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Influence of the swelling history on the swelling kinetics of stimuli-responsive poly[(*N*-isopropylacrylamide)-*co*-(methacrylic acid)] hydrogels

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Abstract

The influence of the swelling history on the swelling behavior of poly[(*N*-isopropylacrylamide)-*co*-(methacrylic acid)] P[(*N*-iPAAm)-*co*-(MAA)] random copolymers hydrogels synthesized by free radical polymerization in solution of *N*-iPAAm and MAA comonomers crosslinked with tetraethylene glycol dimethyl acrylate (TEGDMA) has been studied. The swelling behavior under pH 7 at 18, 29, 39 and 49 °C of this series of copolymers, previously soaked either at pH 2 or 7 has been investigated. The swelling kinetics of these two series of samples displays different behavior as function of the composition and temperature. However, the equilibrium swelling values only show slight dependences on the previous soaking pH and temperature. When samples are soaked at pH 7, then the swelling at pH 7 follows a first order kinetics, irrespective of the copolymer composition or the temperature at which the experiment has been carried out. In this case, the swelling process is very fast and depends only slightly on temperature. The first order rate constant increases with the MAA content in the hydrogel. Furthermore, the swelling rate of copolymer hydrogels soaked at pH 2, show strong dependence on composition and temperature. They follow an autocatalytic swelling kinetics due to the disruption of hydrogen bond arrangements. An initial slow water uptake is followed by an acceleration process, in which water molecules inside the gel help the next water molecules to come in. Two rate constants, a first-order rate constant and an autocatalytic one have been obtained from the kinetics analysis. They have revealed different temperature dependence which may be due to a balance between hydrophobic and hydrogen bond interactions. The temperature dependence of the swelling kinetics is stronger and more complex for copolymers treated under pH 2 than for copolymers soaked under pH 7.

Keywords: Poly[(*N*-isopropylacrylamide)-*co*-(methacrylic acid)]; Sigmoidal swelling; Swelling history

1. Introduction

Hydrogels of poly(*N*-isopropylacrylamide) P(*N*-iPAAm) and poly(methacrylic acid) P(MAA) have been thoroughly investigated, the first as a thermoresponsive hydrogel, the second because its sensitivity to the environment pH changes. P(*N*-iPAAm) exhibit an 'inverse temperature-dependence', i.e. its water solubility decreases with increasing temperature. It presents a lower critical solution temperature LCST. It is above 32 °C, being due to a strengthen of the hydrophobic interactions [1]. Copolymers and interpenetrating polymer networks (IPNs) of *N*-isopropylacrylamide and methacrylic acid have been very recently matter of many studies due to their interesting properties and novel applications [2–19]. Hydrogels copolymers containing MAA have shown a sharp sensitivity to external pH [7,20–22]. Usually they swell extensively in high pH media, as the pendant carboxylic groups become ionized. The equilibrium swelling is a strong function of composition and pH of the swelling medium. In pH solutions, below the pK_a of P(MAA), the pendant groups are not ionized, and repulsion between polymer chain vanishes leaving the polymer in a relatively collapse state [7]. Actually, depending on composition,

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some poly[(*N*-isopropylacrylamide)-*co*-poly(methacrylic acid)] P[(*N*-iPAAm)-*co*-(MAA)] copolymers display a particular sensitivity to pH, overcoming that one of P(MAA) [12]. However, the ability to response to temperature changes is restrained to copolymers with a high *N*-iPAAm content at acidic pH values, where the hydrophobic interaction among chain segments becomes stronger than the hydrophilic ones among the polymer with water [12]. Some of the most remarkable properties of these copolymer hydrogels were attributed to the strong interactions among their comonomeric units [12,13]. By means of solid state NMR, hydrogen bond arrangements between the carboxylic groups of methacrylic acid (MAA) and the amide groups of the *N*-iPAAm units has been detected [14, 15]. The anomalous behavior found in the swelling experiments was related to the reversible character of the hydrogen bonds when the pH of the medium is changed [16, 17]. It has been found that swelling curves for some of these copolymer hydrogels at pH 7 exhibit sigmoidal shapes [12, 16,18]. This fact was related to the dynamic disruption of hydrogen bonding arrangements between both comonomeric units, following an autocatalytic kinetics [16]. On the other hand, swelling curves under acidic medium exhibit an overshoot, which has been attributed to a swelling–deswelling process due to the hydrogen bond formation during swelling [17]. The shape of the swelling curve was found to depend on the previous swelling history, namely the previous soaking pH at which the hydrogels have been submitted [16,17]. The sigmoidal shape increases with decreasing the previous pH, which may be related to the amount of hydrogen bond arrangements in the sample [16]. P(MAA) also forms hydrogen bonds among their carboxylic groups [23], but its swelling curves does not exhibit such sigmoidal shape [16]. It was suggested a hydrophobic character of the complexes responsible for the autocatalytic process and consequently for the sigmoidal shape of the swelling curves [16]. The hydrophobic interaction among the isopropyl group of the *N*-iPAAm and the methyl group of MAA, will contribute to the hydrogen bond stabilization. Such stabilization has been suggested by other authors, thus for instance Staikos et al. [24] concluded that the presence of the isopropyl groups in P(*N*-iPAAm) contributes to a major stabilization of the complex between P(*N*-iPAAm) and P(AA) through hydrogen bonding in aqueous solution at low pH. The strength of both, hydrophobic interaction and hydrogen bonding depends on temperature in an opposite manner. Hydrophobic interaction increases with increasing temperature, whereas hydrogen bonding weakens when temperature is raised. The swelling behavior will be a balance between the contributions of both forces at a given temperature. In this paper, the influence of temperature on the swelling kinetics of P[(*N*-iPAAm)-*co*-(MAA)] hydrogels is investigated to get a deep insight on the interactions taking place between the pendant groups of *N*-iPAAm and MAA comonomeric units.

