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Diffusive Behavior of Physically Cross-linked Hydrogels

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Diffusive Behavior of Physically Cross-linked Hydrogels

Morgan Stilke

Department of Applied Mathematics and Polymer Engineering

**Honors Research Project**

Submitted to

*The Honors College*

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Introduction

A hydrogel is a water swollen polymeric network composed of chemically and/or physically crosslinked hydrophilic polymers.¹ Hydrogels have the potential for transforming many biomedical applications such as drug delivery systems and tissue engineering. The high water content of a hydrogel makes it biologically compatible. Its permeability, swelling properties, and surface functionality become essential in drug delivery systems.² They can be made to be temperature responsive so that once the drug-filled hydrogel reaches the desired area inside of the body, a specific environmental temperature can trigger the release of the drug. Within tissue engineering, hydrogels can act as support structures for cellular growth.³ One of the main problems encountered with hydrogels is their typical poor mechanical robustness. While there are several strategies for improving hydrogel toughness, it is difficult to provide a combination of high modulus, failure toughness, and fatigue resistance. These properties have to be measured in a controlled manner, and water uptake is a key feature. Typically, the swelling of a hydrogel decreases its crosslink density, causing the mechanical properties to become weaker. Part of the problem of improving the mechanical robustness is that certain mechanical properties such as crosslink density and water uptake tend to contradict others. This is one of the main concerns regarding hydrogel toughness. Unfortunately, no synthetic hydrogel can compete with the toughness of any natural hydrogel found in the body such as skin or collagen.⁴ An important realization is that no efficient method exists for determining how the molecular properties affect the optimal mechanical performance for any application. A hydrogel can be composed of physical crosslinks, covalent crosslinks, or a combination of both. I am focusing on physically crosslinked hydrogels and putting together an understanding of its molecular properties. The main role of physical crosslinks is to provide a way for energy dissipation via breaking of sacrificial bonds. This will lead to knowledge of how to incorporate physical crosslinks into a mechanically robust hydrogel.

Natural and synthetic materials based upon associating networks are of deep-rooted interest across a wide variety of different industries.⁵⁶ These materials share a common feature that the network junctions are formed by various physical interactions such as hydrogen bonding,⁷⁻⁹ ionic bonding,¹⁰¹¹ and hydrophobic interactions.¹²¹³ One of the main advantages of having physical crosslinks within a system is that they provide a way for energy to be dissipated. The association energies of physical bonds are typically on the order of $k_B T$, meaning that these bonds can dissociate and recombine due to thermal
fluctuations when triggered by some environmental stimuli. The energy dissipated from these fluctuations during crack growth, \( G_d \), is part of the contribution to fracture toughness, \( G_c \).\(^{15}\) One of the essential challenges of creating a hydrogel with a high fracture toughness emerges from the fact that toughness requires energy dissipation. The reversible crosslinks can dissociate and reform during any type of deformation, dissipating energy.\(^{16}\) Unfortunately, the transient nature of the physical crosslinks can cause dimensional creep, especially at high temperature. Physical and covalent crosslinks both have their own advantages and disadvantages. This is why the ideal hydrogel would have a combination of both networks. Several approaches have been proposed for designing hydrogels that incorporate the advantages of both types of crosslinks. They need a method for energy dissipation while retaining toughness. A promising approach is introducing a double network hydrogel.\(^{17,18}\) One network is sacrificial and mostly load bearing. These networks are the associative junctions that effectively dissipate energy in order to prevent concentrated stress at the early stages of deformation. The other more robust network contributes to the toughness by storing energy and maintaining deformation reversibility. This combination of physical and covalent networks enable soft materials to achieve dramatic enhancements in toughness.\(^{19,20}\) However, before it is possible to understand how to synthesize such a hydrogel, the knowledge of the molecular behavior of each individual network needs to be presented.

The goal of this research is to understand how the dynamics of the hydrogel depend on the attractive energy between crosslinks. The first area of interest for this paper is the linear behavior, which involves observing the diffusive behavior of each hydrogel as well as the distribution of cluster sizes. The cluster distribution shows how many single stickers are present in each hydrogel depending on the attractive energy between crosslinks. The amount of single crosslinking sites compared to occupied sites is a critical variable in predicting the diffusion time of a hydrogel. The diffusion of the hydrogel is expected to follow the Sticky Rouse Model.\(^{21}\) This means that the chains diffuse according to the Rouse model for unentangled polymer chains, however, the sticker beads in the system cause the diffusion to become hindered, leading to an increased diffusion time, \( \tau \). The linear analysis validates the model as well as predicts the results of the nonlinear behavior, the second area of interest. The nonlinear behavior includes any deformation induced on the system, which is the next step but is not covered in this research. The diffusive behavior and aggregate structure leads to information about the linear dynamics of a physically
crosslinked hydrogel, leading to uses in a hybrid network. Hybrid hydrogels are a promising approach to producing more mechanically robust networks for use in biomedical applications.

