ABSTRACT

Title: HYBRID POLYMER HYDROGELS WITH REGIONS OF DISTINCT PROPERTIES

Stephen J. Banik II, Master of Science, 2012

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This thesis investigates a new approach to create hybrid polymer hydrogels that comprise multiple gel types juxtaposed in predetermined zones, with the unique properties of each gel being retained. The key is to ensure that the viscosities of pre-gel mixtures are sufficiently high when brought into contact and subsequently polymerized, preventing convective mixing at gel/gel interfaces. The final gel appears as a single, homogeneous material with robust interfaces between the dissimilar zones. By modifying the pre-gel viscosity, we construct hybrid hydrogels by a procedure that is quick, simple, and has fewer limitations than alternate methods. By varying the components of each gel, we have produced a vast array of hybrid hydrogels with regions of distinct chemical, optical, and mechanical properties. This has enabled the creation of strong, highly-extensible soft materials (e.g. a spinal disc mimic), and of gels bearing hidden patterns that can be revealed with a variety of stimuli.

HYBRID POLYMER HYDROGELS WITH REGIONS OF DISTINCT PROPERTIES

by

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Dedication

This thesis is dedicated to my family for its unending love and support through both the good times and the bad.

Acknowledgements

First, I would like to thank my advisor Dr. Srinivasa Raghavan for the incredible opportunity to be a part of his lab. His creativity, enthusiasm, and encouragement kept me working hard in the pursuit of good science.

I was also fortunate to have had the assistance and companionship of my many labmates in Dr. Raghavan's Complex Fluids group. Thank you Hee Young, Hyuntaek, Peter, Vishal, Bani, Yanjun, Charles, Neville, Kevin, Chanda, Anand, Annie, YoungKoan, Renu, Kunqiang, Veena, Kunal, Jasmin, Ian, Matt Dowling, Matt Allsopp, Nick, Reza, Feili, and the many others who I have failed to mention. I would also like to express my gratitude to my undergraduate researchers, Dominic and Michael, for their countless hours working with me in the lab.

I want to thank Dr. Javier Atencia at NIST for his inspiration and guidance extending the world of gels to other exciting areas.

I of course must thank and acknowledge my family. I am grateful to my father for instilling in me a love of nature, science, and history, and for his willingness to drop everything else if one of us needed him to. I thank my mom for the countless hours she worked while still making time to see that my siblings and I never went without; I don't know how she did it. I thank my stepmom for her hard work and patience over the years.

And I thank all of my siblings--Jacob, Amanda, Cassie, and Alexis--my playmates and confidants as both a child and adult. Notably, I thank my brother Jacob for unknowingly paving the way for me in high school. I worked as hard as I did so that I could one day follow in his footsteps.

I also must thank my girlfriend, Grace, for always being there to help me, even when I was too stubborn to admit that I needed it. She is my sweetheart and best friend; I look forward to our future together.

Lastly, but most importantly, I thank the Lord, God. I am so grateful for the many gifts He has blessed me with, and I pray that I can use them in His name to spread comfort and joy to people everywhere.

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Chapter 1: INTRODUCTION AND OVERVIEW

Polymer hydrogels are three-dimensional networks of polymer chains crosslinked by chemical or physical bonds and swollen in water.[1,2] Their wide ranging and tunable properties have propelled them to the forefront of many current technological applications. Typically, these gels are formed by free-radical polymerization of a monomer such as N-isopropylacrylamide (NIPA) in water using a chemical crosslinker such as N,N′-methylenebis-acrylamide (BIS).[3,4] NIPA gels are known for their temperature-dependent response: they shrink when heated above ~ 32 °C.[3] Other monomers or monomer combinations have been used to create a variety of stimuli-responsive gels including those that shrink upon cooling,[1,2] those that shrink in certain aqueous solvent mixtures,[1] or in response to pH[5] or ionic strength.[6] Many potential applications have arisen for stimuli-responsive hydrogels including in drug delivery,[7,8] tissue engineering,[9,10] and as biomaterials.[8] As research on hydrogels has progressed, scientists have been looking to engineer gels with a combination of properties (e.g., gels that are responsive to more than one stimulus, etc.) This challenge has been largely approached from the standpoint of polymer chemistry, i.e., in suitably engineering the molecular structure of the monomer and/or the crosslinker.

An alternative way to engineer new gels is to physically combine multiple gel components into a single material, while still retaining the unique features of each component. This cannot be achieved by simply mixing two different monomer solutions before polymerization--in that case, the monomers would be copolymerized into a single

network that would not retain the properties of each individual gel. Instead, the approach that is usually adopted to combine different gels into the same material is a variation of Chatterji's interpenetrated network[11]--more commonly associated with the work of Gong[12] and Hu.[13,14] In their approaches, the first monomer solution is allowed to completely polymerize and is then soaked in a pre-gel solution of the second monomer and subsequently polymerized. Thereby, the two monomers do not mix, yet the polymer networks interpenetrate. This approach has been used to create high-strength double-networks,[12] patterns of one gel in another,[13] and also to impart shape memory effects to the combined material.[14] However, the method does have its limitations in that it is time consuming (requiring multiple polymerizations) and is best suited to patterning in two dimensions. Furthermore, the components do not remain fully separated; the first gel is partially interwoven with the second gel, thereby producing a gel with a mixed set of properties.

In this thesis, we present a new approach for combining dissimilar gels into one whole material while fully preserving the unique character of each individual gel. The key to our approach is that we bring dissimilar pre-gel mixtures into contact when their viscosities are sufficiently high and thereafter polymerize the hybrid. The high viscosities eliminate convective mixing and slow down diffusive mixing at gel/gel interfaces. Our approach allows the two individual gel components (which can have vastly different characteristics) to be spatially juxtaposed in a desired fashion in the hybrid gel. As seen in Figure 1.1, the final gel visually appears as a single, homogeneous, transparent material. The blowup schematics in the figure illustrate that though the hybrid is a single

medium, each gel has retained its distinct chemical and physical characteristics. Furthermore, the interfaces between the component gels in the hybrid are smooth, i.e., not apparent on visual inspection, and (as shown later), highly robust.

