

Sensing of Adsorption Induced Phase Behavior of Stimuli-sensitive Polymer Hydrogel Using Quartz Crystal Microbalance

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Abstract

Quartz crystal microbalances (QCM) loaded with poly(N-isopropylacrylamide; NIPA) or poly(N-isopropylacrylamide-acrylic acid, sodium salt; NIPA-SA) micro-hydrogels were prepared. Oscillation frequency of the QCMs for the series of solutions was measured as a function of solution temperature and concentration of additive adsorbates (acrylic acid; AAc and Cu^{2+} ion) in the solutions. The QCM loaded with the gels showed the characteristic oscillation behavior responding to the phase behavior of gels. Drastic shift of the oscillation frequency was observed at the phase transition temperature, T_p , of the gels. The critical temperature T_p at which the drastic change in the oscillation frequency shift appeared decreased by the addition of adsorbates. The change in hydrophobic/hydrophilic balance of the gels due to the adsorption of additives onto the gel resulted in the shift of the critical temperature. The results obtained in this study demonstrated that stimuli-sensitive polymer hydrogel coupled with QCM is a promising device for molecular sensing through the adsorption induced phase change of the gel.

Key words: Polymer hydrogel, quartz crystal microbalance, Phase transition, Resonator, Adsorption

1. INTRODUCTION

Stimuli-sensitive polymer hydrogels have been attracting much attention due to their scientific and engineering importance. Many kinds of the gels that reveal volume phase transition responding to various stimuli and/or environmental change such as light, pH, electric field, solvent and temperature have been investigated¹⁾. The phase behavior and/or swelling volume of gels can be predicted based on the Flory-Huggins and Tanaka's theory^{2,3)} in which osmotic pressure of gel due to mixing between polymer and solvent, elasticity of polymer network and mobile ions are considered. Microscopic reaction occurring in hydrogels can be macroscopically observable by change in phase and/or swelling of the gels in the case of crosslinked polymer hydrogels. The phase change of hydrogels can also be interpreted to occur through a change in hydrophobic/hydrophilic balance of the polymer induced by the stimuli and/or the change in environmental condition⁴⁾. According to the principle of phase behavior of gels, adsorption of a molecule onto the polymer will also be a potential trigger of the phase change of gels if the change in hydrophobic/hydrophilic balance of the polymer can be induced by the adsorption. This simple assumption enables the gels a candidate for sensing device of a target molecule with amplification function of signal through the phase (volume) change of the gels with apparently infinite molecular weight.

In the present study, stimuli-sensitive polymer

hydrogels coupled with quartz crystal micro balance, QCM, were prepared. Oscillation behavior of the QCM with the loaded gels was investigated as a function of temperature and the concentration of adsorbate molecules.

2. ADSORPTION INDUCED PHASE TRANSITION OF HYDROGEL

Figure 1 shows the principle of adsorption induced phase transition of stimuli-sensitive polymer hydrogel. The principle is shown using the case of poly(N-isopropylacrylamide; NIPA) hydrogel, the representative thermo-responsive polymer hydrogel with volume phase transition at a critical temperature, T_{p0} . When functional monomers with different hydrophobicity from poly(NIPA) are copolymerized, shift of the original swelling curve of poly(NIPA) gel (bold line) occurs due to a change in hydrophobic/hydrophilic balance of the polymer network⁵⁾. Introduction of a hydrophilic functional monomer results in the shift of original swelling curve toward higher temperature region (①). On the contrary, introduction of a hydrophobic functional monomer results in the shift toward lower temperature region (②). When the introduced functional monomers adsorb a molecule and the functional monomers reveal the change in hydrophobic/hydrophilic balance by the adsorption, the shift of swelling curve will occur depending upon the apparent change in the hydrophilic/hydrophobic balance of the network. Volume

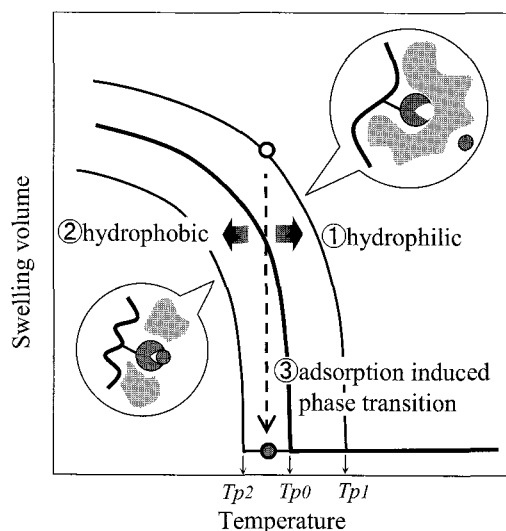


Figure 1 Schematic diagram of the adsorption induced phase change of stimuli-sensitive polymer hydrogel. Bold line; poly(NIPA) gel, thin lines; poly(NIPA) copolymer gels