2. Materials and methods

2.1. Materials

N-Isopropylacrylamide (*N*-iPAAm) (Acros Organics, Morris Plains, NJ) 99% purity, methacrylic acid (MAA) 98% purity, tetraethylene glycol dimethyl acrylate (TEGDMA), ammonium persulfate (APS), N,N,N',N'-tetramethylethylenediamine (TEMED), ethanol, (Panreac Monplet & Esteban, S.A., Barcelona, Spain) were used. All products were used as received, except for *N*-iPAAm, which was purified by recrystallization from a mixture of *n*-hexane/toluene (90/10, v/v) at room temperature and MAA was vacuum distilled at 50 °C/667 Pa. Deionized water from a Millipore Milli-U10 water purification facility was used where appropriate.

2.2. Synthesis

P(MAA) and P(*N*-iPAAm) homopolymers and P[(*N*-iPAAm)-*co*-(MAA)] random copolymers crosslinked with 0.25, 0.50 and 1.00% wt of crosslinker agent TEGDMA were synthesized by free radical polymerization in solution as it has been described in detail elsewhere [13,15]. Each polymer composition estimated by elemental analysis is given in Table 1. Uniform discs were punched out of the hydrogel sample following the procedure described previously [12].

2.3. Swelling experiments

In order to obtain samples with uniform controlled structures two swelling protocols were applied to the hydrogels. Two series of samples were treated by soaking at two different pH media (pH 2 and 7) during 48 h. until equilibrium was achieved and then dried. Then, these samples were swollen again to carry out swelling kinetic experiments in a buffer solution of pH 7. The nomenclature for these samples is, for instance, ‘pH 7 (pH 2)’, that is, a

Table 1
Molar composition of hydrogel samples as determined by elemental analysis

Sample	TEGDMA (wt/wt%)	*N*-iPAAm (mol%)
P(*N*-iPAAm) (100/0)	1.00	100.0
P[(*N*-iPAAm)-*co*-(MAA)] (85/15)	1.00	85.1
P[(*N*-iPAAm)-*co*-(MAA)] (70/30)	1.00	68.8
P[(*N*-iPAAm)-*co*-(MAA)] (50/50)	0.25	50.5
	0.50	46.5
	1.00	50.6
P[(*N*-iPAAm)-*co*-(MAA)] (30/70)	1.00	30.1
P[(*N*-iPAAm)-*co*-(MAA)] (15/85)	1.00	15.4
P(MAA) (0/100)	1.00	0

sample soaked at pH 2, then dried, and subsequently swelled at pH 7. Applying this protocol, hydrogen bonding between both comonomeric units is allowed. We expect to obtain samples with non-hydrogen bond arrangements when samples are soaked at pH 7, these samples will be referred as pH 7 (pH 7).

Swelling and equilibrium data were determined gravimetrically. Dried preswollen-hydrogel disks were left to swell in phosphate buffer solutions at pH 7 (ionic strength = 0.1 M) at the experimental temperature. After regular time intervals, samples were taken out, wiped superficially with blotting paper, weighed, and placed again in the same immersion bath. Swelling data are usually expressed in terms of water uptake, defined as the weight of water imbibed by the sample per unit weight of dry polymer. The percentages of mass or normalized swelling degree (Q_t) at time t were calculated in grams of water per gram of dry gel using the following expression,

$$Q_t = (m_t - m_0)/m_0 = (W_t/m_0) \tag{1}$$

where m_0 is the initial weight of the dried disk (xerogel), namely, the weight at $t=0$, m_t is weight after a time t and W_t is the weight of the water uptake at a time t.