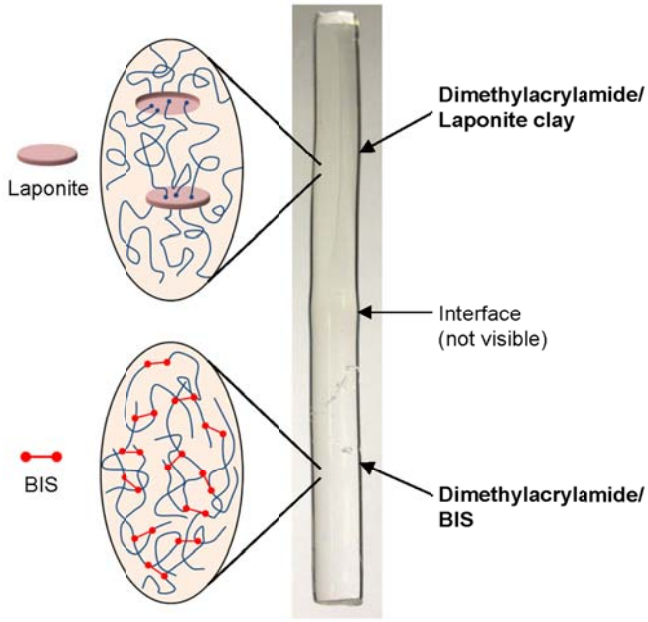

Figure 1.1. A hybrid gel rod (5 mm diam, 7 cm long) made from dimethylacrylamide (DMAA) monomer with a Laponite (LAP) clay particle-crosslinked portion (top half) and a BIS-crosslinked portion (bottom half). Schematics of the two regions of the hybrid are shown on the left. Note that the interface between the regions is smooth and hence not visible.

The utility of our approach is demonstrated in this thesis by multiple examples where we leverage the chemical, mechanical, and optical heterogeneity of our hybrid gels. We have created hybrids that have different monomers, different crosslinkers, and various combinations of the two. Many of our gels incorporate synthetic clays from the Laponite® (LAP) family as physical crosslinkers.[15] The use of Laponite nanoparticles as substitutes for conventional chemical crosslinkers was first demonstrated by Haraguchi et al. about a decade ago.[16,17] The resulting gels have mostly physical rather than covalent

crosslinks,[18,19] and compared to conventional gels, they have much higher mechanical strength and extensibility.[19,20] Recently, Thomas et al. showed that Laponite-crosslinked gels can separate cationic dyes from solution due to the strong chemical affinity of Laponite particles for cationic species.[21] This result is extended to our hybrid gels. We demonstrate that the Laponite-crosslinked regions of our hybrids exhibit a strong affinity for cationic dyes, which is not present in BIS-crosslinked regions. In addition, clay-crosslinked regions are shown to have distinct mechanical properties as well as optical (birefringence) properties. An application of the latter is shown where high-Laponite gel regions are embedded as a hidden pattern or "message" within a matrix of low-Laponite gel. The "message" is revealed either when the hybrid gel is viewed under crossed polarizers or when heated. A similar "message" hybrid gel that was also created with slightly different clay content that reveals its hidden message only when it is subjected to a uniaxial stress.

We have also created some interesting macroscale gels. Our squid-like gel (which combines three gel types of various crosslinkers and monomers) is an example of large-scale assembly of soft matter in a robustly-connected, highly malleable, functional hybrid. We then extend this macroscale assembly to a practical application, using our hybrid technique to form a gel for spinal disc replacements. Finally, we note that our overall approach is simple and versatile; it can be easily extended in a variety of ways to create new gels with unusual and unique properties.

Chapter 2: BACKGROUND

In this chapter, we discuss basic aspects pertaining to the formation of hydrogels via free-radical polymerization and some interesting stimuli-responsive gels. We also review the current-state-of the art in hydrogel networks--an important section as it lays out the foundation upon which our research aims to improve. Also covered are some properties of clay particles and their use as physical crosslinkers in polymer hydrogels.

2.1. HYDROGEL FORMATION VIA FREE-RADICAL POLYMERIZATION

Polymer hydrogels are typically formed by free-radical polymerization of a monomer and a crosslinker in water. Necessary to begin the reaction are an initiator and oftentimes an accelerant. Many are familiar with polyacrylamide gels due to their frequent use in gel electrophoresis[22]. Accordingly, the basic components necessary to form a typical polyacrylamide gel are shown in Figure 2.1.

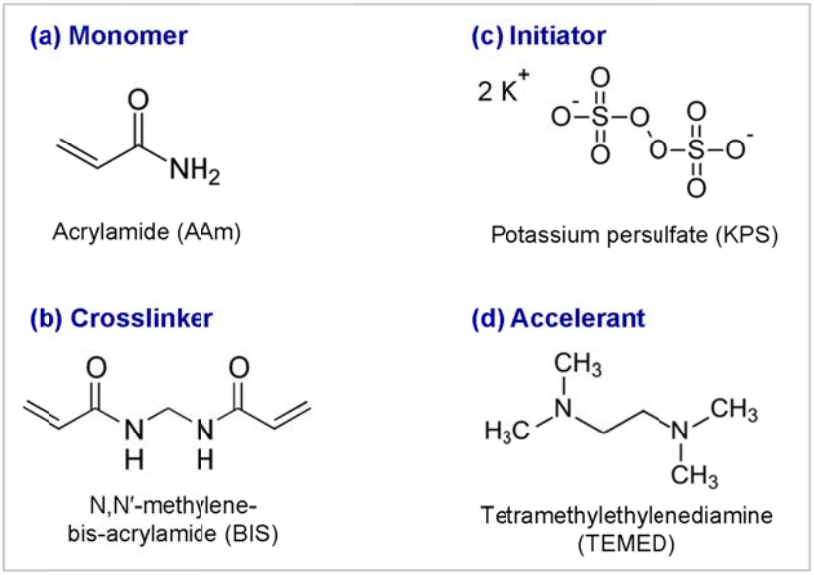

Figure 2.1. Basic components involved in the free-radical polymerization to form polyacrylamide hydrogels at room temperature.

Many different monomers can be used; the main criteria are that they are water soluble and contain a vinyl group (i.e. an available carbon-carbon double bond). The carbon-carbon double bond is the reactive site of the monomer that will be opened up during polymerization to be connected to other monomers and/or crosslinkers. The first step of a free-radical polymerization involves activating the initiator, such that it begins to break down into radicals, as shown in Figure 2.2.

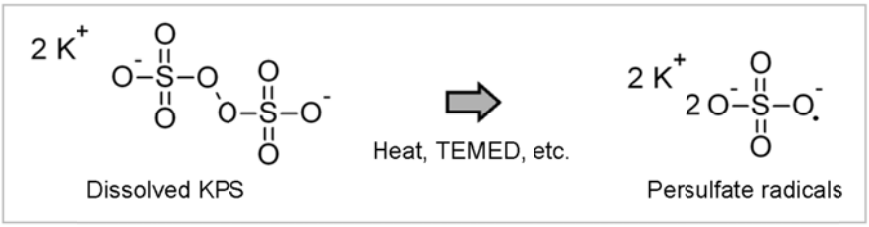

Figure 2.2. Initiation stage of free-radical polymerization. Through heat, TEMED, or other methods, the initiator (KPS) breaks down into highly reactive radicals.

