SYNTHESIS AND CHARACTERIZATION OF BIOACTIVE PANI-PAMPSA NANOPARTICLES DISPERSED IN POLY(HEMA)-BASED HYDROGELS

An Undergraduate Research Scholars Thesis

by

BLAKE ANDREW SMITH

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ABSTRACT

Synthesis and Characterization of Bioactive PAn-PAMPSA Nanoparticles Dispersed in Poly(HEMA)-based Hydrogels

Blake Andrew Smith
Department of Biomedical Engineering
Texas A&M University

Research Advisor: Dr. Anthony Guiseppi-Elie
Department of Biomedical Engineering
Texas A&M University

The distribution of water within and its relation to the electrical impedance of electroconductive hydrogels (ECH) is of interest in developing stimuli-responsive hydrogel membranes for in-dwelling biomedical sensors. Poly(2-hydroxyl methacrylate)-based hydrogels possessing 2-aminoethyl methacrylate hydrochloride (AEMA) and 2-(dimethylamino)ethyl methacrylate (DMAEMA) were synthesized and studied for their degree of hydration, water distribution (free and bound water content), and glass transition temperature. Additionally, AC electrical impedance spectroscopy (EIS) and equivalent circuit analysis of synthesized hydrogels with increasing amounts (0, 0.1, 1.0 and 10.0 wt%) of PAn-PAMPSA was conducted. Using gravimetric analysis and differential scanning calorimetry (DSC), the degree of hydration and distribution of water was found to be significantly affected by inclusion of DMAEMA (hydrophobic) but not AEMA (hydrophilic). The inclusion of DMAEMA significantly decreased overall hydration, increased free water content, and decreased bound water content in the hydrogel. Additionally, the glass transition temperature determined using DSC was found to be significantly increased by the inclusion of DMAEMA, but no significant change was observed

for AEMA inclusion. EIS revealed a significant impact of both AEMA and DMAEMA on the membrane resistance of ECHs. The inclusion of PAn-PAMPSA in 5M% HEMA hydrogel produced a simple scaling of the membrane resistance, R_M, with inclusion composition. The membrane resistance for the AEMA and DMAEMA containing ECHs showed membrane resistances that were dependent upon the nature of the hydrogel as well as the wt% of the PAn-PAMPSA inclusion.

NOMENCLATURE

AEMA	2-aminoethyl methacrylate hydrochloride
DMAEMA	2-(dimethylamino)ethyl methacrylate
DoH	Degree of hydration
DSC	Differential Scanning Calorimetry
ECH	Electroconductive hydrogel
EIS	AC electrochemical impedance spectroscopy
ICP	Inherently conductive polymer
PAMPSA	poly(2-acrylamido-2-methylpropanesulfonic acid) (a macromolecular dopant for PAn)
PAn	Polyaniline (an inherently conductive electroactive polymer)
TFE	Thin film electrodes
wt.%	Weight percent

CHAPTER I

INTRODUCTION

Electroconductive hydrogels (ECH) [1] are stimuli responsive nanocomposites of poly(HEMA)-based hydrogels containing a dispersion of nanostructured inherently conductive polymers (ICPs). ECH synthesized with polyaniline doped with water-soluble poly(2-acrylamido-2-methylpropanesulfonic acid) (PAn-PAMPSA) are promising candidates for serving as the abio-bio interface of implantable devices and as functional, biologically-responsive circuit elements for indwelling electronics [2]. Incorporating water-soluble PAn-PAMPSA in the formulation of hydrogels is a potential solution for the problem of electroconductive hydrogels typically being brittle, not readily processable, and insoluble in biocompatible solvents [2]. Additionally, 2-(dimethylamino)ethyl methacrylate (DMAEMA) and 2-aminoethyl methacrylate hydrochloride (AEMA) have been used as pH modulators within the hydrogel matrix in pH-responsive drug delivery [3] and biosensor applications [4]. There is need for an evaluation of the impact of such modulators on the physicochemical properties of poly(HEMA)-based hydrogels. This study aims to characterize the impact of minor molar concentrations of DMAEMA and AEMA on the physicochemical characteristics (hydration, water distribution, and electrical impedance) of the poly(HEMA)-based hydrogels matrix as well as the electrical impedance characteristics with increasing amounts (wt%) of PAn-PAMPSA within the electroconductive hydrogel.

Synthetic hydrogels are three-dimensional polymer networks that retain a significant weight fraction of water compared to the total polymer content. Within the field of biomaterials, hydrogels have emerged as a promising biomaterial with a diverse array of applications.

Traditionally, synthetic hydrogels have been applied as contact lenses, linings for artificial hearts, materials for artificial skin, three-dimensional scaffolds for tissue regeneration, biorecognition membranes for biosensors, and drug delivery devices [5].

A major challenge faced by biomedical engineers is the need to tailor hydrogels to the specific needs of the environments in which they are applied while also making them have a desired response in that environment. In order to impart a desired functionality, monomer constituents and chemical modifiers are added to hydrogels. For example, polyethylene glycol (PEG), in the form of PEG-acrylates, may be added to hydrogels to mitigate protein adsorption and hence provide biocompatibility, but the inclusion of PEG has an effect on the bulk modulus and surface properties of hydrogels [1, 6]. Characterizing how and to what extent medically relevant hydrogel properties are impacted by PEG inclusion is within the domain of biomedical engineering. It is first necessary to understand the bulk properties of modified hydrogels, as these characteristics have a significant impact on the desired functional role of hydrogels in their final biomedical application.

The degree of hydration (DoH), which is the total amount of water imbibed by the hydrogel, and the distribution of that water between free and bound states, are key hydrogel properties to take into consideration as they have a profound effect on the functionality of hydrogels for biomedical application [7]. For example, the quantity and distribution of water within hydrogels have been shown to alter the sorption and transport of drugs into hydrogels [8], and have also been tailored for the fabrication of injectable hydrogels for surgery and localized therapy [7]. The type of functional groups on the polymeric backbone and the segmental dynamics of the polymer network are responsible for the amount of water that can be imbibed (DoH), and the spatial distribution of water within the polymer network (free and bound water)

[7]. Once imbibed, water within a hydrogel is known to exist as freezable free water, freezable bound water, and non-freezable bound water [9]. For simplicity, the freezable free water and freezable bound water are grouped together as freezable water. The freezable water is taken to be the water that is imbibed but not bound to the polymer network of hydrogels. This water freezes at the regular freezing temperature of water and is easily removed from the hydrogel. The non-freezable water is the water that is strongly bound to the polymer network of hydrogels once imbibed. This portion of the water does not freeze at the regular freezing temperature of water and is not easily removed from the hydrogel.

In addition to monomer constituents, chemical and nanoparticle additives may also be included in the hydrogel formulation in order to engineer novel properties. Inherently conductive polymers (ICPs) are an example of nanoparticle additives that may be incorporated into hydrogel networks to impart electronic conductivity and increase elastic modulus. Polyaniline (PAn) is an example of a well-known ICP. PAn has been used to make electroactive scaffolds for cardiac and neuronal cell regeneration [10] and biologically responsive circuit elements for implantable electronics [2]. Additionally, PAn has been incorporated into hydrogel networks for pH-sensing and electro-actuated drug delivery applications [3, 4]. Unfortunately, ICPs are often brittle and insoluble in biological solvents [2]. In order to address these issues, PAn is doped with the water-soluble dopant poly(2-acrylamido-2-methylpropanesulfonic acid) (PAMPSA) and synthesized as high aspect ratio nanofibers [11]. While a wide array of monomer constituents, chemical and nanoparticle modifiers are known, a major challenge when tailoring hydrogels is the lack of systematic understanding of the impact of individual hydrogel constituents on the water content and its functional distribution. The hydration characteristics of the hydrogel, could in turn affect the overall bulk properties and application scope of a hydrogel. Accordingly, this study had two

objectives. The first was to study the impact of minor changes in monomer constituent and composition on the water content and its functional distribution within the hydrogel. The second was to synthesize nanocomposites of PAn-PAMPSA within these hydrogels and measure their electrical impedance properties.