3. Results and discussion

In Figs. 1 and 2, the swelling curves at pH 7 for two series of P[(*N*-iPAAm)-*co*-(MAA)] hydrogels, previously soaked at pH 7 (Fig. 1) and at pH 2 (Fig. 2), are given. A comparison of these two series of data shows strong differences on the swelling behavior of these samples. On one hand, the swelling rates of samples soaked under pH 2 are lower than those ones of samples soaked at pH 7, and on the other, swelling curves exhibit sigmoidal shape for hydrogels previously submitted to an acidic treatment.

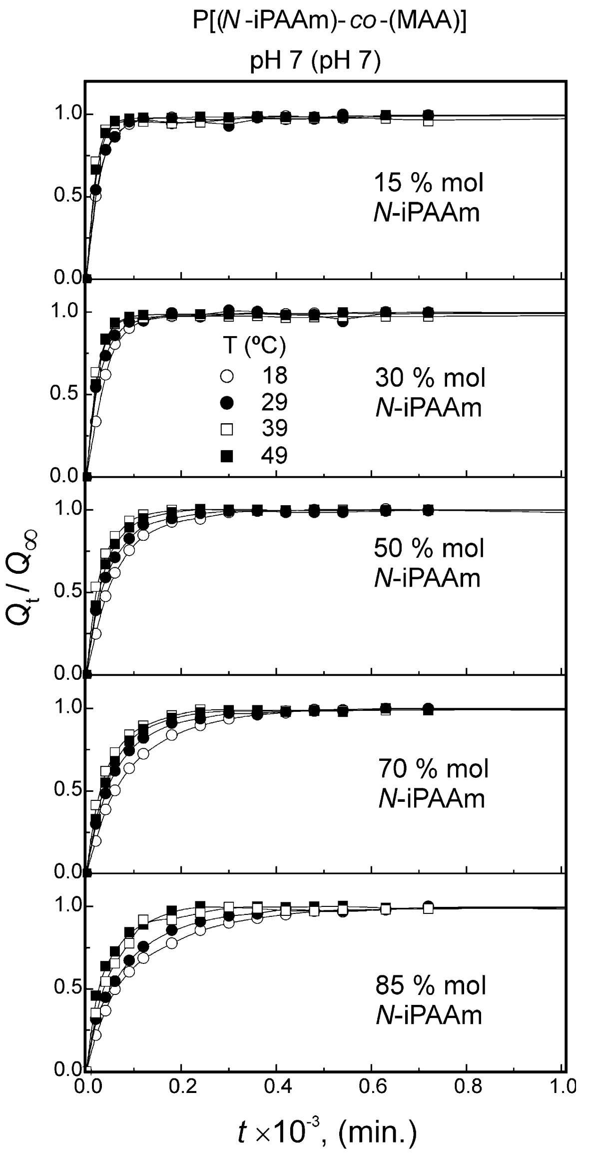

Fig. 1. Plot of Q_t/Q_∞ experimental data versus t for a series of P[(*N*-iPAAm)-*co*-(MAA)] copolymers crosslinked with 1.00% wt/wt of TEGDMA. Previous to the swelling experiment at pH 7, the samples were soaked at pH 7.

In order to clarify these differences, in Fig. 3(a) and (b) the half swelling time, i.e. the time needed for a sample to reach the half of the swelling at equilibrium, $t_{1/2}$ for hydrogels previously soaked at pH 7 (Fig. 3(a)) and at pH 2 (Fig. 3(b)), at the four selected temperatures: 18, 29, 39 and 49 °C, are plotted against the *N*-iPAAm molar percentage. As it can be seen for hydrogels previously soaked at pH 7 (Fig. 3(a)), $t_{1/2}$ changes very slightly with varying either copolymer composition or temperature. With this soaking treatment the disruption of the hydrogen bond interaction between both comonomeric units have to be expected. It can also be observed in Fig. 3(a), $t_{1/2}$ smoothly increases with increasing *N*-iPAAm content in the sample. The swelling is faster, almost instantaneous, when the sample contains great amount of $COO^- Na^+$ due to the osmotic pressure inside the gel. With respect to the temperature dependence, it seems that the swelling rate slightly increases with increasing temperature. When samples were incubated under pH 2 (Fig. 3(b)) a different dependence on the copolymer composition has been observed, the slowest swelling process, takes place for copolymers with almost the equimolecular composition. It has been attributed to a higher amount of hydrogen bond arrangements among amide and carboxylic groups [16]. In Fig. 3(b), as can be seen, $t_{1/2}$ increases considerably with decreasing temperature for P(MAA) and for 15 and 30 mol% *N*-iPAAm content copolymers. However, this effect is much less remarkable in P(MAA) homopolymer. This dependence may be explained by taking into account the fact that the strength of hydrogen bonding decreases with increasing temperature. For copolymers with 50 mol% of *N*-iPAAm, $t_{1/2}$ decreases with increasing temperature, however only a slight difference between $t_{1/2}$ at 18 and 29 °C has been found. For hydrogels