The initiator can be broken down into radicals in a number of ways. Temperature is a very common one--depending on the pH, the half-life of KPS at room temperature is on the order of days, whereas it is on the order of hours at 50 °C.[23] If elevated temperatures are undesirable (as is the case when using a thermoresponsive polymer such as NIPA), a redox-accelerated initiation system is often used. Thus, TEMED and transition metal salts (e.g. ferrous chloride) find common use in promoting the breakdown of KPS into free radicals. The free radicals then begin to convert acrylamide monomers to free radicals that in turn react with other monomers, propagating the chain reaction. As the number of monomer molecules is usually much greater than the number of crosslinkers, the elongating polymer chains grow to substantial lengths until they meet a BIS and are randomly crosslinked, eventually forming a gel network. Figure 2.3 shows

the acrylamide and bis-acrylamide molecules and the gel structure that they form via free-radical polymerization. Notice that the BIS molecule is essentially a monomer with two carbon-carbon double bonds. Thus, it is tetrafunctional and has the ability to crosslink (the minimum requirement being functionality > 2).

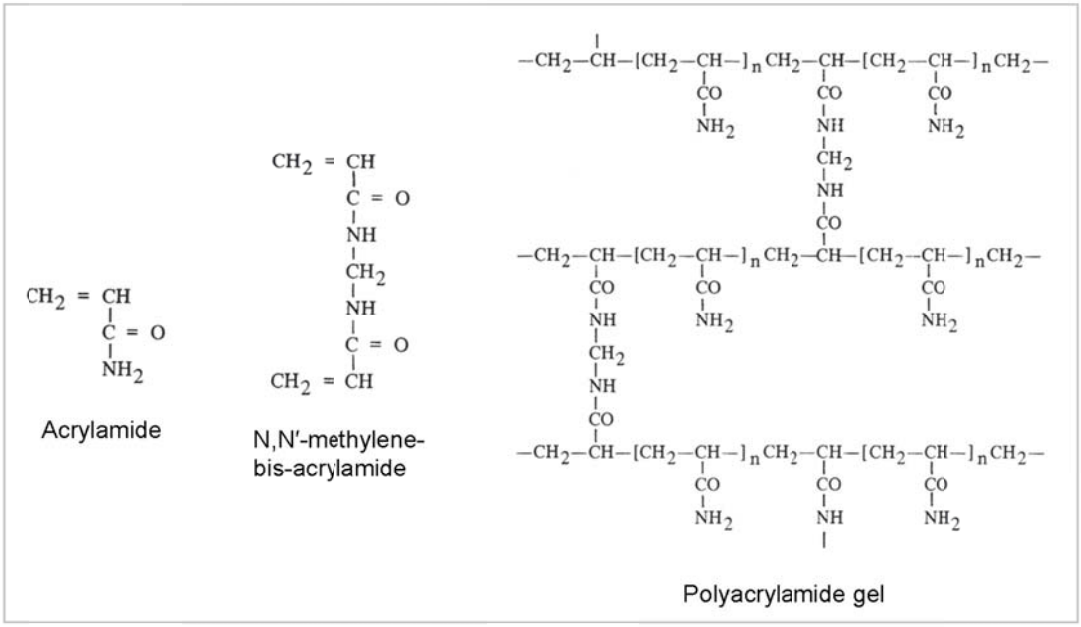

Figure 2.3. Acrylamide and bis-acrylamide react during free-radical polymerization to form a polyacrylamide gel network.[22]

The propagation phase of the polymerization continues until either all of the monomers are consumed or all of the radicals are terminated. It is important to note that the polymerization is very sensitive to the reaction conditions and potential impurities. For example, oxygen is an excellent scavenger for free radicals, preventing proper propagation and chain growth. Thus, in very slow free-radical polymerization reactions, it is crucial to keep the mixture in an oxygen-free environment. If not, a very weak gel or paste-like substance will result.

2.2. STIMULI-RESPONSIVE GELS

There is much interest in polymer gels that undergo a change (in shape, strength, or appearance) in response to an applied stimulus. Gels have been created that shrink upon cooling,[1,2] that shrink in certain solvent mixtures,[1] or in response to pH[5] or ionic strength.[6] Most of these stimuli-responsive characteristics are the result of careful selection of the monomer(s) from which the gel is created. The most ubiquitous thermoresponsive monomer that is employed in polymer hydrogels is N-isopropyl-

