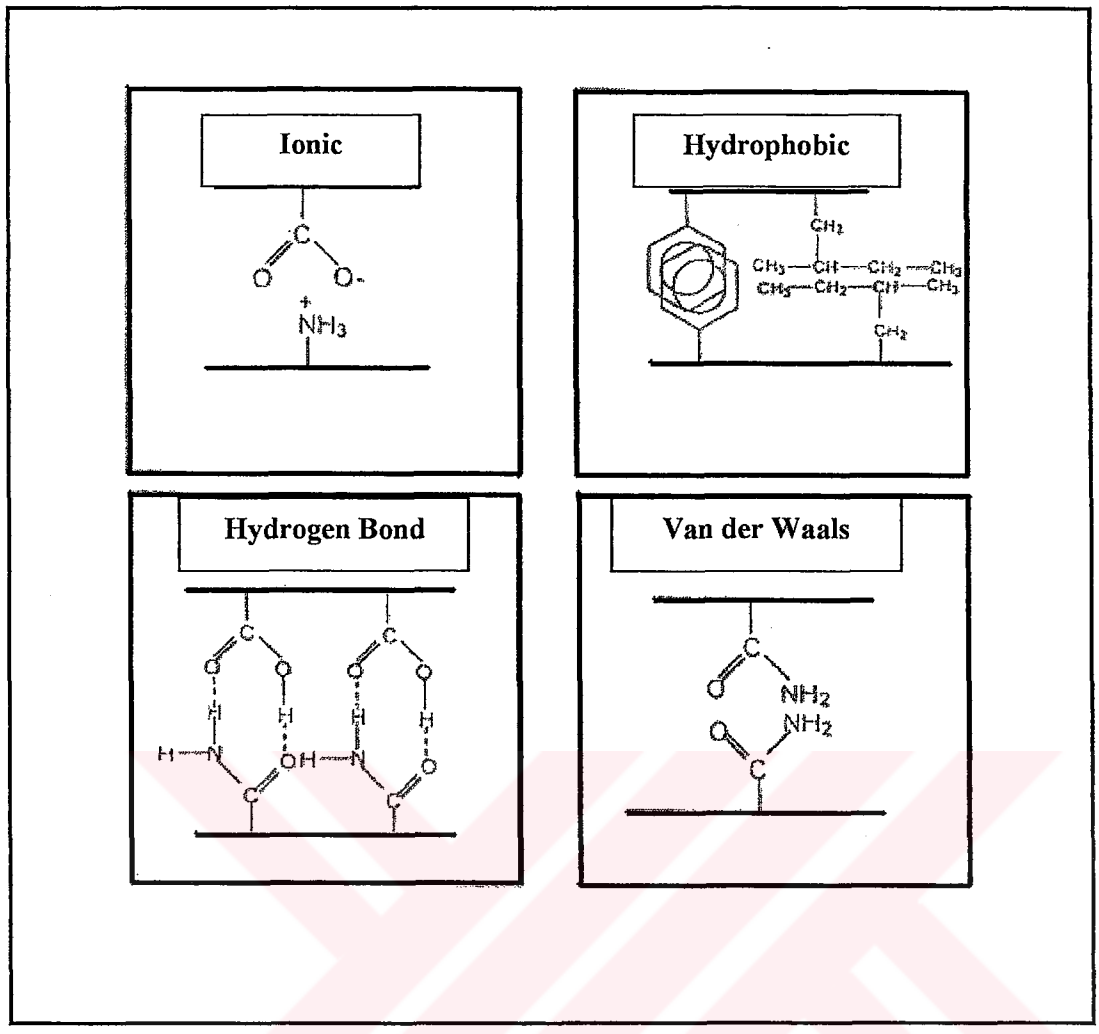


Figure. 2.3: Fundamental Interactions

2.7. The Physical Nature of the Collapse of a Gel

Three forces that act to expand or shrink the polymer network have been identified to examine physical nature of the collapse of a gel. These are the rubber elasticity, the polymer-polymer affinity and the hydrogen ion pressure. Total pressure acting on the gel is the sum of these three components. This sum is called the osmotic pressure of the gel, because it determines whether the gel tends to take up fluid or to expel it.

For a chain in any given configuration the strength of the rubber elasticity depends on how actively the polymer segments are moving. Since the motions are thermally induced, they are proportional to the absolute temperature; hence restoring force that tends to extend or contract the chain is also proportional to the temperature. It should be emphasized that the temperature has no effect on the direction of the force, which

is determined by whether the chain is stretched or compressed compared with the equilibrium length. The temperature affects only the magnitude or the force.

If the gel is swollen, so that the network chains are stretched beyond their equilibrium length, the rubber elasticity tends to make the gel contract. Conversely, a collapsed gel tends to expand under the influence of the rubber elasticity. In this way a directed force of tension or compression along the chains gives rise to a pressure in the gel as a whole. The pressure is positive if it tends to expand the gel and negative if it tends to make the gel shrink. Whereas the sign of the pressure depends only on the volume of the gel, its magnitude is determined by temperature. Raising the temperature strengthens the tendency of a collapsed gel to expand and the tendency of a swollen gel to contract.

The second force acting on the gel, the polymer-polymer affinity can be traced to an interaction between the polymer and the solvent. Interactions can be attractive or repulsive, depending mainly on the electrical properties of the molecules. If the interaction is attractive the polymer can reduce its total energy by surrounding itself with solvent molecules; if the interaction is repulsive the solvent is excluded.

The third and final contribution to the osmotic pressure of the gel, the hydrogen ion pressure, is associated with ionization of the polymer network, which releases an abundance of positively charged hydrogen ions into a gel fluid. However, the positive ions are immersed in a sea of negative charges attached to the polymer network, with the result that the gel as a whole maintains exact electrical neutrality. The mutual repulsion of the hydrogen ion is effectively screened by the background of the negative charges and the ions act much as if they are neutral particles.

The hydrogen ions give rise to pressure. They cannot leave the gel due to the strong electrical attraction between the ions and the negatively charged polymer random motions of the hydrogen ions generate a positive pressure. The pressure is directly proportional to the absolute temperature. If the volume of the gel is held constant, raising the temperature increases the hydrogen ion pressure.

The effect of each of the three components of the osmotic pressure is readily analyzed in isolation. What makes the properties of the gel interesting is the competition among the components. It is the changing balance of forces that gives rise to phase transitions [1].

3. TEMPERATURE SENSITIVITY

3.1. Temperature Sensitive Gels

Temperature is the one of the most significant parameters which affects the phase behavior of gels. Three types of phase transitions have been reported due to the temperature dependence [33]. The first is thermo-swelling type or expansion with temperature [34]. The second is thermo-shrinking type or collapse with temperature [30]. The third is the convexo type that is a mixture of the two types described above [5].

The type of phase transition depends largely on the affinity of monomer units for water. It is important to consider the molecular structure of monomer units in a gel. Thermo-swelling hydrogels mostly contain hydrophilic monomers such as acrylamide (AAm), acrylic acid (AAc) and methacrylic acid. Their transition can be explained by Tanaka's thermal mixing model [5, 30, 34]. On the other hand, the main examples of thermo-shrinking hydrogels are composed of monomers like N-methylacrylamide, N,N'-dimethylacrylamide (NDMA) and N-isopropylacrylamide (NIPA). Also poly(N-vinyl caprolactam) and ethylene oxide containing polymers are examples of thermo-shrinking hydrogels. Transition in their cases cannot be explained by the Tanaka model. These polymers show the same behavior in their aqueous solutions and their solubility decreases when the temperature is increased above the lower critical solution temperature (LCST), so that polymer precipitates. PNIPA is well-known example of thermo-shrinking polymers. The aqueous solution of this polymer can undergo a reversible phase change at approximately 32 °C. The volume phase transition in PNIPA was first reported by Hirokawa [30].

The temperature sensitivity of polymer solutions or polymeric gel is associated with the temperature dependence of the hydrogen bonding and hydrophobic interactions [35]. At lower temperatures, water molecules form cage like structures around the hydrophobic polymer chains with hydrogen bonds. As a result of these hydrogen bonds, nonpolar polymer chains become soluble or swell in water at low

temperatures. At higher temperatures, the hydrogen bonds weaken and the total number of water molecules structured in the vicinity of hydrophobic surfaces decreases and this promotes hydrophobic interactions [36]. Consequently, a rise in temperature strengthens the hydrophobic interactions. On heating a polymer solution or a polymer gel, a transition from swollen to collapsed or soluble to insoluble state occurs at a critical temperature. The total entropy of the polymer-solvent or network-solvent system must increase at higher temperatures. However, the entropy of the network or polymer solution decreases when it becomes insoluble or it shrinks into a more compact and ordered state. The reduced motional freedom of polymer chains in the compact state is compensated by a gain in entropy due to the destruction of structured water around the hydrophobic parts of polymer chains.

There have been many reports of attempts to control the thermally induced volume phase transition in gels, for example through the use of mixed solvents, the addition of salt, the copolymerization of an electrolyte monomer and the addition of surfactants [37,38,39,40]. Previous results show that the polymer structure and composition not only determine the swelling characteristics of the gel but also influence the LCST of the hydrogel [33].

3.2. Properties of Poly(N-isopropylacrylamide) Gels

There is a hydrophilic and hydrophobic balance of polymer side chains corresponding to hydrophilic (-CONH-) and hydrophobic (-CH $(CH_3)_2$) regions in the PNIPA gel [41]. The gel is swollen and the polymer chains expand in water at temperature below $\approx$ 34 °C which is lower critical solution temperature (LCST) of PNIPA gel.

Due to hydrogen bonds between the hydrophilic groups and water, water molecules are structured around the hydrophobic groups. These structured water molecules act cooperatively to form a cage-like structure which leads to a good solubility of the whole gel system. As the temperature is raised, these hydrogen bonds are destroyed, the hydrophobic groups are naked and the hydrophobic interactions become strong. The polymer chains begin to dehydrate. When the temperature is above the LCST, the hydrophobic interactions turn to be dominant and the polymer chains collapse and aggregate abruptly. Thus, phase transition course occurs. On the other hand, due to the increased thermal energy (at the temperature above LCST), the thermal motion

of the polymer chains gets enhanced. The attractive forces induced by the increased hydrophobic interactions also drive the chains to collapse and tangle with each other and the structured water is excluded to the free water. During this course, the entropy of the polymer chains is decreased and the entropy of pristinely structured water surrounding the polymer chains of gel gets increased. But as a whole, the total entropy of the gel system including the polymer chains and the surrounding water is increased [42].

The temperature sensitivity of PNIPA gel has attracted great attention in the last years due to both fundamental and technological interests. PNIPA gels having phase separation property has been used in many devices, for instance, controlled drug release [43], protein solution dehydrating [44], phase separations in biotechnology, processing of agricultural products, sensors and actuators [20, 41].

It was experienced to prepare interpenetrating polymer network produced from PNIPA for drug delivery [43]. Dried interpenetrating PNIPA by freeze-dry system was equilibrated in a 1 mg/ml 5-fluorouracil solution at 25 °C for two days to load the drug into the gel. Then it was dried by the same method and immersed in 0.1 M phosphate buffer solution at 25 °C. Another polymer sample was immersed in the same solution at 37 °C. After measurements of 5-fluorouracil release it was observed that at the lower temperature, the release of the drug was controlled by diffusion of water molecules in the gel network and at the higher temperature, the drug inside the gel could not diffuse into the medium after a burst release of the drug on the surface of the gel.

Macroporous PNIPA hydrogels were synthesized with poly(ethylene glycol) (PEG) as pore-forming agent for controlled release of proteins(bovine serum albumin) [44]. Gels with larger pore size caused by PEG adhered to and loaded more proteins into its network. The reason of this event is that bovine serum albumin molecules may enter into the gel network and later be released with a nearly uniform speed.

3.3. Methods for the Preparation of Fast-Responsive Hydrogels

In many applications, such as for drug delivery systems, separation operations in biotechnology, progressing of agricultural products, sensors and actuators, a fast response rate of the hydrogel to the external stimuli is needed. In order to increase the response rate of gels, several techniques were proposed:

1. Sub-micrometer sized gel particles [45]: Since the rate of response is inversely proportional to the square of the size of the gel [46], small PNIPA gel particles respond to the external stimuli more quickly than bulk gels.

2. Gels having dangling chains [47, 48]: Dangling chains in a gel easily collapse or expand upon an external stimulus because one side of the dangling chain is free.

3. Macroporous PNIPA gels [20]: The kinetics of gel volume change involves absorbing or desorbing solvent by the polymer network, which is diffusive process. This process is slow and even slower near the critical point. However, for a network having an interconnected pore structure, absorption or desorption occurs through the pores by convection, which is much faster than the diffusion process that dominates the non-porous gels.

To prepare macroporous PNIPA networks, one idea is to start the NIPA polymerization below the lower critical solution temperature (LCST) of PNIPA and then elevating the temperature above it. Macroporous PNIPA gels were synthesized above their LCST in the presence of hydroxypropyl cellulose acting as a pore-forming agent. Other idea is to apply a radiation induced polymerization method. Use of inert diluents such as poly(ethylene glycol) during the network formation process was also suggested for the preparation of macroporous PNIPA [20].

4. MACROPOROUS HYDROGELS

Macroporous hydrogels have an interconnected pore structure and, they are able to absorb high amount of solvent molecules as quickly as possible. Crosslinked polymers with a macroporous structure are widely used in separation processes as ion exchange resins and as specific sorbents. Application areas of the macroporous hydrogels have been promoted such as in drug delivery systems, manufacturing of agricultural products, actuators, separation processes in biotechnology and sensors [20, 49].