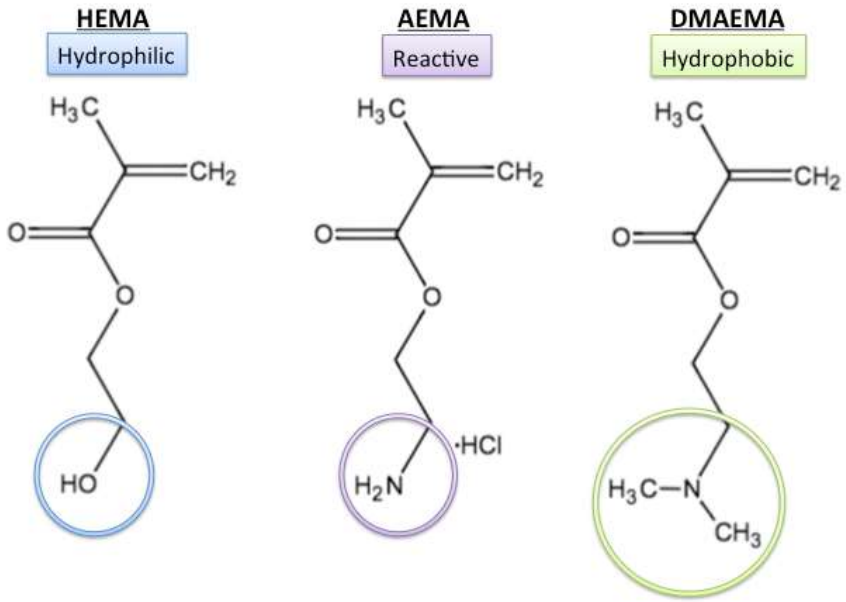

Figure 1: The chemical structures of HEMA, AEMA, and DMAEMA are shown. The differences in the functional groups of each constituent have been highlighted in respective circles and the characteristic traits are highlighted under each label.

The monomer constituents evaluated in this study include 2-hydroxyethyl methacrylate (HEMA), 2-(dimethylamino)ethyl methacrylate (DMAEMA), and 2-aminoethyl methacrylate hydrochloride (AEMA). The chemical structures and end-groups of HEMA (-OH), AEMA (-NH_2), and DMAEMA (-$N(CH_3)_2$) are illustrated in Figure 1. As seen from Figure 1, the hydroxyl end-group in HEMA, a common monomer used in hydrogel formulation [12], was responsible for the hydrophilic property. Similarly, the primary amine group in AEMA and the tertiary amine end-group in DMAEMA were responsible for the reactive and relatively hydrophilic, and relatively hydrophobic, behavior of the constituents. The presence of the hydrophobic and

ionizable tertiary amine in DMAEMA and the reactive primary amine in AEMA were expected to have an impact on hydration characteristics of the hydrogels. The question then becomes, are these expectations manifest when constituents are as low as 5M% or 1:20 repeat units. The hydration characteristics of the hydrogel were determined using differential scanning calorimetry. Subsequently, the bulk electrical properties of the hydrogel, both neat and upon adding different weight percent (wt.%) of PAn-PAMPSA to the base hydrogel were assessed. Electrical properties were assessed using a 2-point probe conductivity method and AC electrical impedance spectroscopy (EIS) with subsequent equivalent circuit analysis.

CHAPTER II

MATERIALS AND METHODS

2.1. Synthesis of Hydrogels

The study was done in two parts. In the first part of the study, the effects of monomer components on the swelling and hydration properties for four base hydrogel formulations were assessed. Subsequently, in the second part of the study, the effects of monomer components on the electrical properties of the hydrogels were assessed following the addition of PAn-PAMPSA.

2.1.1. Chemicals and Reagents

2-hydroxyethyl methacrylate (HEMA), tetra(ethylene glycol) diacrylate (TEGDA, technical grade), poly(ethylene glycol)(360)methacrylate (PEG(360)MA), N-[Tris(hydroxymethyl)methyl]acrylamide (HMMA, 93%), polyvinylpyrrolidone (pNVP, Mw ~1,300,000), 2-aminoethyl methacrylate hydrochloride (AEMA, 90%), 2-(Dimethylamino)ethyl methacrylate (DMAEMA, 98%), the photo-initiator 2,2-Dimethoxy-2-phenylacetophenone (DMPA, 99+%), octadecyltrichlorosilane (OTS), toluene, and all other common solvents and buffers were purchased from Sigma Aldrich Co. (St. Louis, MO, USA). Methacrylate and diacrylate reagents were passed through an inhibitor removal column (Sigma-Aldrich) in order to remove the polymerization inhibitors hydroquinone and monomethyl ether hydroquinone. The HEPES buffer used was prepared to be 25 mM and pH = 7.4. A Milli-Q® plus (Millipore Inc.) ultrapure water system was used to prepare deionized water.

2.1.2. Hydrogel Cocktail Formulation

For the first part of the study, four different hydrogels that varied in composition were synthesized from monomeric components HEMA, DMAEMA, and AEMA each cross-linked with 3M% TEGDA. Sample-A was the reference formulation for all hydrogel samples and was composed of HEMA. Samples B and C were composed of 5-mol% AEMA and 5-mol% DMAEMA, respectively; achieved by replacing 5-mol% of HEMA from the base hydrogel. In sample-D, 5-mol% HEMA was replaced with a mixture of 2.5-mol% AEMA and 2.5-mol% DMAEMA. **Table 1** lists the hydrogel constituents and composition.

Table 1: Monomer composition (mol%) for hydrogel preparation

Sample	**Sample-A**	**Sample-B**	**Sample-C**	**Sample-D**
HEMA *(Base Monomer: hydrophilic)*	79	79	79	79
TEGDA *(Cross-linker)*	3	3	3	3
PEGMA(360) *(Confers biocompatibility)*	5	5	5	5
HMMA *(Support monomer: hydrophilic)*	5	5	5	5
pNVP *(Pre-polymer: Increases viscosity)*	2	2	2	2
HEMA *(Monomer: hydrophilic)*	5	0	0	0
DMAEMA *(Monomer: hydrophobic)*	0	5	0	2.5
AEMA *(Monomer: hydrophilic)*	0	0	5	2.5
DMPA *(Photoinitiator)*	1.0	1.0	1.0	1.0

For the second part of the study, the effect of monomer components on the electrical properties of the samples A-D were assessed, first at 0.0 wt %, and then by increasing the weight percent of PAn-PAMPSA in the following sequence – 0.0, 0.1, 1.0, and 10 (wt.%), making a total of sixteen distinct hydrogel formulations.

2.1.3. Fabrication of Hydrogels

The hydrogel formulations were cast inside silicone hybridization chambers (GBL664206 Grace Biolabs) of 4.5 mm diameter by 2.0 mm depth and placed between two chemically modified glass microscope slides. Prior to casting, the glass slides were thoroughly UV-ozone

cleaned on both sides and sonicated in isopropyl alcohol to further remove contaminants. The slides were then plasma cleaned and incubated in a solution of 0.1% octadecyltrichlorosilane (OTS) in toluene for 45 minutes. The glass slides were then sonicated in isopropyl alcohol for 5 minutes, and were cured in an oven, sequentially at 40°C, 110°C, and 40°C for 20 minutes at each temperature. Within the silicone hybridization chambers, hydrogels were UV cross-linked for five minutes. Upon completion of cross-linking, the polymerized hydrogels were removed from the glass slides for monomer extraction and hydration. The hydrogels were then gradually hydrated by soaking for one hour each in ethanol (99%) and 25 mM HEPES buffer (pH 7.4) mixtures in proportions of 100/0, 75/25, 50/50, 25/75 and 0/100 (mL/mL %).

