Characterization of the Water Environments in Thermosensitive NiPAAm Gels using ^{1}H HRMAS NMR

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Photograph by Sarah K. McIntyre

Abstract

Thermosensitive gels are polymers that modify their conformation in response to temperature change. Many polymers exhibit this property, including N-isopropylacrylamide (NiPAAm). NiPAAm polymer gels are perhaps the most studied thermosensitive polymer because it has a low critical solution temperature (LCST) at 32 °C, and the transition period from a homogenous mixture to a phase-separated polymer is small, within 1-2°C. The LCST is close to a human's body temperature, making it particularly desirable for drug delivery and tissue engineering. Even with this popularity, the water environments above and below the LCST are not completely understood. In this poster, ^{1}H high-resolution magic-angle spinning (HRMAS) nuclear magnetic resonance (NMR) spectroscopy was used to identify and characterize the different water environments present near the LCST. The improved spectral resolution afforded by HRMAS NMR allowed the identification of multiple water environments in these gels, which were observed to depend on the temperature and cross-link ratios. By coupling HRMAS NMR with pulse field gradient (PFG) experiments, it was also possible to measure the self-diffusion rates for these different water environments. Spin-spin relaxation times (T_2), and self-diffusion results were obtained as a function of temperature for two different gels preparation protocols. These HRMAS NMR results provide additional insights to describe the water environments in thermo-responsive gels such as NiPAAm.

Experimental

Sample Preparation:

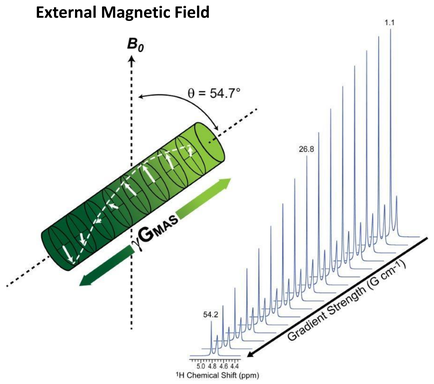
Sample 1: Prepared using a free-radical polymerization initiated by heating for 18 hours in DMSO (dimethyl sulfoxide)

Sample 2: Prepared using a free-radical photopolymerization process that formed gel in 3-4 minutes in aqueous solution

HRMAS NMR Spectroscopy:

All ^{1}H NMR experiments were performed on a Bruker Avance-III Spectrometer at 600.135MHz using a 4mm HRMAS probe. One-dimensional variable temperature (VT) experiments were obtained at increasing temperatures through the LCST with a controlled temperature unit that guaranteed thermal stability with ±0.1°C accuracy. A stimulated bipolar sequence with a gradient ramp containing either 16 or 32 values and 8 scans was used to obtain diffusion coefficients. The self-diffusion coefficients (D) were determined from the signal decay using the Stejkal and Tanner equation where S(g) and S(0) are the integrated signal intensities obtained with and without gradients, DT is the translational self-diffusion coefficient, γ is the gyromagnetic ratio, g is the gradient strength, δ is the duration of the gradient pulse, and Δ is the diffusion time between pulses. At 308K a second peak to the right of the free water peak starting forming, and a diffusion coefficient was obtained for this peak by increasing the interpulse delay, thus amplifying its intensity. Transverse spin-spin relaxation times (T_2) were obtained using inversion recovery and a CPMG (Carr-Purcell-Meiboom-Gill) pulse sequence at temperatures through the LCST. Rates were found using the inverse of the relaxation times.

External Magnetic Field



Todd M. Alam, Janelle E Jenkins, HR-MAS NMR Spectroscopy in Material Science

Stejkal and Tanner Equation

$$S(g) = S(0)\exp[-D_T\gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right)]$$