Porous structure in a polymer network can be created by using inert diluents called pore-forming agent. In this technique, the inert diluent is soluble in the monomer phase: After polymerization-crosslinking reactions, removing the diluent from the network results in a porous structure inside the gel matrix. The network synthesized without inert diluent consists of a continuous polymer phase while the network synthesized with inert diluent consists of voids (pores). Several diluents were used in the polymerization to create pores such as solvents or nonsolvents for polymer chains or inert linear polymers. In order to form macroporous structure in dried state, a phase separation must occur during the crosslinking process. Phase separation generally takes place on a macroscale called macrosyneresis or deswelling [19, 20].

4.1 Approaches for the Preparation of Macroporous Copolymer Networks

Several polymerization techniques have been used to generate macroporous structure within the gels. In order to obtain macroporous copolymer networks in the form of beads which have the sizes ranging from 0.1 to 1.5 mm in diameter, the suspension polymerization technique has been used (Fig. 4.1) [19]. Inert diluent is first dissolved in the mixture consisting of monomer, crosslinker and the initiator and then transferred to the continuous phase under agitation. Monomer droplets, in which free-radical crosslinking copolymerization occurs, are distributed within the continuous phase. Finally, the beads produced are extracted with a good solvent to remove soluble polymers and diluents from the network.

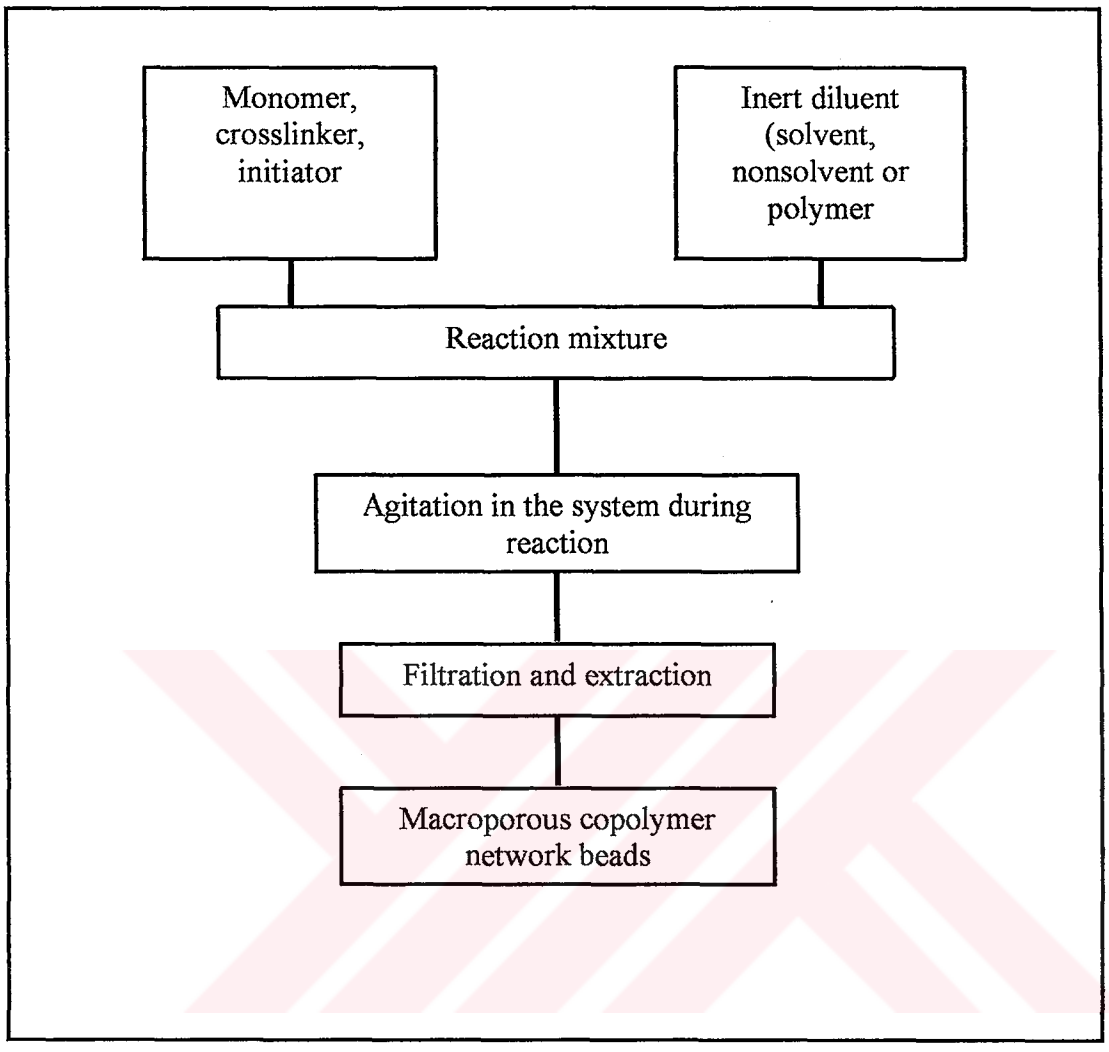


Figure. 4.1: Suspension polymerization system for the synthesis of macroporous networks [19].

For water insoluble monomers such as styrene, the inert diluent used to create pores should also be insoluble in water, but soluble in the droplet (monomer) phase. Conversely, for water soluble monomers, such as acrylamide, hydrophilic inert diluents are used.

Another method for obtaining macroporous structure is the freeze-thaw technique that consists of freezing the initial polymerization mixture (monomer + crosslinker + diluent) to a solid monomer matrix containing diluent crystals. Polymerization of monomer matrix using UV radiation and removing of the diluent by thawing result in a macroporous film or bead. Such gels are also called "cryogels".

The cryo word is from a Greek word kryos that has meaning frost or ice. The desired property of the cryogel, continuous supermacroporosity, is established by solvent crystallization, when the temperature is held below the freezing point of the solvent which is generally water. The monomers and initiators are concentrated in unfrozen micro zones of the apparently frozen system. The polymerization reactions proceed in the unfrozen micro zones. The crystals of reagent-free solvent grow during freezing, merge with other crystals until a continuous system of a frozen framework is created. Upon thawing after completed polymerization, the system consists of a monolithic matrix with continuous macroporous channels filled with liquid solvent (Fig 4.2). Since the cavities are made by the frozen solvent, its crystals act as a pore-forming agent [50].

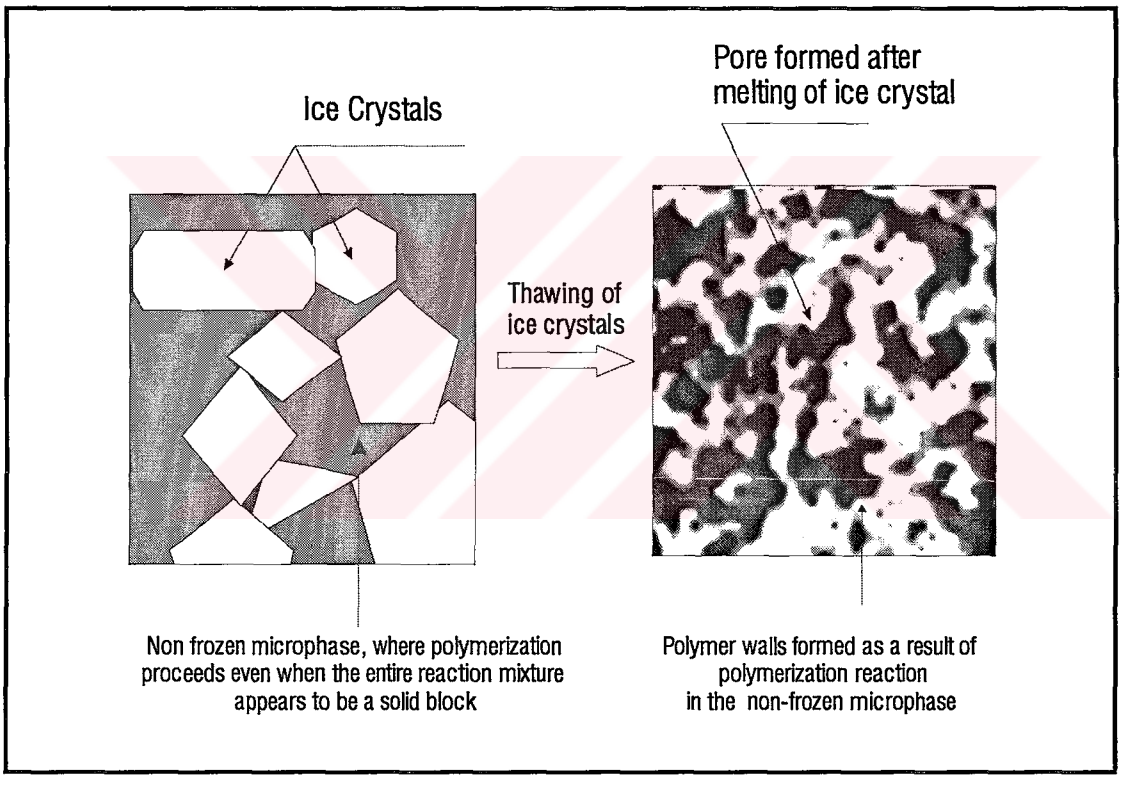


Figure. 4.2: Schematic presentation of cryo-polymerization and formation of macroporous structure in a continuous polymer matrix [50].

The appearance of the cryo-polymerized NIPA-based gel is completely different as compared to the gels produced from exactly the same reaction mixture in a liquid state. These gels prepared by the conventional methods are transparent and rather brittle. In contrast, cryo-polymerized gels are opaque, sponge like and elastic. These gels can be easily compressed by hand to remove water accumulated inside the

pores. When the compressed piece of gel was submerged in water, it swells within 1-2 s and restores its original size and shape [50].

PNIPA cryogel was synthesized in an organic solvent (dimethylsulfoxide, DMSO) at a temperature below the melting point of DMSO [51]. The porous structure of cryogels was attributed to the pore-forming capability of DMSO crystals generated during polymerization at a temperature below DMSO melting point. In a frozen system, there exist two phases, a solid and a liquid phase. During the polymerization of cryogels, the reaction was carried out in the liquid phase that was dispersed within the solid phase. The solid phase is composed by many DMSO crystals which could act as a pore-forming agent during the polymerization. After thawing at room temperature after cryo-polymerization, many pores would be formed in the spaces originally occupied by DMSO. Since these DMSO solvent crystals acted as pore-forming agent, the number and size of the pores formed would depend on the number and size of the DMSO crystals formed during cryo-polymerization which, in turn, would depend on the relative concentration of the solution.

Inorganic salts were also used to produce a macroporous structure in PNIPA gels [52]. In this method polymerization proceeds in NaCl solution in which phase separation occurs due to the fact that PNIPA chains cannot dissolve in the reaction medium and they precipitate.

Another idea to prepare macroporous PNIPA networks is to start the NIPA polymerization below (22.5 °C) the lower critical solution temperature of PNIPA at a range of crosslinker concentration between 0.2 and 30 % wt (with respect to monomers) [20]. After passing a critical crosslinker concentration (2-5 % BAAm), the network structure changes from homogeneous to heterogeneous ones as shown in Fig. 4.3. Further increase of crosslinker content increases both the rate of swelling and the porosity of the networks. Heterogeneous PNIPA networks consist of spherical globules called microspheres of 0.1-0.5 μm in diameter aggregated to large, unshaped, discrete clusters with dimensions of a few μm. At 30 % BAAm, the structure looks like cauliflowers, typical for a macroporous network.

4.2 Formation of Porous Structures during Crosslinking

A macroporous gel is formed by the free-radical crosslinking copolymerization (FCC) reactions. This reaction system consists of monomer, crosslinker, initiator and diluent. The reaction is initiated by the decomposition of the initiator; After a given time (gelation time), a polymer network forms, which is swollen in the monomer-solvent mixture. As the reaction time is further increased, the amount of soluble components decreases while the amount of crosslinked polymer (network) increases. Finally only the network and diluent remain in the reaction system. Amounts of the crosslinker and the inert diluent are the main factors determining the structure and properties of crosslinked copolymers.

Fig. 4.3 demonstrates various gel structures formed depending on the synthesis parameters. If the gel preparation reactions proceed in bulky system and in the presence of small amount of crosslinker, inhomogeneous (A) gel forms. In this type of gel, the network consists of regions of different crosslinking densities. This difference of the crosslink density is due to the fact that the crosslinker usually has a reactivity twice that of monomer since it has two vinyl groups while monomer has one. At the beginning of the copolymerization, higher amount of crosslinker is spent than the monomer. At later reaction times, however, the monomer is consumed more than the crosslinker. This type of gel is called inhomogeneous gel. ((A) gel in Fig. 4.3)

(B) gel shown in Fig. 4.3 with an expanded structure is obtained when the polymerization system consists of a large amount of a good solvent as an inert diluent. This type of gel is turned into a collapsed form by removing of diluent after its preparation. Because of this fact it is nonporous in the glassy state. Finally, (B) gel swells in good solvents much more than (A) gel prepared in bulky system.

Heterogeneous (C) gel forms if the crosslinker content in the reaction mixture containing monomer + diluent is increased above a critical level. This type of gel formation arises according to the macrosyneresis model [19, 20]. This model leads to the formation of microgels as an intermediate step of macrogel formation. During polymerization and crosslinking processes, new microgels form as a discontinuous phase. Separated liquid from the microgels is in the form of the continuous phase. These microgels react each other through their radical centers and pendant vinyl

groups to form agglomerates. Finally, a macrogel consisting of two continuous phases will form; voids of different sizes are created after removing of the diluent from the macrogel.

If a good solvent is used as the inert diluent, a discontinuous macrogel phase is generated due to the fact that the amount of monomer and growing chains cannot occupy the whole polymerization system ((D) gel). Further increasing the amount of solvent brings about decrease in the size of gel particles as small as ordinary macromolecules ((E) gel).