2.2. Characterization of Hydrogels

2.2.1. Water States in Hydrogels

The degree of hydration was determined using gravimetric analysis and freezable free water content and the non-freezing bound water content were determined using a multi-step process involving differential scanning calorimetry.

2.2.1.a. Gravimetric Analysis

First, the degree of hydration (DoH) of the hydrogels was determined with gravimetric analysis. In this process, hydrogels were weighed when fully hydrated (W_h) and then weighed again once they were completely dehydrated (W_d). Dehydration was accomplished by storing hydrogels in an -80°C freezer for twelve hours and then lyophilizing them for two days under 0.01 mbarr at -50°C. DoH can then be calculated using Eq. (1).

$$DoH = \frac{W_h - W_d}{W_h} \times 100 \quad (1)$$

2.2.1.b. Differential Scanning Calorimetric (DSC) Analysis

DSC was performed using the Q2000 differential scanning calorimeter (TA Instruments). Following established methods [12], approximately 5-10 mg of hydrated hydrogel was placed and sealed into a hermetic pan (Tzero hermetic lid, 901684.901; Tzero pan, 901683.901), equilibrated at -40°C and heated to 30°C at 10°C/min under purging nitrogen (50mL/min). The ΔH_m of hydrogels at 0°C was then found by integrating the endothermic peak in TA Universal analysis software and then normalizing the data with respect to W_h. Assuming the enthalpy of the freezing and bound water to be the same as that of bulk water (ΔH_0 = 334 J/g), the freezing free water content was calculated using Eq. (2), and the non-freezing bound water content was calculated using Eq. (3).

$$\frac{W_f}{W_h}(wt\%) = \frac{\Delta H_m}{\Delta H_0} \times 100 \quad (2)$$

$$\frac{W_{\mathrm{nfb}}}{W_h}(wt\%) = DoH - \frac{W_f}{W_h} \quad (3)$$

To determine the glass transition temperature (T_g) of the hydrogels, DSC was performed on dehydrated hydrogels using the Q2000 differential scanning calorimeter (TA Instruments). The hydrogels were first be dehydrated by placing them in an -80°C freezer for twelve hours and then lyophilizing them for 24 hours under 0.01 mbarr at -50°C. The dehydrated samples were placed and sealed into hermetic pans (Tzero hermetic lid, 901684.901; Tzero pan, 901683.901), equilibrated at -20°C and heated to 200°C at 10°C/min for two cycles. The first cycle was performed in order to erase the thermal history of the hydrogels, and the second cycle was

performed in order to determine the inherent thermal properties of the hydrogels. The T_g was then extrapolated from the data using TA Universal Analysis software.

2.2.2. Electrical Characterization

Initial resistivity measurements were performed using a 2-point probe conductivity method on formulated, cast and UV-cured hydrogels. The measurements were taken using a Keithley Multimeter (Model 2010), keeping the distance between the hydrogels and conductivity probe constant between measurements. At least five measurements were taken in order to collect a representative sample data set. The resulting resistance readings were then used as a relative gauge for the conductivity of the hydrogels and to guide expectations with regard to EIS measurements.

AC electrochemical impedance spectroscopy (EIS) measurements (sine wave, 50mV p-t-p, 0.01Hz – 1.0 MHz) were then taken for the formulated hydrogels set between two opposing fold Thin Film Electrodes (TFEs, ABTECH Scientific, Inc.). The EIS measurements were taken using a Versastat 4 (Princeton Applied Research). Hydrogels were placed between two TFEs, which were pressed with a constant force in order to ensure the hydrogels were in complete contact with the TFEs and also to ensure reproducibility for all EIS measurements.

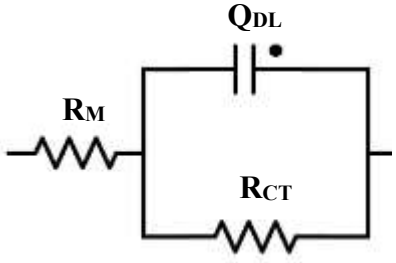

Figure 2. Representation of a Randles equivalent circuit used to calculate membrane resistance (R_M), charge transfer resistance (R_{CT}), and double layer capacitance (Q_{DL}).

Equivalent circuit analysis was performed in order to model the electrical characteristics of the hydrogels. The analysis was completed using ZSimpWin (v3.60, Princeton Applied Research, PLACE). A modified Randles circuit, (R(QR)) (Figure 2), was used to calculate the resistance and capacitance elements from the gathered impedance data of the hydrogels.

CHAPTER III

RESULTS AND DISCUSSION

3.1. Monomer Composition Influences Water Content and Distribution

Initially, the total degree of hydration (DoH) of the hydrogels was determined using gravimetrical analysis. Next, the freezable free water and non-freezable bound water were determined using differential scanning calorimetry in order to further understand how the two monomers AEMA and DMAEMA effected hydration.

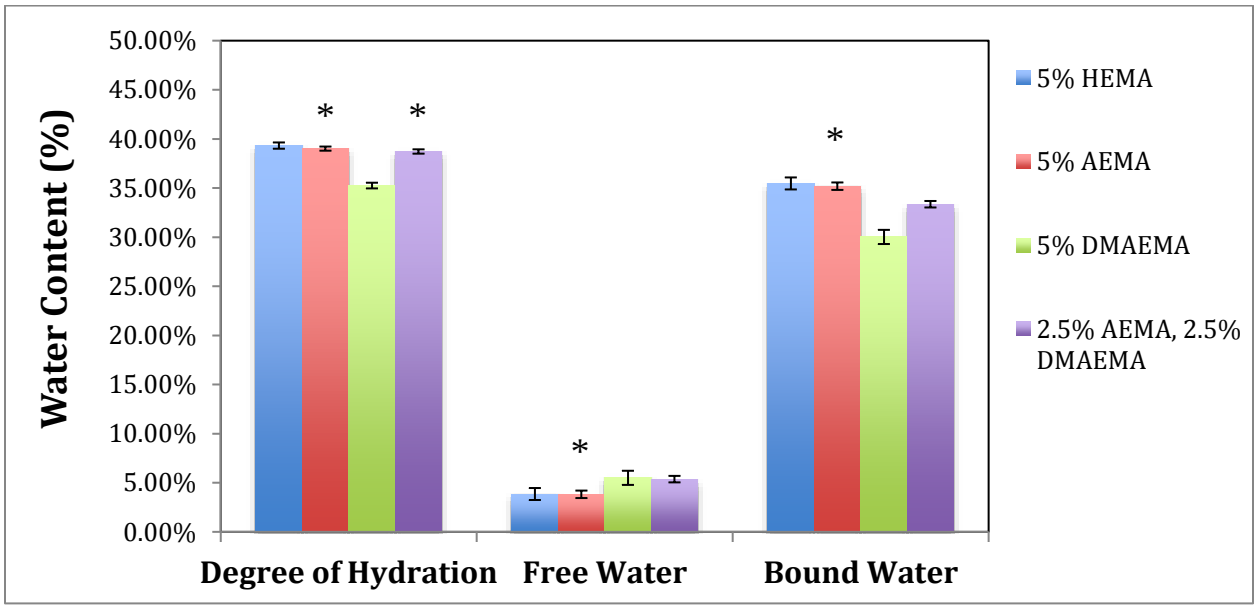

Figure 3: Degree of hydration, free water content, and bound water content of Sample-A (blue), Sample-B (red), Sample-C (green) and Sample-D (purple) are provided. The bar graphs and error bars represent the mean ± 95% C.I. (n=3). * Indicates statistical similarity to Sample-A.