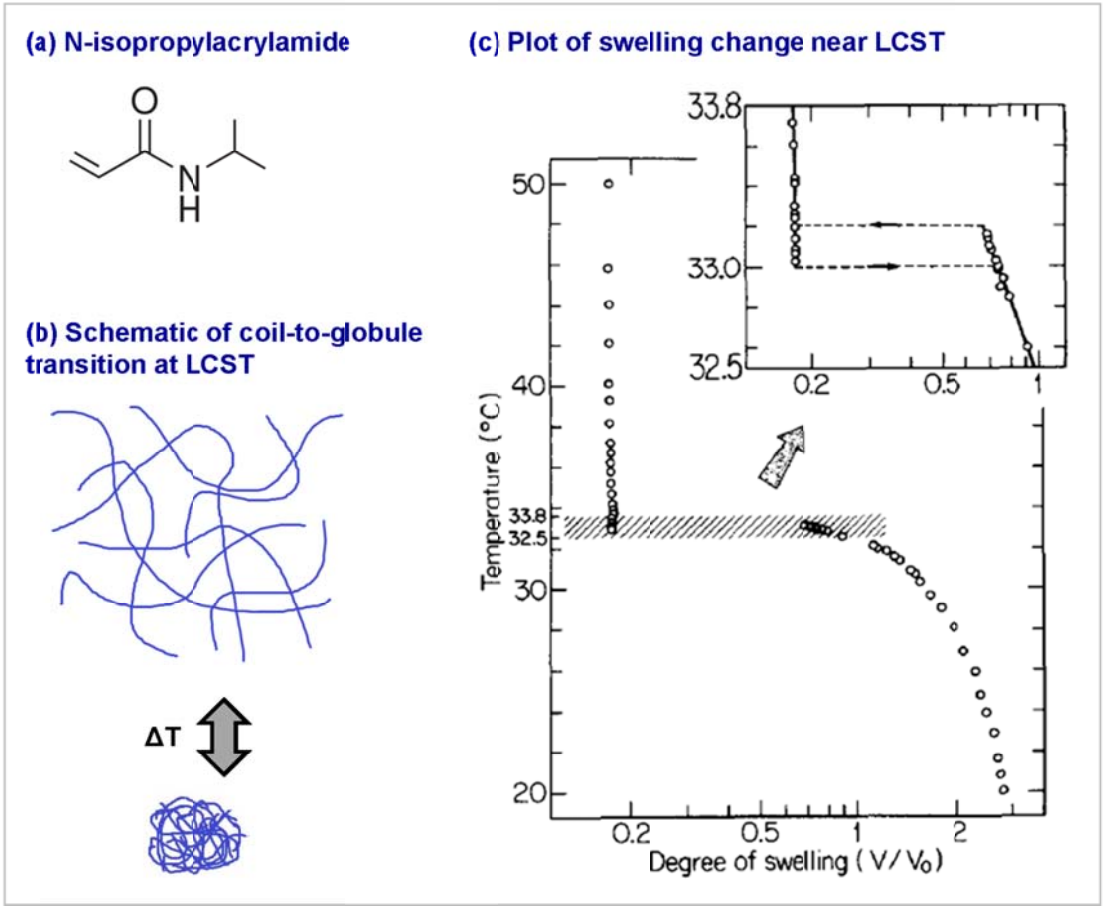

Figure 2.4. (a) Molecular structure of N-isopropylacrylamide. (b) Schematic showing reversible collapse of the polymer chains during coil-to-globule transition at the lower critical solution temperature (LCST). (c) Plot of the degree of swelling of a NIPA gel in pure water as a function of temperature.[3]

acrylamide (NIPA). As shown in Figure 2.4 (a), the structure of NIPA differs from that of acrylamide by the presence of the isopropyl group attached to the nitrogen. The isopropyl group gives the monomer and resulting polymer chain hydrophobic characteristics. While the monomer is still largely hydrophilic, its solubility in water is much less than that of AAm and DMAA.

Below 32 °C, the isopropyl groups are hydrophobically hydrated in water via the formation of a clathrate structure (i.e. hydrophobic hydration cluster).[19] As the poly(NIPA) solution is heated, the clathrate structure becomes less stable and eventually collapses, causing the poly(NIPA) chains to aggregate due to the hydrophobic interactions between the isopropyl groups. The rapid change in solubility at 32 °C is what is referred to as the lower critical solution temperature (LCST) of poly(NIPA). This produces a well-defined coil-to-globule transition, as shown in Figure 2.4 (b), where the poly(NIPA) chains collapse together, expelling water from between them, rapidly shrinking/deswelling. Figure 2.4 (c) illustrates the discontinuity of the transition--how a temperature difference of a few degrees can cause a very large volume-phase transition. Because of the large deswelling at a temperature that is biologically relevant, NIPA has been studied quite thoroughly and has shown promise in areas such as drug delivery.[7]

Another interesting stimulus-response response system is that involving polyacrylamide gels and the combined stimuli of temperature and solvent composition, originally investigated by Tanaka in 1981.[1] Tanaka found that polyacrylamide gels showed similar collapse and volume-phase transition properties as that of the NIPA

system, yet with some key differences. Tanaka first noticed that for a given temperature, a polyacrylamide gel would transition from swollen to collapsed with increasing acetone content in the surrounding solution, as shown in Figure 2.5. Tanaka also found that the acetone values that caused collapse varied with temperature, though in the opposite direction as NIPA. Essentially, the AAm/acetone system would exhibit upper critical solution behavior (UCST). That is, for a given acetone content in the surrounding solution, a polyacrylamide gel transitions from swollen to collapsed as temperature decreases.

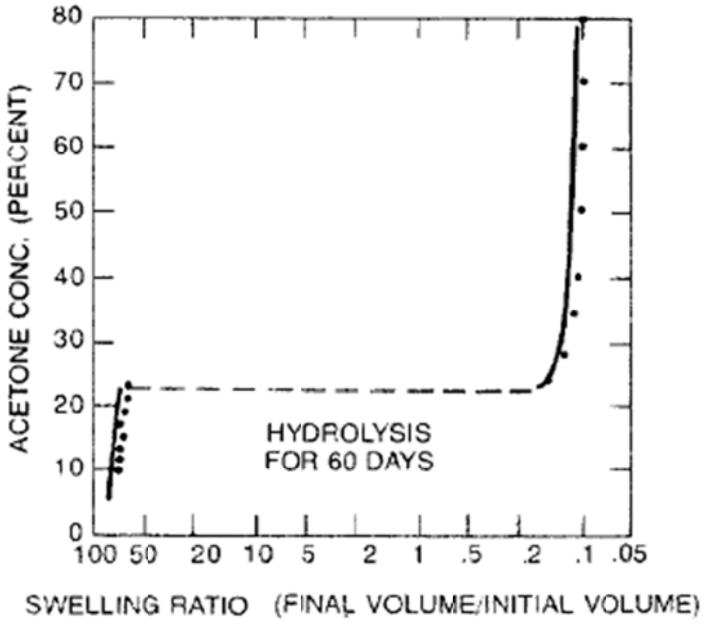

Figure 2.5. Change in degree of swelling of a polyacrylamide gel as a function of acetone concentration in the surrounding solution for a given temperature. (Note that the gel used in the above figure has been soaked in sodium hydroxide for sixty days to hydrolyze a portion of the amide groups, increasing the discontinuity of the collapse.)[1]

Work done by Beltran et al. in the 1990s found that adding a weakly ionizable comonomer to a polymer hydrogel dramatically affected its swelling behavior.[5] The two

monomers they studied, sodium acrylate (SA) and 2-(dimethylamino)ethyl methacrylate (DMEM), are shown in Figure 2.6 (a). Depending on the pH of the surrounding solution, portions of each polymer chain in the gel alternate between a neutral and charged state, affecting inter- and intra-chain interactions. For example, at neutral and higher pH, the carboxylic acid group on SA carries a negative charge. The negative portions of the polymer chain thereby repel each other, expanding the gel network and allowing it to swell. At low pH, however, the carboxylic acid group loses its negative charge, minimizing the repulsive force between polymer chains, forming a tighter, less swollen state. Conversely for DMEM, the polymer chains becomes protonated and positively charged at low pH, where the repulsive interactions cause swelling, yet are uncharged at high pH and the network remains closely packed. These behaviors are illustrated in Figure 2.6 (b) which plots the effect of pH on the swelling capacity of copolymer gels.