If a non-solvent or a linear polymer is used as the inert diluent, a macrophase separation will occur. Discontinuous macrogel phase is distributed in the continuous liquid phase containing monomer and diluent ((D) gel). With increasing reaction time, the polymer content increases so that the agglomeration processes between the polymeric phases arise. As a result of these agglomeration processes, macrogels turn into larger clusters called microspheres and then, new clusters generated by polymerization become continuous polymer phase. Thus a polymeric system consisting of two continuous phases forms. Finally macroporous copolymer is produced by removal of the diluent from the gel.

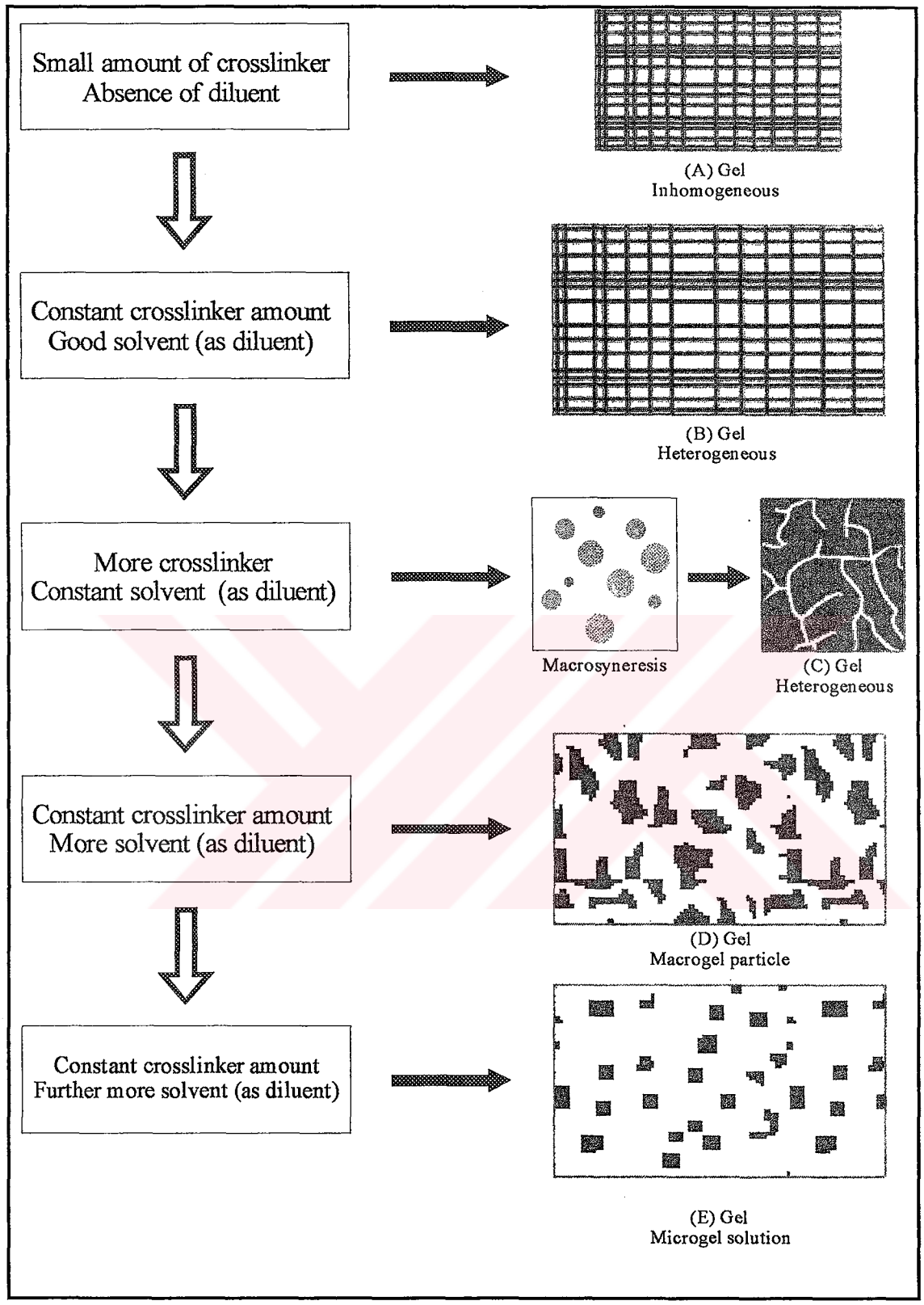


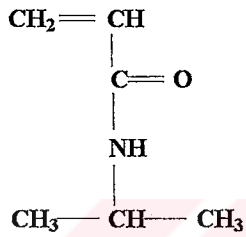
Figure. 4.3: Formation of various structures in free-radical crosslinking copolymerization of vinyl/divinyl monomers with or without using a diluent [19].

5. EXPERIMENTAL PART

5.1. Materials and Chemicals

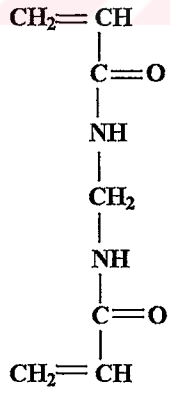
a) Monomers:

N-isopropylacrylamide (NIPA, Aldrich) was used as received. Its molecular weight is 113.16 g/mol.



NIPA

N,N'-methylenebisacrylamide (BAAm, Fluka) was used as the crosslinking agent in the polymerizations and used as received. Its molecular weight is 154.17 g/mol.

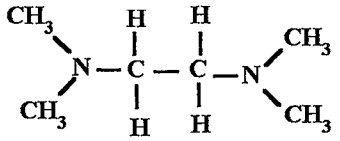


BAAm

b) Initiators:

Ammonium persulfate ($(NH_4)_2S_2O_8$, APS, Merck) was used as received. Its molecular weight is 228.20 g/mol.

N,N,N',N'- tetramethylethylenediamine (TEMED, Carlo Erba) was used as received. Its molecular weight is 116.21 g/mol.



TEMED

c) Pore-forming Agent:

Poly(ethylene glycol) (PEG, Fluka) was used as a pore-forming agent and used as received. Its molecular weight is 300 g/mol and it is a liquid at room temperature.

d) Solvent:

Distilled water was used for the synthesis of the hydrogels, as well as for the swelling and deswelling processes.

5.2. Experimental Set-up and Equipment:

5.2.1. Hot Water Bath

The hot water bath (BÜCHI Waterbath B-480) is used for the deswelling processes.

5.2.2. Digital Thermometer

The digital thermometer (Checktemp 1 Pocket Thermometer) is used for both deswelling and reswelling processes.

5.2.3. Electronic Balance

The electronic balance of Precisa 205A was used in the experiments. It displays to four decimal places and its weighting capacity is 205 g.

5.2.4. Temperature-Sensitive Oven

The oven (Nüve EN 400) is used for the polymerization reactions at 50 °C. It runs in range of 0 - 80 °C with a sensitivity of 1 °C.

5.2.5. Digital Compass

The diameters of the cylindrical gel samples were measured using a calibrated digital compass (Mitutoyo). The device has a measuring range between 0-150 mm with an accuracy ± 0.02 mm.

5.2.6. Tubes

3.90-4.05 mm internal diameter and 10 cm long glass tubes were used in the gelation experiments.

5.2.7. Uniaxial Compression Apparatus

In order to measure mechanical properties of the gel samples, a home-made uniaxial compression apparatus was used. This apparatus consists of four parts as shown in Fig.4.1.

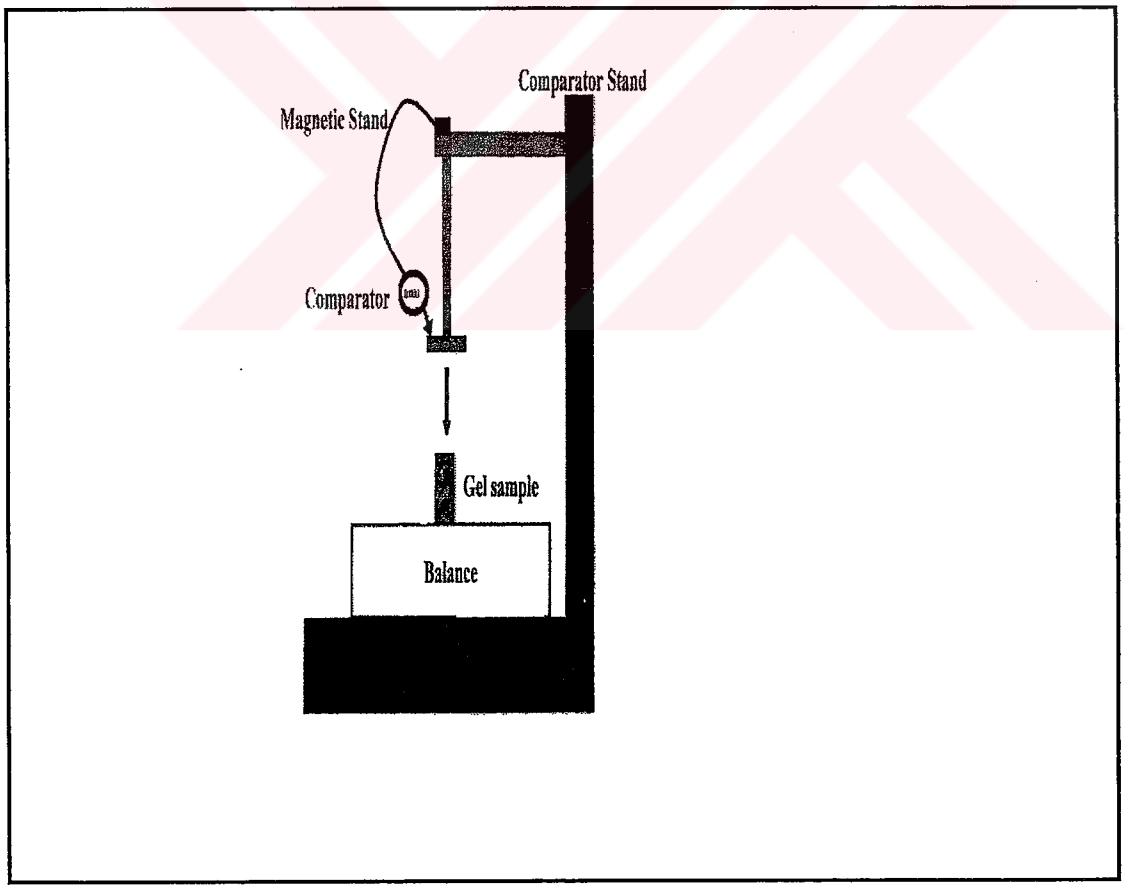


Figure. 5.1: Elastic modulus measurements and these of the gels during measure.

5.3. Experimental Procedure

5.3.1. Synthesis of PNIPA Hydrogels

The gels were prepared by free radical crosslinking copolymerization of NIPA and BAAm at both 9 and 50 °C in the presence of TEMED (0.25 ml / 100 ml reaction solution) and APS (0.0035 M) as the redox initiator system. Aqueous PEG-300 solutions of various compositions were used as the polymerization solvent and as pore-forming agent. The initial monomer concentration was fixed at 0.7 M, which corresponds to 7.92 w/v %. Two sets of experiments were carried out: In the first set, the crosslinker (BAAm) content was fixed at 1.2 mol % (with respect to the monomer), while the PEG content of the PEG-water mixture was varied between 0 and 70 v/v %. This set of experiments was carried out both at 9 °C and 50 °C. In the second set, PEG content was fixed at 70 v/v % and the polymerization temperature was 9 °C. Here, only the amount of the crosslinker BAAm was varied between 1.2 and 15 mol %. The amounts of the chemicals used in the gel preparation are compiled in Table 1 and Table 2. General synthetic procedure is given below:

NIPA, BAAm and APS were weighed in amounts listed in Table 1 and Table 2. They were then dissolved in a few ml of distilled water. After addition PEG-300, nitrogen gas was bubbled through the mixture for 15 minutes in order to eliminate oxygen from the system. Finally, 1 ml TEMED stock solution (2.5 ml TEMED / 100ml water) was added and then, the reaction solution was completed to 10 ml with distilled water in a volumetric flask. After shaking the flask, the solution was poured into the glass tubes. The tubes were sealed and then the reaction was conducted at the desired temperature for 48 h. Homologous series of hydrogels were prepared in this way. The formation reactions of PNIPA hydrogel is given in Fig.4.2.

After polymerization, the crude hydrogels were freed from the glass tubes and they were cut into samples of about equal length. Each gel sample was then placed in an excess of distilled water at room temperature.

