VISCOELASTIC STUDY OF PH-RESPONSIVE HYDROGELS

A Thesis

by

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ABSTRACT

The viscoelastic behavior of two pH-sensitive hydrogels hydroxyethyl methacrylate dimethyl aminoethyl methacrylate (HEMA - DMAEMA) and hydroxyethyl methacrylate acrylic acid (HEMA-AA) in acidic and basic mediums were studied. The three-dimensional network structure of hydrogels along with high water content make them an ideal bio-material. The hydrogels were prepared by co-polymerization of one inert and one stimuli-responsive monomer. The structural characterization of hydrogels is needed due to its bio-medical applications. Large amplitude oscillatory shear tests were conducted on the hydrogel samples using a rheometer to find the energy dissipated. The degree of viscous behavior can be determined by the amount of energy dissipated in the material. The LAOS test helps in better understanding of the non-linear visco-elastic behavior of a material. The result obtained showed an increase in the energy dissipation with the increase in the shear strain unique to both the buffer solutions. The energy dissipation obtained for the HEMA-DMAEMA samples was greater in 11.0 pH buffer solution as compared to 3.0 pH buffer solution and the opposite for HEMA-AA samples. The results helped in further understanding the material properties of the two hydrogels. Temperature imposed relaxation tests were also conducted on the HEMA-DMAEMA samples which is to be a part of a much larger project.

DEDICATION

For you dad, my greatest strength and inspiration

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1. INTRODUCTION

1.1 pH-responsive Hydrogels

The pH responsive hydrogels are one of the promising classes of hydrogels due to their ability to change state, volume and even undergo self-healing [35]. These hydrogels respond to a change in the pH by swelling or de-swelling as water is absorbed or expelled from the network depending on the type of ionizable pendant group present. Such systems are required for bio-medical applications involving the human body which exhibits a substantial change in the pH level. Some of the commonly studied ionic polymers include poly(acrylic acid) [4, 25, 55], poly(methacrylic acid), poly(diethylaminoethyl methacrylate) and poly(dimethylaminoethyl methacrylate).

The pH sensitive hydrogels have a tendency to ionize resulting in swelling or de-swelling when exposed to an aqueous solution. A number of attempts have been made to understand and model the swelling behavior of the pH-sensitive hydrogels [39, 45, 60, 23, 59, 62, 13].

Brannon et al. [13] identified that the abrupt change in swelling ratio is due to the pH of the medium, the pK_a (measure of acid strength) and the structural parameters of the gel. This was studied using structural models based on Flory-Huggins thermodynamic theory, the rubber elasticity theory and ionic interaction deviations therefrom.

The anionic and cationic hydrogels differ in their swelling behavior. The anionic hydrogels swell at pH ¿ pK_a because of the large osmotic pressure due to the presence of the ions whereas cationic hydrogels swell at pH ¡ pK_a [45]. The swelling of anionic hydrogel was investigated experimentally by Jabbari et al [39]. Drozdov [23] developed the constitutive model of cationic hydrogels under swelling and also carried out its numerical analysis. A simulation model for predicting the dynamic response of the transient swelling behavior of pH sensitive hydrogels over time was presented by William et al [62].

Targeted drug delivery is one of the main applications of pH sensitive hyrogels and has been studied extensively for various drugs [68, 60, 4, 12, 35]. The swelling behavior of the pH sensitive hydrogels has been of particular importance in formulation of drug delivery like the drugs and protein delivery [4] and release of paclitaxel within a tumor environment [68]. The demand for controlled delivery of insulin has been the greatest by far. Brahim et al [12] studied the insulin and protamine release in an amphiphilic hydrogel incorporating a hydrophobic comonomer and pH-responsive DMAEMA. A self-regulated insulin delivery system was studied by Satish et al [60] which resulted in a bi-sensitive hydrogel responding to both pH and glucose concentrations. Similar investigation of a bi-sensitive hydrogel was carried out by Rueda et al [59] which responded to pH as well as temperature and could be used as actuators and sensor gels in smart chemo-mechanical valves, pumps, or chemical transistors. A successful study has been conducted to characterize the inulin hydrogel for its application in colonic drug targeting [65]. Guo et al [35] studied the pH-switchable and self healable properties ketone type acylhydrazone dynamic covalent bonds hydrogels which finds potential application in bio-medicines and tissue

The inherent sensitivity of pH responsive hydrogels make them ideal for fabrication of autonomous fluid control devices. Arbabi et al [5] concluded that a fluid-structure interaction simulation was essential for accurately designing the micro-valves based on pH-sensitive hydrogels. The smart hydrogels are also used to selectively measure the concentration of a biochemical substance without the help of any other instrument or reagents [63]. Such a device is called a biosensor and it combines the biological entities (Enzymes, Antibodies, Nucleic acid, Whole cells) with the transduction principles (Electro-chemical, Optical, Thermometric, Gravimetric, Mechanical).

Commercial contact lenses are based on two pH-sensitive hydrogels- poly - 2 - hydroxyethyl methacrylate (HEMA) and acrylic acid (AA). Moradi et al [51] concentrated on the adsorption of protein, albumin and lysozyme onto the hydrogel surface since these cause problems in their applications. Adsorption of protein increased with its concentration while adsorption of albumin and lysozyme depended on the type of hydrogel. AA was observed to have higher tendency to absorb sodium ions due to its negative surface charge.

Jiang et al [40] tried to mimic the creatural soft tissue deformation during mini invasive surgery with needle intervention by investigating a kind of transparent PVA hydrogel. The results from the experiment showed that the PVA hydrogel has same deformation property as prostate tissue. The PVA hydrogel obtained by varying the freeze/thaw cycles had similar mechanical and morphological properties to that of the porcine liver, which is used as a reference material for human soft tissue.

A successful attempt has been made to understand the mechanism of mucoadhesion of the poly acrylic acid hydrogel for retarding the gastric emptying by adhering to the gastric mucus layer [55]. This study was an attempt to enable not only the prolongation time but also to control the retention time of oral dosages anywhere in the gastrointestinal tract apart from the stomach. The results suggested that mucoadhesion occurs when the polymers with functional groups have hydrogen bond forming capacity above the critical concentration and is flexible enough to hold as many hydrogen bonds as possible.

Some of the conventional techniques to mechanically characterize the hydrogels are strip extensiometry, ring extensiometry, compression test, bulge test and indentation test [2]. Ahearne et al [2] measured the mechanical properties of thin hydrogels by using the long focal microscopy based spherical micro-indentation approach and the optical coherence tomography approach for thicker hydrogels.