Methodology

To model a physically crosslinked hydrogel, Brownian dynamics are employed, using the Large-scale Atomic/Molecular Massively Parallel Simulator\textsuperscript{22} software package to simulate the linear and nonlinear behavior. Brownian motion uses Langevin dynamics to describe the random motion of particles suspended in a fluid, which is characteristic of a hydrogel. The hydrogel consists of telechelic chains. A telechelic polymer is one that is di-end functional and has the same functionality on each end. The gel is represented by a coarse grained bead spring Kremer-Grest (KG) model.\textsuperscript{23} Hydrophilic beads are the backbone in the chains, represented in Figure 1 as the blue beads, and there are also hydrophobic beads delineated by the orange beads. The hydrophobic beads act as the physical crosslinks within the network and will also be defined as ‘sticker’ groups. These sticker groups are what form the physically crosslinked system within the hydrogel. Non-bonded monomers interact through the Lennard-Jones (LJ) potential shown in equation 1:

![Figure 1](image)
\[ E_{LJ}(r) = 4\epsilon \left[ (\sigma/r)^{12} - (\sigma/r)^6 \right], \quad r < r_c \] (1)

where \( \epsilon \) is the LJ energy scale, \( \sigma \) is the monomer diameter, and \( r_c \) is the radial cutoff distance of the potential. The LAMMPS simulations use a reversible reference system propagator algorithm (RESPA) time integration scheme with a time step of \( \Delta t = 0.01\tau \), where

\[ \tau = \left( m\sigma^2/\epsilon \right)^{1/2} \] (2)

and \( \tau \) is the LJ unit of time and \( m \) is the mass of the monomer. For the LJ interactions of the hydrophobic beads with themselves, the LJ interaction cutoff is \( r_c = 2.5\sigma \). Any beads that are farther away than this distance have no interactions with each other. Brownian dynamics within LAMMPS uses an implicit solvent to save on simulation time. The hydrophilic beads are made repulsive with each other, mimicking the effective hydrophil-hydrophil pair interaction, which is repulsive in the presence of a solvent. As a consequence, hydrophilic domains will swell and assume extended coil conformations comparable to a water-swollen hydrogel, but without an explicit water molecule. The only attractive forces within the hydrogel are the sticker beads with each other because that is how the crosslinks form. The interactions between molecules are represented through the cut-off distance in the Lennard Jones potential. The cutoff distance for the LJ interactions of the hydrophilic beads with each other and the hydrophilic beads with the hydrophobic beads is \( r_c \approx 2^{1/6}\sigma \) which is the minimum in the LJ potential curve. This means that only the repulsive interactions are taken into account and the attractive interactions are turned off.. A Langevin thermostat with a damping parameter of \( 2\tau \) models the interactions of a group of atoms. The damping parameter determines how fast the temperature is relaxed. A low parameter means the thermostat is aggressive and more effective. The thermostat has three different terms that help contribute to the model:

\[ F = F_c + F_f + F_r \] (3)

\[ F_f = -(m/damp)/v \]

\[ F_r \approx \sqrt{(K_b*T*m)/(dt*damp)} \]

\( F_c \) is the conservative force computed via the usual inter-particle interactions. The \( F_f \) and \( F_r \) terms are specific to this fix. \( F_f \) is the frictional drag force proportional to the particles’ velocity, where \( m \) is the mass of the particle and \( \text{damp} \) is the damping factor specified by the user. \( F_r \) is a force due to solvent atoms at a
specific temperature bumping into the particle. $K_b$ is the Boltzmann constant, $T$ is the desired temperature, $m$ is the mass of the particle, $dt$ is the timestep size, and damp is the damping factor. The Langevin thermostat does not perform time integration, which is necessary for the simulation. This is the reason fix NVE is used solely as the time integrator to update the velocities and positions of the atoms. For any simulation needing a barostat to control the pressure, a Berendsen barostat with a damping parameter of $2\tau$ is employed because it does not perform time integration. The barostat resets the pressure of the system, which rescales the atom coordinates within the simulation box every timestep. Periodic boundary conditions are also imposed in all directions. The combination of these parameters is what makes the simulation specific to a hydrogel.