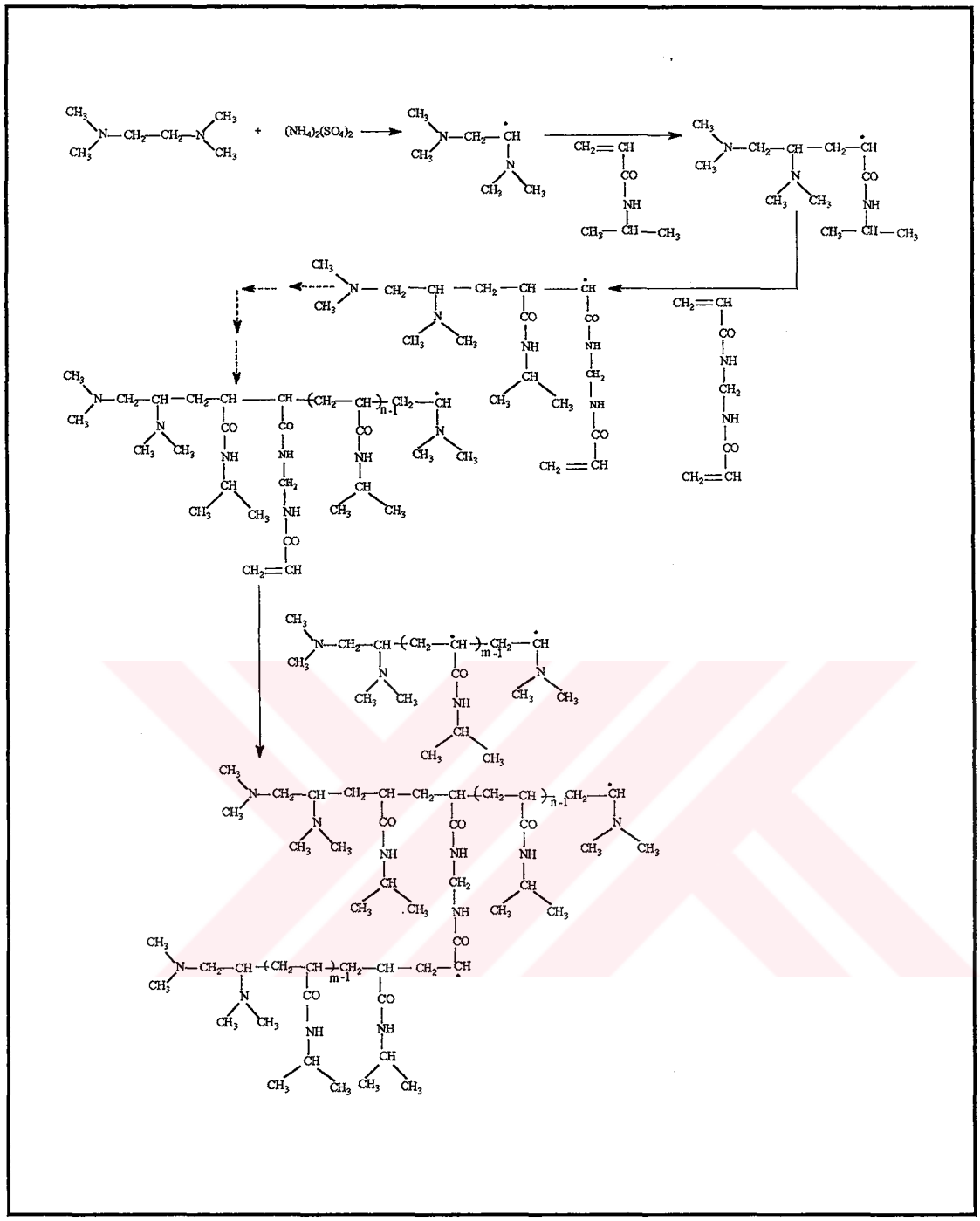


Figure. 5.2: Synthesis Reactions of PNIPA Hydrogels

Table 5.1. Feed compositions for the synthesis of PNIPA hydrogels at both 9 and 50 °C in the presence of various PEG-300 contents. Total reaction volume is 10 ml, completed with water.

PEG (ml)	PEG % content	NIPA (g)	BAAm (g)	APS (g)	TEMED (ml)
0	0	0.792	0.0126	0.008	0.025
1	10	0.792	0.0126	0.008	0.025
2	20	0.792	0.0126	0.008	0.025
3	30	0.792	0.0126	0.008	0.025
4	40	0.792	0.0126	0.008	0.025
5	50	0.792	0.0126	0.008	0.025
6	60	0.792	0.0126	0.008	0.025
7	70	0.792	0.0126	0.008	0.025

Table 5.2. Feed composition for synthesis of PNIPA hydrogels at 9 °C at various crosslinker contents. The total reaction volume is 10 ml, completed with water.

BAAm (g)	mol BAAm %	NIPA (g)	APS (g)	TEMED (ml)	PEG (ml)
0.0126	1.2	0.792	0.008	0.025	7
0.0216	2.0	0.792	0.008	0.025	7
0.0431	3.9	0.792	0.008	0.025	7
0.0718	6.3	0.792	0.008	0.025	7
0.1079	9.1	0.792	0.008	0.025	7
0.1472	12	0.792	0.008	0.025	7
0.1906	15	0.792	0.008	0.025	7

5.3.2. Synthesis of PNIPA Cryogel [50]

The gels were prepared by free radical crosslinking copolymerization of PNIPA and BAAm in water at -25 °C. TEMED (1.2 % of the total NIPA + BAAm mass) and APS (0.83 % of the total NIPA and BAAm mass) were used as the redox initiator system. The mole ratio of monomer to crosslinker (NIPA:BAAm) and the initial monomer concentration were fixed at 30:1 and 4.5 wt/v %, respectively. The synthetic procedure is given below:

NIPA (1.337 g), BAAm (0.006 g) were weighed and dissolved in distilled water. After nitrogen bubbling for 15 minutes, TEMED (0.013 ml) was added from the same stock solution mentioned above. Then, the reaction mixture was taken into a water-ice bath for 2-3 minutes. After addition APS (0.0116 g), the reaction mixture was poured into a plastic 5-ml syringe with closed outlet at the bottom. The plastic syringe was placed into the deep-frost refrigerator at -25 °C. The sample was kept at -25 °C for 24 h and then thawed at room temperature. The cryogel matrix was taken out of the syringe and washed in distilled water.

5.4. Characterization Methods

5.4.1. Equilibrium Swelling Measurements

The gel samples were incubated in distilled water for two weeks to reach equilibrium swelling state at room temperature. The swelling ratios of the hydrogels were measured by using volumetric and gravimetric techniques. For volumetric measurements, the diameters of the gel rods after preparation (D_o) and after swelling (D) were measured by a calibrated digital compass. The equilibrium swelling ratio of the gel samples with respect to the after preparation state, V/V_o, was calculated as

$$volume\ swelling\ ratio = \frac{V}{V_o} = \left(\frac{D}{D_o}\right)^3 \tag{5.1}$$

For gravimetric measurements, the weights of the gel rods after preparation (m_o) and after swelling (m_{sw}) were measured by the electronic balance. The equilibrium weight swelling ratio of the gel samples with respect to the after preparation state was calculated as

$$\text{Weight swelling ratio} = \frac{m_{sw}}{m_o} \tag{5.2}$$

5.4.2. Deswelling Kinetic Measurements

For the deswelling kinetics measurements, the hydrogels equilibrium swollen in water at room temperature were jumped into hot water at 48 °C. Deswelling kinetics of the hydrogels was measured gravimetrically after excess water was wiped off the hydrogel surface. The weight changes of the hydrogels were recorded during the shrinking process at regular time intervals. Water retention was defined by the relative mass (m_{rel}) parameter, which was calculated according to the following formula:

$$m_{rel} = \frac{m_t}{m_{sw}} \tag{5.3}$$

where m_t is the mass of the gel sample at time t and m_{sw} is its swollen mass at room temperature.

5.4.3. Reswelling Kinetic Measurements

After collapsing of PNIPA gels in water at 48 °C, they were again jumped into water at room temperature (25 °C). The reswelling kinetics of the shrunken samples was determined gravimetrically after the excess water was wiped off the hydrogel surface. The weight of the hydrogels was recorded at convenient time intervals. The water uptake or the water retention was calculated in terms of the relative mass parameter m_{rel}, given by eq. (5.3).

5.4.4. Mechanical Measurements

Uniaxial compression measurements were performed on hydrogels after their preparation state. All the mechanical measurements were conducted in a thermostated room at 25 °C.

Briefly, cylindrical gel sample after preparation was placed on the electronic balance (Fig. 5.1). A load was transmitted vertically to the gel through a road fitted with a PTFE (Teflon) end-plate. The force acting on the gel was calculated from the reading of the balance m as F=mg, where g is gravitational acceleration (g = 9.803002 $m.s^{-2}$). The resulting deformation $\Delta\ell = \ell_o - \ell$, where ℓ_o and ℓ are the initial undeformed and deformed lengths, respectively, was measured using a digital comperator (IDC type

Digimatic Indicator 543-262, Mitutoyo) which was sensitive to displacements of 10^{-3} mm. The force and the resulting deformation were recorded after 20 sec of relaxation. The measurements were conducted up to about 20 % compression. The deformation ratio α (deformed length / initial length) was calculated as $\alpha = 1 - \Delta\ell/\ell_o$. The corresponding f was calculated as $f = F / A$, where A is the cross-sectional area of the specimen, $A = \pi (D_o/2)^2$, where D_o is its initial diameter.

The elastic modulus G_o was determined from the slope of the linear dependence of stress-strain isotherms by using the equation

$$f = G_o (\alpha - \alpha^{-2}) \qquad (5.4)$$

6. RESULTS AND DISCUSSION

As pointed out in the introduction, two sets of experiments were carried out in order to prepare fast-responsive PNIPA hydrogels. The hydrogels were prepared by free-radical crosslinking copolymerization of NIPA monomer and BAAm crosslinker in aqueous PEG solutions. PEG-300/water mixtures of various compositions were used as the polymerization solvent and as the pore-forming agent.

In the first set of gelation experiments, PEG-300 content of the solvent mixture was varied between 0 and 70 v/v %. The crosslinker (BAAm) content was fixed at 1.2 mol %. In the second set, the PEG content of the solvent mixture was fixed at 70 v/v % while BAAm content was varied over a wide range. In order to observe the effect of the gel preparation temperature on the swelling behavior of the resulting hydrogels, the gelation experiments were carried out both at 9 °C and 50 °C.

Before presenting results of the swelling kinetics measurements, in the following section, the equilibrium swelling behavior of PNIPA gels will be given for the two sets of hydrogels.

6.1. Equilibrium Swelling Behavior of PNIPA Hydrogels:

Equilibrium swelling degree of PNIPA hydrogels prepared in the presence of various amounts of the pore-forming agent PEG-300 and of the crosslinker BAAm was determined at 25 °C in water. Fig. 6.1 shows the swelling ratio V/V_0 of the hydrogels plotted as functions of the PEG v/v % in the polymerization mixture and of the crosslinker BAAm. Open symbols represent data of PNIPA hydrogels prepared at 50 °C, while filled symbols represent those obtained at 9 °C. It is seen that the equilibrium swelling ratio V/V_0 of PNIPA gels in water increases with increasing amount of PEG-300 present in the gel formation system. Another point shown in Fig. 6.1 is that, if PEG content is less than 40 v/v %, the gels formed at 50 °C swell in water much more than those formed at 9 °C. However, if the PEG content is 40 % or more, both 9 °C and 50 °C- gels exhibit the same swelling behavior in water. This

behavior can be explained with the extent of the van der Waals and Hydrogen-Bonding interactions present in the gel formation system; if the PEG content is less than 40 v/v %, these interactions dominate during the gel formation process, so that the growing PNIPA chains in the gelation system exhibit temperature sensitivity. Thus, if the gel preparation temperature (T_{prep}) is 50 °C, they separate out of the gel phase and lead to the formation of polymer aggregates. This results in the formation of macroporous hydrogels with a high swelling capacity. However, if T_{prep} is 9 °C, which is below the LCST of PNIPA, the growing chains remain in the solution phase and result in a less porous hydrogel matrix with a relatively low swelling capacity. On the other hand, in PEG-water mixtures with PEG contents more than 40 %, PNIPA chains become temperature-insensitive, so that the resulting hydrogels prepared both at 9 °C and 50 °C show the same swelling behavior.

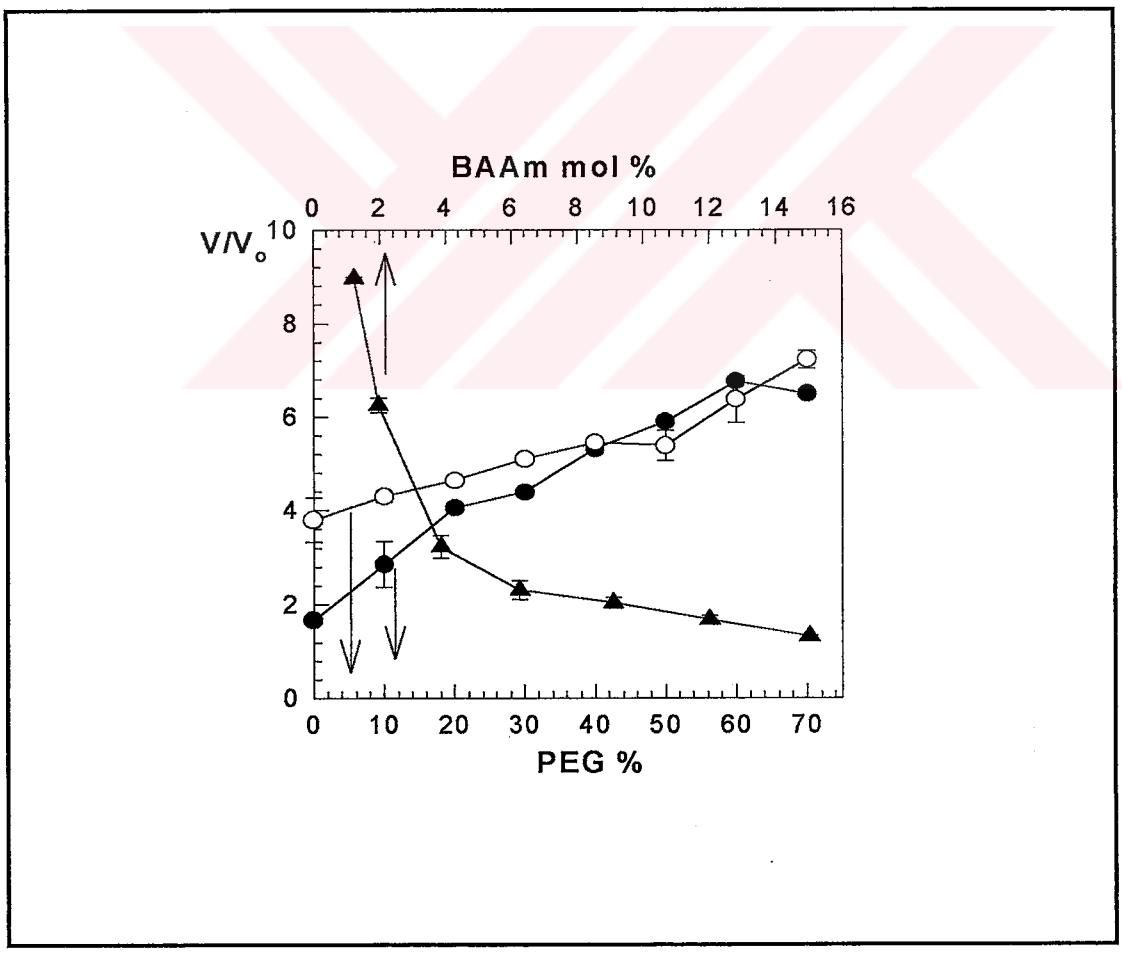


Figure. 6.1: The equilibrium swelling ratio V/V_o of PNIPA hydrogels shown as a function of PEG % and BAAm %. The gel preparation temperature (T_{prep}) = 9 °C (filled symbols) and 50 °C (open symbols)

Fig. 6.1 also shows that, the higher the crosslinker (BAAm) content, the lower the swelling capacity of the resulting hydrogels. This is expected. Rising the crosslinker content in the gel brings about a decrease in the mesh size of the gel network. This event causes the hydrogel to absorb less amount of water in the equilibrium swelling state.

