# Stimulations of Responsive Hydrogels: Experimental Investigations and Modelling

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**Summary:** Modelling the responses of hydrogels to external stimulations requires a thermodynamic framework for the phase equilibrium between a gel and a surrounding phase and models for describing the Gibbs energies of both phases. The phase equilibrium conditions are described and some appropriate models for describing the thermodynamic properties are presented. These methods are applied to describe (correlate/predict) the swelling of nonionic hydrogels (of n-isopropyl acrylamide) and ionic hydrogels (of n-isopropyl acrylamide and sodium methacrylate) in various nonionic and ionic aqueous solutions at 298 K.

**Keywords:** modelling; phase equilibrium in hydrogel systems; swelling of nonionic and ionic hydrogels in water and aqueous solutions

## Introduction

Responsive hydrogels are three dimensional networks composed of crosslinked hydrophilic polymers. They respond to external stimulations (for example, temperature, pH and liquid phase composition) by changing their degree of swelling, e.g. the amount of solvent components they absorb from their surroundings. The swelling/shrinking phenomena are governed by the properties of the hydrogel phase and the liquid phase that coexists with that gel. The basic thermodynamic relations of such phase equilibria are at first summarized and at second, applied to correlate and predict the response of some synthetic hydrogels (of n-isopropyl acrylamide (NIPAAm) and sodium methacrylate (NaMA)) to aqueous electrolyte solutions as well as to aqueous/organic solvent mixtures. The models for the hydrogel require parameters which have to be determined from some results of experimental investigations with well-defined gels. Such models then allow to predict the influence of some important characteristics of such hydrogels on the stimulated response. Typical examples for such correlation and predictions are presented.

### Thermodynamics of Phase Equilibrium in Systems with Hydrogels

The phase equilibrium conditions are derived from the 2nd law of thermodynamics. For a given amount of substance the 2nd law of thermodynamics at constant temperature and constant (external) pressure states that when a liquid phase I coexists in equilibrium with a gel phase II the sum of the Gibbs energies G of both phases must attain a minimum:

$$G^{I}+G^{II} \rightarrow \text{Min.} \qquad (1)$$

Here the surrounding liquid is either an aqueous organic solvent mixture or an aqueous electrolyte solution. Well-established models exist for the Gibbs energy of such solutions (e.g., the UNIQUAC relation of nonelectrolyte mixtures and Pitzer's equation for aqueous electrolyte solutions (see, for example, Prausnitz et al.[1]). The gel phase differs from a conventional liquid phase due to its elastic properties (similar to a solid). The Gibbs energy of the gel phase $G^{II}$ is split into two parts: one part

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($G^{II,liq}$) describes the liquid-like behaviour whereas the other ($G^{II,elastic}$) results from the elastic properties:

$$G^{II} = G^{II,liq} + G^{II,elastic}. \tag{2}$$

For describing $G^{II,liq}$ the gel is virtually split into polymeric chains of even length at all crosslinking positions, i.e. the gel phase consists of polymeric chains dissolved in a liquid solution. The elastic properties of the gel phase are expressed using an equation for the Helmholtz energy $A^m$ of an elastic network:

$$G^{II,elastic} = A^m. \tag{3}$$

The final result for the phase equilibrium between a liquid phase I and a gel phase II can then be written as (cf. Maurer and Prausnitz[2]):

At constant temperature T and constant external pressure p:

$$\begin{aligned}\ln a_j^I(T,p,n_k^I) &= \ln a_j^I(T,p,n_k^{II}) \\ &\quad + \frac{v_j^{II}}{RT}\left(\frac{\partial A^m}{\partial V^{II}}\right)_T \\ &\quad + \frac{z_j}{z_q}\left\{\ln\left(\frac{a_q^I(T,p,n_k^I}{a_q^{II}(T,p,n_k^{II}}\right) - \frac{v_q^{II}}{RT}\left(\frac{\partial A_m}{\partial V^{II}}\right)_T\right\}\end{aligned} \tag{4}$$

where $a_j^I$ and $a_j^{II}$ are the thermodynamic activities of component j in the liquid phase I and the gel phase II, respectively. These activities are calculated from expressions for the Gibbs energy. $n_k^I$ and $n_k^{II}$ are the number of moles of component k in phase I and II, respectively. $V^{II}$ and $v_j^{II}$are the volume of the gel phase and the partial molar volume of component j in the gel phase. $z_j$ is the electric charge number of component j. R is the universal gas constant. Eq. (4) holds for all nonionic and ionic species j that partition between the coexisting phases, but not for an arbitrarily selected ionic species q that is used to fulfil the side condition of electroneutrality of each of the coexisting phases.