The study of flow and deformation of viscoelastic materials, called rheology, is important to determine their material property. The feasibility of a hydrogel for a specific bio-medical application is judged based on its mechanical properties. The mechanical properties are explored primarily using the small deformation rheology which are small amplitude oscillatory shear (SAOS) measurements as well as creep, creep recovery and relaxation [67]. The storage modulus G' and loss modulus G" is used to describe the elastic and viscous property of the material respectively. For small strains, the polymer gels follow Hookean behavior and deviates for large strains [42]. The viscoelastic nature of the material is obtained from the creep profile.

Rheometry has also been successfully used to determine the linear viscoelastic behavior of various tissues [64, 36, 30]. Mechanical properties of the tissues suggested the independence of the storage and loss modulus (G' and G") with respect to the strain. Results obtained for the brain tissue was used to describe a new differential viscoelastic model.

Rheology was used to conclude the effectiveness of 50% cross-linked Hyal hydrogel for treatment of osteiarthritis as compared to the natural polysaccharide hyaluronic acid [6].

Rammensee et al [57] studied the rheology of nanofiber-based hydrogels produced from engineered and recombinantly produced spider silk proteins. A parallel plate-plate rheometer was used to obtain the dynamic rheological measurements of the crosslinked and non-crosslinked hydrogels. The results obtained showed the dependence of storage and loss modulus (G" and G') on the oscillation frequency. The non-crosslinking fiber network demonstrated a viscous behavior at low frequencies and elastic behavior at moderate frequencies while the crosslinking fiber network showed only elastic behavior at all the frequencies tested. The results also indicated a high storage modulus and low loss modulus for crosslinked silk hydrogel as compared to non-crosslinked silk hydrogel. These spider silk hydrogels developed are suited for a variety of application due to its stability over time and high elastic modulus.

Rheological characterization of synthesized inulin hydrogels was described by Vervoort et al [65]. A strain controlled rheometer with a parallel plate geometry was used for the dynamic oscillatory measurements of the hydrogel formation as well as the network. Hydrogel formation was monitored by applying small strain oscillations at a fixed frequency while a frequency sweep was performed on fully cured hydrogel. The results obtained shows the independence of frequency over storage modulus, G' for hydrogels with lower degree of substitution or feed concentration. Consequently the storage modulus, G' decreased with frequency for other hydrogels. This result was used to conclude that a higher degree of substitution or feed concentration accelerates the network formation process. It was also observed that addition of initiating species of the free radical polymerization reaction (Ammonium persulphate (APS) and N,N,N',N'-tetramathylethylenediamine (TMEDA)) accelerates the hydrogel formation process but resulted in hydrogels with lower G' values.

Marra et al [50] characterized the mechanical properties of two active polymer gels - poly vinyl alcohol and poly acrylic acid gel which are used as actuators and artificial muscles.

The uni-axial tensile strength test was used by Jiang et al [40] to test the PVA hydrogels with varying freeze/thaw cycle repetitions. The results obtained shows an increase in the Young's modulus to a point where it is similar to that of a porcine liver tissue. The test was conducted on cylindrical shaped samples of the PVA hydrogel.

Nakajima et al [52] used the uni-axial testing results to characterize the internal fracture process of double network hydrogels. The fracture energy of the double network hydrogels is very large and is also comparable to that of some industrial rubber even though their water content is high.

1.2 Large Amplitude Oscillatory Shear (LAOS)

Oscillatory shear tests are used to measure the mechanical response as a function of time of a material subjected to a sinusoidal deformation. The response can transition from a linear to non-linear regime as the applied amplitude is increased from small (small amplitude oscillatory shear,SAOS) to large (large amplitude oscillatory shear,LAOS) at a fixed frequency respectively and have been extensively studied [38, 1, 11, 37, 56]. The storage (G') and the loss modulus (G") are independent of the strain amplitude in the linear regime and results in a sinusoidal stress response. On the contrary, they depend on the strain amplitude in the non-linear regime and the stress response deviates from a sinusoidal waveform. In other words, when the strain amplitude is smaller, the material is characterized by the viscoelastic moduli G'(w) and G"(w) but are not uniquely defined at a higher strain amplitude or when the material enters the non-linear regime [27]. The raw material test data obtained from LAOS are commonly called Lissajous curves. LAOS tests are preferred over SAOS test since it attains a broad spectrum of conditions when the strain amplitude and frequency is varied independently.

LAOS test are conducted on commercially available strain-controlled rheometers to obtain the torque and displacements. Trevor et al [53] used LAOS to mechanically characterize a gluten gel. This data was used to devise a constitutive equation to describe the progressive transition to nonlinear behavior of the gel. The model predicted for this study showed that the transient rheological behavior of this gel could be captured by using just four linear (relaxation time, modulus of the Rouse segments, gel strength, gel index) and three nonlinear (Constant that characterizes the rate of network breakage, FENE parameter that characterizes the limit of extensibility of the polymeric strand, δ that modifies the FENE function by allowing the junction points to be destroyed close to but before the finite extensibility limit b is reached) viscoelastic parameters.

Ewoldt et al.[27] introduced a comprehensive framework for physically interpreting deviations from a linear response to an imposed oscillatory shear deformation that can describe the nonlinear viscoelastic response in general terms.

A quantitative way to represent the nonlinear response is by using methods such as Fourier Transform analysis [33, 38] and Lissajous plot [28]. The Fourier transformation results can not be easily associated with the other physical properties of the material due to the difficulty in detecting the higher harmonics which makes it a satisfactory tool for determining the LAOS behavior. Ewoldt [26] proposed a convention to define the unclear signs of the higher harmonics theoretically and practically by using the Chebyshev coefficients and referencing to a sine or a cosine input respectively. On the other hand, Lissajous curve , which is the graphical representation of the non-linearity does not identify the underlying. Cho et al.[15] proposed a method based on the symmetry of stress, making it easier to determine the nonlinear parameters and a more powerful method than the previous two methods. But in this method, the coefficients representing the material properties are not unique and depend on the fitting coefficients chosen. Ewoldt et al. [29] introduced a framework to physically quantify the elastic and viscous non-linearities simultaneously by representing the curves using a set of Chebyshev polynomials, which can easily be converted to the Fourier coefficients.