6.2. Effect of PEG-300 Concentration

In this section, the crosslinker (BAAm) content was fixed at 1.2 mol %. T_{prep} was also fixed at 9 °C. The amount of PEG-300 in the PEG/water mixture was varied between 0 and 70 v/v %. The resulting hydrogels were subjected to swelling and deswelling kinetics measurements. For this purpose, they were first swollen in water at 25 °C to their equilibrium state. Thereafter, they were immersed in water at 48 °C and the deswelling process was monitored by recording the relative gel mass m_{rel} as a function of the time of deswelling. After attaining the gel samples to the equilibrium collapsed state in water at 48 °C, they were immersed again in water at 25 °C and the reswelling behavior was monitored until the new equilibrium state is obtained. The results of measurements are presented in Fig. 6.2, which shows the deswelling and reswelling processes of PNIPA gels at 48 °C and 25 °C, respectively. The PEG-300 contents used in the hydrogel preparation are indicated in the Figure.

Let us first discuss the deswelling behavior of gels at 48 °C (left part of the dotted vertical line in Fig. 6.2). The deswelling response rate of the gels to an external temperature change from 25 °C to 48 °C increases with increasing amount of PEG used in the hydrogel preparation. For example, PNIPA gel prepared in the absence of PEG-300 reaches to the equilibrium collapsed state in 20 minutes. This time decreases with increasing PEG content and becomes only 4 minutes at 70 v/v % PEG. Moreover, in the first minute of the deswelling process, PNIPA gel without PEG loses only 20 % of its water content, while this amount increases to 85 % in PNIPA gel prepared with 70 % PEG. These results can be explained with the fact that PEG-300 present in the gel formation system act as a pore-forming agent [53, 54] so that the porous structure formed in the resulting hydrogels allows an easy diffusion of the water molecules outside of the gel phase. Thus, the pores can offer enough water-releasing channels for the inner water molecules and the water can easily be squeezed out of the gel matrix at 48 °C, which leads to a much faster

deswelling rate [54]. The higher the PEG-300 content of the gel formation system, the higher the porosity of the resulting networks, the faster the deswelling rate of the hydrogels above their LCST.

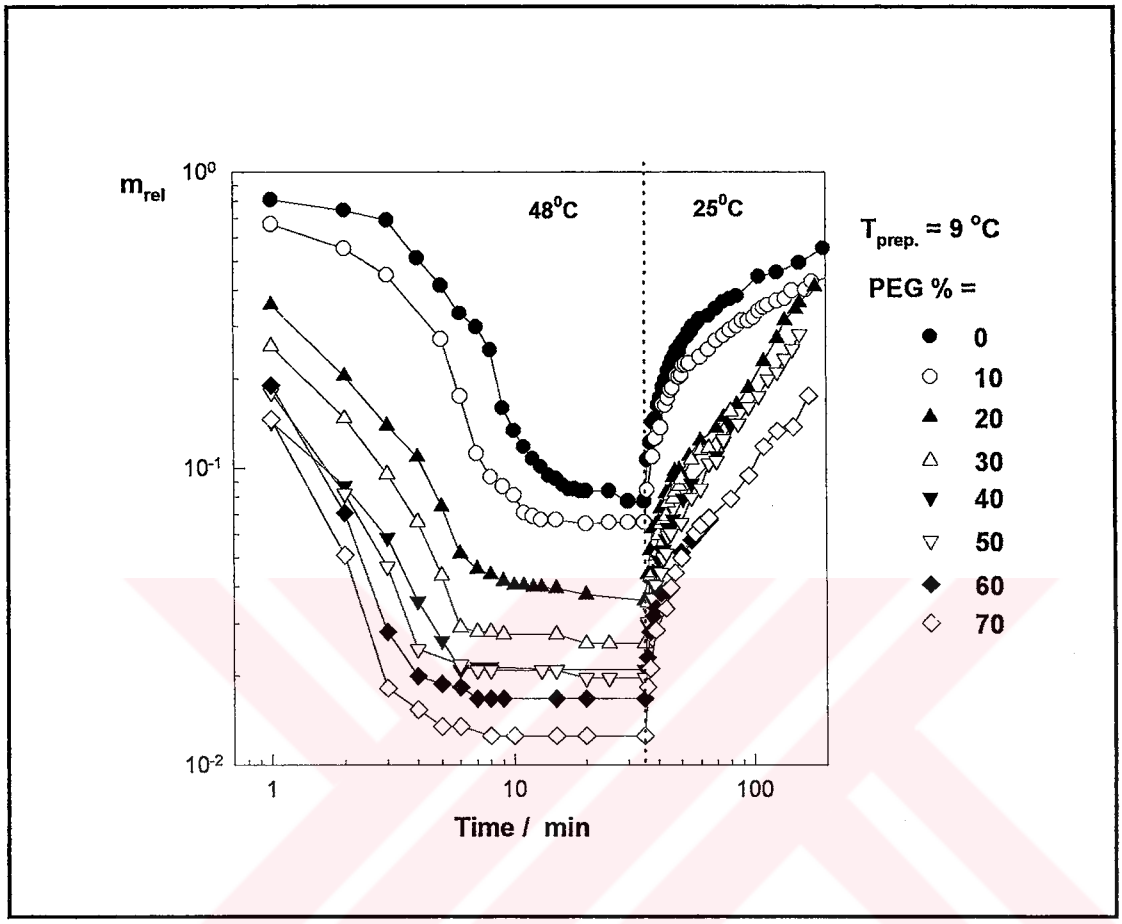


Figure. 6.2: Deswelling - reswelling kinetics of PNIPA hydrogels shown as the change in the relative mass m_{rel} of gels as a function of time in minutes. The PEG-300 contents used in the hydrogel preparation are indicating in the Figure.

Another point shown in Fig. 6.2 is that, the higher the PEG content, the smaller the mass of PNIPA gels in their equilibrium collapsed state. For example, $m_{rel} \approx 10^{-1}$ and 10^{-2} for gels without PEG and with 70 % PEG, respectively. Thus, the total amount of losing water during the deswelling process is an increasing function of PEG content used in the hydrogel preparation. This result can be explained with the "skin layer formation" mechanism [42, 54, 55], as schematically illustrated in Fig. 6.3. During the deswelling process, the gel starts to shrink and this shrinkage starts in the surface layer first; the collapsed chains in the surface region of the gel sample may form a dense skin layer, which prevents further water diffusion from in-to-outside of the gel sample. However if the gel is porous, that is, if there are interconnected pore channels inside it (Fig. 6.4), water can easily diffuse outside of the gel phase so that a

skin layer formation during shrinking does not prevent water diffusion. From our results, we can conclude that, the higher the PEG content, the larger the pore channels in the gel, so that the losing amount of water increases with increasing PEG content.

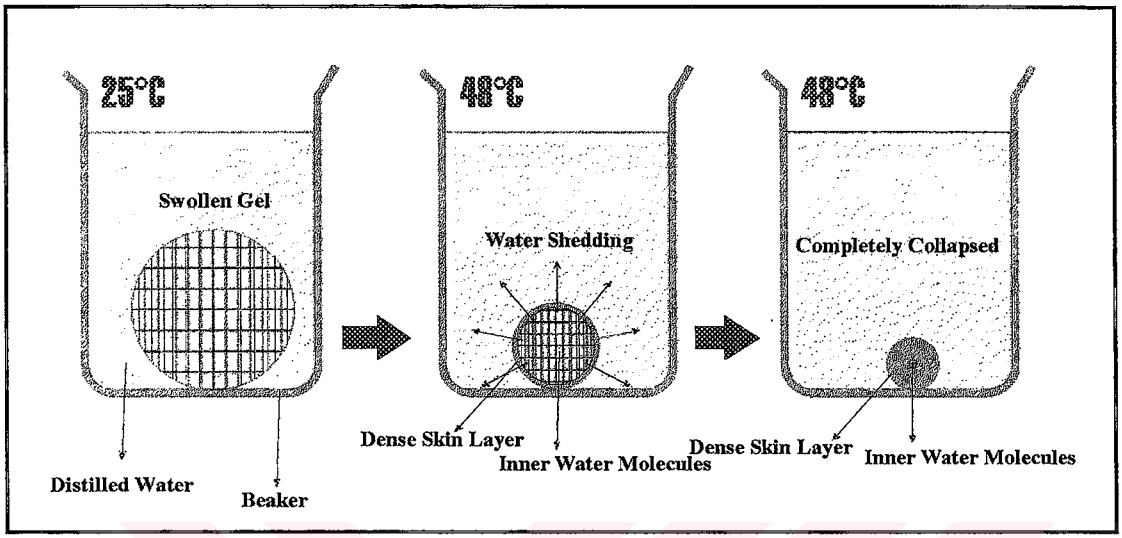


Figure. 6.3: Dense skin layer formation results in slower deswelling rate for insufficiently porous or nonporous gels. Hatched area of the gel is crosslinked region swollen with water molecules. The arrows from the gel represent direction of water diffusion out of the gel surface. Grey region of the gel is dense skin layer formed during the deswelling process.

Let us know discuss the reswelling behavior of the collapsed PNIPA gels at 25 °C (right part of the dotted vertical line in Fig. 6.2). According to Fig. 6.2, the reswelling process of gels can be divided into two periods: A rapid reswelling period followed by a slow reswelling period until the equilibrium swollen state. For example, for the PNIPA gel prepared without PEG, the rapid reswelling period lasts 20 minutes, while the slow second period continuous for about 5 days (Fig. 6.5), until attaining the initial swollen gel mass. Compared to this gel, PNIPA gel prepared with 70 % PEG exhibits a faster response rate in the first reswelling period which only takes 15 minutes. However, the second period is still slow and even slower than the standard PNIPA gel.

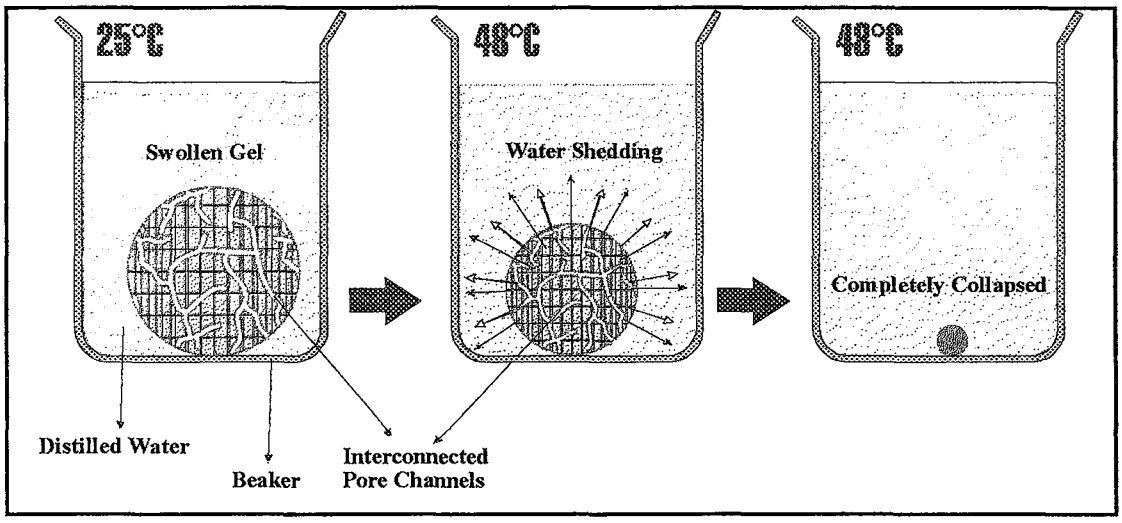


Figure. 6.4: Mechanism rapid deswelling of PNIPA gel prepared in the presence of PEG-300. Hatched areas represent crosslinked region of the gel. White lines in hatched areas represent interconnected pore channels. White arrows represent direction of water shedding from the pore channels. Black arrows represent direction of water shedding from the crosslinked region of the gel in the middle beaker.