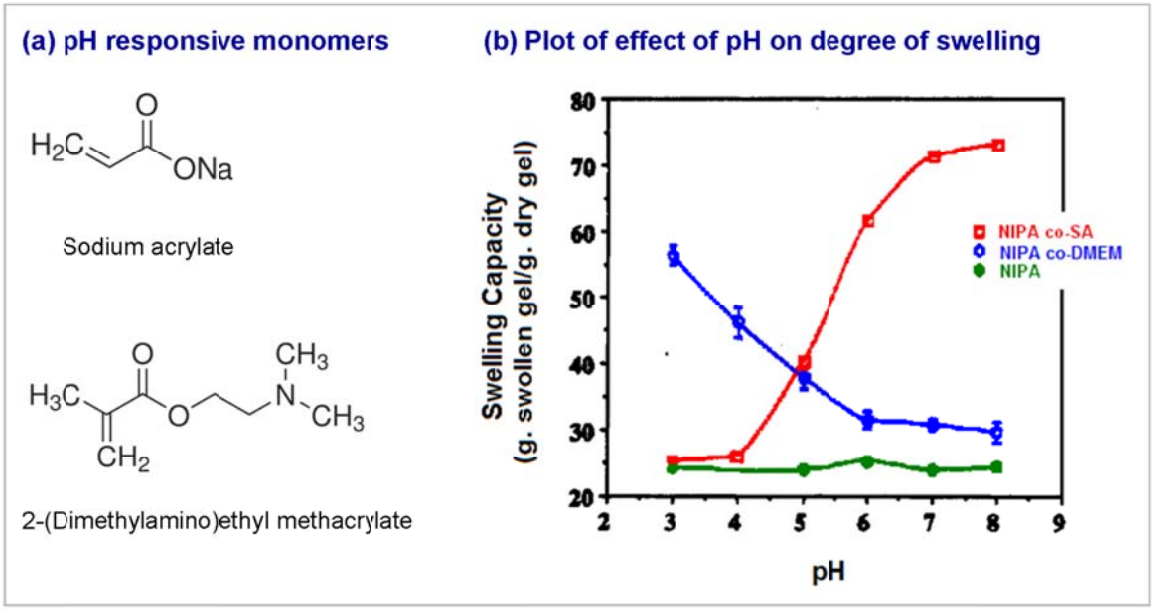

Figure 2.6. (a) Two ionizable, pH responsive monomers. (b) Effect of pH on the swelling capacity of various copolymer gels.[5]

2.3. CURRENT STATE-OF-THE-ART IN GEL-COMBINATION NETWORKS

Gels have been combined in various forms for the last few decades. Chatterji et al. first coined the term "interpenetrated network" (IPN) in 1989 when they combined gelatin and polyacrylamide.[11] Their method was to prepare a pre-gel containing both dissolved gelatin and acrylamide monomer. They then polymerized the acrylamide, entrapping the gelatin network in the acrylamide network (later soaking the gel in glutaraldehyde to permanently crosslink the gelatin network).

A derivation of the IPN was established by Gong et al. when they found that specific combinations of networks in an IPN-fashion result in improved mechanical properties, calling these "double-networks."[12] Their procedure (outlined schematically in Figure 2.7) started by fully preparing and polymerizing gel A. Gel A was then taken and soaked in monomer B for a significant amount of time. After soaking, polymerization/crosslinking of diffused monomer B was initiated, resulting in a gel with network B interpenetrated into network A.

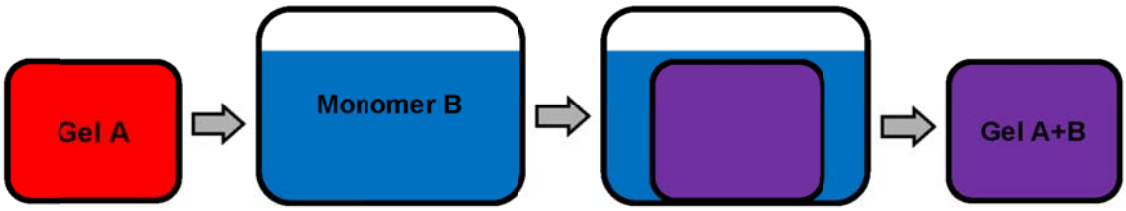

Figure 2.7. Typical procedure for forming double networks (a derivation of an interpenetrated network.) All components of gel A are combined and polymerized to completion. Gel A is then soaked in monomer B. After soaking, polymerization/crosslinking of diffused monomer B is initiated, resulting in a gel with network B interpenetrated into network A.[12]

Hu et al. derived another variation of the interpenetrated network where they were able to create interesting surface patterns and gel combinations.[13,14] Their approach was to fully form gel A and soak it in monomer B, much like Gong et al.[12] Hu et al. would then selectively initiate regions of monomer B using UV irradiation and a photo mask. Their particular choice of monomer B produced a stimuli-responsive polymer network that could then be revealed or modulated on command. Examples of double-network gels by Gong et al. and surface-patterned gels by Hu et al. can be seen in Figure 2.8.

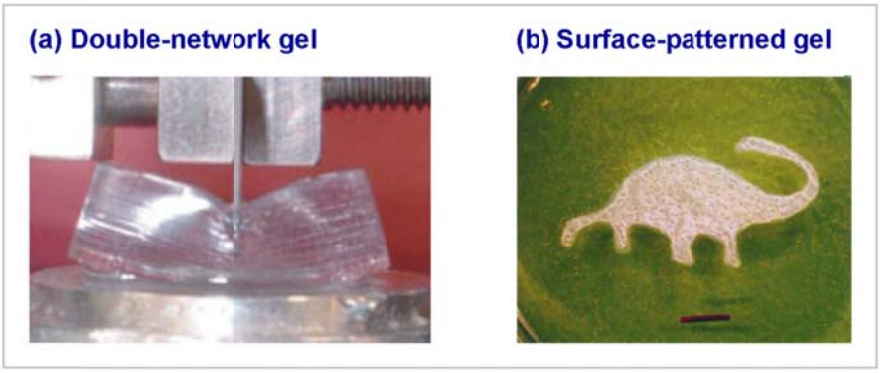

Figure 2.8. Variations of the traditional interpenetrated networks: double-networks[12] and surface-patterned gels.[13]

2.4. CLAY PARTICLES

2.4.1. CLAY PARTICLE STRUCTURE AND INTERACTIONS IN AQUEOUS SOLUTIONS

Clays are hydrous flat sheets of minerals containing combinations of aluminum, magnesium, and silicate, oftentimes with variable amounts of iron, alkali metals, alkaline earth metals, or other cations.[24] Laponite® is a synthetic clay manufactured by Southern Clay Products, produced by combining salts of sodium, magnesium, and lithium along with sodium silicate. Since Laponite is manufactured and not mined, it can be milled to

very fine sizes with tight control over contamination and impurities. Because of this, it has been commonly used to enhance the properties of a wide range of industrial and consumer products, like paints and toothpastes.[25]