Inhomogeneity Dipolar Equations

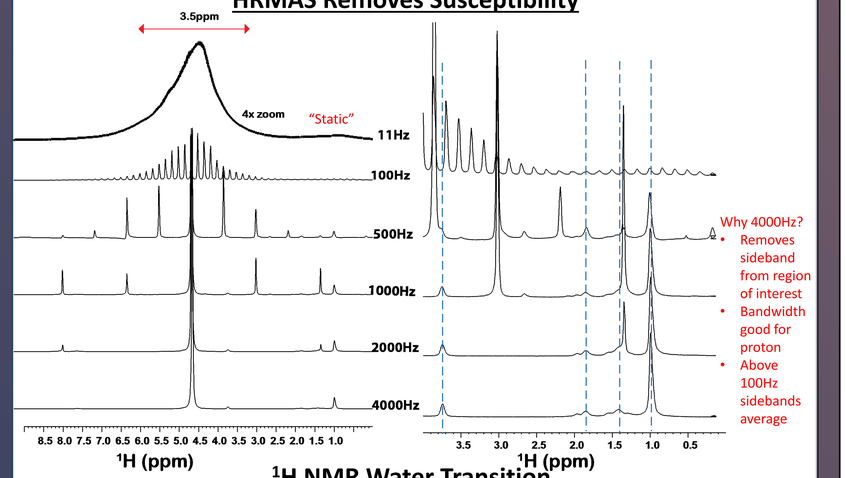
$$B(r_i, \theta_i, \phi_i) = \sum_i \frac{M_j}{r_{ij}^3}\frac{1}{2}(3cos^2\theta_{ij} - 1)$$

$$B(r_i, \theta_i, \phi_i, t) = \sum \frac{M_j}{r_{ij}^3}[\frac{1}{4}(3cos^2\beta - 1)(3cos^2\beta_{ij}' - 1) + \frac{3}{4}sin2\beta sin2\beta_{ij}' \cos(\omega_R t + \phi_{ij}) + \frac{3}{4}sin^2\beta sin^2\beta_{ij}' \cos(2\omega_R t + 2\phi_{ij})]$$

$(3cos^2\beta - 1) = 0$ when $\beta = 54.7°$

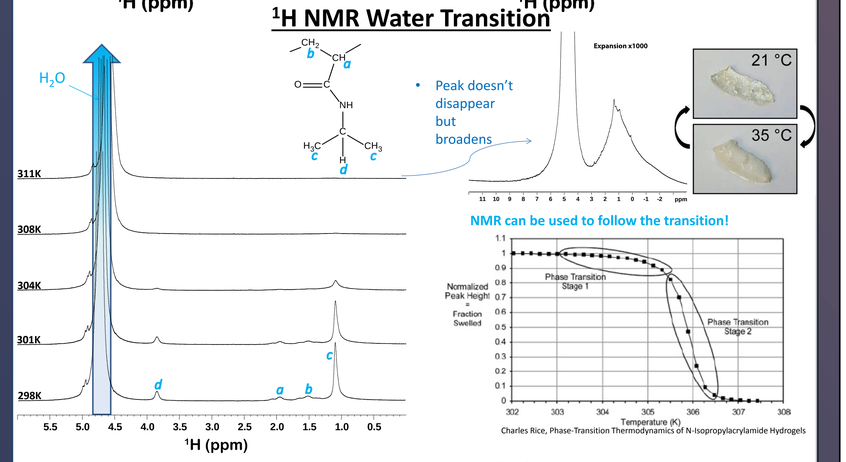
- "Magic angle" at which magnetic susceptibility goes to zero

HRMAS Removes Susceptibility



Why 4000Hz?
- Removes sideband from region of interest
- Bandwidth good for proton
- Above 100Hz sidebands average

^{1}H NMR Water Transition

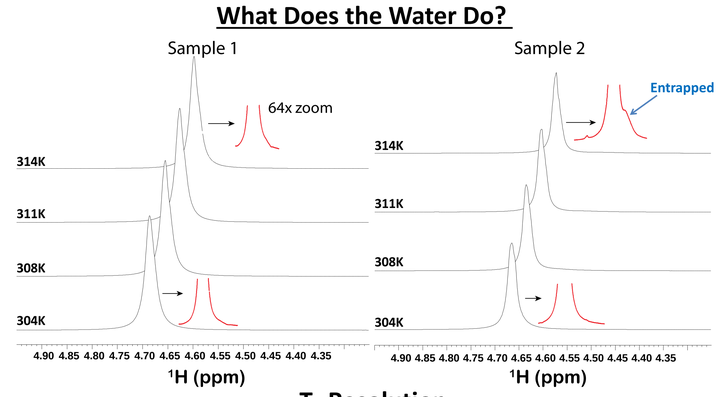


- Peak doesn't disappear but broadens

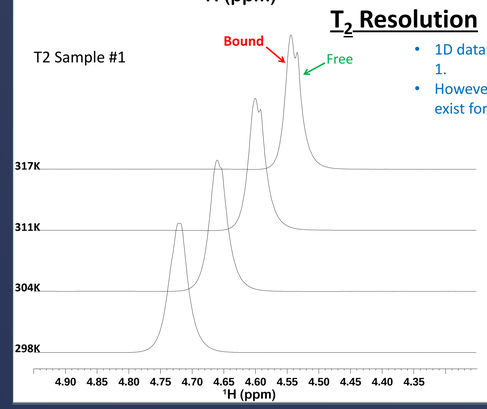
NMR can be used to follow the transition!