The Gibbs energy of a nonionic mixture is calculated applying the UNIQUAC-expression for the Gibbs excess energy in combination with a "Free Volume" correction that is to account for the size differences between solvent molecules on one side and the polymeric chains on the other side (see, for example, Hüther et al.[3]). When the hydrogel contains an ionic comonomer, it is assumed that the comomomers are either completely dissociated or are subject to dissociation equilibrium. All electrolyte solutions are treated applying an extension of Pitzer's equation for the Gibbs excess energy of aqueous electrolyte solutions. The extension takes the differences in the sizes of the components into account (for more details, see for example, Hüther et al.[4]). The models require pure components size/surface parameters and binary parameters for interactions between solute species. Those parameters have to be determined as far as possible from independent thermodynamic investigations, for example from the osmotic coefficient of aqueous electrolyte solutions and the vapour-liquid equilibrium of aqueous/organic liquid mixtures. Only a few interaction parameters (for example between a salt and n-IPAAm) and a network parameter are to be determined from phase equilibrium data of the hydrogel/solvent systems.

The Helmholtz energy $A^m$ for an elastic volume expansion of a hydrogel is described here only for nonionic polymer chains. The extension to ionic polymer chains is available elsewhere (Orlov et al.[5]). The Helmholtz energy of an expanded (from its volume in the stress-free state $V_0$ to the actual volume $V^{II}$) nonionic hydrogel is given by the phantom network theory.[6]

$$\frac{A^m}{RT} = C_{nonion} n_{poly}\left[\left(\frac{V^{II}}{V_0}\right)^{\frac{2}{3}} - 1\right] \tag{5}$$

$C_{nonion}$ and $n_{poly}$ are adjustable parameters which characterize the stiffness of the nonionic hydrogel and the number of polymer chains, respectively. Assuming a perfect tetrafunctional network allows to calculate the number of polymer chains from the parameters used to characterize the polymer network (see below). The volume of the polymer network in the stress-free state $V_0$ is approximated by the volume of the liquid phase before polymerization/crosslinking. Both volumes ($V_0$ and $V^{II}$) are calculated assuming ideal mixing – i.e. neglecting any excess volumes. Only the network parameter $C_{nonion}$ has to be determined from experimental swelling equilibrium data (typically from the swelling equilibrium in pure water).

## Characterization of Hydrogels

One of the most important problems in systems with hydrogels as well as in comparing the experimental data with such calculation results consists in a sufficient characterization of the polymer network. Within the scope of the present investigations, the hydrogels are characterized by the process of the polymerization and by three additional parameters: the total mass fraction $\xi_{gel}$ of polymerizable material ($\xi_{gel} = (m_{mono} + m_{cr})/m_{feed}$), the mole fraction of cross linking agent $y_{cr}$ ($y_{cr} = n_{cr}/(n_{mono} + n_{cr})$) and the comonomer mole fraction $y_{co}$ ($y_{co} = n_{co}/(n_{mono} + n_{co})$) $m$ and $n$ are amount of mass and mole number, respectively. The subscripts *mono*, *cr*, *co*, and *feed* designate "monomer", "crosslinker", "comonomer", and the "feed solution". The production procedure has to be described in such detail, that the gel can be reproduced sufficiently.

## Experimental Data for the Swelling Equilibrium

The modeling has to be based on reliable data for the phase equilibrium of hydrogel systems. Figure 1 is to demonstrate that such experimental data have to be carefully evaluated. Figure 1 shows the degree of swelling $q$, i.e., the ratio of the masses of the equilibrated gel $m_{gel}$ and the polymeric network $m_{gel}^{(dry)}$ ($q = m_{gel}/m_{gel}^{dry}$) of a non-ionic hydrogel of NIPAAm in aqueous solutions of ethanol at 25 °C.[3] One set of experimental data was obtained by immersing the "dried" hydrogel into the liquid solutions, whereas the other set was determined by immersing the swollen gel (swollen in pure water) into the aqueous solution ("wet" gel). The experimental results differ when the ethanol concentration of the liquid solvent mixer lies between about 20 and 45 mass percent. There the "dried" gel exists in a shrunken state, whereas the "wet" gel looks like to be in a swollen state. That behavior might be due