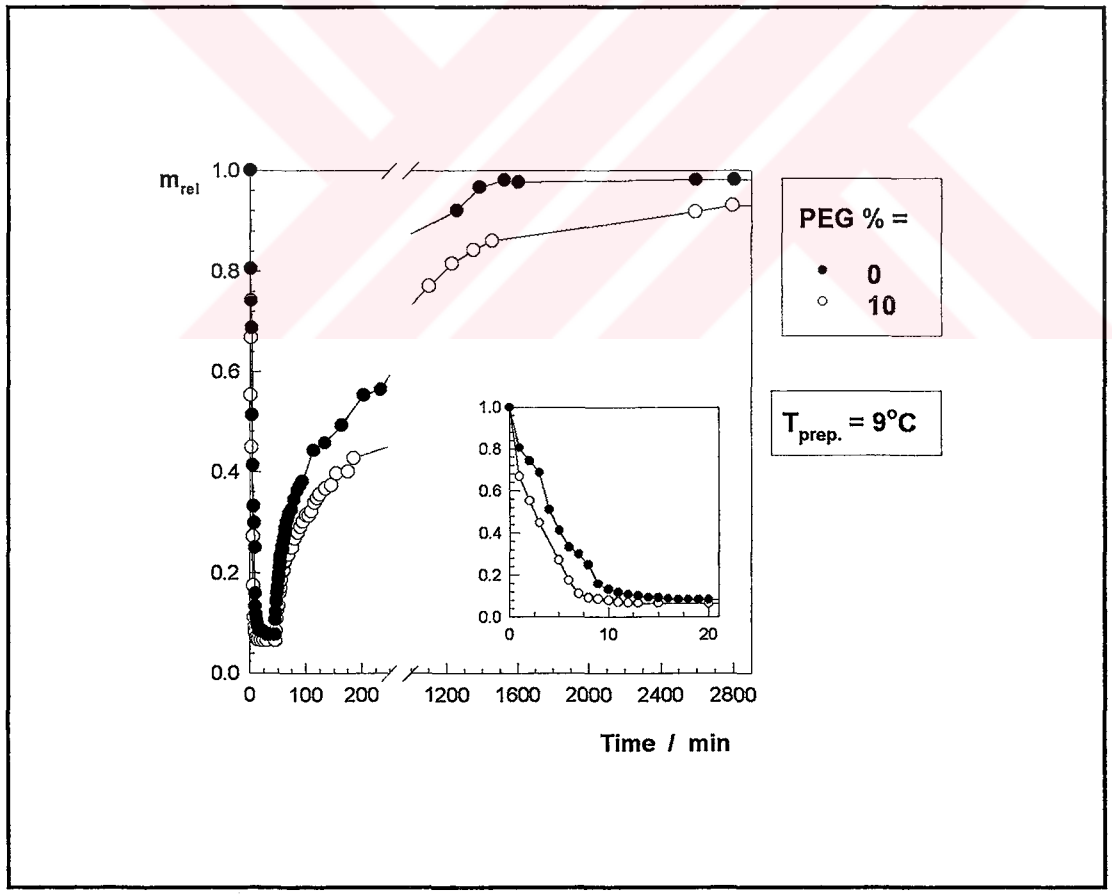


Figure. 6.5: Deswelling-reswelling kinetics of PNIPA hydrogels prepared with 0 and 10 % PEG content.

The two-step reswelling profile of PNIPA gels can be explained with the shell-core mechanism, as schematically illustrated in Fig. 6.6. When a collapsed PNIPA gel sample is dropped in cold water, i.e., in a good solvent, the outer surface of the sample will first be in contact with water molecules and, the collapsed network chains at the gel surface will start to relax. Initially, the surface area of the collapsed gel is large, so that water absorption occurs easily. However, as the gel swells, since swelling starts from the surface region of the gel, a two-phase structure will form: one containing relaxed network chains at the gel surface (relaxed part) and the other containing unrelaxed network chains in the inner part of the gel sample (unrelaxed part). Unrelaxed part of the gel sample becomes smaller as the gel swells, so that the reswelling process slows down after the initial rapid swelling period. Another point shown in Fig. 6.2 is the decrease of the reswelling rate of the gels, as the amount of PEG is increased. This may be due to the different initial states of the gel samples. As seen in Fig. 6.2 the gels prepared with PEG are in a more collapsed state at 48 °C, compared to the gel without PEG. As a result, they will need additional time to attain the swelling equilibrium. Another explanation for this behavior is the collapse of the porous structure in gels at 48 °C. Thus, all the gels at 48 °C behave as non-porous materials, so that the reswelling needs a long time.

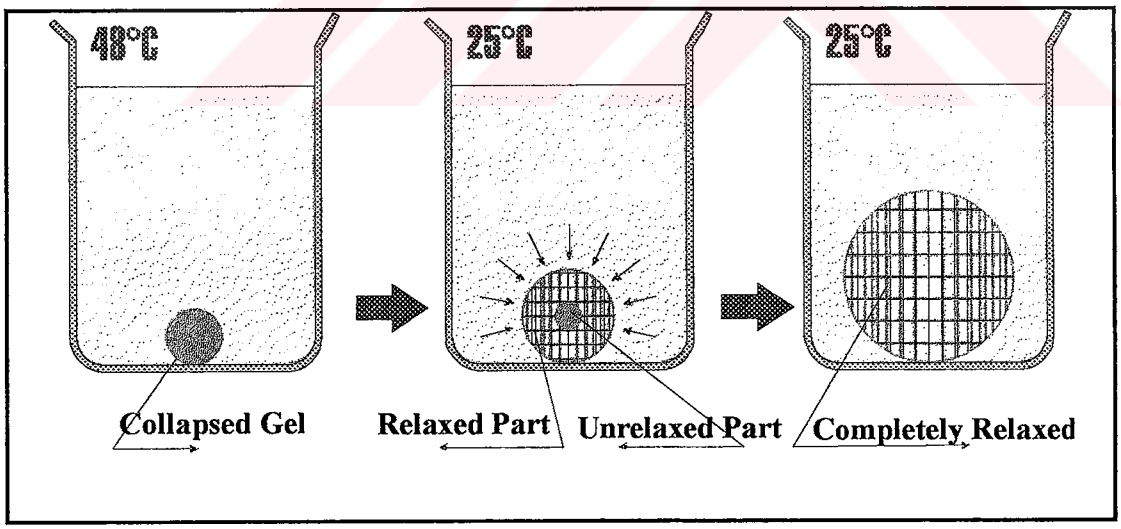


Figure. 6.6: Shell-core mechanism suggested for the two-step reswelling behavior of PNIPA hydrogels. Hatched area represents crosslinked region of the gel. Grey region represent collapsed part of the gel. Arrows represent direction of water molecules entering into the gel matrix.

The experimental swelling-deswelling behavior of the gels can thus be explained with the pore structure formation in the presence of PEG-300. Indeed, the visual appearance of the gel samples supports this explanation. Gels prepared without PEG

were transparent, while those prepared with 20 % PEG or more were opaque, indicating existence of phase separated domains. Interestingly, gels prepared with 10 % PEG were partly transparent and opaque; this PEG concentration thus represents a critical concentration for the formation of a macroporous structure. Fig. 6.7 shows the elastic modulus of gels G_o plotted as a function of PEG content used in the hydrogel preparation. Note that the PNIPA gels prepared with more than 50 % PEG were too weak to withstand the elasticity tests. It is seen that the modulus of elasticity decreases with decreasing amount of PEG. This is expected since increasing PEG content in the gel formation system promotes the phase separation process, so that the degree of macroporosity of the resulting hydrogel increases with PEG %. Increasing macroporosity makes the network system weaker so that the modulus decreases. As seen in Fig. 6.7, two G_o values are given for the gel formed at 10 % PEG; one measured from the transparent part of the gel sample and the other measured from the opaque part. Modulus of elasticity of the opaque part of the gel is lower than that of the transparent part, which is in accord with the above explanation.

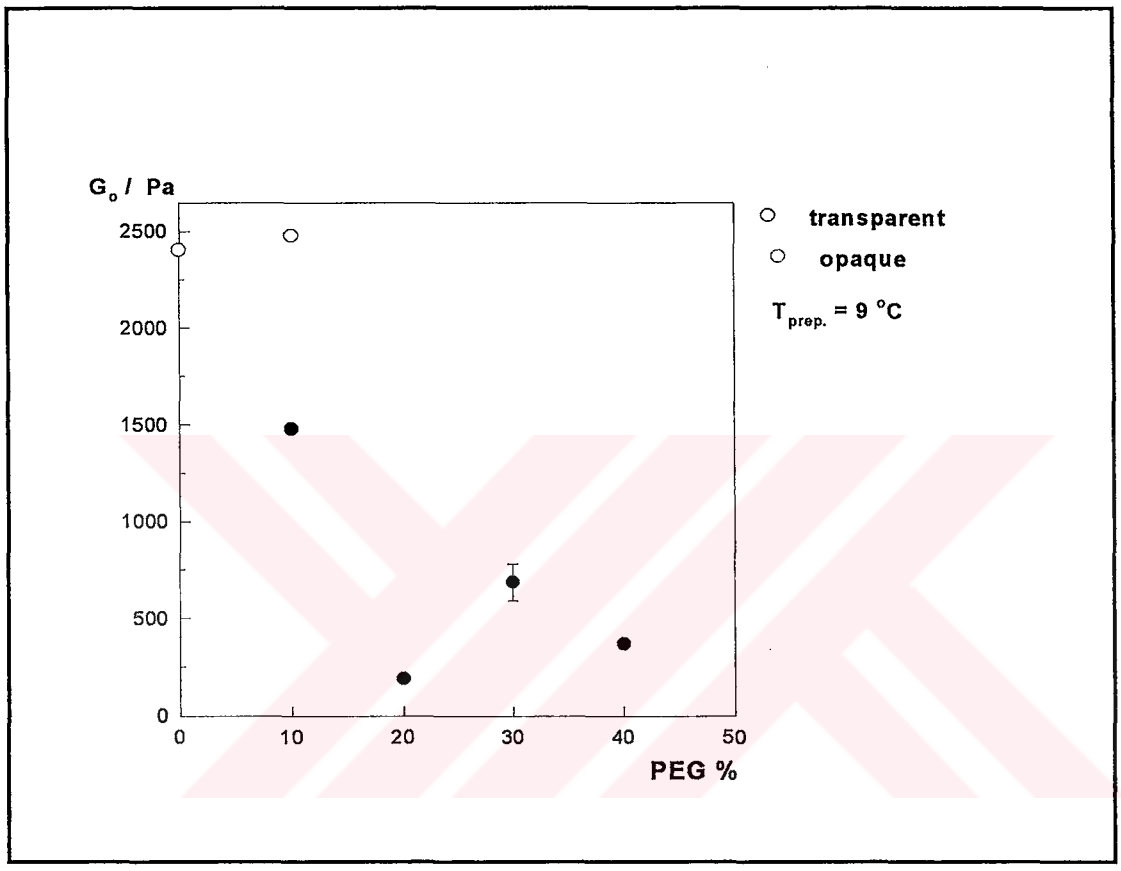


Figure. 6.7: Elastic modulus G_o of PNIPA hydrogels plotted against the PEG content used in gel preparation.

In order to find out, whether the swelling-deswelling kinetics of the gels shown in Fig. 6.2 is reversible, we also conducted oscillating deswelling-reswelling measurements. For this purpose, PNIPA gels prepared with 0 and 10 % PEG were subjected to deswelling-reswelling process twice. The results are shown in Fig 6.8. It is seen that almost the same behavior was observed both in the first and the second cycle of experiments. Consequently, the gels exhibit reproducible and reversible deswelling-reswelling kinetics.

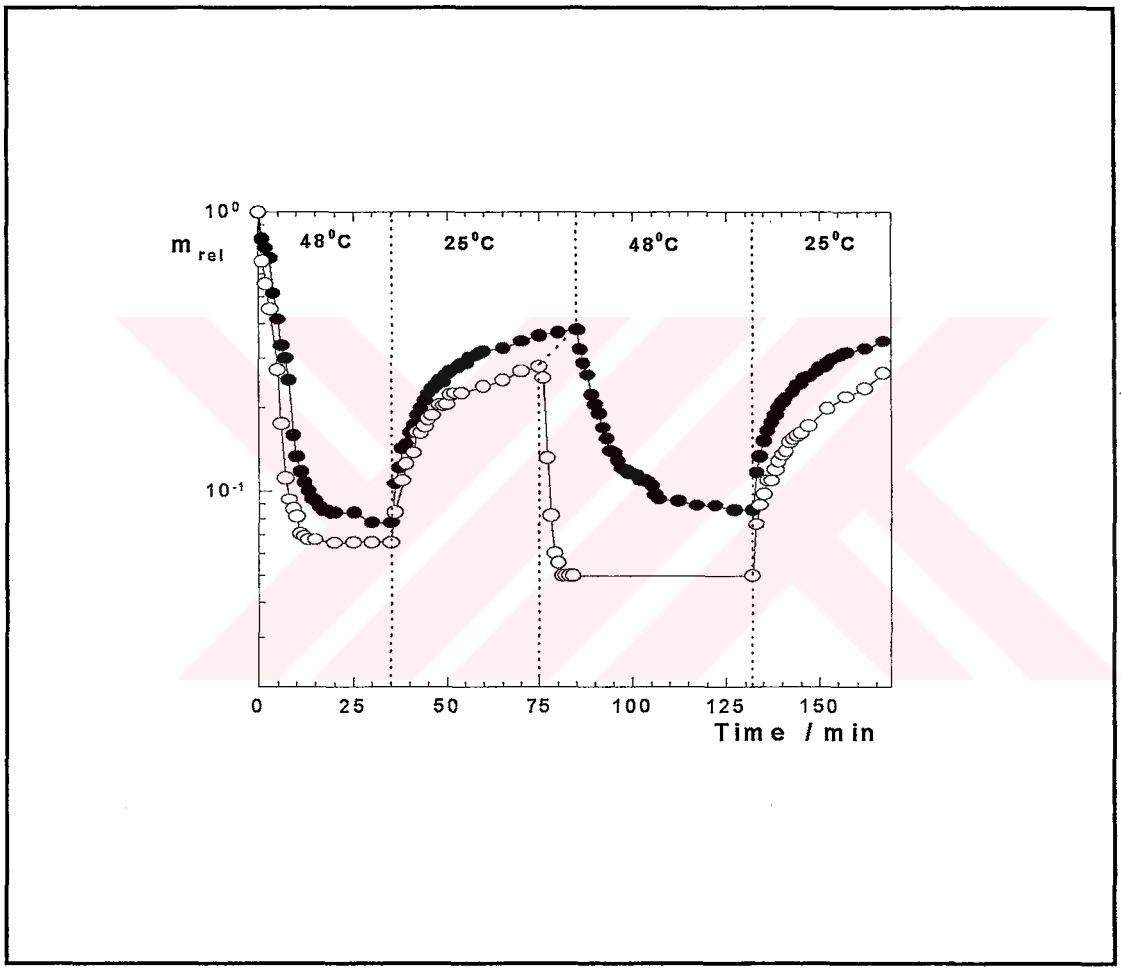


Figure. 6.8: Oscillating deswelling-reswelling behavior of PNIPA gels. Deswelling (48 °C) and reswelling (25 °C) courses are separated by the dashed lines in the figure. $T_{prep.}$ = 9 °C. PEG % =0 (filled symbols) and 10 % (open symbols)

6.3. Effect of Gel Preparation Temperature

In this section, the experiments reported in 6.2 were repeated, with the difference that, the gels were prepared at 50 °C instead of 9 °C. In this way, we aimed to observe the effect of the gel preparation temperature on the swelling kinetics of PNIPA hydrogels. In Fig. 6.9, the relative mass of gels m_{rel} prepared at 50 °C is plotted against the deswelling time. The PEG contents used in the hydrogel preparation are indicated in the Figure. In accord with the previous results, deswelling response rate becomes faster as the amount of PEG present in the gel formation system is increased. This indicates increasing degree of porosity with increasing PEG %, also at a gel preparation temperature of 50 °C.