The two different systems that are analyzed in the molecular dynamics simulations differ by two variables. As shown in Figure 2, one system has 18 hydrophilic beads in the middle of each chain and one sticker bead on each end. The other system also has 18 hydrophilic beads in the middle but it has 3 sticker beads on each end. The linear chains are well below entanglement length in both hydrogel systems. Initial positions of the 100 polymer chains in each system were generated in a low-density configuration using Packmol, and constant temperature molecular dynamics where then conducted in the NPT ensemble for $T=1$, where $T$ is the reduced LJ temperature and $\sigma=1$, where $\sigma$ is the bead diameter as mentioned above. The simulation protocol is started with generating the hydrogel and forming the physical crosslinks. During these simulations, the bonds will be modeled with the FENE potential which resists a physical chain-crossing events. At a constant temperature of $T=1$ and a pressure of 0.1 in all directions, all

Figure 2 Depiction of polymer chains within the hydrogel. The three sticker system (top) and the one sticker system (bottom).
attractions between beads are turned off. The pressure is necessary in order to prevent the simulation box from coming apart. After 1000τ, the attractions between the sticker beads are turned on and epsilon is gradually ramped at a rate of $25 \tau / 0.01\epsilon$ to the desired value. To form the crosslinks within the hydrogel, the epsilon potential mentioned above is manipulated. Epsilon is a Lennard Jones variable that symbolizes the attractive energy between two beads. Epsilon is varied in the hydrogel simulations to give a range of size and attraction of crosslinks. The higher the epsilon, the stiffer and more glassy the crosslinks become. The crosslinks also become larger with a higher epsilon because the beads are more attractive towards each other. The number of sticker beads is the same, but the crosslinks are more distributed into smaller clusters with a smaller attractive energy. Epsilon is not the same value for both systems. Instead, the same epsilon in the one sticker system is distributed between the three beads in the three sticker system. There were no assumptions made that these systems could be comparable to each other. This method was simply a decision made about the simulated hydrogel systems. Once the epsilon is reached and the crosslinks have formed, the pressure can be taken off the system and the hydrogel can be equilibrated. For high epsilon values, this is simple and the pressure is slowly ramped from 0.1 to 0.0 over 2000τ. However at the lower epsilons, the crosslinks are not strong enough to remove the pressure without having the simulation box explode. Because of this issue, an equilibrated system with a formed network at a high epsilon is used and then the epsilon is decreased to a lower value. Taking an already equilibrated hydrogel means the crosslinks have been able to fully form, keeping them from falling apart without the stabilizing pressure. The systems with a lower epsilon have to be run in the NVT ensemble rather than the NPT ensemble. This is performed to freeze the box size and keep it from bursting. This causes the simulation box to not be equilibrated to the size specific to the lower epsilon value. However, the attractive energy is so low that the networks have trouble forming and retaining the shape of the hydrogel.

The size of the equilibrated box depends on the epsilon. This is because a higher attractive energy typically yields a smaller box size because the hydrogel is more compact since the crosslinks are stronger. The average size of the box is around $22\sigma$, where $\sigma$ represents approximately 1 nanometer. The hydrogels generated for the linear analysis in the one sticker system and the three sticker system have a varying number of epsilon values shown below, while all other parameters are equal.
One sticker system: 9, 8, 7, 6, 5, 4.8, 4.6, 4.4, 4.2, 4, 3.8, 3.6, 3.4, 3.2, 3, 2, 1

Three sticker system: 3.3, 3, 2.7, 2.3, 2, 1.7, 1.6, 1.5, 1.47, 1.4, 1.3, 1.27, 1.2, 1.13, 1.07, 1, 0.7, 0.3

The linear analysis performed includes 2000 beads for the system with one sticker on each end, and 2400 beads for the system with three stickers on each end. Each system has 1000 chains. Note that four trials were completed for every separate simulation. The appropriate equilibrium times depending on epsilon is as follows: Epsilons 1-4 and 0.3-1.4: $10^7$ timesteps, epsilons 4.2-5 and 1.47-1.83: $10^8$ timesteps, and finally epsilons 6-9 and 2-3.3: $10^9$ timesteps. These times will be explained in the diffusive behavior section.