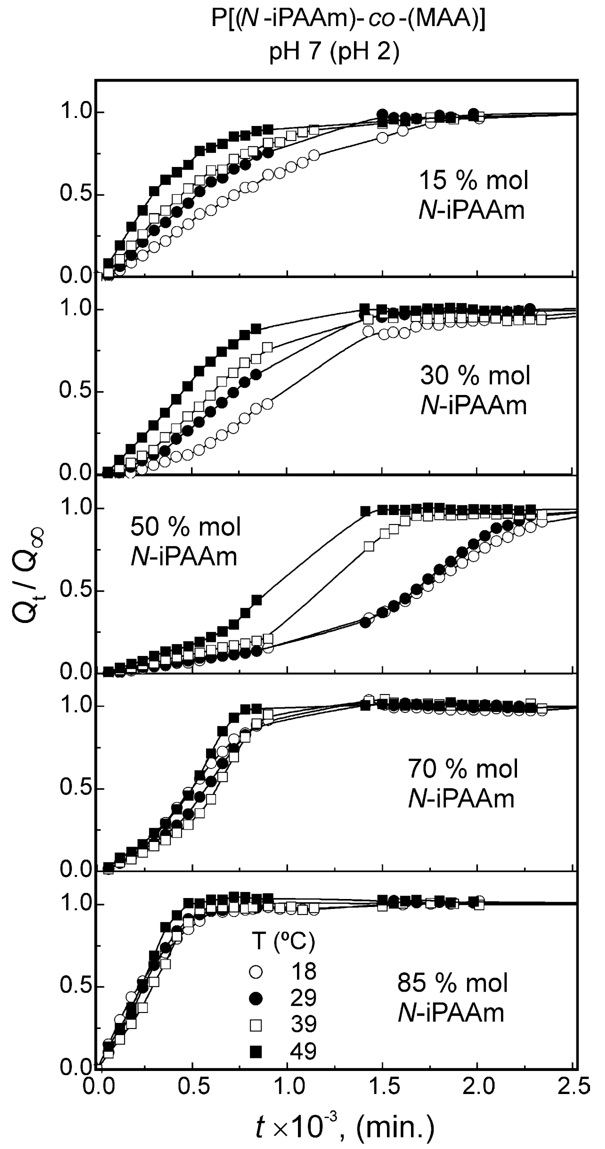

Fig. 2. Plot of Q_t/Q_∞ experimental data versus t for a series of P[(*N*-iPAAm)-*co*-(MAA)] copolymers crosslinked with 1.00% wt/wt of TEGDMA. Previous to the swelling experiment at pH 7, the samples were soaked at pH 2.

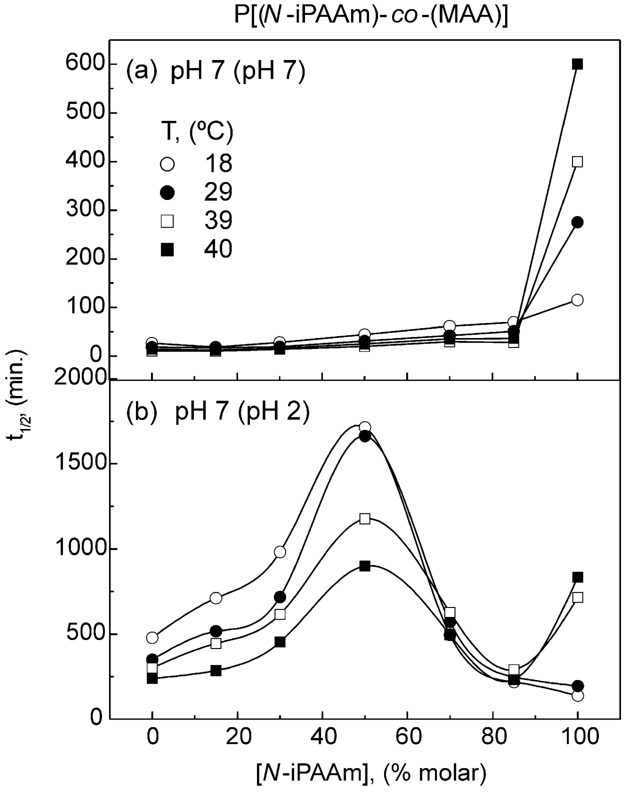

Fig. 3. Half swelling time, $t_{1/2}$ at pH 7 and at four different temperatures, plotted against molar percentage of *N*-iPAAm in the copolymer [*N*-iPAAm] for a series of copolymers and their homopolymers previously soaked at pH 7 (a) and at pH 2 (b).

with 70 and 85 mol% of *N*-iPAAm, $t_{1/2}$ is not so different for the four temperatures 18, 29, 39, 49 °C. Although an inversion of the temperature dependence is observed for these copolymers, because the swelling is slower at 39 °C than at 18 and 29 °C. This fact may be related to the hydrophobic interactions occurring at these compositions.