2. SUMMARY: ENERGY DISSIPATION IN PH-SENSITIVE HYDROGELS SUBJECTED TO LARGE AMPLITUDE OSCILLATORY SHEAR

2.1 Synopsis

Stimuli-responsive hydrogels belong to a class of shape-memory elastomers that have gained immense popularity due to their applications in the fields of drug delivery, tissue engineering, implants, bio-sensors and many more. The pH-responsive hydrogels exhibit swelling behavior in response to changes in pH. The present study characterizes the energy dissipation of the pH sensitive hydrogels 2-hydroxyethyl methacrylate (2-dimethylamino) ethyl methacrylate (HEMA-DMAEMA) and 2-hydroxyethyl methacrylate acrylic acid (HEMA-AA) subjected to large amplitude oscillatory shear. The experiments were conducted at strain levels 0.5%, 1.0% and 5% maximum amplitude strain at a constant frequency of 1Hz. The result obtained showed an increase in the energy dissipation with the increase in the shear strain unique to both the buffer solutions. The energy dissipation obtained for the HEMA-DMAEMA samples was greater in 11.0 pH buffer solution as compared to 3.0 pH buffer solution. On the contrary, the energy dissipation for HEMA-AA samples was found to be greater in 3.0 pH buffer solution as compared to 11.0 pH buffer solution.

Keywords: Microfluidics, Hydrogel, Viscoelasticity, Interfacial, Large Amplitude Oscillatory Shear (LAOS)

2.2 Introduction

Stimuli-responsive hydrogels belong to a class of shape-memory elastomers that have gained immense popularity due to their applications in the fields of drug delivery, tissue engineering, implants, bio-sensors, contact lenses and many more. The three-dimensional network structure of hydrogels along with high water content makes them an ideal bio-material. The structural characterization of hydrogels is needed due to its biomedical applications[20, 21, 5].

The swelling behavior of hydrogels has been of particular interest in various fields and has been studied extensively [39, 45, 60, 23, 59, 62, 13]. These ”smart” materials exhibit swelling behavior in response to different stimuli (temperature, pH, chemical, light, electro, shear-sensitive). Rheometry has also been successfully used to determine the non-linear viscoelastic behavior of various hydrogels[18, 44].

The pH-responsive hydrogels are one of the promising classes of hydrogels due to their ability to change state and volume[34]. Two stimuli-responsive hydrogels of interest are hydroxyethyl methacrylate dimethyl aminoethyl methacrylate (HEMA - DMAEMA) and hydroxyethyl methacrylate acrylic acid (HEMA-AA). The HEMA-DMAEMA represents a cationic hydrogel network and is extensively used in tissue growth and controlled drug delivery[60]. On the other hand, HEMA-AA represents an anionic hydrogel known for its application in drug delivery systems[4]. For proper designing and effective use of these hydrogels, it is important to study their mechanical as well as material properties. The swelling of stimuli-responsive hydrogels is a well studied area, but the mechanical properties associated with this swelling is still an open field of research. Stimuli-responsive hydrogels are key components in microfluidic devices used in scientific fields such as genomics, metabolimics and proteoemics[66, 47, 46].

Current microfluidic device designs have been developed based on trial and error approaches. Microfluidic device designers currently use theories that assume the hydrogel obey’s Hooke’s law[31, 17, 24] or linear viscoelasticity[3, 61, 22]. Device designers know that responsive hydrogels are non-linear viscoelastic materials but there are very few non-linear viscoelastic models in the literature for them to use. When subjected to large amplitude oscillatory shear, these hydrogels display complex rheological responses due to the finite strains imposed[16]. In general, a material subjected to a small amplitude oscillatory shear (SAOS) can be described well using linear viscoelasticity. Under the condition that strain amplitudes are small and the applied strain is, $\varepsilon = \varepsilon_o sin(\omega t)$, where ε_o is the strain amplitude, and ω is the frequency of oscillation and t is time. When this applied strain is put into the Boltzmann integral formulation of linear viscoelasticity, $\sigma = \int^t G(t-\tau)\frac{d\varepsilon}{d\tau}d\tau$ the solution of this integral can be written as, $\sigma = G' sin(\omega t) + G'' cos(\omega t)$, where G' is the storage modulus and is analogous to an elastic modulus and G'' is called the loss modulus and is analogous to viscosity. The output stress is sinusoidal, and G' and G'' have meaning. If the strain amplitude ε_o is increased, a point is reached at which the output stress loses the sinusoidal form. Under these conditions the relaxation modulus $G(t-\tau)$ can be a function of strain amplitude or the frequency of oscillation or the assumption of small strain gradients is no longer valid and a finite strain formulation is needed. In either case, the storage and loss modulus lose their meaning, and a new constitutive equation is warranted. To the best of this authors knowledge, a widely accepted formulation to handle LAOS behavior does not exist[27, 38, 18]. In a standard oscillatory shear test using a parallel plate rheometer, a sinusoidal strain is applied and torque is measured. From this data, a Lissajous plot is made, and the area inside the ellipsoid is the energy dissipated during oscillation. This remains the case for SAOS and LAOS tests and is a starting point by which nonlinear behavior is studied. Energy dissipation is an essential feature of stimuli-responsive hydrogels because of their ability to be used as both a sensor and an actuator simultaneously. The pH-sensitive hydrogels operate in a hydrated external environment, and their mechanical properties have been shown to change based on environmental conditions[8, 7]. The amount of energy dissipated varies dramatically between external environments and can be a critical factor in device designs. Many researchers have studied the ability to tune the dissipation capabilities of hydrogels[69, 14] to take advantage of the stimuli-responsive hydrogels unique features. The primary objective of this study is to characterize the energy dissipation of HEMA-DMAEMA and HEMA-AA stimuli-responsive hydrogels in different external environments during LAOS tests. There are many different methods of characterizing nonlinear behavior in polymers under cyclic loading. Depending on the domain investigated, (time domain[49, 54] or strain/strain rate domain[15]) the nonlinear moduli are different and direct physical meaning can be difficult to determine. We investigate here the difference in dissipation for SAOS and LAOS tests and different hydrated environment. Attempts have been made to extend linear viscoelasticity into the nonlinear regime. Ewodlt et al.[27] extended the storage and loss modulus from linear viscoelasticity and modeled the nonlinearity by taken the storage and loss moduli to be functions of frequency and strain. There are, however, appropriate nonlinear viscoelastic theories that can be applied to hydrogels, such as quasi-linear viscoelasticity[48], K-BKZ[43], the Rivlin-Sawyers equation[58], and the Doi-Edwards model[19] that can be used as a starting point for a nonlinear viscoelastic model that can describe the nonlinear viscoelasticity that governs responsive hydrogels. These theories can be a starting point for describing the energy dissipation that viscoelastic materials exhibit due to cyclic loading. Energy dissipation is used because the test is the same for linear or nonlinear viscoelasticity. Non-linear viscoelastic theories can then be validated with the experimental data obtained from non-linear energy dissipation tests.