Charles Rice, Phase-Transition Thermodynamics of N-Isopropylacrylamide Hydrogels

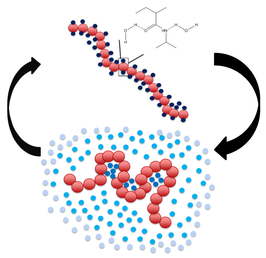
What Does the Water Do?



T_2 Resolution

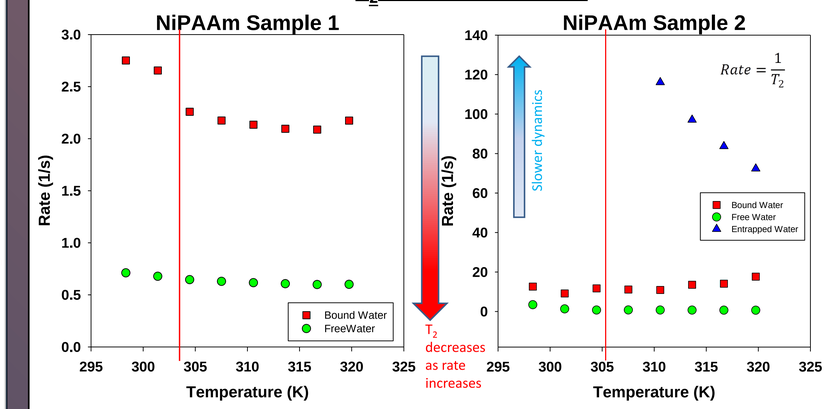


- 1D data showed only one water environment for Sample 1.
- However, T_2 data suggests multiple water environments exist for Sample 1.



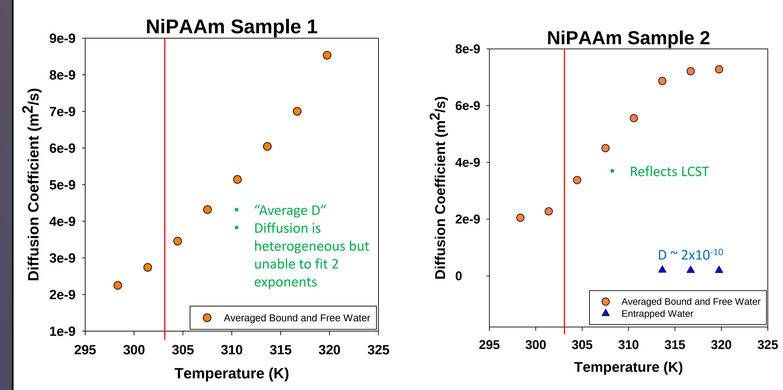
Multiple H_2O environments exist

T_2 Relaxation Results

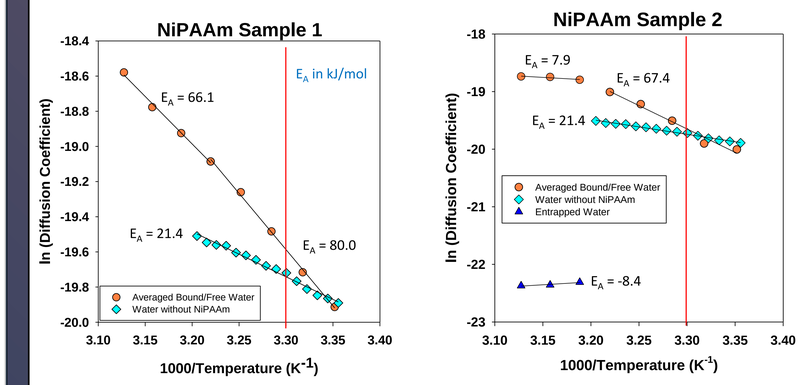


T_2 decreases as rate increases

Diffusion Results



- "Average D"
- Diffusion is heterogeneous but unable to fit 2 exponents



CONCLUSIONS

- HRMAS NMR was able to resolve different H_2O environments in NiPAAm gels.
- Slow and fast R_2 relaxation results discriminate different environments.
- R_2 results suggest these two environments represent water, "free" water and water with only a small polymer interaction.
- Diffusion does not resolve these two environments in Sample 1.
- A " bound" or entangled environment is observed in Sample 2. The diffusion rate is significantly slower, and the relaxation rate is ~10 times larger, resulting from a very slow motion.

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