It is worth mentioning that the swelling history only affects the swelling rate but not the value of the swelling equilibrium. In Table 2, the equilibrium of swelling values, Q_∞, for P(MAA), P(*N*-iPAAm) and their copolymers previously soaked either at pH 7 or at pH 2, are gathered. As can be easily seen, Q_∞ values depend only slightly on temperature up to copolymers with a 70 mol% *N*-iPAAm content. Only for high content *N*-iPAAm copolymers and for P(*N*-iPAAm) homopolymer, a dependence with temperature is observed, which may be due to the strengthening of the hydrophobic interactions with increasing temperature.

The swelling kinetics of samples which were previously soaked at pH 7, shown in Fig. 1, follows a first order process. In Table 3, first order rate constant k_1 and determination coefficient R^2 extracted from the best fitting are collected. As it can be seen, R^2 values are higher than 0.99 in most cases, indicating the goodness of the fitting assuming a first order process.

From the analysis of the data corresponding to samples soaked at pH 2, which are given in Fig. 2, it was found that only the swelling curves corresponding to the homopolymers may be described according to a first order rate equation. The first order rate constant and the determination coefficient R^2, extracted from the best fitting are collected in Table 4. For P(MAA), the value of k_1 increases with increasing temperature. For P(*N*-iPAAm) the opposite effect is observed, namely the increasing of temperature from 18 to 29 °C reduces the value of the rate constant k_1. This effect is related to the neighborhood LCST. At 39 and 49 °C, kinetics parameters have not been estimated due to the sample collapse. In this case the experimental error is quite high (Table 4).

Looking at the swelling curves corresponding to the

Table 2
Equilibrium swelling values Q_∞ at pH 7 for a series of cross-linked (1.0 wt/wt% TEGDMA) P[(*N*-iPAAm)-*co*-(MAA)] copolymers at 18, 29, 39 and 49 °C, previously soaked either at pH 2 or 7

N-iPAAm (mol%)	Soaking pH	Q_∞			
		$T=18$ °C	$T=29$ °C	$T=39$ °C	$T=49$ °C
100	2	10.3	4.0	0.1	0.8
	7	11.6	5.9	0.7	1
85	2	24.1	23.1	20.3	18.4
	7	22.8	21.4	19.3	18.1
70	2	27.1	27.8	25.0	24.3
	7	24.0	22.5	21.2	21.3
50	2	23.9	24.4	23.5	23.2
	7	19.6	19.1	17.4	18.7
30	2	14.3	14.6	13.7	14.5
	7	11.5	11.5	11.3	11.3
15	2	11.4	11.4	11.8	12.2
	7	9.9	8.7	8.8	10.9
0	2	7.7	8.0	8.2	8.7
	7	5.9	6.5	6.4	6.1

copolymers soaked a pH 2, given in Fig. 2, it can be seen that any of these curves can be described neither by a first order nor according to a second order kinetics. The swelling curves exhibit a sigmoidal shape which is more remarkable seen for samples with 30, 50 and 70 mol% of *N*-iPAAm contents. The sigmoidal shape remains with increasing temperature.

Sigmoidal swelling curves have been reported by some authors [25–30] in different systems. Siegel et al. [26,27] found these anomalous behavior for a hydrophobic weak polyelectrolite copolymer of methyl methacrylate (MAA) and *N*,*N*-dimethylamino methacrylate (DMA). This copolymer on the contrary to the system studied in the present paper behaves as a weak base, it ionizes under acidic pH, where the gel swelling is maximum. They widely studied the effect of pH, buffer identity, buffer concentration and temperature on the equilibrium and kinetics swelling properties of this copolymer. Thus, for a P(MMA-*co*-DMA) 70/30 copolymer in citrate buffer at low pH a sigmoidal swelling curve appears, however when the gels were exposed to unbuffered media, the sigmoidal pattern disappears. They did not make mention of the pH history at which the hydrogels may be submitted as it has been done in the present paper. The sigmoidal shape curve may have been explained by Siegel et al. [26,27] as follows. After the commencement of swelling and prior to the acceleration point, the slab consists of a dry glassy core surrounded by a hydrated rubbery periphery with positive fixed charged groups. At these pH values is it reasonable to assume that all amino in the hydrated region are charged, since $\mathrm{pH} \ll \mathrm{p}K_a$ of the amines. In order for swelling to progress, protons must be transported from the outer solution to uncharged amines at the swelling front. The protons may be either bound to the water as hydronium ions, or bound to the buffer in the latter's acid form. Hydronium ions will be Donnan excluded by the positively charged gel, but the protonated neutral buffer will be able to enter the gel, diffuse to the front, and deliver the proton to the unionize amine.