2.3 Large Amplitude Oscillatory Shear

We impose a sinusoidal strain on the sample of the form,

$$\varepsilon = \varepsilon_o sin(\omega t), \tag{2.1}$$

where ε_o is the strain amplitude and ω is the angular frequency defined by $\omega = 2\pi f$. When the amplitude of strain is small the stress can be written as $\sigma_{\theta z} = \sigma_o sin(\omega t + \delta)$. This stress can be decomposed into elastic and viscous components,

$$\sigma_{\theta z} = G' sin(\omega t) + G'' cos(\omega t), \tag{2.2}$$

where $G'(\omega)$ and $G''(\omega)$ are the storage and loss moduli from linear viscoelasticity. For small strains the storage and loss moduli are functions of only the angular frequency ω. When the strain amplitude becomes large the stress response is no longer sinusoidal and G' and G'' lose their meaning. The point at which this transition occurs can be easily seen in a strain amplitude sweep at constant frequency. When the functions G' and G'' become functions of the strain we see that a different interpretation of the material functions is needed. One of the widely accepted nonlinear formulations for LAOS is to decompose the stress into elastic and viscous components defined as an infinite Fourier series containing only the odd harmonics[15],

$$\sigma_{\theta z} = \sigma_e + \sigma_v, \qquad \sigma_e = \varepsilon_o \textstyle\sum_{nodd} G'_n sin(n\omega t), \qquad \sigma_v = \varepsilon_o \textstyle\sum_{nodd} G''_n cos(n\omega t)$$

Where G'_1 and G''_1 are analogous to the storage and loss modulus from linear viscoelasticity, and the higher harmonics account for the nonlinear stress response[32]. We note that there are several different methods for characterization of nonlinear viscoelastic moduli and it is important to emphasize the method of testing and the pros and cons of each method. In this work, we emphasize calculation of energy dissipated. It is a calculation that is the same for SAOS and LAOS tests and for responsive hydrogels the difference in environmental conditions is dramatic and is shown in the data collected.

2.3.1 Energy Dissipation

The stress calculated from oscillatory shear in a parallel plate rheometer at the upper edge is given by,

$$\sigma_{\theta z}(R) = \frac{T}{2\pi R^3}\left[3 + \frac{dln(T)}{dln(\dot{\varepsilon_R})}\right], \tag{2.3}$$

where T is the torque measured with the rheometer, R is the outer radius of the parallel plate, and $\dot{\varepsilon}_R$ is the strain rate at the edge of the plate defined as,

$$\dot{\varepsilon}_R = \varepsilon_o \omega cos(\omega t). \tag{2.4}$$

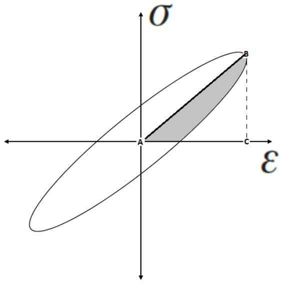


Figure 2.1: A representative Lissajous plot with the gray area representing the dissipated energy for one cycle and the area under the triangle (ABC) representing the stored energy during oscillation.

For a linear viscoelastic material the term $dln(T)/dln(\dot{\varepsilon_R})$ is approximately equal to one[10]. We will determine stress using equation Stress:01. A sinusoidally varying strain is applied in torsional shear to the hydrogel sample in a parallel plate rheometer that has the following form, $\varepsilon = \varepsilon_o sin(\omega t)$. This strain produces a stress output given by equation Stress:01. When the oscillatory stress and strain are plotted they produce what is known as a Lissajous plot as shown in figure 2.1. The area underneath the triangle (ABC) is the stored energy and the grey area in figure 2.1 is the dissipated energy. For both small and large amplitude test the percentage of energy dissipated to energy lost can be calculated by taking the area of the gray portion of the ellipse and dividing it by the area of the triangle (ABC). Energy dissipation is a property of all materials and shows the degree to which the viscous behavior of a material is present.

2.4 Material Fabrication:

2.4.1 Sample Preparation

The hydrogel pre-polymer solution for HEMA-DMAEMA was prepared by mixing two monomers 2-hydroxyethyl methacrylate (HEMA) and 2-(dimethylamino) ethyl methacrylate (DMAEMA), a cross-linker ethylene glycol methacrylate and a photo-initiator 2,2 - dimethoxy - 2 - phenylactophenone (DMPA) in the ratio of 27.627:5.718:0.467:1 respectively. The hydrogel pre-polymer solution for HEMA-AA consisted of the same monomer, cross-linker, and photo-initiator but DMAEMA monomer was replaced by acrylic acid (AA) monomer. The weight percentage of components needed for both HEMA-DMAEMA and HEMA-AA are as shown in Table 2.1

Component	HEMA-DMAEMA(wt %)	HEMA-AA(wt %)
Monomer 1	HEMA (80)	HEMA (84)
Monomer 2	DMAEMA (16)	AA (11)
Crosslinker	EGDMA (1)	EGDMA (1)
Photo-initiator	DMPA (3)	DMPA (4)

Table 2.1: Weight % of components needed in preparation of pre-polymer solution of HEMA-DMAEMA and HEMA-AA

Polydimethylsiloxane (PDMS) with circular wells were used for easy fabrication of hydrogel samples. The samples had the same thickness as that of the PDMS wells and thus helped in controlling the thickness of the samples. An assembly consisting of a PDMS well holding the pre-polymer solution sandwiched between two glass cover-slip was prepared and placed in a petri-dish. It was ensured that no air bubbles were formed while the glass cover-slip was placed. A photo-mask with a circular pattern was used for blocking the UV light such that curing occurs only in the desired pattern. The sample was then exposed to UV light using an Omnicure series 1500 at an intensity of 20 mW/cm^2 for 110 seconds which resulted in cured hydrogel samples.

(i) (a)A HEMA-DMAEMA sample soon after curing (b)A photomask used for curing (c)PDMS well used for fabrication of hydrogel samples

(ii) Experimental setup of hydrogel placed between the parallel plates

Figure 2.2: Sample preparation and experimental setup

2.4.2 Pre-conditioning

The cured hydrogel samples were first swollen in Phosphate Buffer solution for 24-48 hours to easily remove the hydrogel from the glass cover-slip. The samples were then swollen in two different buffer solutions of 3.0 and 11.0 pH for 48 hours after which no significant change in the volume was observed. One inch samples were then punched out to meet the specifications of the parallel plate used in the rheometer for testing. The hydrogels were exposed to the atmosphere while testing since the test lasted for only 2 minutes.