change of the hydrogel will be induced by the adsorption at an isothermal condition. For instance, when a copolymer hydrogel between the NIPA and a hydrophilic monomer adsorbs a molecule, and reveals the decrease in the hydrophilicity of the copolymer by the adsorption due to any reasons such as compensation of charge or hydrophilic part, and adsorption of molecule with strong hydrophobicity, the swelling curve of the gel with phase transition at a temperature, T_{p1} , shifts toward lower temperature with phase transition temperature, T_{p2} . In case of the gel, the adsorption induced volume change of gel can be induced effectively at an isothermal condition in the temperature range between T_{p1} and T_{p2} (③). Any kind of functional molecules which reveal the change in their hydrophobic/hydrophilic balance by the adsorption of its affinitive molecules will be applicable to the adsorption induced phase transition in principle when introduced in the network.

3. Quartz crystal microbalance; QCM

Sauerbrey ⁷⁾ investigated mass/frequency shift relation for rigid foreign layers that are firmly attached to the surface of a resonator. The theoretical derivation of the relation assumes that a thin layer of foreign material is the antinode of the standing wave in the quartz crystal. The change in oscillation frequency of resonator, $-\Delta F$, is defined by the following equation (1).

$$-\Delta F = 2F_0^2 / (A\rho_q^{-0.5}\mu_q^{-0.5})\Delta m \quad (1)$$

Where $-\Delta F$ is the change in oscillation frequency of the resonator (QCM) due to added mass (Δm) on the surface of resonator. F_0 is oscillation frequency of the unloaded resonator. ρ_q and μ_q are the density and shear modulus of

quartz, respectively. A is surface area of the resonator. Phase change of the loaded hydrogel causes a change in apparent Δm , resulting in the change in $-\Delta F$. Kanazawa *et al.*⁸⁾ extended the theory for resonator immersed in a viscous medium of infinite extent and provided the extended relationship between solution properties and oscillation frequency shift as shown in equation (2), where ρ_L and η_L are density and viscosity of liquid in contact with the resonator, respectively. The equation (2) means that the viscosity and density of a medium in contact with the resonator affect the oscillation frequency.

$$-\Delta F = F_0^{3/2} [(\rho_L \eta_L) / (\pi \rho_q \mu_q)]^{1/2} \quad (2)$$

4. EXPERIMENTAL

4.1 Preparation of resonator loaded with the hydrogels

5MHz AT-cut quartz crystal resonator with gold electrodes ($\phi=10\text{mm}$, supplied from Mita-Denpa Co. Ltd. of Japan) were used in the present study. One side of the resonator was sealed using a silicon rubber not to contact with solution in its use. Poly(N-isopropylacrylamide) (NIPA) or poly(NIPA- Sodium acrylate) (NIPA-SA) copolymer hydrogels were loaded on the open surface of resonator. 0.5~1.0 μl of pregel reaction mixture containing 700mM NIPA+SA; 7mM N,N'-methylene-bisacrylamide; (crosslinker) and 20mM V-50; initiator was dropped on the surface followed by polymerization under *uv*-light irradiation for 3 min. The prepared gels on the resonator were washed by a large amount of distilled water to wash away residual chemicals. Thickness of the loaded gel was around 0.1mm

4.2 Oscillation of the resonator

Figure 2 shows schematic diagram of the experimental apparatus. The prepared resonators with the hydrogels were oscillated using an oscillator circuit assembled in our laboratory ⁹⁾. The resonators loaded with the hydrogels were immersed in 50ml of temperature controlled aqueous solutions containing adsorbates. Acrylic acid; AAc and copper ion (CuCl_2) were used as the adsorbate for NIPA and SA, respectively. NIPA

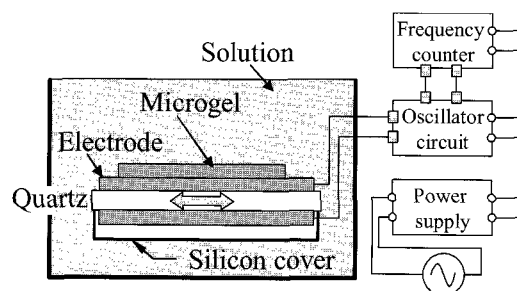


Figure 2 Schematic diagram of the QCM device loaded with the stimuli-sensitive polymer hydrogels and the experimental apparatus for the measurement of oscillation frequency shift.