On other hand, Okano and co-workers [28,29], found sigmoidal swelling for the thermoresponsive hydrogels of poly[(*N*-iPAAm)-*co*-(*n*-butylmethacrylate)], a system with some different characteristics to that one which Siegel and co-workers studied. They also proposed a swelling model for explaining sigmoidal swelling at 10 °C. They suggest that the acceleration was due to a rapid increase in swelling with disappearance of the glassy core which had constrained swelling. They reconcile their model with that one of Siegel et al. [30] of the called 'swelling front model' i.e. in the early stage of swelling stage swelling, the swelling front separates a swollen outer region from a glassy core. The front proceeds toward the interior as the polymer absorbs water. In this process, the glassy core largely constrains swelling in the direction normal to the front. When the front meets at midplain of polymer core, the glassy region vanishes and the polymer starts to swell largely unidirectionally because the swelling constraint disappears. Therefore, swelling of the gel is accelerated. They argued that the sigmoidal swelling patterns are intrinsically linked to the architecture of the gel and its unique physical chemistry [28]. Hydrophobic interactions must be disrupted in order to hydrate the gel below the LCST. They made swelling experiments at 10 °C by changing the initial state of the sample and they found that the sigmoidal pattern was related to this factor [29].

More recently, some of the present authors have proposed a mechanism based on hydrogen bonding disruption which has been kinetically quantified assuming an autocatalytic process for the water uptake of P[(*N*-iPAAm)-*co*-(MAA)] hydrogel which were submitted to a preestablished pH history prior to the swelling studies [16].

All of the systems, which show sigmoidal swelling patterns, have in common, the hydrophobicity. We propose

Table 3
First order rate constant k_1 and determination coefficient R^2 for hydrogels crosslinked with 1.0 wt/wt TEGDMA swollen at pH 7 and previously soaked at pH 7

T (°C)	N-iPAAm (% molar)													
	0		15		30		50		70		85		100	
	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2	$k_1 \times 10^{-2}$ (min^{-1})	R^2
18	2.7	0.9739	3.8	0.9931	2.5	0.9901	1.6	0.9979	1.1	0.9967	1.0	0.9872	0.6	0.9916
29	3.8	0.9837	4.0	0.9941	3.6	0.9734	2.2	0.9930	1.6	0.9945	1.4	0.9810	0.3	0.9901
39	6.7	0.9930	6.6	0.9961	5.1	0.9983	3.4	0.9973	2.4	0.9960	2.5	0.9904	0.3	0.4982
49	4.9	0.9912	5.6	0.9991	4.4	0.9990	2.8	0.9965	2.0	0.9990	1.9	0.9948	–	–

that the initial hydrophobic aggregates of the gels constrain the water penetration, the structural reorganization under swelling giving rise to the sigmoidal shape of the curves. In the case of P[(N-iPAAm)-*co*-(MAA)], hydrophobic aggregates are related to the hydrogen bonding [14]. That is the reason because soaking the hydrogels under acidic pH produces a great amount of hydrogen bond arrangements with hydrophobic character. These hydrogels with this pretreatment are very hydrophobic, so that water can not come in, but under neutral or basic pH these complexes can slowly break, controlling the swelling.

In the autocatalytic process [16], the first molecules penetrating in the gel, help to the next ones to come into the gel. The process of swelling was described according to the following equation,

$$\frac{Q_t}{Q_\infty} = \frac{(k_1/k_2)(1 - \mathrm{e}^{-(k_1+k_2)t})}{(k_1/k_2) + \mathrm{e}^{-(k_1+k_2)t}} \tag{2}$$

where k_1 is a first order rate constant, corresponding to the penetration of the initial water molecules and k_2 is the autocatalytic rate constant. The shape of this curve depends on the balance between the two rate constants. If $k_1 \gg k_2$, then the above equation can be simplified to a first order kinetics:

$$\frac{Q_t}{Q_\infty} \approx 1 - \mathrm{e}^{-k_1 t} \tag{3}$$

Rate constants k_1 and k_2 obtained from the best fitting to Eq. (2) are gathered in Table 5. In most of the cases, a good agreement between the experimental values and the autocatalytic model was found. In the case of 30, 50 and 70 mol% of N-iPAAm content, there exists an induction period or lag period. This period has been already observed and was attributed to the glassy state of the dry polymer where the diffusion coefficient is very small [31,32]. The polymer requires a conditioning time, during which the sample is swelled and platicized by water absorption to allow accessibility to complexed sites.