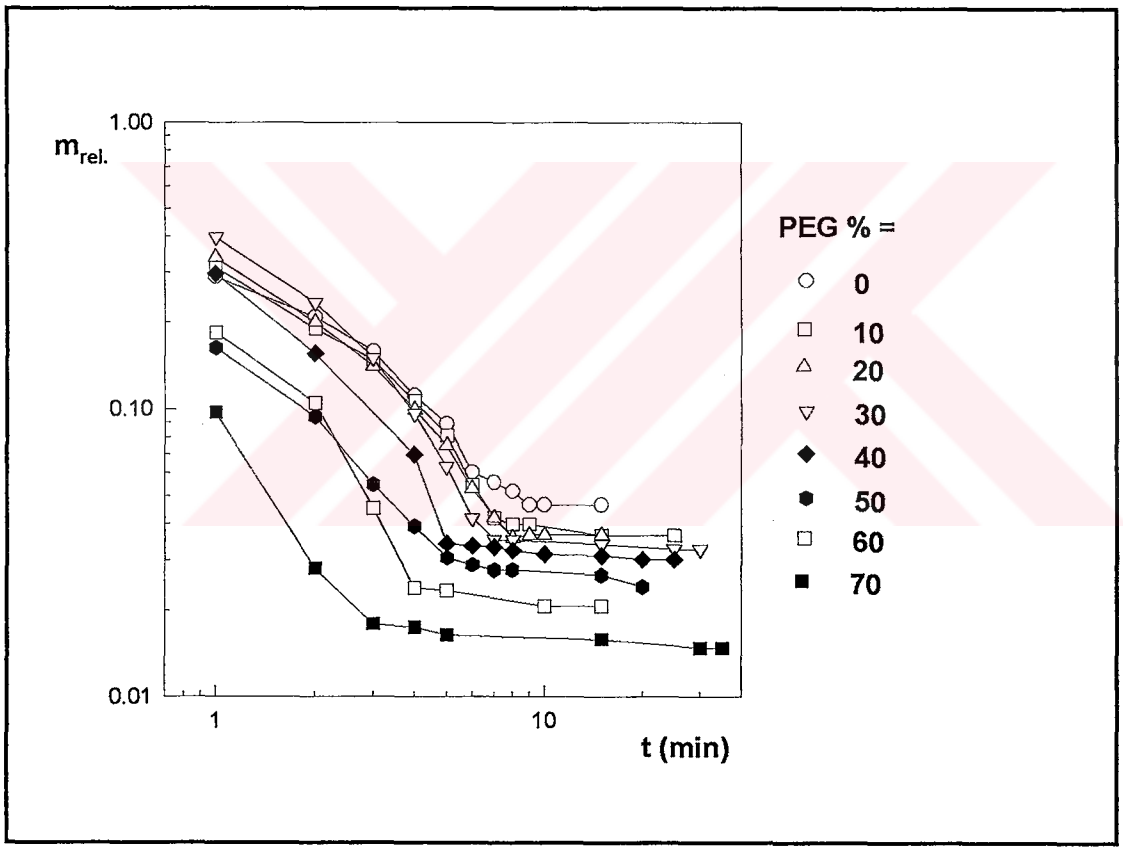


Figure. 6.9: Deswelling kinetics of PNIPA hydrogels synthesized at 50 °C. The relative gel mass m_{rel} is plotted as a function of the deswelling time in minutes. PEG-300 contents used in the hydrogel preparation are indicated.

In Fig. 6.10, the deswelling-reswelling kinetics of PNIPA gels formed at 50 °C (filled symbols) is compared with gels formed at 9 °C (open symbols). It is seen that, if the PEG content is 20 % or more, both 9 °C and 50 °C gels exhibit the same deswelling-reswelling cycles. A difference between the two series of gels appears if the PEG content is less than 20 %: The gels prepared at 50 °C show a much more rapid

deswelling course at 48 °C than those prepared at 9 °C. Also, the reswelling course becomes rapid by increasing the gel preparation temperature.

For a temperature–sensitive polymer, increasing the gel preparation temperature (T_{prep}) above its LCST will induce a phase separation during the polymerization-crosslinking reactions, so that a macroporous structure will form. As a result, the gels formed at $T_{prep} > T_{LCST}$ will exhibit a rapid deswelling-reswelling course than those formed below LCST. This explanation is supported by our gelation experiments conducted in water or in PEG solutions with less than 10 % PEG (Fig. 6.10). However, experiments conducted in PEG solutions with more than 10 % PEG show no T_{prep}-effect on the swelling kinetics of PNIPA gels. This unexpected result can be explained with the equilibrium swelling behavior of PNIPA gels in PEG solutions, as shown in Fig. 6.11. These swelling data were taken from the literature [56]. It is seen that, if the PEG content is above 20 % the swelling temperature, whether above or below the LCST of PNIPA, does not affect the swelling behavior of PNIPA gels in PEG solutions. Thus, the gels become temperature-insensitive in these PEG solutions. Accordingly, if the PEG solutions with more than 20 % PEG are used as the polymerization solvent for NIPA, the growing PNIPA chains during gelation will not be affected from the gel preparation temperature T_{prep}, as also observed experimentally in Fig. 6.10.

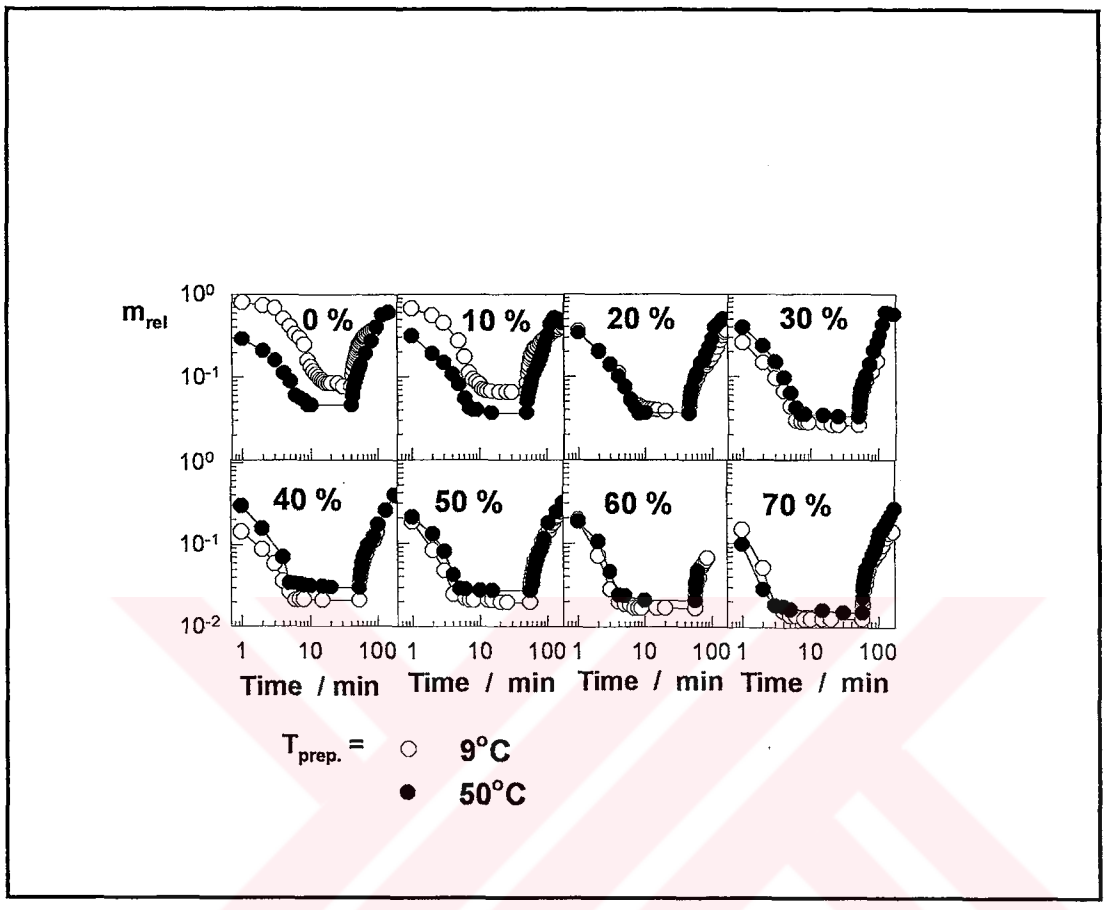


Figure. 6.10: Comparison of deswelling-reswelling kinetics of PNIPA hydrogels prepared at 9 °C and 50 °C.

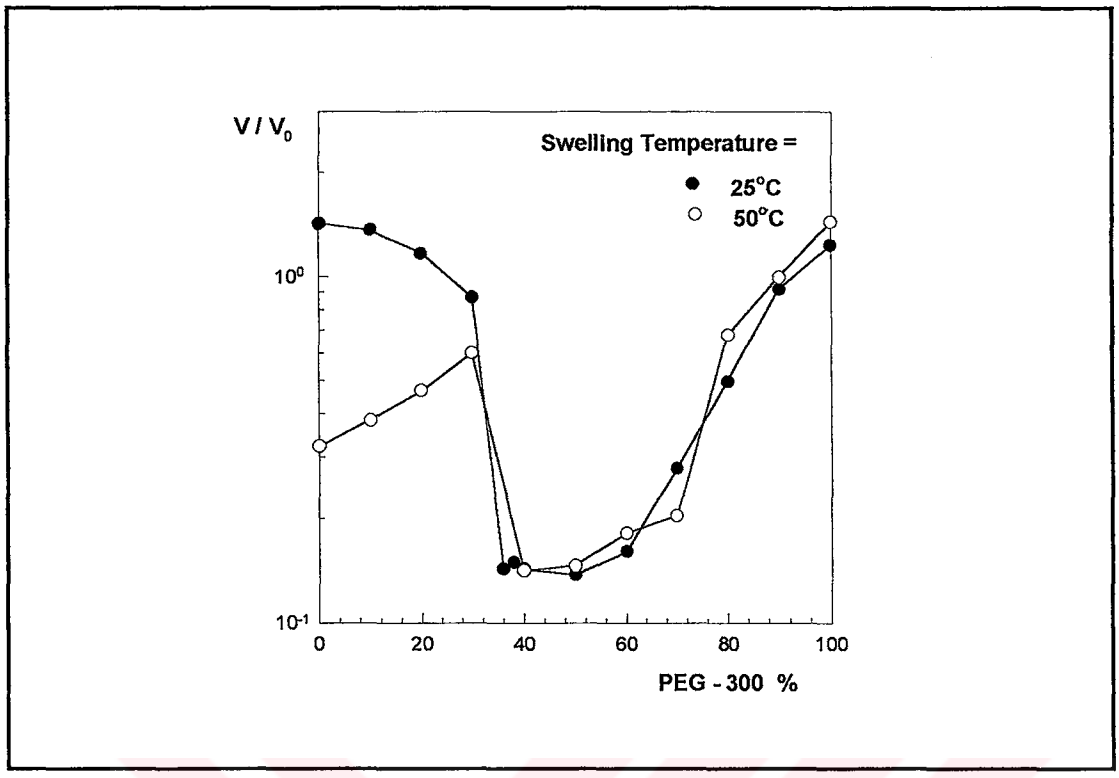


Figure. 6.11: Swelling behavior of PNIPA hydrogels in PEG-300 /water mixtures. The equilibrium swelling ratio V/V_0 is plotted against the solvent mixture composition. The data were taken from the literature [56]. Swelling temperature = 25 °C (filled symbols) and 50 °C (open symbols).

6.4. Effect of the Crosslinker Content

From the previous sections, one may conclude that a PNIPA hydrogel with the fastest response rate to an external temperature change from 25 °C to 48 °C and vice versa can be obtained under the following gel preparation conditions:

PEG content = 70 v/v %

T_{prep} = 9 °C or 50 °C.

In these experiments, however, the crosslinker (BAAm) content was set to 1.2 mol %. From the literature [19], it is well known that the crosslinker content also affects significantly the porosity of the networks. Therefore, in this section, we prepared a series of PNIPA gels with various amount of the crosslinker BAAm, while T_{prep} and PEG content were fixed at 9 °C and 70 %, respectively. In Fig. 6.12, the modulus of elasticity G_o of gels is plotted against the BAAm content in the feed. It is seen that G_o does not change much between 6 and 10 mol % BAAm, while it rapidly increases as the BAAm content is further increased.