After the hydrogel has fully equilibrated for the appropriate time length, the short cluster analysis is performed. The sizes of the cluster vary depending on the epsilon and it is beneficial to see how large or how small the clusters are in the equilibration phase. As mentioned previously, the number of single stickers is critical in validating the Sticky Rouse model. The LAMMPS simulation package has a command that will calculate the neighbor list of each bead and group them together, given a certain cutoff distance. The cutoff distance needs to be something larger than $2^{1/6} (~1.12)$ because as mentioned before, this is the lower limit for repulsive interactions. The sticker beads contained within the clusters are attracted to each other so no repulsive interactions should be considered. The cutoff value chosen is 1.2 because the value must be close to the repulsive limit. However, any thermal fluctuations that would cause the illusion of more beads being within the clusters need to be avoided. For acceptable statistics, the average of the cluster distribution is computed out of 1000 trajectory outputs. The calculated values are then used within the distribution for each epsilon. The system is in equilibrium so it is unnecessary to see how the cluster distribution changes over time. Using a trajectory output by LAMMPS, a code that was written in Matlab performs the analysis of the size of the clusters, and how many aggregates of each size are present in each system. This information will help see how the physical crosslinks behave depending on the attractive energy between each other and the number of sticker beads in the simulation. Once the short cluster analysis has been completed, an even longer equilibration run is performed in the NVT ensemble for all epsilon values. This run will be referred to as a production run for clarity. The appropriate time lengths of each production run are shown in Table 1 along with the original equilibration times. The reason for the production run is to output a trajectory file for all of the beads so the relaxation behavior can be interpreted.
The trajectory file is an output of all of the X, Y, and Z coordinates for each timestep. The mean squared displacement of the hydrogel is a measure of the changes over time between the starting position and ending position of the beads. This value helps measure the diffusion of each system and gives information about how the gel relaxes over time. The cluster analysis as well as the relaxation behavior analysis mentioned above are necessary for understanding how the physical crosslinks behave under linear behavior.

There are multiple types of simulations that are performed in order to fully understand the diffusive properties depending on the sticker energy and sticker length. The cluster distribution yields information about the mean aggregate sizes and the number of single sticker beads in each system. The results from this analysis will be described first. The next factor of interest is the mean squared displacement, describing the diffusive behavior according to the Sticky Rouse model. Both of these responses represent the linear behavior that is used to better understand the nonlinear behavior, which will not be discussed here. All of these simulations and analysis methods are necessary for the understanding of physical networks within a hydrogel.

Derivation of Diffusive Time

The linear behavior involves observing diffusion as well as cluster sizes. The physically crosslinked hydrogel is expected to follow the Sticky Rouse model for diffusion. An important question that could be asked is why the model would follow the Rouse model and not the Zimm model. The hydrogel does not have an explicit solvent because Langevin dynamics is used in the LAMMPS simulations. There are no hydrodynamics, which would lead to the Zimm model. Therefore, Rouse diffusion is expected to occur and is explained in the mean squared displacement section. The diffusive behavior is expected to start out with a ballistic regime, where the molecules bounce around in the beginning until they become constricted. Since the chains in the hydrogel model are telechelic, after the sticker groups relax, the whole chain relaxes and becomes fully diffusive. There is expected to be an Arrhenius relationship between the sticker energy and the sticker relaxation time denoted as $\tau_{\text{out}}$, according to the Sticky Rouse theory. “Out” simply means the time it takes the sticker bead to escape the cluster and
become a single sticker. $\tau_{\text{out}}$ is the time that determines when the whole system diffuses since it is longer than the Rouse time, $\tau_{\text{rouse}}$. The fraction of free stickers becomes important in determining the relationship between the sticker energy and relaxation time and can be determined from the cluster distribution. The dependence between the fraction of free stickers and the rates of either joining a cluster or leaving a cluster is shown below

$$\frac{k_{\text{out}}}{k_{\text{in}}} = \frac{X}{1 - X} \quad (4)$$

where $X$ denotes the fraction of free stickers, $n_{\text{free}}/(n_{\text{free}} + n_{\text{bound}})$. It is also important to note that $k$ is a rate and is in units of time$^{-1}$. The number of free stickers and the number of bound stickers is related to the energy the stickers in an Arrhenius relationship

$$\frac{n_{\text{free}}}{n_{\text{bound}}} = \frac{e^{(E_{\text{free}}/kT)}}{e^{(E_{\text{bound}}/kT)}} = e^{(E_{\text{free}} - E_{\text{bound}}/kT)} = e^{(\Delta E/kT)} \quad (5)$$

where $\Delta E = an_{\text{eff}}\varepsilon$, showing that the energy of the stickers depends on epsilon and $n_{\text{eff}}$ is a correction term for the different sticker lengths between the two systems. The reaction rate from chemical kinetics is related to the rate constant and the concentration of materials by