From a qualitative point of view, in Figs. 2 and 3(b), the dependence of the swelling rate on composition and temperature for samples previously soaked at pH 2, could be observed. The temperature dependence is also different for each copolymer composition. As it may be observed in Table 5, the value of the autocatalytic constant k_2 is higher than the value of the non-catalytic one k_1. Furthermore, as can be seen k_2 remains almost constant with increasing temperature for 15 and 30 mol% N-iPAAm copolymers and increases with increasing temperature for the 50, 70 and 85 mol% N-iPAAm copolymer. The behavior of k_1 is more complex. This rate constant increases with increasing temperature for the higher MAA content copolymers. And it does not change for the equimolecular composition hydrogel and decreases with increasing temperature for 70 and 85 mol% N-iPAAm copolymers. In Fig. 4, the values of k_2 and k_1 are presented as function of the copolymer

Table 4
First order rate constant k_1 and determination coefficient R^2 for P(MAA) and P(*N*-iPAAm) homopolymers hydrogels crosslinked with 1.0 wt/wt TEGDMA swelled at pH 7 and previously soaked at pH 2

T (°C)	P(MAA)		P(*N*-iPAAm)	
	$k_1 \times 10^{-3}$ (min^{-1})	R^2	$k_1 \times 10^{-3}$ (min^{-1})	R^2
18	1.33	0.9845	5.770	0.9860
29	1.90	0.9681	2.620	0.9670
39	2.07	0.9852	–	–
49	2.54	0.9764	–	–

composition. The autocatalytic constant k_2, increases with increasing *N*-iPAAm content, reaches a maximum at 70 mol% *N*-iPAAm composition and decreases again for the highest *N*-iPAAm content copolymer. The non-catalytic rate constant k_1 reaches a minimum for 30, 50 and 70 mol% *N*-iPAAm.

In Fig. 5, swelling curves at pH 7 of a series of 50 mol% *N*-iPAAm copolymers with 0.25, 0.50 and 1.00 wt% crosslinker agent are shown. These hydrogels were previously soaked at a buffered pH 2. One can observe that the swelling behavior is almost independent of the chemical crosslinker amount used. The dependence on the temperature is also very similar indicating that swelling is controlled by 'physical crosslinking' in the hydrogel, i.e. the crosslinking due to hydrogen bonding and hydrophobic interactions.

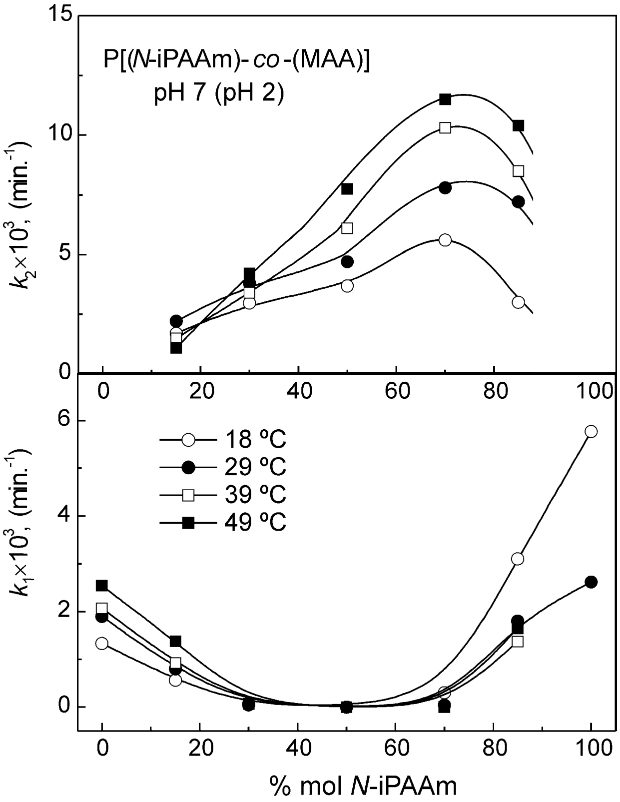

Fig. 4. Non-autocatalytic rate constant k_1 and autocatalytic rate constant k_2, obtained from the swelling curves of samples at pH 7 and previously soaked at pH 2, as a function of the molar percentage of *N*-iPAAm content in the hydrogel at 18, 29, 39 and 49 °C.