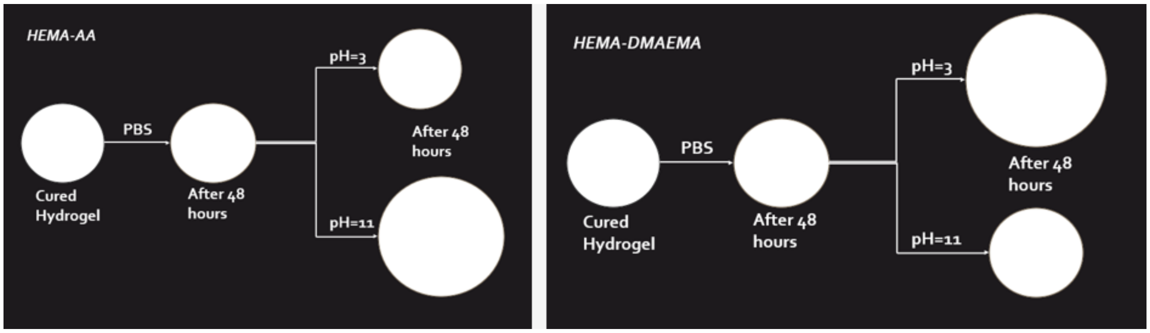


Figure 2.3: Swelling behavior of the two hydrogels in 3.0 pH and 11.0 pH buffer solution

2.5 Testing Method:

The mechanical properties of HEMA-DMAEMA and HEMA-AA were measured by oscillatory shear tests conducted using the Anton Paar Rheometer MC 305 with the 1-inch parallel plate setup. The samples of 1 inch diameter were punched before testing and had a thickness ranging from 1.5-2.8mm. The samples were placed between the parallel plates, and a normal force of 1.5N was applied to prevent slippage during the test. The tests were conducted at 0.5%, 1%, and 5% strain and a frequency of 1Hz. Figure 2.2ii shows the experimental setup of the hydrogel in the rheometer used for testing.

2.6 Results

The hydrogel samples were subjected to oscillatory shear at strain amplitudes of 0.5%, 1% and 5% and a frequency of 1Hz. The shear stress and shear strain data obtained was used to plot Lissajous curves for each sample and the energy dissipated was computed by computing the area under the curve. The percentage of energy dissipated was tabulated by taking the average of the samples.

Figure 2.4i and 2.4ii displays the comparison between the Lissajous plots obtained for HEMA-DMAEMA samples strained up to 0.5% and 1%, pre-swollen in 3.0 and 11.0 pH buffer solution respectively. One data point per 10s was taken for a total interval of 100s. A comparison between the amount of energy dissipated by the HEMA-DMAEMA samples pre-swollen in two buffer solutions and tested at strain amplitudes of 0.5% and 1% is shown in Figure 2.4iii and Figure 2.4iv respectively. Figure 2.4v shows the Lissajous plots for HEMA-DMAEMA samples pre-swollen in the two different buffer solutions and strained up to 5% .

Plots obtained from tests conducted on HEMA-AA at strain amplitudes of 0.5% and 1% are shown in Figure 2.5i and Figure 2.5ii pre-swollen at 3.0 pH and 11.0 pH buffer solutions respectively. Figure 2.5iii, 2.5iv, 2.5v displays the Lissajous plots obtained for HEMA-AA samples pre-swollen in 3.0 pH and 11.0 pH and strained up to 0.5%, 1% and 5% respectively.

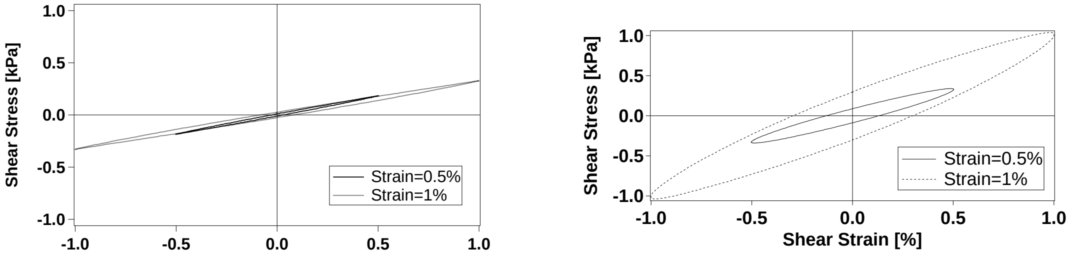
Energy Dissipation (HEMA-DMAEMA)

pH	Strain (%)	Energy Dissipated (%)
3.0 (10 samples)	0.5	15.3 (±2.26)
3.0 (10 samples)	1	19.9 (±4.00)
3.0 (9 samples)	5	62.4 (±17.8)
11.0 (10 samples)	0.5	55.1 (±3.12)
11.0 (10 samples)	1	56.5 (±3.77)
11.0 (10 samples)	5	83.4 (±10.1)

Energy Dissipation (HEMA-AA)

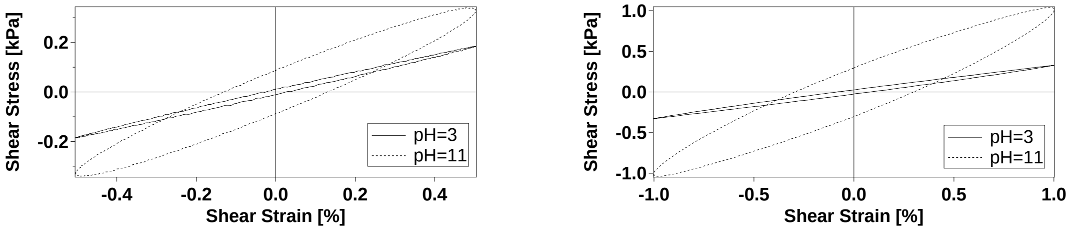
pH	Strain (%)	Energy Dissipated (%)
3.0 (8 samples)	0.5	40.6 (±4.84)
3.0 (8 samples)	1	43.6 (±4.61)
3.0 (8 samples)	5	55.6 (±3.1)
11.0 (8 samples)	0.5	15.2 (±5.03)
11.0 (8 samples)	1	21.3 (±9.79)
11.0 (8 samples)	5	58.5 (±20.6)

Table 2.2: Energy Dissipation results computed for the hydrogels



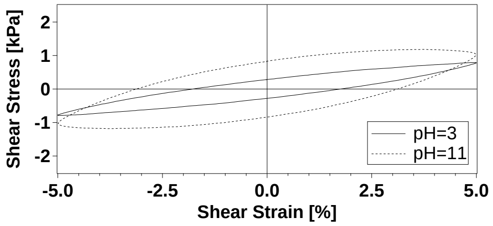
(i) The Lissajous plots obtained for HEMA-DMAEMA
sample swollen in 3.0 pH buffer solution

(ii) The Lissajous plots obtained for HEMA-DMAEMA
sample swollen in 11.0 pH buffer solution