$$K = r[C], \quad (6)$$

$$r = Ae^{-E/kT} \quad (7)$$

The rate constant is the inverse of the time for the sticker bead to either escape or join a cluster. The concentration of clusters is related to the density, therefore a relationship between the density and the rate constant can be evaluated using the fraction of free stickers, $X$, as follows:

$$X = \frac{n_{\text{free}}}{n_{\text{free}} + n_{\text{bound}}} = \frac{\rho_{\text{free}}}{\rho_{\text{free}} + \rho_{\text{bound}}} \quad (8)$$

$$\rho_{\text{free}} + \rho_{\text{bound}} = \rho_{\text{total}} \quad (9)$$

where $\rho_{\text{total}}$ is a known value. Using the relationship between the rate and the density

$$k_{\text{out}} = r_{\text{out}} \rho_{\text{bound}} \quad (10)$$

$$k_{\text{in}} = r_{\text{in}} \rho_{\text{free}}$$
the focus will be on the first equation because $\tau_{\text{out}} = 1/k_{\text{out}} \propto \tau_p$ since the sticker lifetime is the variable that determines when the chain becomes fully diffusive. From Equations 8 and 9, $X \rho_{\text{total}} = \rho_{\text{free}}$, and performing this substitution with Equation 9 gives an equation for $k_{\text{out}}$ in terms of $\rho_{\text{total}}$ and $X$, which are both known variables.

$$k_{\text{out}} = r_{\text{out}} \rho_{\text{total}} (1-X) \quad (11)$$

It is shown from Equation 10 that the reaction rate is dependent on the density, and in turn the temperature, and is not a function of $\Delta E$. Therefore, the relationship between the fraction of free stickers and the diffusion time is:

$$\tau_{\text{out}} = \frac{1}{k_{\text{out}}} = \frac{1}{r_{\text{out}} \rho_{\text{total}} (1-X)} \quad (12)$$

The final step in the derivation is to convert $1-X$ into the Arrhenius relationship relating the fraction of free stickers with the sticker energy found in Equation 5.

$$1-X = 1 - \frac{n_{\text{free}}}{n_{\text{free}} + n_{\text{bound}}} = \frac{n_{\text{bound}}}{n_{\text{bound}} + n_{\text{free}}} = \frac{1}{1 + \frac{n_{\text{free}}}{n_{\text{bound}}}} = \frac{1}{1 + e^{(\Delta E/kT)}} \quad (13)$$

Therefore, substituting this into Equation 12,

$$\tau_{\text{out}} = \frac{1 + e^{(\Delta E/kT)}}{k_{\text{out}} \rho_{\text{total}}} \quad (14)$$

yields the Arrhenius relationship between the sticker energy and the sticker relaxation time. The equation for the sticker diffusion time is a check that the Sticky Rouse theory correctly predicts the diffusive time based on the sticker energy. The Arrhenius relationship between the two variables is verified below in the results section of the mean squared displacement. First we look at the cluster distribution of the hydrogel in equilibrium to see how many single stickers are present in each system depending on the epsilon value.
The distribution also yields information about how the mean aggregate size is affected by epsilon. After that, the diffusion time from the mean squared displacement is shown to agree with the Sticky Rouse model.

Aggregate Structure

The first variable of interest in the linear behavior is the aggregate structure in the equilibrated state of the hydrogel. It is important to understand how the sizes and number of aggregates depend on the attractive energy of the crosslinks. The aggregate distributions are found for each epsilon. However, only a few epsilons of varying attraction will be discussed and the remaining distributions can be found in Appendix A. The distributions can be explained in the following way. The X-axis represents the size of the clusters within the system looking at the weight distribution, depicted by n. The Y-axis indicates how many clusters of that specific size n are present. The Y-axis is plotted on a log-scale so the distribution can be seen more clearly. Also it should be noted that the values of cluster sizes on the X-axis in the three sticker distribution are in multiples of three. Along with this distinction, the three sticker distributions have not been normalized by three, therefore the Y-values will be larger in these cases. Each distribution was averaged over 100 different files and the output is shown below in Figure 3. The corresponding depictions of the hydrophobic beads of the hydrogel are shown below in Figure 4. These figures show how the distribution changes with different attractive energies. It can be seen that the single stickers are extremely prevalent when the attractive energy is low. There is not a network at this point, it is basically a depiction of chain extension, meaning that the hydrophobic groups act as if they are just part of a chain with no individual properties. As epsilon increases, the single stickers decrease and more of a network starts to form. At the highest epsilon shown, the distribution becomes more spread out and the aggregates becomes larger and more compact with each other. The larger aggregates also mean the less number of total aggregates in the system.