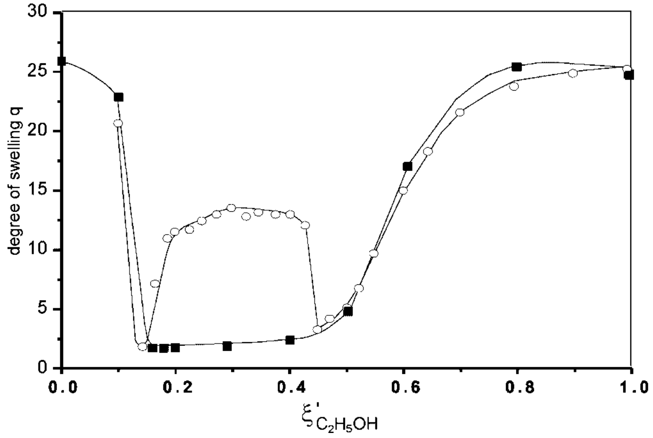

**Figure 1.**

Exp. results for the swelling of NIPAAm hydrogels ($\xi_{gel} = 0.08$, $y_{cr} = 0.015$) in aqueous solutions of ethanol at 25 °C [3]: ○, "wet" gel, i.e., gel swollen in pure water before immersion in aqueous solution; ■, gel dried before immersion in aqueous solution.

to a multiple phase transition. However, a detailed investigation of the structure of the gel in that region shows that the gel consists of a swollen core and a shrunken shell. When the "wet" gel is immersed into the liquid solution, the outer regions shrink quickly forming a shell that does not allow the core of the gel to reach equilibrium with the surrounding liquid. Thus the results for the "wet" gel are influenced by the shrinking kinetics and cannot be considered as equilibrium results.

Typical results for the equilibrium swelling of NIPAAm/NaMa hydrogels in aqueous solutions at 25 °C are presented below together with correlation/prediction results. All examples are taken from publications of my group. The detailed characteristics of the gels as well as the details of the modeling are described in those publications.

### NIPAAm/NaMA Hydrogels in (Water + Di-sodium Hydrogen Phosphate)

Figure 2 presents experimental data for the swelling equilibrium of four non-ionic NIPAAm hydrogels in aqueous solutions of di-sodium hydrogen phosphate. The hydrogels differ in two characteristic properties (the total mass fraction $\xi_{gel}$ of polymerizable material and the mole fraction of cross linking agent $y_{cr}$). At low salt concentrations the gels are swollen, whereas they shrink at high salt concentrations. The transition from a swollen to a shrunken state appears at salt concentrations $\xi^{I}_{Na_2HPO_4}$ of about 0.01 g/g. The experimental results for the degree of swelling in pure water were used to determine the gel-specific parameter in the equation for the Helmholtz energy of the network. The experimental results for the degree of swelling for a single gel were used to adjust some parameters for interactions between the salt ions and the NIPAAm-groups in the network. All other parameters were determined from independent experimental data. With the resulting set of parameters the model reliably predicts the degree of swelling of the other investigated nonionic hydrogels.

Figure 3 shows a comparison between experimental data and prediction results for the degree of swelling of three ionic IPAAm/NaMA hydrogels in the same aqueous solutions.

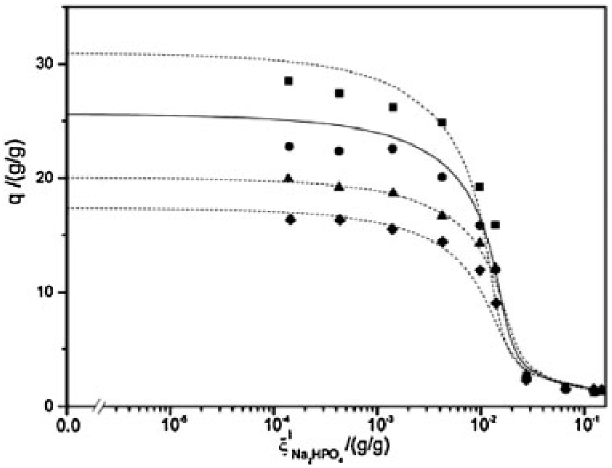

**Figure 2.**
Swelling of non-ionic NIPAAm hydrogels in aqueous solutions of di-sodium hydrogen phosphate [7]: Experimental results: ■, $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.01$ mol/mol, ● $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.015$ mol/mol,▲ $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.02$ mol/mol,◆ $\xi_{gel} = 0.1$ g/g;, $y_{cr} = 0.015$ mol/mol. Calculation results: (——) correlation and (- - - -) predictions.