4. Conclusions

The swelling history exerts a strong influence on the swelling properties of P[(*N*-iPAAm)-*co*-(MAA)] copolymer because their ability to form hydrogen bond arrangements with hydrophobic character. Two series of these samples that were soaked either at pH 2 or 7, exhibit very different swelling kinetics and a different temperature dependence of the swelling kinetics. Swelling history must be controlled

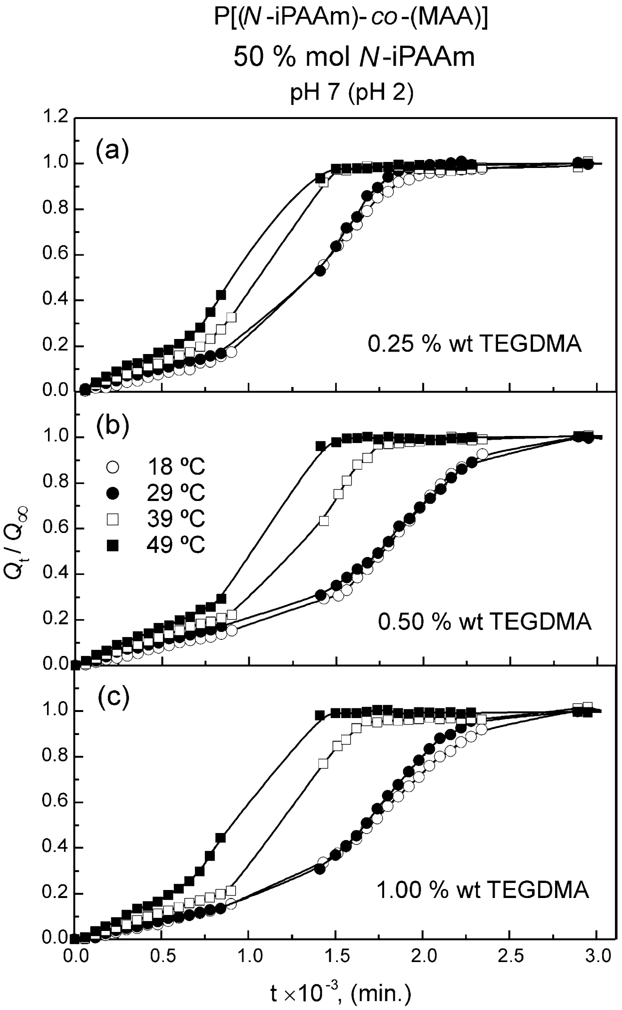

Fig. 5. Plot of Q_t/Q_∞ experimental data versus t for a copolymer with 50 mol% *N*-iPAAm with 0.25 (a), 0.50 (b) and 1.00 (c) % wt/wt of TEGDMA. Previous to the swelling experiment at pH 7, the samples were soaked at a pH 7.

Table 5
Non-catalytic rate constant k_1, autocatalytic rate constant k_2 and determination coefficient R^2 for copolymers with 1.0 wt% crosslinker swollen at pH 7 and previously soaked at pH 2

T (°C)	N-iPAAm (% molar)														
	15			30			50			70			85		
	$k_1 \times 10^{-3}$ (min^{-1})	$k_2 \times 10^{-3}$ (min^{-1})	R^2	$k_1 \times 10^{-3}$ (min^{-1})	$k_2 \times 10^{-3}$ (min^{-1})	R^2	$k_1 \times 10^{-3}$ (min^{-1})	$k_2 \times 10^{-3}$ (min^{-1})	R^2	$k_1 \times 10^{-3}$ (min^{-1})	$k_2 \times 10^{-3}$ (min^{-1})	R^2	$k_1 \times 10^{-3}$ (min^{-1})	$k_2 \times 10^{-3}$ (min^{-1})	R^2
18	0.53	1.71	0.9979	0.14	2.97	0.9970	0.03	2.65	0.9917	0.33	5.58	0.9978	2.43	3.01	0.9962
29	0.76	2.20	0.9979	0.23	3.81	0.9993	0.01	3.27	0.9867	0.19	6.07	0.9981	1.25	7.22	0.9982
39	1.14	1.48	0.9968	0.39	3.44	0.9878	0.05	4.02	0.9944	0.11	6.89	0.9928	0.74	8.54	0.9936
49	2.01	1.06	0.9927	0.62	4.17	0.9991	0.09	4.49	0.9957	0.20	7.65	0.9936	1.02	10.36	0.9856

and it can be use to tailor the swelling rate of hydrogels, i.e. sigmoidal swelling patterns can be obtained. Copolymers until a 70 mol% [*N*-iPAAm] content previously soaked at pH 2 display swelling curves at pH 7, which are remarkably affected by changing the temperature. This effect resulting in several different release profiles and therefore to tailoring drug delivery systems.

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