These individual distributions can then be modeled in another way by looking at the mean aggregate size of each system depending on epsilon. This way the systems can be compared with each other and the aggregate structure can provide information on how the chains will diffuse. The mean
aggregate structure is shown in Figure 5. It can be seen that there is a sort of self assembly transition occurring as epsilon increases. The figure can be split into four different regimes. The first regime is at low epsilon where the sticker groups are mostly singles. This corresponds to the distribution where there is

Figure 3  Aggregate Distributions of both systems. The one sticker system is the left column and the three sticker system is the right column. There are three epsilon values shown for each, starting with the lowest and increasing to the highest attractive energy shown.
Figure 4  Corresponding aggregate structures to the aggregate distributions in Figure 5. The one sticker system is in the left column and the three sticker system is in the right column,
not much of a network to form. The second regime can be seen from the first part of the transition period. This is when the sticker lifetime, \( \tau_s \), is shorter than the chains longest Rouse mode, \( \tau_p \). From Rouse theory, we know that the Rouse modes will be the first to relax in the telechelic chains. These modes are represented by the hydrophilic backbone. The sticker groups will be the last to relax from Sticky Rouse theory, therefore, when epsilon is low enough before the transition occurs, the longest Rouse mode is the governing time, not the sticker diffusion time. However, the third regime is the second half of the self assembly transition and this is when the sticker lifetime becomes longer than the Rouse modes. This causes the diffusion to be hindered. The fourth regime is when \( \tau_s \) is much greater than the longest Rouse mode. This is when epsilon is extremely large and the mean aggregate size plateaus at a certain value. The aggregate structure can tell us what we should expect from the diffusion of these different epsilon values.

**Figure 5** Mean aggregate size for each epsilon. There are four different regimes throughout the self assembly transition. The one sticker system is on top and the three sticker system is on the bottom.
The last thing to observe from the cluster analysis is the number of stickers in the large population and the small population shown in Figure 6. A scaling factor $n=3$ to account for the different epsilon values between systems was used on the three sticker system to make the numbers of sticker beads more comparable to each other. Instead of plotting the number of stickers in each population, the fraction of stickers was chosen. Both types of crosslinks plateau at small epsilon and at large epsilon. The only observable difference between both crosslinks is that the single sticker system increases or decreases more rapidly with epsilon from 0-2000 or 2000-0 stickers, depending on whether the small or large population is of interest. This distinction is not apparent enough to have a reasonable explanation. The other feature that gives insight about the effect of epsilon on the system is the plateau at high epsilons. This plateau indicates that the equilibration time does not have a pronounced effect on the cluster sizes since the plateau has already been reached. A higher epsilon would still lead to all of the sticker beads being part of the large

![Fraction of Stickers in Each Population](image1)

**Fraction of Stickers in Each Population**

- small pop:1
- large pop:1
- small pop:3
- large pop:3

![Fraction of Stickers in Each Population using scaling factor n](image2)

**Fraction of Stickers in Each Population using scaling factor n**

- small pop:1
- large pop:1
- small pop:3
- large pop:3

Figure 6  Fraction of stickers in each population. 1 indicates one sticker system and 3 represents the three sticker system. Fraction of stickers with unaltered epsilon (top) and eps/3 multiplied by 3 to scale the 3 sticker system (bottom).
population and no stickers in the small population. One modification that could be made if interested in any systems with a higher attractive energy is to either call the hydrogel one population or split up the system in a different way so that there could be a significant number of sticker beads in both populations.

From the cluster analysis, multiple conclusions can be attained. The cluster size distribution is dependent on epsilon as well as the number of sticker beads in a chain. While the one sticker system and the three sticker system follow analogous tendencies, there are some obvious differences as discussed above. The clusters are larger in the three sticker system because of the increased number of stickers per chain. The distribution is also wider which could be because there are three bonding points per chain end, meaning that the beads can connect and disconnect at a greater rate than if there was only one bonding site. This transient nature of the bonds could lead to a broader distribution because a wide variety of cluster sizes can be explored throughout the equilibrated run.