Figure 3 shows the degree of hydration, free water content and the bound water content for the four different hydrogel formulations. As mentioned in the introduction section, the bound water that is hydrogen-bonded to the hydrogel polymer network is an integral part of the polymer

and cannot be easily removed. This also means that this water is not freezable at the freezing temperature of free, un-bound water. The free water, on the other hand, is water that is not strongly hydrogen-bonded to the polymer network, which may be easily removed and frozen at 0°C.

Similarly, the glass transition temperature (T_g) of hydrogels determined using DSC, represents the physical state of the hydrogels at different temperatures. The T_g is the temperature at which there is an increase in segmental mobility of the polymer backbone. It is characterized as a transition from a glassy (hard) to a rubbery (soft) state. The ability of each hydrogel to undergo this transition is dependent on the flexibility of the polymer chains, which is influenced by the bound water within the hydrogel. For this reason, analysis of T_g is closely related and compared to hydration and water distribution. Table 2 provides the T_g estimate for all hydrogel samples that were used in the current study. Values were obtained from the second DSC heating cycle, erasing any influence from the thermal history of the hydrogels.

Table 2. T_g for all four hydrogel formulations (n=3, mean ± 95% C.I.)

Sample Name	Control	Hydrophilic	Hydrophobic	Mix
T_g (°C)	93.2 ± 2.9	86.3 ± 1.3	114.2 ± 0.7	96.3 ± 0.4

3.1.1. Water Content Analysis of Sample-A-HEMA

Figure 3 shows that ~39.3% of the Sample-A hydrogel weight consisted of water. Of this 39.3% water, 91% was bound water and 9% was unbound water. The T_g for the control samples was found to 93.2°C. The T_g values reported in the literature for polyHEMA hydrogels vary

generally from 86°C - 100°C. The results from the current study does fall within the range. The wide variations in T_g values from literature were due to the variations in cross-linking density, the overall water content, and drying method used prior to DSC. In general, higher water content generally lowered the T_g values.

3.1.2. Water Content Analysis of Sample-B-AEMA

The replacement of 5-mol% HEMA with 5-mol% AEMA did not significantly affect the DoH of the hydrogel, and the distribution of the bound and free waters that were present in the hydrogel. With regard to T_g, the mean values for AEMA hydrogels (86.3°C) was slightly lower than the control sample (93.2°C). However, these estimates were not significantly different from the control sample. The relative similarity in the water content and the distribution of water were not surprising as both AEMA and HEMA are relatively hydrophilic monomers with relatively similarly sized functional groups.

3.1.3. Water Content Analysis of Sample-C-DMAEMA

The replacement of 5-mol% HEMA with 5-mol% DMAEMA in Sample-C had a significant effect on water content and the distribution of water around the polymer. In general, the overall water content in the sample-C hydrogel dropped by ~10%, as evident from the drop in DoH from 39.32% in the control samples to 35.25% hydration in the Sample-C hydrogels. More importantly the DMAEMA addition decreased the bound water content by a factor of ~14% while increasing the free water content by a factor of ~45% relative to the control hydrogels. The decrease in hydration and the shift in the water distribution was expected and was consistent with previous studies [12]. The impact of DMAEMA addition was also evident on the

T_g. Inclusion of DMAEMA caused a significant increase in the T_g, from an average of 93.2°C for Sample-A to 114.2°C for Sample-C.

DMAEMA, unlike the HEMA and AEMA, is relatively hydrophobic with bulkier functional groups. The inclusion of DMAEMA was thus expected to cause a decrease in the hydrogels ability to bond strongly to water, leading to higher free water content and lower bound water content. The lower bound water also raised the energy required to incite mobility in the polymer chains within the hydrogel. Hence, the chains are not flexible until a T_g, of 114.2 °C.

3.1.4. Water Content Analysis of Sample-D-Mixture

The effect of 2.5-mol% AEMA and 2.5-mol% DMAEMA mixture on the water content and distribution was interesting. In general, the overall water content and the T_g for sample-D hydrogels were statistically similar to that of the polyHEMA base hydrogel. However, the amount of bound water in the sample-D was reduced by a factor of ~6%, and the free water increased by a factor of 42% relative to the equivalent water content in polyHEMA hydrogel. The overall results were quite different from the individual addition of AEMA or DMAEMA. In fact, the T_g for the mixture was significantly different from that of the AEMA or the DMAEMA hydrogels. Based on the combined results, it was evident that the water content and distribution within a hydrogel with equivalent mixtures of hydrophilic and hydrophobic monomers do not follow the rule of mixtures but instead reflect a distinct behavior of its own.

3.2. Monomer Composition Influences the Electrical Properties

For this part of the study, the bulk electrical properties of the hydrogel were determined when PAn-PAMPSA concentrations in the hydrogel were increased in the sequential order – 0.0,

0.1, 1.0, and 10.0 wt.%. Subsequently, the electrical conductivity of the hydrogels were characterized using a DC power source and the interfacial behavior was investigated using an AC impedance spectroscopy.

3.2.1. Monomer Composition Influences the Resistance of the Hydrogel

Figure 4 shows the resistance to electrical conductance for hydrogels with different monomeric constituents as the PAn-PAMPSA concentration in the hydrogels was increased in the sequential order – 0.0, 0.1, 1.0, and 10.0 wt.%. As mentioned in the introduction section, the PAn is an ICP and its addition to the hydrogel was expected to decrease the overall electrical resistance within the hydrogel.

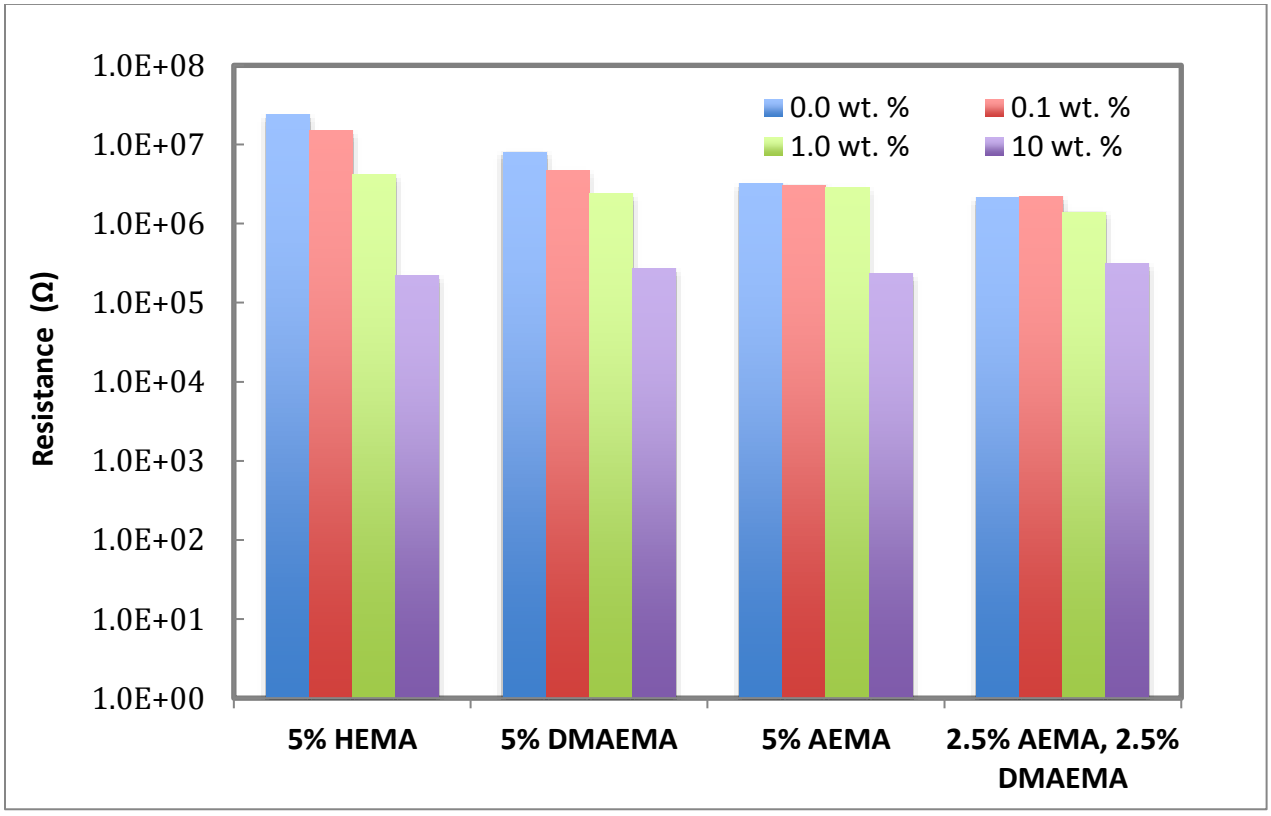

Figure 4. Conductivity of sample-A (blue), sample-B (red), sample-C (green) and sample-D (purple) with 0.0, 0.1, 1.0 and 10.0 wt.% of PAn-PAMPSA are provided.