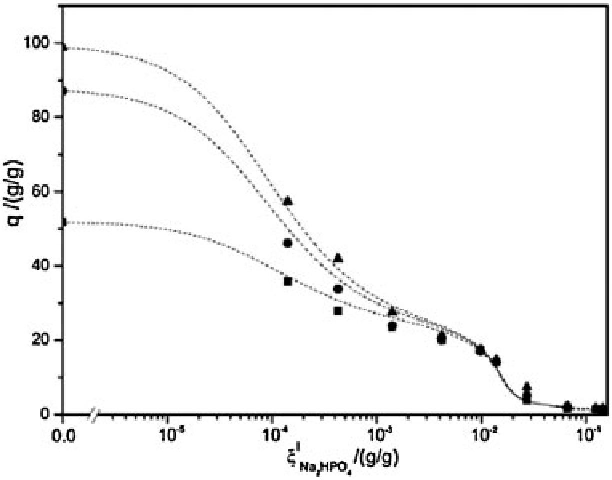

*Figure 3.*
Swelling of NIPAAm/NaMA hydrogels in aqueous solutions of di-sodium hydrogen phosphate [7]: $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.015$ mol/mol. Experimental results: ■, $y_{co} = 0.01$ mol/mol, ● $y_{co} = 0.02$ mol/mol, ▲, $y_{co} = 0.03$ mol/mol. Prediction results: (– – – –).

There is only a difference in the swelling behavior of the ionic and non-ionic hydrogels in very diluted salt solutions, where the ionic hydrogels reveal a higher degree of swelling as the nonionic gels. With increasing salt concentration these differences disappear before the hydrogels shrink. The model quantitatively predicts that behavior.

## NIPAAm/NaMA Hydrogels in Miscible Aqueous/organic Solvent Mixtures

Figure 4 shows a typical example for experimental data and correlation/prediction

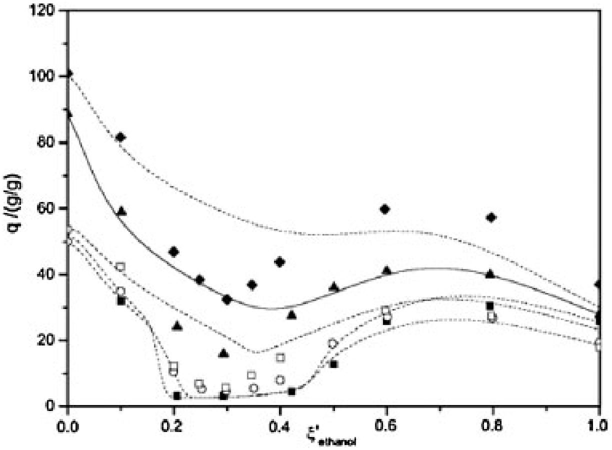

*Figure 4.*
Swelling of PNIPAAm/NaMA hydrogels in aqueous solutions of ethanol at 298 K [5]. Experimental results for hydrogels characterized by a) $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.015$ mol/mol and $y_{co} = 0.01$ mol/mol (■), $y_{co} = 0.02$ mol/mol (▲), $y_{co} = 0.03$ mol/mol (◆); b) $\xi_{gel} = 0.08$ g/g; $y_{cr} = 0.02$ mol/mol, $y_{co} = 0.02$ mol/mol (□), c) $\xi_{gel} = 0.1$ g/g; $y_{cr} = 0.015$ mol/mol, $y_{co} = 0.02$ mol/mol (○) and calculation results: (——) correlation; (– – – –) prediction.

results for the degree of swelling of some ionic NIPAAm/NaMa hydrogels in aqueous solutions of ethanol at 25 °C. Such nonionic gels are in a shrunken state at about 30 mass percent ethanol in the coexisting liquid phase (cf. also Figure 1). With increasing comonomer concentration $y_{co}$ the concentration range where the gel is shrunken, decreases and at higher comonomer concentrations the gel swells in all solvent mixtures. The model is suited to describe that behavior adequately.