Mean Squared Displacement

Brownian motion of particles in polymer networks can be experimentally studied through measuring their mean-squared displacement, \( \langle r^2 \rangle \), as a function of time. The slope of the mean squared displacement is expected to follow the Sticky Rouse model outlined in the introduction.\(^{29}\) This model models diffusion time in the following way according to Figure 7. The slope of the mean squared displacement starts at two and then decreases to 0.5, indicating the Rouse modes. After a slope of 0.5, the slope decreases to zero, indicating that the Rouse modes have relaxed, but the sticker groups have not. After the second plateau, the stickers have fully relaxed, leading to diffusion. The chains in this model are telechelic, meaning that there are no sticker groups present within the backbone of the chain. The crosslinking sites are only at the ends. In a normal Sticky Rouse model, there would be a second region where the slope is 0.5, where the Rouse modes occur again after the sticker groups in between the backbone chain relax. In this case, only one region of Rouse modes occur and it happens before the sticker relaxation time. The physical crosslinked hydrogel is expected to follow these characteristics of the mean squared displacement and will now be verified. The slope of the mean squared displacement is more appropriate in understanding how the diffusion occurs within each hydrogel. The mean squared
Figure 7 Mean Squared Displacement according to the Sticky Rouse model for telechelic chains. These are the features we expect to see in the hydrogels that follow this model. Mean squared displacement (top) and corresponding slope (bottom).
displacement and the slope are both shown in Figures 8 and 9. According to the mean squared displacement, there are three main regimes in both the one sticker system and three sticker system. There is a regime where the slope stays linear at low times, followed by a region where a plateau can be observed for certain epsilon values. At long times, it can be regarded that the plateau ends and the mean squared displacement has a different linear slope. We can look at the slope of the mean square displacement to understand at what time the regimes occur and what they depict. The first regime is the ballistic regime. This is where the system first starts to relax. Basically the bond vibrations happen in this step, causing the slope to start out as two and then rapidly decrease. It can be seen that the behavior is still subdiffusive in these short time scales. However, at slightly larger times, a plateau appears for the systems with a high epsilon. This is called the Rouse regime where the slope is around 0.5. At this point, the Rouse modes are occurring. Each mode has its own relaxation time and the beads continue switching directions, trying to diffuse as time increases. The Rouse model describes the conformational dynamics of an ideal chain, where single chain diffusion is represented by Brownian motion of the beads.\(^3\) This region either plateaus over a time of two decades for the high epsilon values, or it only plateaus for a decade or less for low epsilon values. This is because the crosslinks haven’t formed, allowing the chains to diffuse easily. The Rouse modes are never reached when the sticker groups are weakly attracted. The higher the slope, the easier it is for the chains to diffuse. For higher epsilons, the slope of the plateau drops below 0.5, which is due to the stronger crosslinks because of the sticker beads. This leads the chains to diffuse slower, agreeing with the Sticky Rouse model. The network is tighter and the attraction to hold the crosslinks together is stronger. It seems that during this plateau, particles explore all the available volume in the hydrogel and disconnect and reconnect with each other causing a sort of constrained motion. In order to analyze this feature within the mean squared displacement further, the epsilon versus the depth of the first minimum in Figure 10 is shown to illustrate this behavior in a more concise way. This figure shows that the depth of the Rouse modes changes less and less the higher and lower the epsilon value becomes. These are the values where the diffusive behavior is not as affected, where the minimum of the middle epsilon values
Figure 8 Mean squared displacement and corresponding slope for the one sticker system. Observe that multiple epsilons with similar diffusive behavior are omitted for clarity.
Figure 9: Mean squared displacement and corresponding slope of the three sticker system. Observe that epsilon values with similar behavior are omitted for clarity.
changes drastically with one change in epsilon. The rouse modes are never reached at low epsilon and at high epsilon, the Rouse modes either become more restrictive leading to a shallower slope or a second plateau appears representing the sticker diffusion time. It is apparent that after analyzing the slope of the mean squared displacement, the larger and stronger physical crosslinks restrict the motion to a greater extent than the weak crosslinks with low attractive energy.

One thing to notice when comparing the mean squared displacement slopes for the two different systems is that the three sticker system has a second plateau after the original rouse regime. Although a sort of second plateau can be seen in some of the epsilons in the one sticker system, it is not as prominent. This second plateau is characteristic of the Sticky Rouse model. After the Rouse modes relax, a second plateau with a slope around zero occurs because of the sticker groups. The sticker relaxation time is longer than the rouse diffusion time, meaning that it takes longer for the network to diffuse.