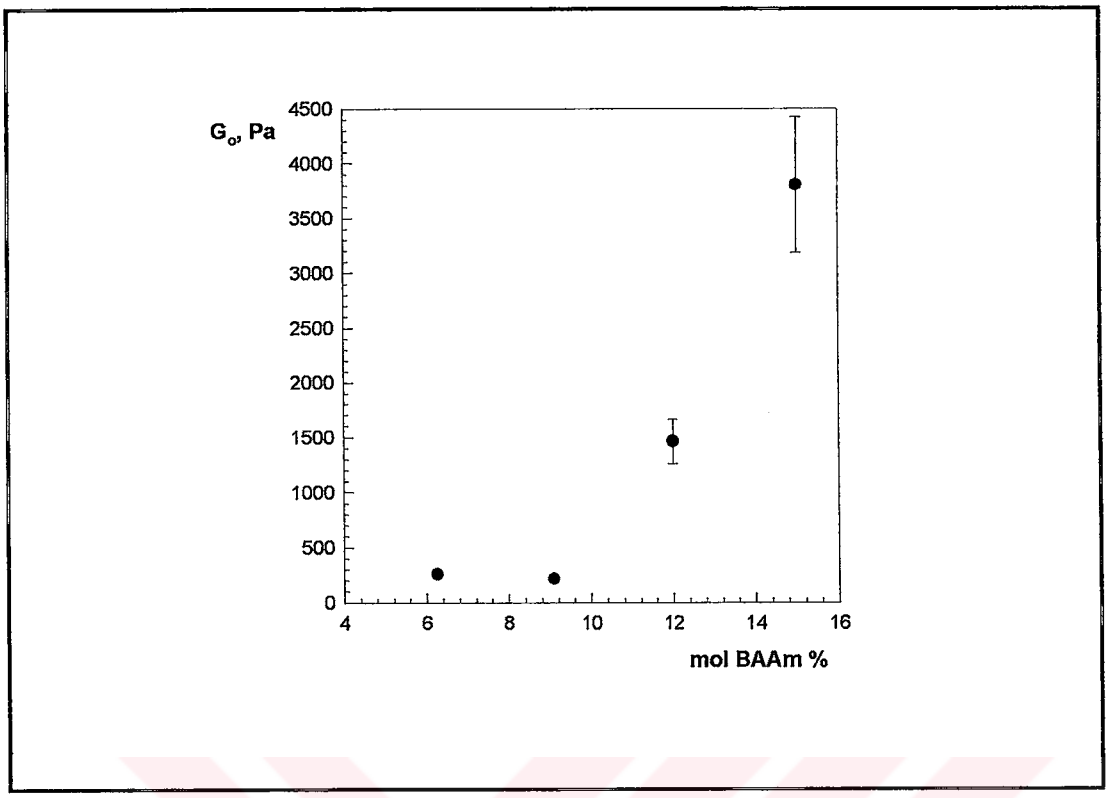


Figure. 6.12: Elastic modulus G_o of PNIPA hydrogels plotted against the crosslinker (BAAm) content

In Fig. 6.13, the reswelling and deswelling cycles of PNIPA gels with various amounts of BAAm are presented. Fig. 6.13 A and 6.13 B show m_{rel} versus time plots for gels with 1.2 – 9.1 mol % BAAm and 9.1 – 15 mol % BAAm, respectively. The small Figure at far right demonstrates the reswelling behavior of the gels. Following features can be seen from the Figures.

(1) Deswelling course: The time to attain the equilibrium collapsed state is 4, 20 and 46 minutes for gels with 1.2, 9.1 and 15 mol % BAAm. Thus, the deswelling response rate of the gels decreases with increasing crosslinker content. This is probably due to the reduction in the mesh size of gel on rising the crosslinker content, which slows down the diffusion rate of water molecules outside of the gel phase.

(2) Reswelling course: In contrast to the deswelling behavior, the reswelling of the gels at 25 °C becomes faster on rising the crosslinker content. Also, the two-step reswelling profile observed at 1.2 mol % BAAm disappears with increasing BAAm content and, a single step reswelling was observed between 9 and 12 mol % BAAm.

(3) Mass of the collapsed gel at 48 °C: Increasing BAAm content also increases the mass of PNIPA gels at 48 °C. Thus, the amount of water released from the swollen gel decreases with increasing content of BAAm. The results thus demonstrate that, increasing crosslinker content decreases the deswelling rate but increases the reswelling rate of PNIPA gels formed in 70 % PEG solution.

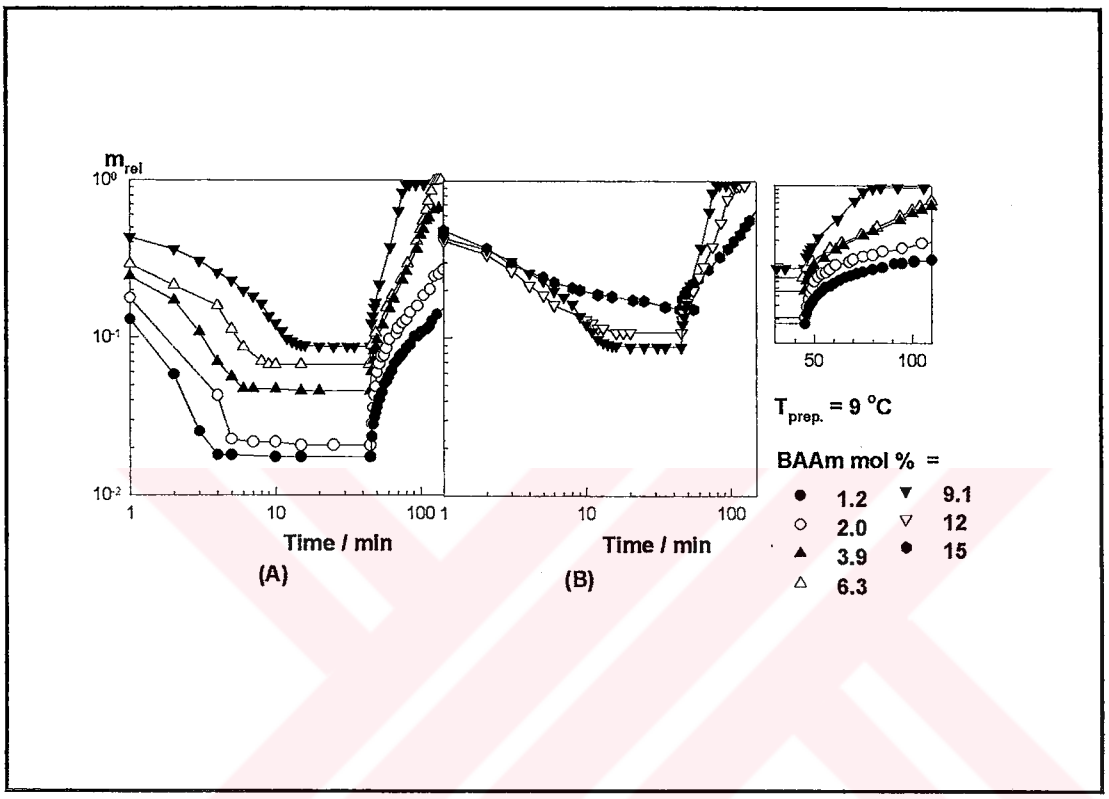


Figure. 6.13: Deswelling-reswelling kinetics of PNIPA hydrogels formed at various BAAm contents. T_{prep}= 9°C. The crosslinker contents are indicated in the Figure. The small Figure demonstrates the reswelling kinetics only.

6.5. Comparison of the PNIPA Hydrogel with a PNIPA Cryogel

We obtained PNIPA hydrogel with a fastest response rate at T_{prep}= 9 °C and in aqueous PEG solutions containing 70 % PEG-300. The deswelling-reswelling cycle of this gel is replotted in Fig. 6.14 by the filled symbols. To compare the response rate of this gel with that of PNIPA cryogels, we prepared a PNIPA cryogel at -25 °C in ice, as reported in the literature [50]. The deswelling-reswelling cycle of this cryogel is also shown in Fig. 6.12 as open symbols. Comparison shows that the cryogel deswells much faster than our gel formed in PEG solution. The deswelling times are 1 and 4 minutes, respectively. On the other hand, the reswelling of the cryogel also occurs much faster than PNIPA gel, as also shown in the Figure.

Moreover, another advantage of PNIPA cryogel is that it returns to its original shape and mass after a short reswelling period, which is less than one minute. PNIPA hydrogel formed in PEG solution, however, cannot reach to its original shape and mass in a reasonable period of time, i.e., within a time period of less than a few days.

In contrast to these disadvantages of PNIPA hydrogels formed in PEG solution, they release a much larger amount of water compared to the cryogel. As seen in Fig. 6.12, $m_{rel} \approx 0.01$ and 0.3 for the hydrogel and for the cryogel, respectively. Thus, our gels are more suitable in application areas, in which the amount of water released in a long run is important.

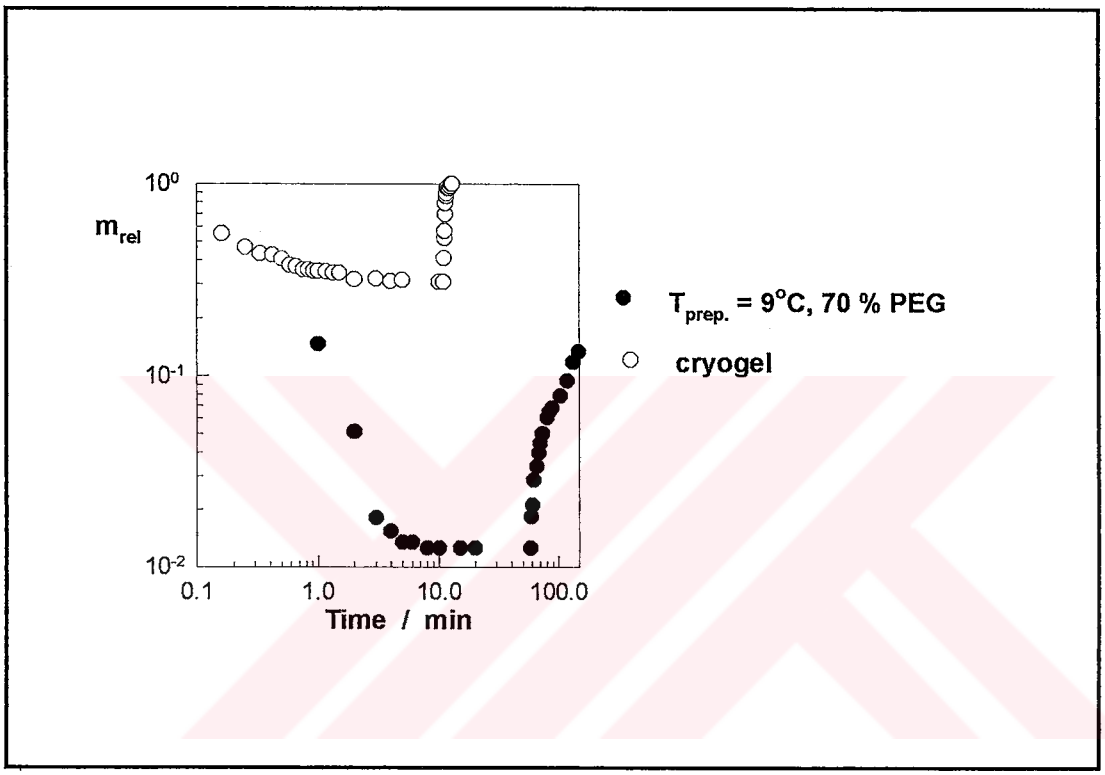


Figure. 6.14: Comparison of PNIPA hydrogel formed in PEG-300 solution (70 %) with a PNIPA cryogel prepared at -25 °C.

CONCLUSIONS

A series of PNIPA hydrogels was prepared in PEG-300/water mixtures of various compositions as well as in the presence of various amounts of BAAm as a crosslinker. The deswelling and reswelling behavior of gels depending on a temperature change between 25 °C and 48 °C was investigated. The conclusions that can be drawn from the experimental results can be summarized as follows:

1) The equilibrium swelling capacity of PNIPA hydrogels increases with decreasing crosslinker ratio, or with increasing amount of PEG-300 used in the gel formation process as a pore-forming agent.

2) The deswelling rate of swollen PNIPA hydrogels in water at 48 °C increases with increasing amount of PEG-300. Also, larger amount of water is released from the gel as the PEG-300 content is increased. These results were explained with the formation of "water channels" in the "dense skin layer" of gels formed in the presence of PEG-300. The higher the amount of PEG used in the gel preparation, the larger are the water channels at the gel surface, so that water molecules can easily diffuse out of the gel phase. In contrast to these observations, the reswelling rate of the collapsed PNIPA gels decreases on rising PEG content, probably due to the smaller mass of the gel samples in their collapsed state.

3) The gel preparation temperature (T_{prep}) affects both the equilibrium swelling capacity and the deswelling-reswelling kinetics of PNIPA hydrogels, if the PEG content is less than 20 %. In this range of PEG, the deswelling and reswelling rates become faster if $T_{prep}>T_{LCST}$. This result was explained with the temperature sensitivity of PNIPA hydrogels in PEG solutions containing less than 20 % PEG.

4) The deswelling rate decreases while the reswelling rate increases as the crosslinker content of the hydrogels is increased. This behavior is due to the decreasing mesh size of gels on rising their crosslinker contents.

5) Comparison of PNIPA hydrogels prepared in PEG/water mixtures with a PNIPA cryogel shows that our gels release a much larger amount of water within a long period of time.

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