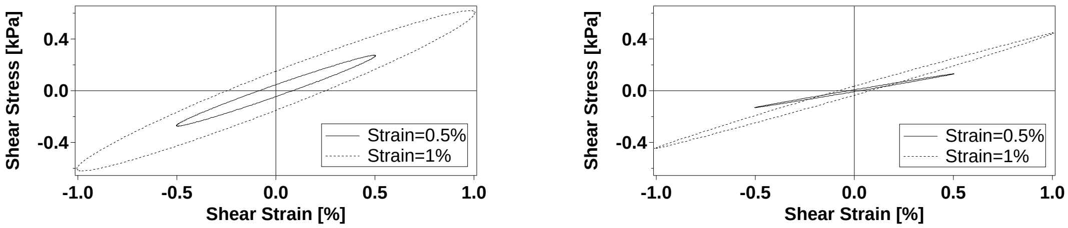
(iii) The Lissajous plots obtained for HEMA-DMAEMA
sample strained upto 0.5%

(iv) The Lissajous plots obtained for HEMA-DMAEMA
sample strained upto 1%



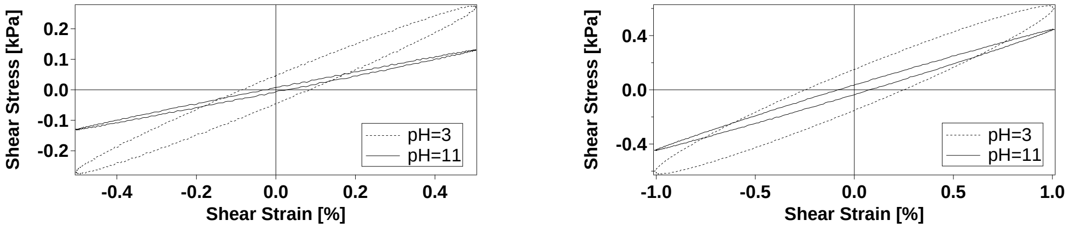
(v) The Lissajous plots obtained for HEMA-DMAEMA sample strained upto 5%

Figure 2.4: Results obtained for oscillatory shear test conducted on HEMA - DMAEMA at different strain levels and pH values



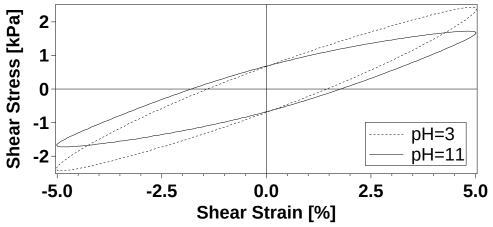
(i) The Lissajous plots obtained for HEMA-AA sample swollen in 3.0 pH buffer solution

(ii) The Lissajous plots obtained for HEMA-AA sample swollen in 11.0 pH buffer solution



(iii) The Lissajous plots obtained for HEMA-AA sample strained upto 0.5%

(iv) The Lissajous plots obtained for HEMA-AA sample strained upto 1%



(v) The Lissajous plots obtained for HEMA-AA sample strained upto 5%

Figure 2.5: Results obtained for oscillatory shear test conducted on HEMA-AA at different strain levels and pH values

2.7 Discussion

The energy dissipated was computed by calculating the area under the Lissajous curves obtained from the resullts of small and large amplitude oscillatory shear tests conducted on HEMA-DMAEMA and HEMA-AA hydrogel samples pre-swollen in 3.0 and 11.0 pH buffer solution using a parallel plate rheometer.

The dissipated energy for HEMA-DMAEMA samples was observed to increase with an increase in the strain amplitude when pre-swollen in 3.0 and 11.0 pH buffer solutions. However, the energy dissipation obtained for these hydrogel samples was greater in 11.0 pH buffer solution as compared to 3.0 pH buffer solution. This may be due to the fact that the crosslinked network in the hydrogel expands in the 3.0 pH buffer solution due to the chemical reaction that leads to the formation of water in the network. On the other hand, the crosslinks in the hydrogels pre-conditioned in 11.0 pH do not undergo significant changes.

The results obtained from dynamic oscillatory tests conducted on HEMA-AA samples pre-swollen in 3.0 pH buffer solution showed a higher dissipation of energy compared to the those pre-swollen in 11.0 pH buffer solution. The energy dissipation was also observed to increase when the applied strain amplitude was increased. HEMA-AA hydrogel samples swell in 11.0 pH buffer solution, which expands the crosslinked network, thus requiring lower energy. The results obtained for HEMA-DMAEMA and HEMA-AA are similar for the opposite buffer solutions viz. acidic and basic.

Previous attempts have been made by researchers to understand the viscoelastic properties of these pH-sensitive hydrogel. A thorough research of the properties of a material is required before using it for any application. The viscoelastic properties in terms of material function like storage modulus, loss modulus and loss tangent was studied by Benjamin et al. [7].The stress relaxation behavior of this pH-sensitive hydrogel within the linear viscoelastic range was accounted in another research by Benjamin et al. [9]. Johnson et al. [41] studied the effect of pH and crosslinker on the mechanical properties of HEMA-AA. In research, the aspect of energy dissipation plays an important role in defining the material property.

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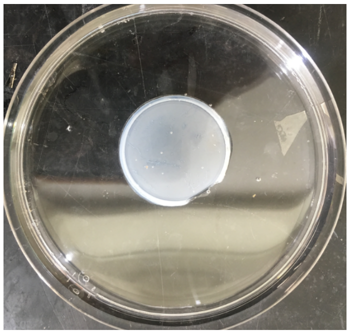
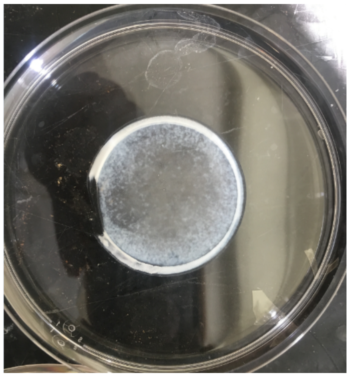
APPENDIX A

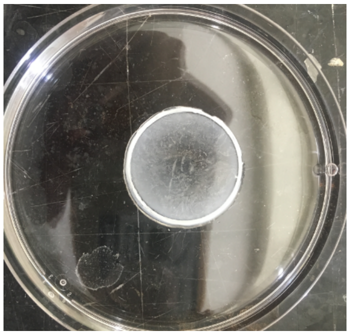
ENERGY DISSIPATION RESULTS



(i) HEMA-DMAEMA sample after placing in PBS solution



(ii) HEMA-DMAEMA sample after placing in 3.0 pH buffer solution



(iii) HEMA-DMAEMA sample after placing in 11.0 pH buffer solution

Table A.1: Results obtained for HEMA-DMAEMA samples swollen in 3.0 pH and strain at 0.5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.92	13.45
2	2.18	19.25
3	1.92	17.6
4	2.18	16.43
5	2.88	15.01
6	2	12.06
7	2.57	16.68
8	1.95	12.93
9	2.57	12.8
10	2.02	16.49