Laponite has a layer structure that when dispersed in water takes the form of disc-like crystals. The empirical formula, $Na^{+}_{0.7}$ $[(Si_8\ Mg_5.5\ Li_{0.3})\ O_{20}\ (OH)_4]^{-0.7}$ can be thought of as a unit cell in the crystal, as shown by the blowup in Figure 2.9. The schematic shows six octahedral magnesium ions sandwiched between two layers of four tetrahedral silicon atoms. These groups are balanced by twenty oxygen atoms and four hydroxyl groups. The height of the unit cell is the thickness of the Laponite crystal, about 0.92 nm. The unit cell is repeated many times in two directions, resulting in the disc shaped crystal shown of ~25 nm diameter.[25]

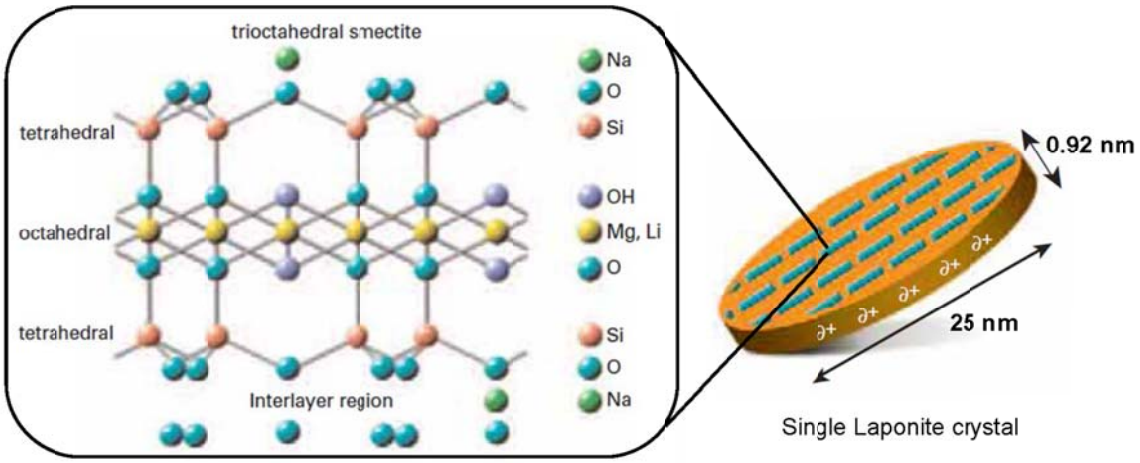

Figure 2.9. Single Laponite clay particle/crystal and its idealized structure.[25]

It should be noted that many natural clays exist as well, e.g. montmorillonite. But because they are naturally occurring, (i.e. they are mined instead of synthesized), their

structures and levels of impurities can vary. Furthermore, the size and complexity of the crystal packing is usually larger for natural clays (as shown in Figure 2.10). For reference, Laponite is generally thought of as a synthetic hectorite, and bentonites are made up mostly of montmorillonite.

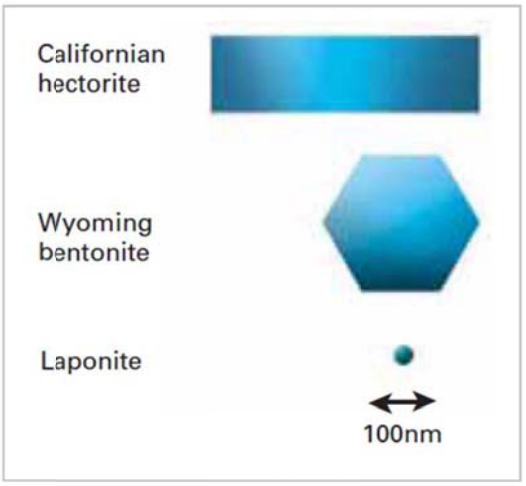

Figure 2.10. Size comparison of clay particles.[25]

As the theoretical formula for a Laponite particle shows, it generally has a negative charge of 0.7 per unit cell that is neutralized as sodium ions adsorb to the surface of the particle during manufacturing. Each Laponite particle face has a strong negative charge (due to the oxygen atoms) and small localized positive charges (generated by absorption of ions where the crystal structure terminates).[25]

In its dry form, the clay particles stack together electrostatically, sharing sodium ions in the interlayer regions between particles. When added to water, the stacks of clay particles begin to disperse, becoming substantially exfoliated (split apart) after about 10 minutes. The clay particles are stabilized in water due to an equilibrium of competing

forces over their sodium ions: electrostatic attractions try to keep the sodium ions near the Laponite surface, yet osmotic pressure from the bulk water tries to pull them away, forming a local "electric double layer" as shown in Figure 2.11 (a).

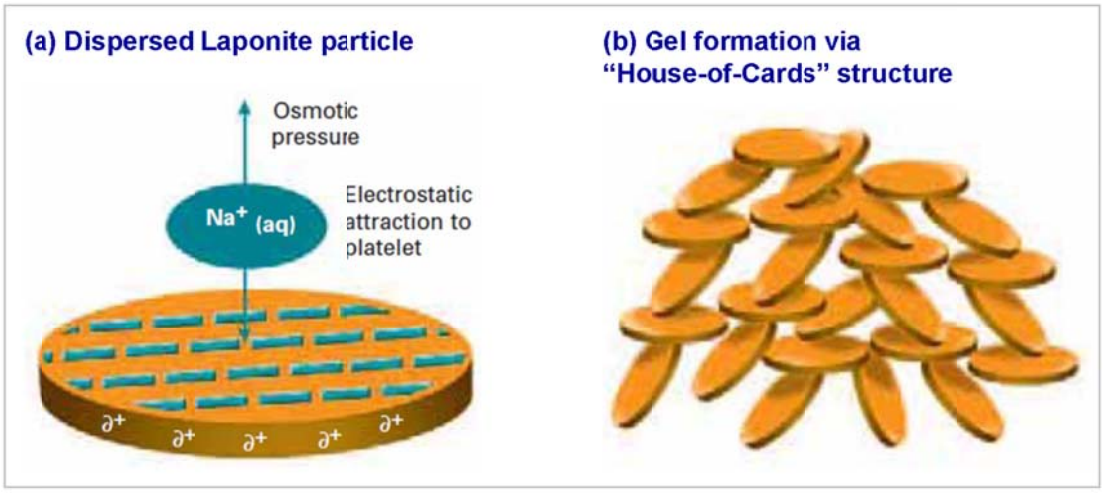

Figure 2.11. (a) A balance of forces keeping each Laponite particle dispersed in water and (b) the "House-of-Cards" gel structure that Laponite can form.[25]