3.2.1.1. Resistance of Sample-A-HEMA

Figure 4 shows that the polyHEMA was inherently resistive as evident from the resistance values (23.8 MΩ) at 0.0 wt.% PAn-PAMPSA. The 0.1 wt.% addition of PAn-PAMPSA to the hydrogel introduced a significant difference to the overall resistance values, and reduced the resistance by a factor of ~37%. Subsequent addition of 1.0% PAn and 10% PAn-PAMPSA reduced the resistance within the hydrogel by a factor of ~82% and ~91% respectively. These measurements thus clearly showed that increasing the wt.% of PAn-PAMPSA in the polyHEMA hydrogels significantly decreased the resistance and increased the overall conductivity of the polyHEMA hydrogel.

3.2.1.2. Resistance of Sample-B-AEMA

In contrast to the control samples, the resistance within the AEMA hydrogel was inherently lower (3.2 MΩ), and did not change significantly with the addition of 0.1 wt.% and 1.0 wt% of PAn-PAMPSA. This trend in resistance values was quite distinct from all other hydrogels with similar PAn-PAMPSA wt.% composition and hints at the dominant influence of AEMA functional groups on the electrical characteristics of the hydrogel. With the subsequent addition of 10 wt.% PAn-PAMPSA, however, the resistance decreased by a factor of ~93%. At this wt.% of PAn-PAMPSA, the resistance values were not significantly different from the resistance values of control sample with 10 wt% PAn-PAMPSA compositions. This illustrates that PAn-PAMPSA dominates conductivity when present in sufficient amounts, even in the presence of strongly influential monomers such as AEMA.

3.2.1.3. Resistance of Sample-C-DMAEMA

The inherent resistance of the Sample-C hydrogels (8 MΩ) to electrical conduction was lower than the control hydrogel (Sample-A) by a factor of ~66%. The addition of 0.1 wt.% and 1.0 wt.% PAn-PAMPSA lowered the resistance by a factor of ~41% and ~70% respectively. The resistance values for these hydrogels were significantly different from the resistance values of the control samples with similar PAn-PAMPSA compositions. The subsequent addition of 10 wt.% PAn-PAMPSA lowered the resistance further by a factor of ~97%. The resulting resistance values were not significantly different from the resistance values of control sample with 10 wt% PAn-PAMPSA.

3.2.1.4 Resistance of Sample-D-Mixture

The inherent resistance of the Sample-D hydrogels (2.2 MΩ) to electrical conduction was lower than the control hydrogel (Sample-A) by a factor of ~91%. Similar to Sample-B, the addition of 0.1 wt.% PAn-PAMPSA did not cause a significant shift in resistance. However, the addition of 1.0 wt.% PAn-PAMPSA lowered the resistance by a factor of ~35%. Although the numerical resistance values were not between the values for Sample-B and Sample-C, Sample-D displayed intermediate behavior in terms of resistance trends with increasing wt.% PAn-PAMPSA. Sample-D behavior was similar to Sample-B at 0.1 wt.% and Sample-C at 1.0 wt.%. The subsequent addition of 10 wt.% PAn-PAMPSA lowered the resistance further by a factor of ~97%. The resulting resistance values were not significantly different from the resistance values of control Sample-A, Sample-B, or Sample-C with 10 wt.% PAn-PAMPSA, indicating that conductivity for all hydrogel formulations was dominated by PAn-PAMPSA at 10 wt.%.

3.2.2. Monomer Composition Influences the Interfacial Behavior of the Hydrogel

To gain a more in-depth understanding of the interfacial behavior of the hydrogel with varying compositions of the monomer and chemical additives, AC electrochemical impedance spectroscopy (EIS) was employed in this part of the study. EIS measurements were made over the frequency range 1MHz to 0.01Hz, and equivalent circuits analysis was performed using the acquired impedance data.

3.2.2.1. Sample-A-HEMA Impedance Analysis

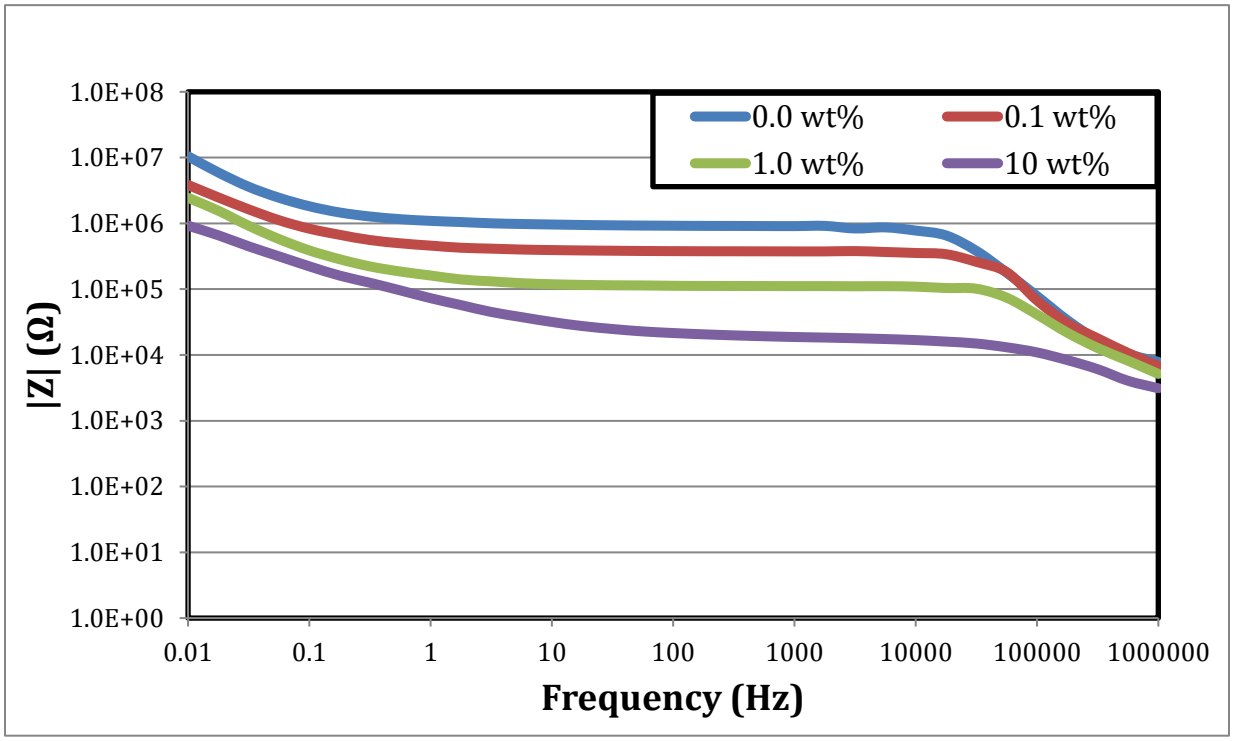

Figure 5. Magnitude of the impedance spectra for 0.0, 0.1, 1.0 and 10 weight percent PAn-PAMPSA in Sample-A-HEMA hydrogel formulation from 0.01 Hz to 1 MHz using a 50 mV peak-to-peak sine wave.