Table A.2: Results obtained for HEMA-DMAEMA samples swollen in 3.0 pH and strain at 1%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.92	16.08
2	2.18	23.08
3	1.92	23.58
4	2.18	19.93
5	2.88	16.24
6	2	14.17
7	2.57	26.85
8	1.95	18.59
9	2.57	16.51
10	2.02	23.61

Table A.3: Results obtained for HEMA-DMAEMA samples swollen in 3.0 pH and strain at 5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.8	88.69
2	1.5	48.89
3	1.5	61.57
4	1.8	90.92
5	2.02	48.37
6	2.1	56.98
7	2.1	78.34
8	1.79	41.59
9	1.89	46.24

Table A.4: Results obtained for HEMA-DMAEMA samples swollen in 11.0 pH and strain at 0.5%

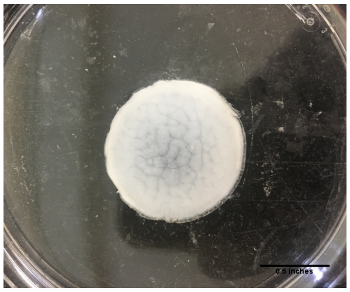
Sample No.	Thickness(mm)	Energy Density(%)
1	2.42	56.76
2	2.42	60.07
3	2.42	53.23
4	2.88	52.83
5	2	52.25
6	1.95	49.94
7	2.57	58.76
8	1.95	54.16
9	1.8	58.51
10	2.6	54.19

Table A.5: Results obtained for HEMA-DMAEMA samples swollen in 11.0 pH and strain at 1%

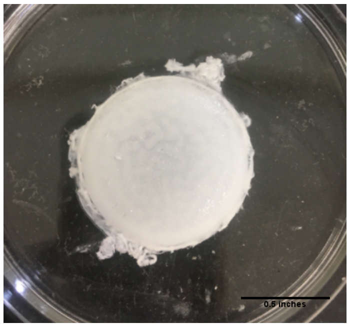
Sample No.	Thickness(mm)	Energy Density(%)
1	2.42	51.76
2	2.42	55.65
3	2.42	55.13
4	2.88	52.17
5	2	59.81
6	1.95	53.28
7	2.57	61.49
8	1.95	57.34
9	1.8	63.51
10	2.6	55.01

Table A.6: Results obtained for HEMA-DMAEMA samples swollen in 11.0 pH and strain at 5%

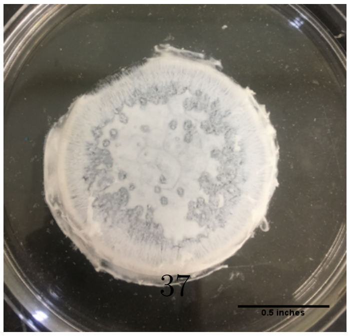
Sample No.	Thickness(mm)	Energy Density(%)
1	1.8	93.14
2	2.6	64.58
3	1.5	90.74
4	2.6	87.09
5	2.6	64.99
6	2.1	88.98
7	2.1	78.59
8	2.02	93.08
9	1.89	88.14
10	1.79	84.86



(i) HEMA-AA sample after placing in PBS solution



(ii) HEMA-AA sample after placing in 3.0 pH buffer solution



(iii) HEMA-AA sample after placing in 11.0 pH buffer solution

Table A.7: Results obtained for HEMA-AA sample swollen in 3.0 pH and strain at 0.5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.79	38.47
2	1.89	37.66
3	1.88	46.1
4	2.278	32.42
5	1.88	38.36
6	2.27	48.69
7	2.27	39.97
8	2.27	43.17

Table A.8: Results obtained for HEMA-AA sample swollen in 3.0 pH and strain at 1%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.79	41.97
2	1.89	41.26
3	1.88	48.54
4	2.278	35.47
5	1.88	42.34
6	2.27	43.86
7	2.27	51.92
8	2.27	43.15

Table A.9: Results obtained for HEMA-AA sample swollen in 3.0 pH and strain at 5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.79	59.48
2	1.89	55.64
3	1.88	55.29
4	2.278	52.98
5	1.88	56.57
6	2.27	60.41
7	2.27	53.88
8	2.27	50.29

Table A.10: Results obtained for HEMA-AA sample swollen in 11.0 pH and strain at 0.5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.8	16.03
2	1.88	15.83
3	2.27	10.41
4	1.88	10.27
5	1.88	26.97
6	2.27	11.19
7	2.27	15.61
8	2.27	15.55

Table A.11: Results obtained for HEMA-AA sample swollen in 11.0 pH and strain at 1%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.8	22.99
2	1.88	20.08
3	2.27	13.92
4	1.88	13.68
5	1.88	45.09
6	2.27	12.95
7	2.27	23.41
8	2.27	18.10

Table A.12: Results obtained for HEMA-AA sample swollen in 11.0 pH and strain at 5%

Sample No.	Thickness(mm)	Energy Density(%)
1	1.88	31.16
2	2.27	73.93
3	1.88	95.36
4	2.27	73.25
5	1.88	62.74
6	2.27	39.66
7	2.27	53.88
8	2.27	37.93

APPENDIX B

RELAXATION TEST

B.1 Methodolgy

2-hydroxymethyl methacrylate 2-dimethylamino ethyl methacrylate (HEMA DMAEMA) is a pH-responsive hydrogel which swells in an acidic medium and deswells in a basic medium. Relaxation tests were conducted on this hydrogel for the purpose of studying its behavior in the acidic and basic medium with respect to a change in temperature. 11 HEMA DMAEMA cylindrical samples were fabricated using PDMS wells and cured using a photomask. The pre-polymer solution was composed of the monomers 2-dimethylamino ethyl methacrylate (DMAEMA) and 2-hydroxyethyl methacrylate (HEMA), the crosslinker ethylene gylcol dimethacrylate (EGDMA) and the photo-initiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) in the ratio 5.718:27.627:0.467:1. The samples had a thickness in the range of 1.32mm to 1.93mm. These samples were then immersed in the respective mediums for 48 hours after which 1 inch diameter samples were punched out for testing. The diameter and thickness of the samples along with the mediums are given in Table 1.