### NIPAAm Hydrogels in Aqueous/organic Two-phase Systems

Figure 5 demonstrates that the thermodynamic framework is evenly suited to describe the swelling of noninionic NIPAAm hydrogels in aqueous solutions of an organic solvent when these mixtures reveal a liquid-liquid miscibility gap. That statement holds when the gel shrinks in the miscibility gap (e.g., with butanol as the organic solvent; left side of Figure 5) but also when the gel swells in the two-phase systems (e.g., with

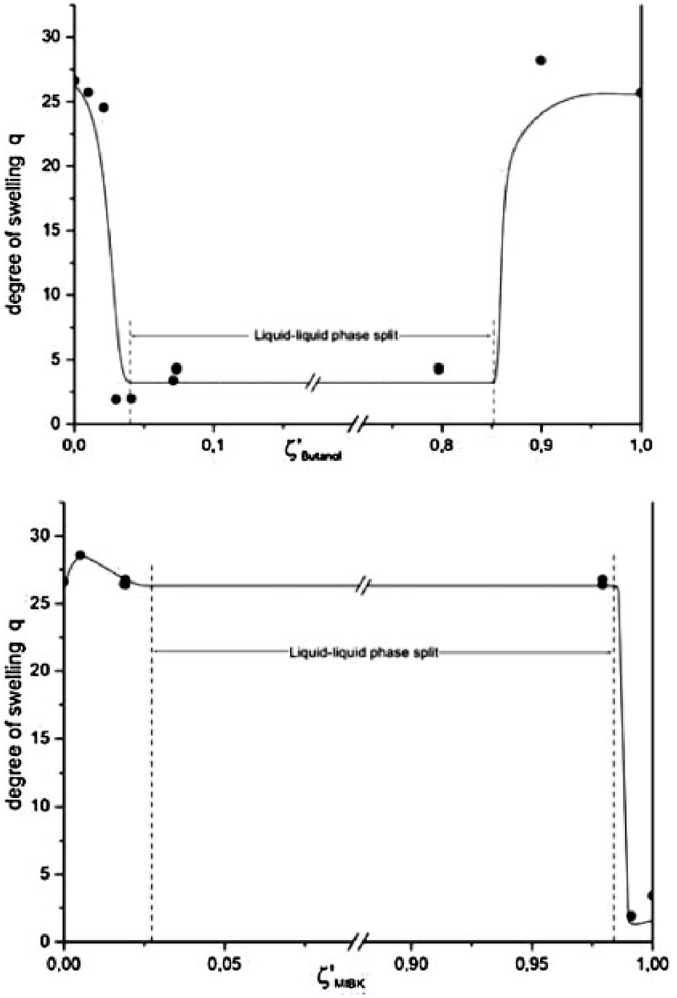

**Figure 5.**
Degree of swelling q $\left(= m_{gel} \big/ m_{gel}^{(dry)}\right)$ of a NIPAAm hydrogel (characterized by: $\xi_{gel} = 0.08$ g·g$^{-1}$; $y_{cr} = 0.015$ mol·mol$^{-1}$) in aqueous solutions of 1-butanol (top) and of methylisobutylketone (bottom) at 298 K: ● exp. data; ——, correlation results. [8]

methyl isobutylketone as the organic solvent; bottom side of Figure 5).

## Conclusion

The swelling equilibrium of NIPAAm/NaMA hydrogels in aqueous solutions of a single solute (electrolyte or organic solvent) is successfully described (i.e., correlated/predicted) by thermodynamic methods. The methods are shortly presented together with some typical examples. More details as well as further examples have been published before.[3–5,7–12] Currently work on extending the framework to other nonionic (of vinyl-2-pyrrolidone) and ionic hydrogels (of vinyl-2-pyrrolidone and sodium methacrylate) is in progress.

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[1] J. M. Prausnitz, R. N. Lichtenthaler, E. Gomes de Azevedo, "*Molecular Thermodynamics of Fluid Phase Equilibria*", Prentice Hall PTR, Upper Saddle River, New Jersey **1999**.
[2] G. Maurer, J. M. Prausnitz, *Fluid Phase Equilib.* **1996**, *115*, 113.
[3] A. Hüther, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2004**, *219*, 231.
[4] A. Hüther, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2006**, *240*, 186.
[5] Y. Orlov, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2006**, *249*, 6.
[6] L. R. G. Treloar, "*The Physics of Rubber Elasticity*", 3rd Ed., Clarendon Press, Oxford **1975**.
[7] Y. Orlov, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2007**, *254*, 1.
[8] Y. Orlov, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2005**, *235*, 18.
[9] J. Thiel, G. Maurer, *Fluid Phase Equilib.* **1999**, *165*, 225.
[10] A. Hüther, B. Schäfer, X. Xu, G. Maurer, *Phys. Chem. Chem. Phys.* **2002**, *4*, 835.
[11] A. Hüther, G. Maurer, *Fluid Phase Equilib.* **2004**, *226*, 321.
[12] Y. Orlov, X. Xu, G. Maurer, *Fluid Phase Equilib.* **2005**, *238*, 87.