The impedance behavior of the Sample-A hydrogel (Figure 5) followed the expected trend for increasing PAn-PAMPSA wt.%. As PAn-PAMPSA wt.% increased, going from 0.0,

0.1, 1.0, and 10 wt.%, the magnitude of the impedance values decreased. This was the same trend seen in the initial conductivity measurements. This shows that the polyHEMA hydrogel formulation maintains its electrical characteristics throughout a wide range of frequencies. As Sample-A is the reference polyHEMA hydrogel, the impedance behavior seen in Figure 5 functions as a reference to compare subsequent impedance data for Sample-B, Sample-C, and Sample-D hydrogels.

3.2.2.2 Sample-B-AEMA Impedance Analysis

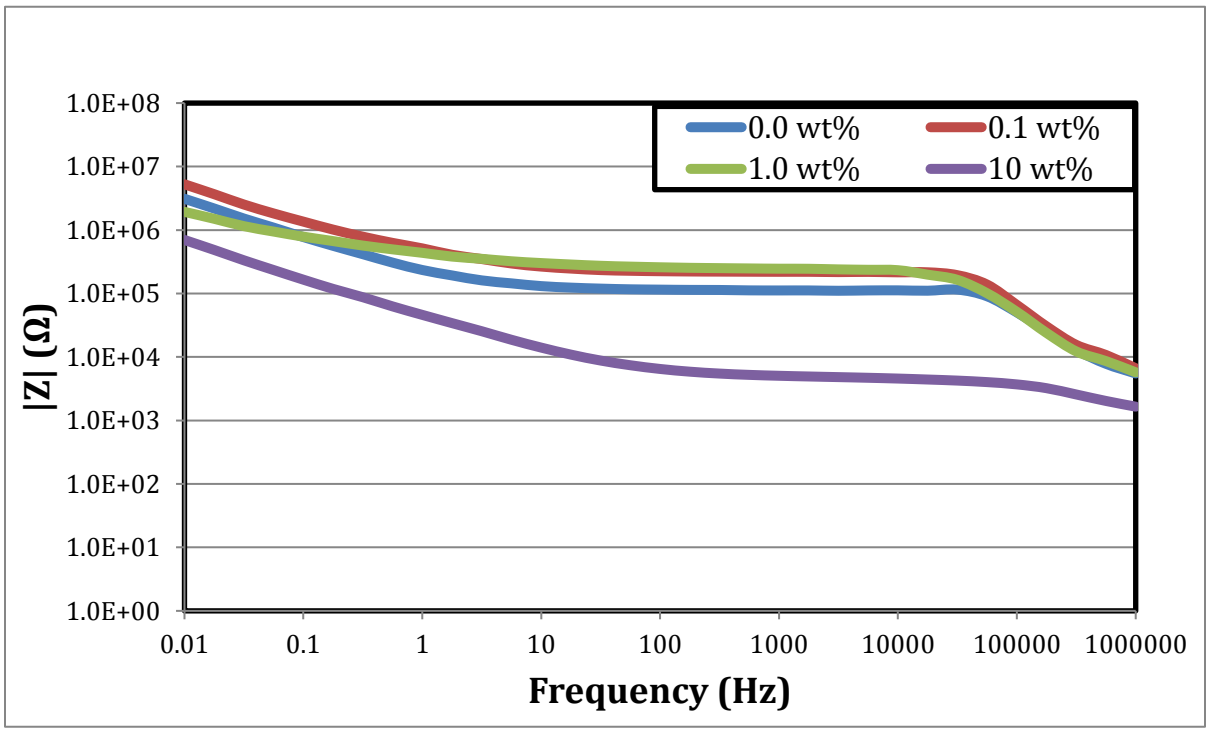

Figure 6. Magnitude of the impedance spectra for 0.0, 0.1, 1.0 and 10 weight percent PAn-PAMPSA in Sample-B-AEMA hydrogel formulation from 0.01 Hz to 1 MHz using a 50 mV peak-to-peak sine wave.

The impedance data for Sample-B hydrogel (Figure 6) is bunched together at 0.0, 0.1, and 1.0 wt.% PAn-PAMPSA, but there is a drop in impedance at 10wt.% PAn-PAMPSA. This is

likely due to the reactive nature of AEMA resulting from the amine group attached to it (Figure 1). Because of this, AEMA hydrogels are fully protonated and the conductivity is dominated by this factor at low PAn-PAMPSA concentrations. However, the conductivity of AEMA is overcome by a higher conductivity caused by PAn-PAMPSA at 10 wt. %.

Similar to Sample-A, the behavior of the impedance data for Sample-B hydrogel seen in Figure 6 matched the behavior of the initial conductivity test. For both tests, the 0.0, 0.1, and 1.0 wt.% hydrogel formulations have roughly equivalent values, while the 10 wt.% has a much lower value. This shows that the electrical characteristics of Sample-B hydrogel formulation are similar across a wide range of frequency values just as Sample-A was.

3.2.2.3 Sample-C-DMAEMA Impedance Analysis

The Sample-C-DMAEMA hydrogels showed anomalous behavior. Figure 7 shows that at low frequencies, the impedance values followed the trend seen for the reference Sample-A impedance, but this trend broke down at high frequencies with no clear order. These unclear readings could possibly be the result of incomplete cross-linking. These hydrogels were one of the first cross-linked with higher wt. % PAn-PAMPSA, and it was found in the process of formulating all of the hydrogels that increasing the wt. % of PAn-PAMPSA increases the time needed to complete cross linking. Even so, there is a possible conclusion that can be drawn regarding the results. The 0 wt. % DMAEMA may have a low impedance by nature, and adding 0.1 wt. % PAn-PAMPSA disrupts this aspect of DMAEMA, acting as a filter. Then when PAn-PAMPSA concentration is increased to 1.0 wt. %, the PAn-PAMPSA nanoparticles are present in a high enough amount to complete their own chain causing a drop in impedance. This

reasoning fits the data collected. However, further testing would be required to affirm this hypothesis.

