Biomedical applications of hydrogel with precisely controlled structure

(*¹Graduate School of Engineering, University of Tokyo*)　○Takamasa Sakai[1]
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Hydrogel is a material in which the polymeric network is swollen with a large amount of water. It is possible to exchange substances with the surrounding environment through the water. Because their composition and properties are similar to biological soft tissue, hydrogels are helpful as biomaterials. When used as biomaterials, hydrogels deteriorate in vivo due to various factors and dissolve with swelling. The swelling pressure of hydrogels is defined as the difference between the osmotic pressure that drives the swelling, and the elastic pressure that resists the swelling. Therefore, it is essential to understand and control the elastic and osmotic pressures of hydrogels.

The various physical properties of polymer gels were extrapolated from those of the single polymer chains, polymer solutions, and rubbers. However, our recent research has revealed that the existing theories cannot explain the elastic and osmotic pressures, which are elementary properties of polymer gels. In the presentation, we first discuss the elastic and osmotic pressures, and will introduce hydrogels for hemostat and anti-adhesion agent.
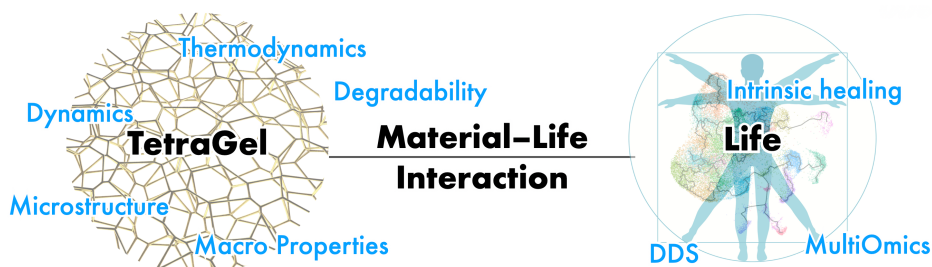

Elastic modulus of Polymer Gels [1]

Materials consisting of a polymeric network structure, such as rubbers and polymer gels, are soft and stretch well. The entropy force explains the elastic property based on the second law of thermodynamics. To confirm this experimentally, we can measure the shear modulus's (G) temperature dependence. Using the relation $G_S = T\partial G/\partial T$, we can separate G into $G = G_S + G_E$, the entropy contribution G_S and the energy contribution G_E. For rubber, experiments have confirmed that $G \approx G_S$ and theories describing rubber elasticity have been developed, focusing only on entropy elasticity (G_S).

On the other hand, the theory of rubber elasticity has been conventionally ($G \approx G_S$) used without any experimental verification for polymer gels, which are rubber swollen by solvents. However, our recent study revealed a non-negligible negative G_E in polymer gels (G-axis intercept of an extrapolated straight line in Fig. 1). This study investigated the physical laws governing the negative G_E using various samples with systematically modulated microscopic structural parameters (prepolymer binding ratio p, branching number f, molar mass M, and concentration C) to elucidate its origin.

We measured the T-dependence of G for all samples and found that the extrapolated line passes through a point (T_0) on the T-axis, independent of p (Figure 1). Thus, the elastic modulus can be written as $G = a(T - T_0)$, where the first and second terms represent the entropy contribution G_S and the energy contribution G_E, respectively. When

the C^* specified by f and M was appropriately chosen and normalized, C-dependence of T_0, which governs the energy elasticity, fell on one master curve. This suggests that T_0 is a universal function of C/C^*. Analysis of the C/C^* dependence of T_0 indicates that the physical origin of the energy elasticity is most likely the interaction of the polymer chain with the solvent.
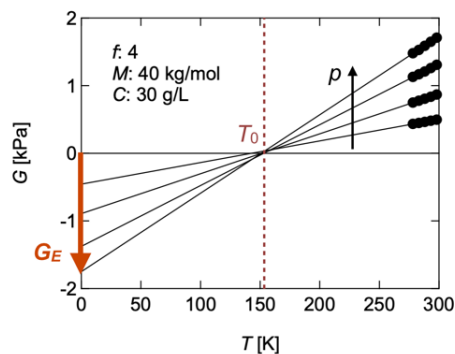

Osmotic Pressure of Polymer Gels [2]

A standard theory and experiments show that the osmotic pressure of a linear polymer solution in a good solvent is described by a universal equation of state $\widehat{\Pi} = f(\hat{c})$ (solid black line in Fig. 2), independent of the length of the polymer chains and the type of solvent. Here, $\hat{c} = c/c^*$ is a dimensionless quantity in which the polymer concentration c is normalized by the overlapping concentration c^*, and $\widehat{\Pi} = \Pi M/(cRT)$ is a dimensionless quantity in which the osmotic pressure Π is normalized by the molar mass M of the polymer, the gas constant R, and the absolute temperature T. In the semi-dilute region where polymer chains penetrate each other, the osmotic pressure approaches asymptotically to the scaling law:

$$\widehat{\Pi} = f(\hat{c}) = K\hat{c}^{1/(3\nu-1)} \quad \text{(for } \hat{c} \gg 1) \qquad (1)$$

, where $K \simeq 1.1$ and $\nu \simeq 0.588$ is the excluded volume index giving $1/(3\nu-1) = 1.31$. In this

study, we measured the osmotic pressure during the gelation process, from the sol state to the gel state, as the end reaction of the polymer chain progresses. It was found that the osmotic pressure can be described by the universal equation of state (1) for linear polymer solutions, even though the polymers form large clusters and a polymer network as the end reaction progresses.
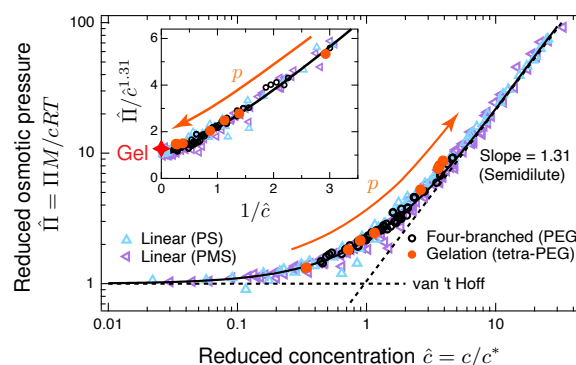
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