At low Laponite concentrations, the positive charges of the electric double layer of each clay particle keep them apart, giving the solution low viscosity. Higher clay concentrations, simple salts, or other soluble impurities reduce the osmotic pressure holding the sodium ions away from each Laponite particle, shrinking its electric double layer. This then allows the weaker positive charge on the edge of the Laponite discs to interact with the negative surfaces of the faces of neighboring particles, producing the "house-of-cards" structure seen in Figure 2.11 (b), resulting in a thick gel. The gel structure is only loosely maintained, however, and can be easily broken down with the application of shear stress. If the shear stress is again removed, the particles will re-orientate themselves with time, again forming the "house-of-cards" gel structure.[25]

2.4.2. PHYSICAL CROSSLINKERS IN POLYMER HYDROGELS

In 2002, Haraguchi et al. reported a notable finding--that clay particles can act as physical crosslinking points in polymer hydrogels, completely replacing conventional covalent crosslinkers.[17] Furthermore, the clay particles gave hydrogels significant improvements in modulus, strength, and elongation. On a number basis, there are far fewer clay crosslinkers than there are in a conventional BIS-crosslinked hydrogel (several orders of magnitude fewer), and each clay particle acts as a multifunctional crosslinker, connecting more than just one polymer chain (as shown in Figure 2.12).

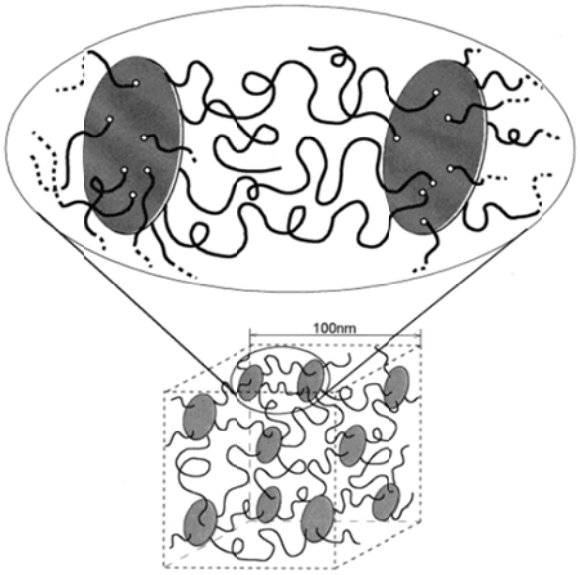

Figure 2.12. Schematic of clay particle-crosslinking in a polymer hydrogel.[17]

This in turn leads to longer and less polydisperse polymer chains between junction points as compared to those in a conventional gel, imparting Laponite-crosslinked gels with higher strength and extensibility (see Figure 2.13).

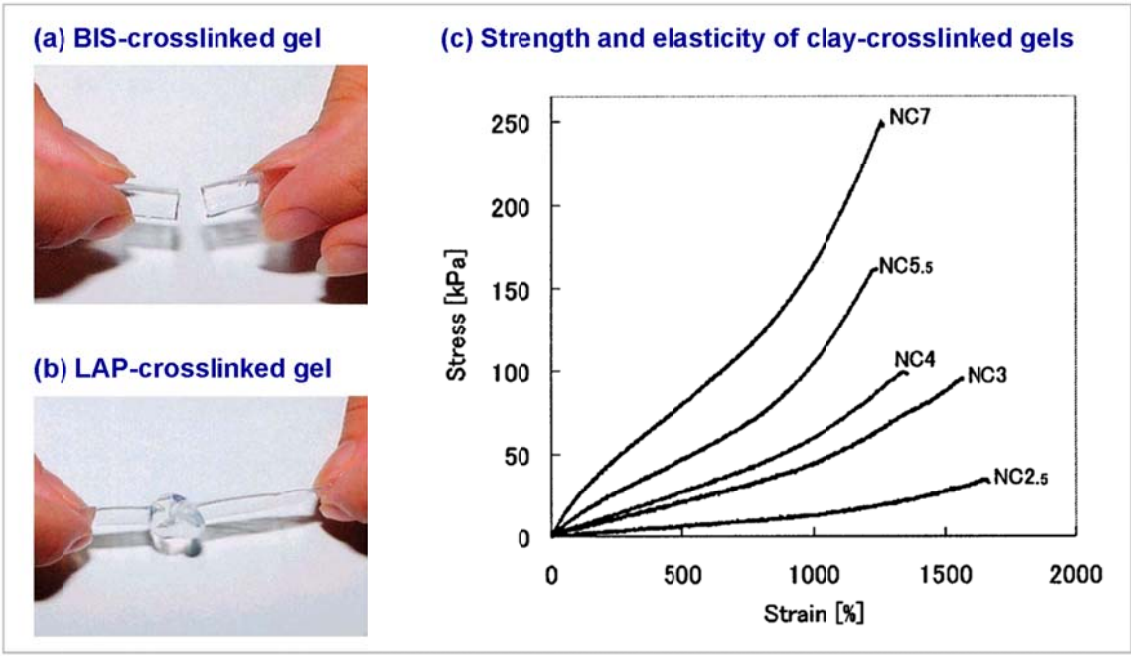

Figure 2.13. (a) Conventional BIS-crosslinked gels are very brittle/fragile. (b)-(c) LAP-crosslinked gels, however, show great strength and elasticity, even sustaining being tied in knots. [17,26]

It is believed that the crosslinking mechanism in clay-based polymer hydrogels is a mixture of physical bonds including hydrogen bonding, ionic bonding, coordinate bonding, and entanglement.[19] One proposed mechanism for the hydrogen bonding between a polyacrylamide chain and clay particle face is shown in Figure 2.14.

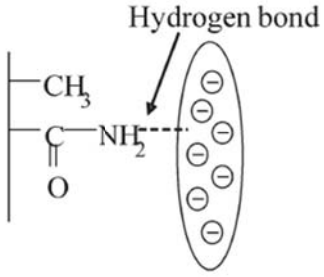

Figure 2.14. Hydrogen bonding mechanism between polyacrylamide and the oxygen atoms on the face of Laponite particles.[27]

Chapter 3: CREATING HYBRID POLYMER HYDROGELS

3.1. INTRODUCTION

In this chapter, we present a new approach for combining distinct gels into a single material while fully preserving the unique character of each individual gel. The key to our approach is that we bring dissimilar pre-gel mixtures into contact when their viscosities are sufficiently high and thereafter polymerize the hybrid. The high viscosities eliminate convective mixing and slow down diffusive mixing at gel/gel interfaces. Our approach allows the two individual gel components to be spatially juxtaposed in a prescribed fashion in the hybrid gel. The final gel visually appears as a single, homogeneous, transparent material. Interfaces between the component gels in the hybrid are smooth, i.e., not apparent on visual inspection; moreover, the interfaces are highly robust and mechanical failure does not occur at these locations.