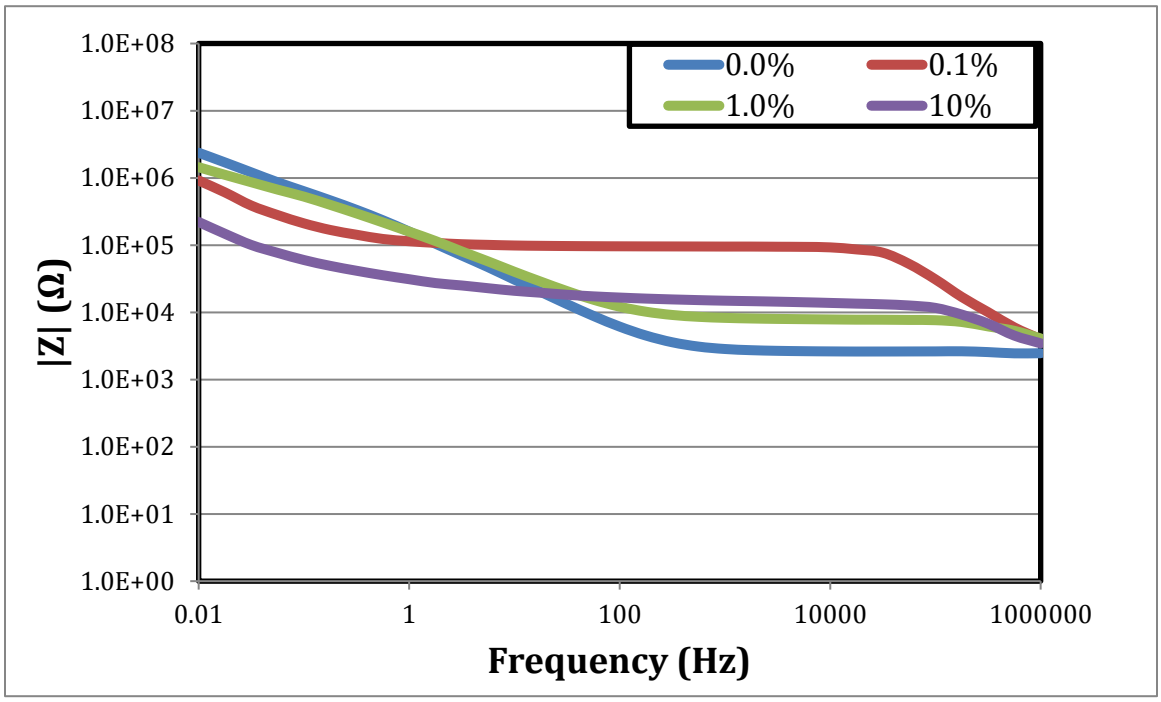

Figure 7. Magnitude of the impedance spectra for 0.0, 0.1, 1.0 and 10 weight percent PAn-PAMPSA in Sample-C-DMAEMA hydrogel formulation from 0.01 Hz to 1 MHz using a 50 mV peak-to-peak sine wave.

3.2.2.4 Sample-D-Mixture Impedance Analysis

The impedance of the Sample-D hydrogel (Figure 8) is similar to both Sample-B and Sample-C in different ways. The impedance values of Sample-D are bunched together for 0.0, 0.1, and 1.0 wt.% PAn-PAMPSA, which is similar to Sample-B. This shows the influence of AEMA in Sample-D. However, the bunching of impedance values for the lower wt.% PAn-PAMPSA breaks down slightly at higher frequencies. There is still some grouping of impedance values at higher frequencies, but there is also anomalous behavior similar to Sample-C. This

indicates that the DMAEMA present in Sample-D plays a roll, but possibly only at higher frequencies. This can also be seen in Figure 7, where the impedance behavior of Sample-C hydrogel shifts behavior at higher frequencies.

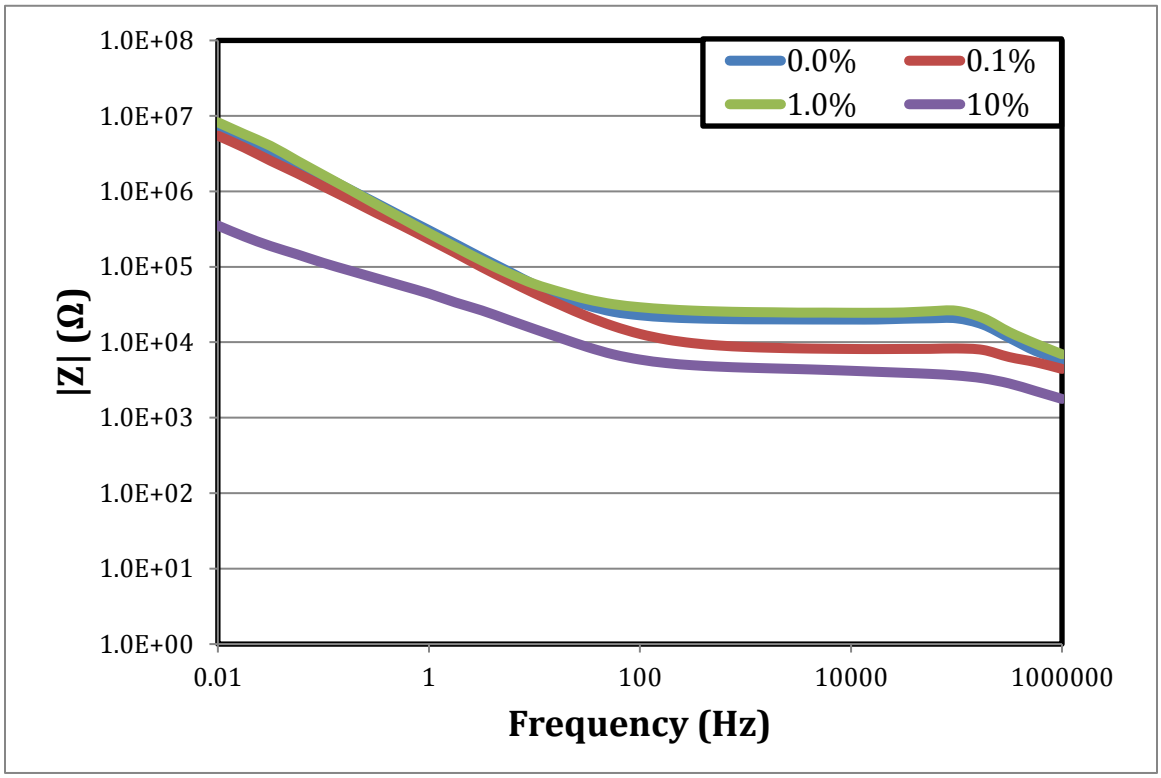

Figure 8. Magnitude of the impedance spectra for 0.0, 0.1, 1.0 and 10 weight percent PAn-PAMPSA in Sample-D-AEMA/DMAEMA hydrogel formulation from 0.01 Hz to 1 MHz using a 50 mV peak-to-peak sine wave.

3.2.2.5. Equivalent Circuit Analysis

Significant trends were seen by applying equivalent circuit analysis to the impedance data collected on each of the hydrogel formulations, modeling them as R(QR) Randle circuits. The graph of Q_{DL} from circuit analysis showed that Q_{DL} values increased with increasing weight percent (Figure 9A). The membrane resistance (R_m) values did not show a general trend, except

for in HEMA hydrogels in which the R_m decreased with increasing PAn-PAMPSA weight percent (Figure 9B.) Finally, the R_{CT} values are all similar until 10 wt. % is reached, at which point the R_{CT} value increases greatly.

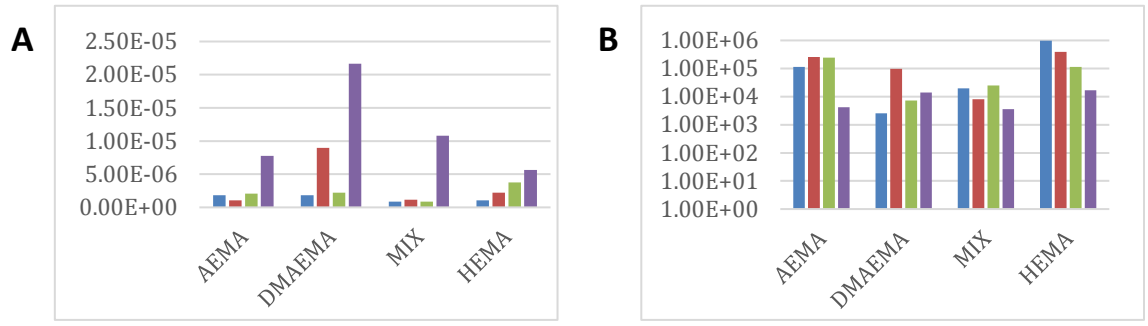

Figure 9. Equivalent circuit analysis: (A) The double layer capacitance (Q_{DL}) values and (B) the membrane resistance (R_M) values of all of the hydrogel formulations.