B.2 Initial Results

Anton Paar MCR 305 rheometer with 1 inch parallel plate configuration was used to conduct temperature imposed relaxation tests at shear strain of 0.5%. The test was run for 100secs with 10 data points at temperature ranging from 5°C-75°C. The normal force was set between a range of 1.2N to 1.8N. The relaxation modulus vs time plots for various samples were obtained and are as shown.

Table B.1: Sample Details

Sample No.	Thickness(mm)	pH
1	1.34	3
2	1.4	3
3	1.34	3
4	1.4	3
5	1.34	3
6	1.4	3
7	1.32	11
8	1.93	11
9	1.32	11
10	1.93	11
11	1.32	11

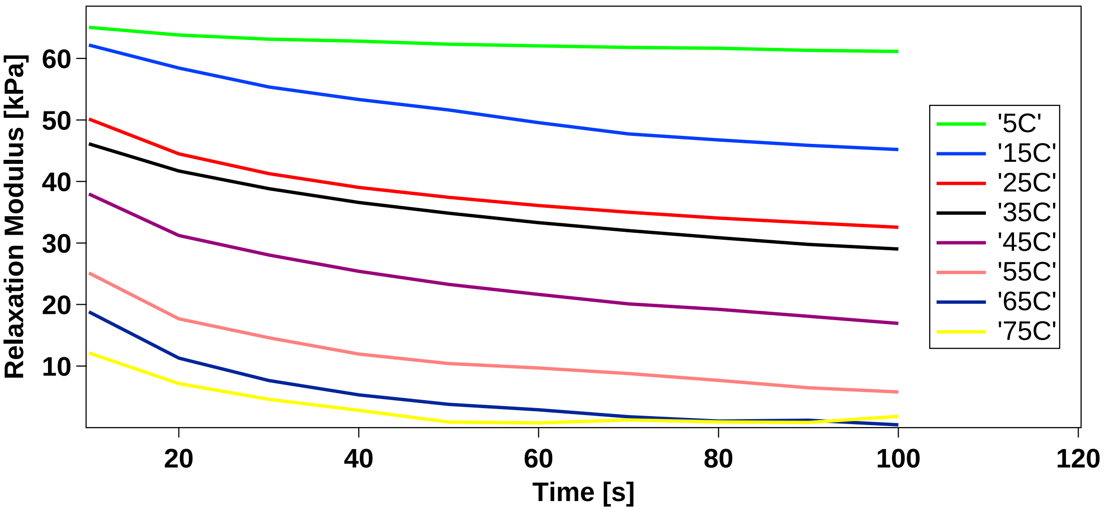


Figure B.1: Relaxation vs Time results for HEMA-DMAEMA in 3.0 pH buffer solution

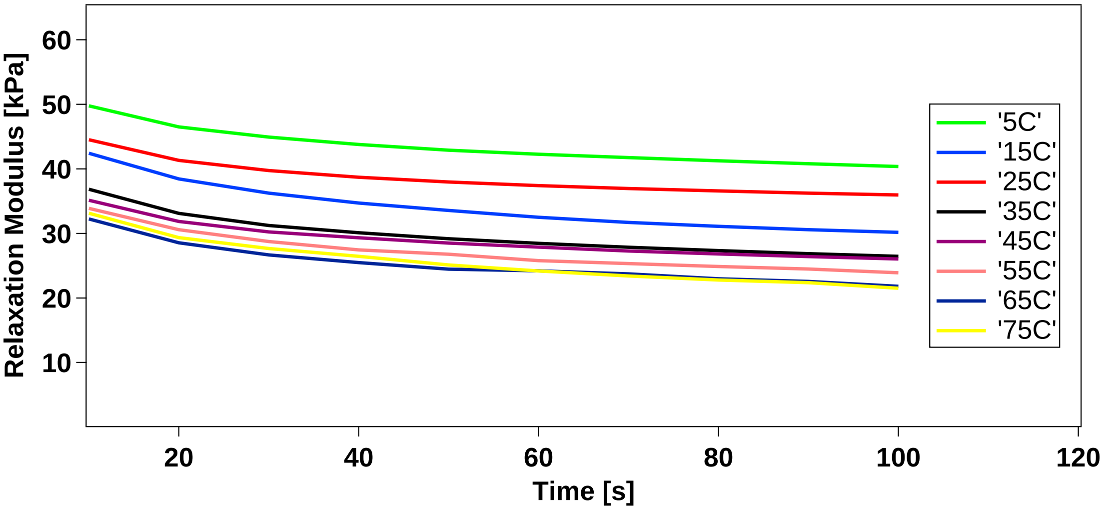


Figure B.2: Relaxation vs Time results for HEMA-DMAEMA in 11.0 pH buffer solution

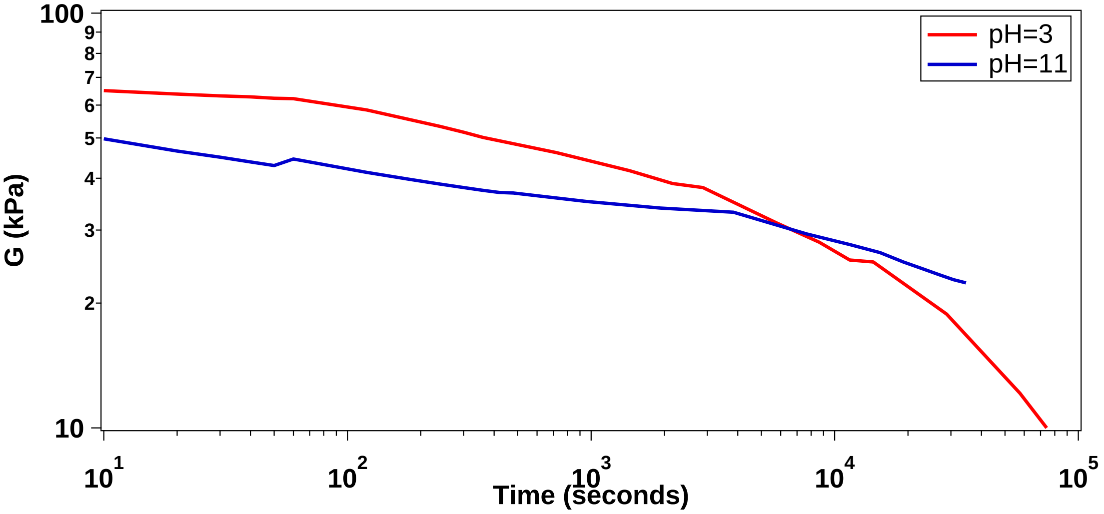


Figure B.3: Master Curve obtained for HEMA-DMAEMA in 3.0 pH and 11.0 pH buffer solution