adsorbs acrylic acid through hydrogen bonding between carbonyl and amide groups of NIPA and carboxyl group of acrylic acid¹⁰. SA adsorbs copper ion through electrostatic interaction via ion-exchange. The oscillation frequency was monitored as a function of solution temperature and concentration of the adsorbates using a frequency counter (Akiba Electric co. Ltd., FC-7150U). Oscillation behavior of the resonator without the gels was also measured for the series of experimental conditions to clarify the effect of gel on the oscillation behavior of resonator. All the reagents were used as supplied without further purification in each experiment.

5. RESULTS and DISCUSSION

Figure 3 indicates time course of oscillation frequency shift, $-\Delta F$, in the case of resonator loaded with poly(NIPA). The change in frequency shift occurred quickly within several ten seconds responding to the stepwise temperature change from 283K to 313K. Shrinking rate of hydrogel is inversely proportional to the square of gel size¹¹. The use of micro gel will be advantage of the present device for quick sensing of phase behavior of gel.

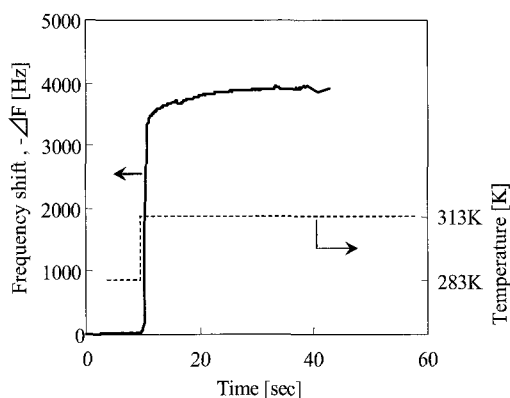


Figure 3 Time-course of the oscillation frequency shift, $-\Delta F$, in the case of resonator loaded with poly(NIPA). The response of resonator to the stepwise temperature change was recorded.

Figure 4 indicates the oscillation frequency shift of resonator loaded with the poly(NIPA) gel as a function of temperature and concentration of acrylic acid; AAc in the solution. Normalized swelling curve of the poly(NIPA) gel¹⁰ is also shown in the figure. The oscillation behavior of resonator at low temperature region below the phase transition temperature, T_p , of poly(NIPA) was similar to the oscillation behavior of resonator in the absence of gel. The oscillation frequency shift, $-\Delta F$, increased drastically at the critical temperature, T_p , of gel, followed by a gentle decrease of the $-\Delta F$. The result indicates that the hydrogel in swelling phase affects the oscillation similar to the solution due to large water content and/or small polymer density of the gel. The small decrease of $-\Delta F$ with increasing temperature is

due to change in viscosity of solution^{8,9}. The steep increase of the $-\Delta F$ at the critical temperature is due to shrinkage of poly(NIPA) gel with the volume phase transition. The collapsed phase of the gel affects resonator as a mass loading due to a large visco-elasticity of the collapsed gel. The sharp and intensive frequency shift at the critical temperature may be due to a critical slowing down of density fluctuation (infinitely small collective diffusion coefficient) of the polymer network at the critical point¹². The gentle decline of $-\Delta F$ at higher temperature region following to the drastic shift at the critical temperature will be due to further dehydration and relaxation of the polymer. Reversibility of temperature dependence of the oscillation behavior of resonator supports the interpretation of the phenomena.

The existence of acrylic acid in the solution affects the oscillation behavior as well as the phase behavior of gel. The phase transition temperature of gel decreases with the increase of concentration of acrylic acid. This is due to the increase of hydrophobicity of the gel through adsorption of acrylic acid onto the hydrophilic functional groups of the poly(NIPA). The increase of acrylic acid in the solution also decreases the viscosity of solution, resulting in the decrease of overall frequency shift depending on the concentration. The contribution of AAc adsorption to the Δm will be small compared with that of gel.