For the fully equilibrated systems, it can be seen that the slope of the MSD curves plateaus to one, indicating that the hydrogel has become fully diffusive. The crosslinks entirely relax and disconnect from each other after enough time has passed. For the higher epsilons in both systems, the crosslinks are too strong to become diffusive in the time frame that we can probe. However, it can be observed at what times the other systems become diffusive. The established times can be fit to an Arrhenius plot of $y = Ae^{bx}$ to

![Figure 10](image.png)

Figure 10  Depth of the first minimum in the mean squared displacement slope. All epsilons values are accounted for. The Rouse modes indicating a slope of 0.5 occur for high epsilons, but not for low epsilon because there is no sufficient network to diffuse.
predict at what times each hydrogel of varying epsilon will become fully diffusive. This agrees with the predicted relationship from the Sticky Rouse theory derived in the introduction. An arbitrary reference point of slope of 0.9 was used to determine the diffusion time for each system. When the slope of the mean squared displacement reaches 0.9, the system becomes fully relaxed. Figure 11 is a plot of epsilon against diffusive time on a semi log scale. The only epsilons shown are the middle epsilons where Arrhenius behavior is observed. Epsilons greater than six in the one sticker system and greater than two in the three sticker system have not been equilibrated long enough. It is noticeable that the slope of the mean squared displacement of these systems never reaches one in the time scale that can be reached in a manageable fashion. It can also be detected that the hydrogel systems with the lowest epsilons have been equilibrated almost a decade longer than necessary. In order to predict the diffusive time for the higher epsilon systems, the middle epsilons are fit to an exponential equation. It is interesting to note that the exponential prefactor for the system with 1 sticker on each end is 3.7421 and the prefactor for the system with 3 stickers on each end is 10.526. The ratio is 2.813, which is almost 3 times as much as the one sticker system. In the beginning there were no assumptions made that epsilon=3 for the one sticker system would behave in an identical way to epsilon=1 in the three sticker system. However, it seems that the assumption of these being similar is fairly reasonable. It makes sense that this is less than three because in the three sticker system, some neighbors of sticker beads are taken up by bonded beads instead of nonbonded. Using $n_{\text{eff}} = 2.813$ to rescale the Arrhenius diffusion plots as shown in Figure 12, it is easier to see how the diffusion
times line up with one another. This makes it easier to compare the two systems. The simple crosslinks diffuse slower than the complex physical crosslinks because the diffusion time is longer. This Arrhenius relationship found between the sticker energy and the diffusion time agrees with the predictions made by the Sticky Rouse theory. The sticker energy per sticker is higher in the simple crosslinked network,

![Graph 1](image1.png)

**Figure 12** Top figure is diffusion times of both systems plotted on the same axes. Bottom figure is same data but with the epsilons in the three sticker system rescaled by $n_{\text{eff}}$.

explaining the longer overall diffusion time for the hydrogels in the one sticker system.

Based on the conclusions drawn from the aforementioned plots, the diffusion time for each system increases as epsilon increases. This observation suggests that the formation of stronger crosslinks induces strong interactions between the beads, causing the network to become stronger, leading to slower diffusion times. This agrees with the relationship derived from the Sticky Rouse theory and chemical kinetics that involves the diffusion time and the activation energy, described by epsilon. Although the perceptions made from analyzing the MSD behavior of the hydrogel system might not be unusual or unique, the analysis
assists in understanding a physically crosslinked hydrogel. It is also necessary in being able to connect the linear behavior with the nonlinear behavior through defining appropriate parameters for simulations involving deformation, which will be explained in the nonlinear section.

Conclusion

The linear behavior of the physically crosslinked hydrogel can be better understood after analyzing the mean squared displacement data as well as the cluster analysis of a fully equilibrated hydrogel. The diffusive behavior of each hydrogel was dependent upon the sticker energy as well as the length of each physical crosslinking site. The $n_{\text{eff}}$ determined from the Arrhenius plots of the diffusion time will be used as a scaling factor for the three sticker system when calculating various failure characteristics in the nonlinear section. The Sticky Rouse theory for the hydrogel model was derived and explained. It was found that there is an Arrhenius relationship between the sticker relaxation time and the sticker energy, agreeing with the model. The sticker relaxation time, $\tau_D$, is the determining factor in the diffusion time of the hydrogel. This is because the sticker beads are the last to relax, after the hydrophilic beads in between the stickers relax via Rouse diffusion. It also became known how the hydrophobic groups aggregate with each other depending on the attractive energy between stickers. The distribution is much broader and non-uniform for attractive networks. The aggregate distribution becomes more compact as epsilon decreases because there aren’t as many large clusters anymore. Once the single stickers become the most prevalent cluster size, the distribution no longer looks Gaussian. It steadily decreases from single stickers, to slightly larger cluster sizes. After examining the diffusive behavior along with the aggregate structure, we can conclude that the hydrogel model is understood and can be used in farther analysis of mechanical behaviors and properties. The analysis of a physical network will aide in understanding how to implement this network as a sacrificial network in a hybrid network hydrogel.
REFERENCES