Equivalent circuit analysis provided insight into resistivity and capacitance for each of the hydrogel formulations. Membrane resistance (R_M) showed a difference in results for hydrophobic (DMAEMA) and hydrophilic (HEMA) formulations. Membrane resistance decreased with increasing PAn-PAMPSA wt. % in HEMA (hydrophilic), and increased with increasing PAn-PAMPSA wt. % in DMAEMA, (hydrophobic). The double layer capacitance (Q_{Dl}) calculated shows an increased capacitance for all formulations as PAn-PAMPSA wt.% is increased. This signifies that increasing the concentration of PAn-PAMPSA increases capacitance.

The charge transfer resistance values obtained from equivalent circuit analysis were on the order of $10^7\,\Omega$ to $10^{15}\,\Omega$, which indicates erroneous equivalent circuit results. However, equivalent circuit analysis is dependent upon the impedance values. Further analysis of the impedance data obtained revealed that the frequency range used in EIS may not have been sufficient to capture the full spectrum of impedance values needed to determine the true charge transfer resistance value. If correct, this explanation makes sense of the unreasonably high

resistance values obtained for R_{ct}, as the modeling program attempted to fit an R_{ct} value without sufficient impedance data to do so. However, further experimental testing would be required to affirm the validity of this hypothesis.

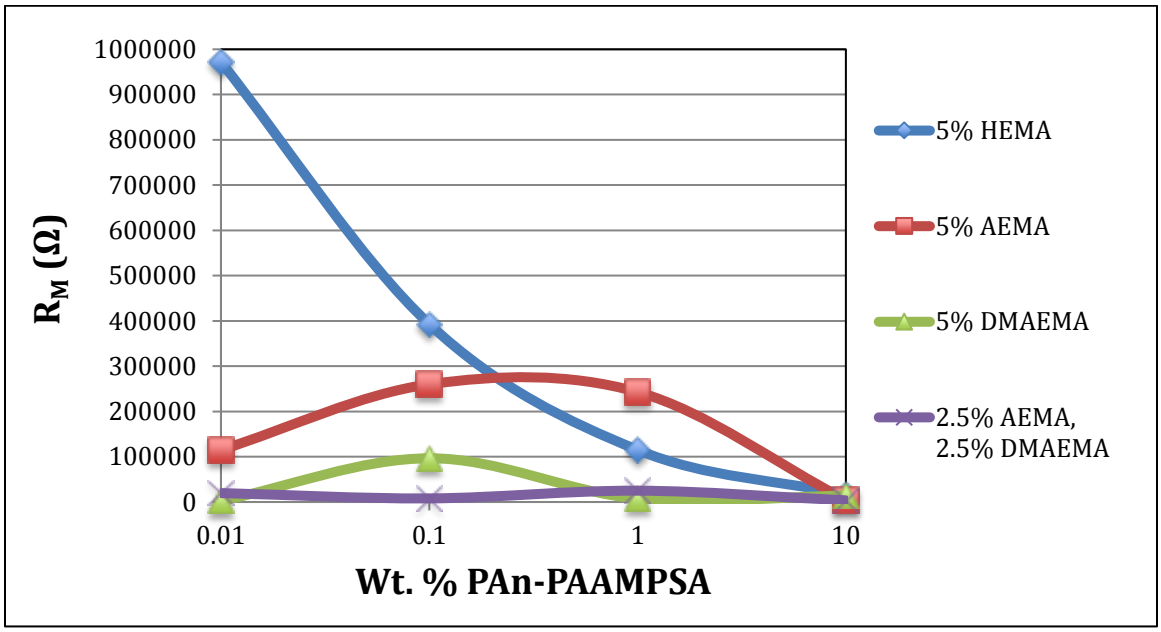

Figure 10. Membrane resistance (R_M) versus weight percent of PAn-PAMPSA for the four hydrogel formulations. A placeholder value (0.01) was used for 0 wt.% PAn-PAMPSA to illustrate the trend.

The change in membrane resistance caused by the monomer differences of the hydrogels is further illustrated by analyzing how R_M changes for each hydrogel formulation as PAn-PAAMPA wt.% is increased (Figure 10). Addition of Pan-PAMPSA results in a sequential decrease in resistance for the reference poly(HEMA) hydrogel. However, the addition of conductive PAn-PAMPSA is not always accompanied by a decrease in resistance, as shown by membrane resistances of 5-mol% AEMA and 5-mol% DMAEMA hydrogels for 0 and 0.1 wt.% PAn-PAMPSA. This illustrates that the conductive hydrogels do not obey a simple rule of mixtures in which adding conductive PAn-PAMPSA to the hydrogel formulation is expected to

result in an equal mix of PAn-PAMPSA and hydrogel properties. Interestingly, the R_M for each hydrogel is distinctly different at lower weight percent PAn-PAMPSA (0.1 and 1 wt. %). However, the R_M for the hydrogels converge at high weight percent PAn-PAMPSA (10 wt.%). This indicates AEMA and DMAEMA imbue unique electrical characteristics to the hydrogels and dictate how the influence of PAn-PAMPSA is manifested at sufficiently low wt.% PAn-PAMPSA. However, the particular characteristics caused by the monomers are overridden when PAn-PAMPSA is present at 10 wt.%. Understanding the synergistic contributions of the ionic conductivity of the hydrogels and the electronic conductivity of the PAn-PAMSA nanofiber inclusions is a forefront area of biomaterials research.

CHAPTER IV

CONCLUSION

The combined data suggests that the uncharged, hydrophilic and small monomeric constituents of poly(HEMA) in Sample-A hydrogel favored hydration and was involved in binding to water, likely via hydrogen bonding. The plasticizing nature of the bound water also imparted flexibility to the hydrogel, decreasing the glass transition temperature. Additionally, as the functional groups of the poly(HEMA) hydrogel were neutrally charged, the systematic addition of PAn-PAMPSA systematically lowered the overall electrical resistance and increased the capacitive nature of the interface. Accordingly, the addition of the conductive component resulted in a simple scaling of the conductivity

At the solution pH values that were used in the current study, AEMA hydrogels (Sample-C) were composed of monomeric constituents with functional groups that were slightly ionized (Hildebrand equation), hydrophilic and small. These functional groups favored hydration and were bound to water, and offered the plasticizing nature to the hydrogel. However, as the functional groups of the AEMA were charged, the hydrogels were inherently more electro-conductive than the poly(HEMA) hydrogels. It was further observed that until a critical limit, the exogenous addition of PAn-PAMPSA did not improve the electrical properties, including the resistive or the capacitive nature of the hydrogels.

The DMAEMA hydrogels (Sample-C) were composed of monomeric constituents with functional groups that were slightly charged, hydrophobic and bulkier than either HEMA or AEMA. Inherently, these functional groups also affected the overall hydration and did not bind with the water molecules. The lack of water within the hydrogel and the bulkier side chains also

affected the segmental mobility of the hydrogel, increasing the glass transition temperature significantly. However, the weak polarization on the tertiary amine significantly reduced the inherent electrical conductivity within the hydrogel compared to Sample-A, but was insufficient in dominating the behavior over PAn-PAMPSA constituents.

The hydrogel formulation composed of equimolar mixtures of AEMA and DMAEMA (Sample-D) was the most interesting. In comparison to the control hydrogels (Sample-A), the Sample-D did not show a significant change in the overall water content (DoH) or in the segmental mobility of the hydrogel (T_g). That is, at these small amounts, 2.5 M% of AEMA and DMAEMA, the polymer behaved much like poly(HEMA). However, both functional groups impacted the interfacial and bulk properties of the hydrogel, albeit differently. The more hydrophobic DMAEMA affected the molecular interaction with water, causing a decrease in the amount of bound water and a significant increase the amount of free water in the hydrogel. The more ionized AEMA (according to its pK_a), on the other hand, dominated the electrical properties of the hydrogel. The dataset for Sample-D therefore suggests that the bulk and interfacial properties of the hydrogel are influenced by the dominant functional groups in the hydrogel and do not necessarily follow the simple rule of mixtures.

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