Figure 5 indicates temperature dependency of the $-\Delta F$ for the resonator loaded with poly(NIPA-SA) gel. The oscillation behavior of the resonator was similar to the behavior of resonator loaded with poly(NIPA). The

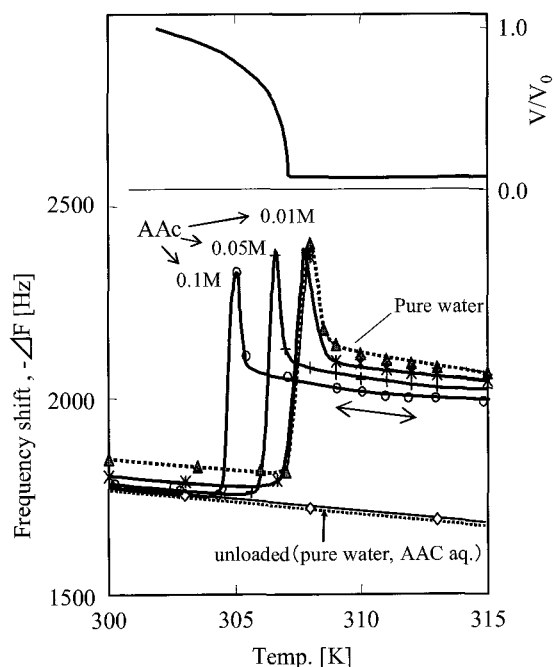


Figure 4 Temperature dependence of the oscillation frequency shift, $-\Delta F$, of the resonator loaded with poly(NIPA) gel for the series of solutions containing acrylic acid.

frequency shift, $-\Delta F$, at low temperature region below the critical temperature of the poly(NIPA-SA) gel was almost the same with the shift of resonator without the gel. The curve of $-\Delta F$ shifted toward the higher temperature region in the solution with pH=9.0. The resonator loaded with poly(NIPA-SA) was washed by large amount of distilled water at the preparation stage. During the wash, the counter ion of SA was exchanged from sodium ion to proton due to the washing of the microgel by the large amount of distilled water, resulting in the oscillation behavior similar to the resonator loaded with poly(NIPA) in pure water with pH=5.7. The phase behavior of poly(NIPA-SA) is almost the same with poly(NIPA) in acidic solutions¹⁰. The counter ion was exchanged again to sodium ion in the alkali solution with pH=10 and the $-\Delta F$ curve shifted toward higher temperature region due to the increase of hydrophilicity of the gel. The curve shifted toward lower temperature region in the solution containing Cu^{2+} ion. The SA in gel adsorbed Cu^{2+} ions through the ion-exchange of its counter ions and reveals hydrophobicity due to the complex formation between the carboxylates and Cu^{2+} ions, releasing hydrated water of them¹³. The critical temperature with the steep frequency shift of the resonator depends upon the concentration of adsorbates, indicating that phase transition of the gel can be induced through adsorption of the adsorbates within a short time in the experimental range.

The QCM loaded with stimuli-sensitive polymer hydrogel reveals quick change in its oscillation frequency responding to environmental change. The oscillation frequency of the QCM changes sensitively reflecting the phase change of the hydrogel so that the use of hydrophilic/hydrophobic balance change of the hydrogel enables the sensitive molecular sensing based on the adsorption induced phase change of the gel.

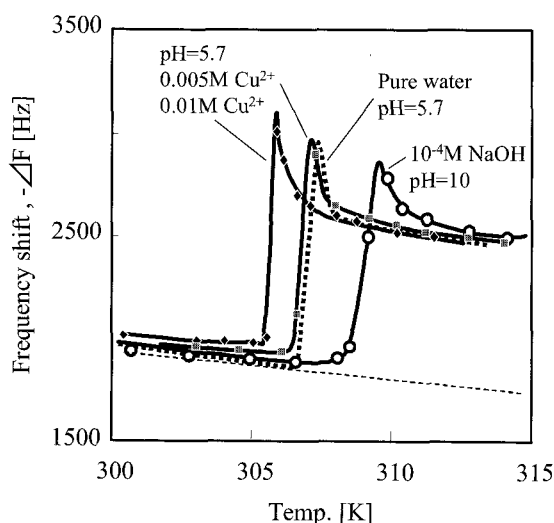


Figure 5 Temperature dependence of the frequency shift of the resonator loaded with poly(NIPA-SA) gel for the series of solutions containing copper ions.

6. CONCLUSION

The oscillation behavior of resonator loaded with poly(NIPA) and poly(NIPA-SA) micro-hydrogels were observed as the function of solution temperature and concentration of the adsorbates. The responsiveness of oscillation frequency of the resonator with gel is quick within several ten seconds to temperature change. In the case of molecules which induce the change in hydrophilic/hydrophobic balance of hydrogel through their adsorption onto the gel, the phase change of the gel can be induced by the adsorption trigger. The results demonstrated in the present paper indicate the feasibility of molecular sensing utilizing the phase change of stimuli-sensitive polymer hydrogels. The coupling of the gel with QCM potentially enables the rapid molecular sensing with high resolution.

7. ACKNOWLEDGEMENT

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