We start out by describing our hybrid method--highlighting the details necessary for successfully implementation and contrasting it with alternative approaches and the current state-of-the-art. We then demonstrate the utility of our approach through multiple examples where we take advantage of the chemical, mechanical, and optical heterogeneity of our hybrid gels. The hybrid gels described here comprise either two or three different gel types that can have different monomer combinations and/or different crosslinker combinations. Many of our gels utilize synthetic clay Laponite nanoparticles as physical crosslinkers. We show hybrids with regions that have different affinities for cationic dyes as well as distinct mechanical properties. We show hybrids with regions of

distinct optical (birefringence) properties that are embedded as a hidden pattern or "message" within a matrix of another gel. The "message" is revealed either when the hybrid gel is viewed under crossed polarizers or when heated. We have also created a hybrid gel that reveals its hidden message only when it is subjected to a substantial uniaxial stress. Our squid-like gel (which combines three gel types of various crosslinkers and monomers) and spinal disc replacement gel are examples of large-scale, soft matter hybrids that exemplify the robustness and practicality of our hybrid technique.

3.2. EXPERIMENTAL SECTION

Materials. The monomers acrylamide (AAm), N,N-dimethylacrylamide (DMAA), N-isopropylacrylamide (NIPA), and N,N′-methylene-bis(acrylamide) (BIS); the initiator potassium persulfate (KPS); and the accelerant N,N,N′,N′-tetramethylethylenediamine (TEMED) were all purchased from Sigma-Aldrich and used as received. Acrylic acid (AA) was purchased from Sigma-Aldrich and was combined in equimolar amounts with sodium hydroxide (NaOH) to produce sodium acrylate (SA). The inorganic clays Laponite® XLG (LAP), a synthetic hectorite, and Cloisite® Na+ (MONT), a natural montmorillonite, were obtained from Southern Clay Products and used as is. The cationic dyes methylene blue (MB) and rhodamine B (RB) were purchased from Sigma-Aldrich while the anionic dye 5(6)-carboxyfluorescein (CF) was purchased from ACROS and used as is.

Basic Gel Preparation. Two types of crosslinkers were used to produce the polymer networks in the hybrid gels: the tetrafunctional acrylamide derivative BIS for chemical crosslinks, and clay particles for physical crosslinks. Gels were prepared using a 15 g water basis. First, nitrogen gas was bubbled through deionized water (18 MΩ, Millipore-spec) for 3 hours prior to use to remove any dissolved oxygen. Monomer was then dissolved in the water at 1 M concentration, following which crosslinker was added. In the case of BIS, the concentration used was typically 2.2 mol% (with respect to the monomer). In the case of Laponite, the content ranged between 3.3 and 6.4 wt% (with respect to total solution weight) and the particles had to be added slowly to avoid clumping. The solution was stirred for ~10 minutes on a magnetic stirrer plate. The accelerant (12 μL of TEMED) and initiator (0.015 g KPS) were then added. At this point polymerization began and was allowed to proceed at room temperature (or in a controlled temperature water bath) in a nitrogen-only environment for 20 hours.

DMAA/LAP(4.0)--DMAA/LAP(3.3) Test Tube Gel for Hybrid Technique Demonstration. The hybrid gel created for demonstration of our approach consisted of 4.0 wt% LAP/DMAA solution with a small amount of blue MB dye for pre-gel A and 3.3 wt% LAP/DMAA solution with a small amount of pink RB dye for pre-gel B. Pre-gel A was first pipetted into the bottom of a glass test tube. After a few minutes, the viscosity of the mixture was quite high, and pre-gel B was pipetted on top--a single, easy step for combining the two gels. The hybrid was polymerized for 20 hours at room temperature in an oxygen-free environment. Afterwards, the test tube was broken and the gel hybrid was removed and rinsed.

DMAA/LAP(4.0)--DMAA/LAP(3.3) Test Tube Gel for Non-Hybrid Comparison.

The "non-hybrid," i.e. sequential polymerization gel was prepared using the same formulation as that in the hybrid technique above, yet this time in a two-step process. A 4.0 wt% LAP/DMAA pre-gel with a small amount of pink RB dye was created, pipetted into a test tube, and allowed to fully polymerize overnight in an oxygen-free environment. The next day, pre-gel B was prepared, consisting of 3.3 wt% LAP/DMAA, with a small amount of blue MB dye. The pre-gel was then poured over top of gel A and polymerized overnight in an oxygen-free environment. Afterwards, the test tube was broken and the gel network was removed and rinsed.

DMAA/BIS--DMAA/BIS Test Tube Gel for Clay-free Hybrid. Our hybrid gel approach was extended to pre-gels containing no Laponite by utilizing the onset of gel polymerization to produce the viscosity increase necessary to prevent convective mixing of the pre-gels. The components of pre-gel A were first combined--AAm/BIS with a small amount of pink RB dye, and then pipetted into the bottom of a glass test tube. In order to produce an appropriate viscosity increase within about 10 minutes, ~0.05 M TEMED (ten times higher than the usual value) was used to accelerate/initiate the polymerization of pre-gel A (along with the normal amount of KPS). As the viscosity began to increase, pre-gel B, containing no RB dye and ~0.005 M TEMED was added over top. After 20 hours of polymerization at room temperature in an oxygen-free environment, the test tube was broken and the gel hybrid was removed and rinsed.

DMAA/LAP(3.3)--DMAA/BIS Dye Separation Rod. The hybrid gel for dye separation and mechanical tests was a 5 mm diameter rod, approximately 7 cm long. One half of the rod was BIS-crosslinked and the other half was LAP-crosslinked (3.3 wt%)--both portions using DMAA as the monomer. The DMAA/LAP mixture was pipetted into a 5 mm diameter glass vial. After a few minutes, the viscosity of the mixture was sufficiently high, and the DMAA/BIS pre-gel solution was pipetted on top of the DMAA/LAP mixture. After 20 hours of polymerization, the vial was broken and the gel hybrid was removed and rinsed.

DMAA/LAP--DMAA Test Tube Gel for Crosslinker-free Hybrid. The hybrid gel of a clay-crosslinked region and a self-crosslinked DMAA region was produced using our general hybrid approach. Pre-gel A consisted of a 4.0 wt% LAP/DMAA (with a small amount of blue MB dye) and pre-gel B consisted of 50 wt% DMAA in water. Both were initiated using the KPS+TEMED system, which in the case of the high DMAA monomer pre-gel, caused self-crosslinks to occur. After pipetting pre-gel A into a glass test tube, pre-gel B was slowly pipetted on top. Both were left to polymerize for 20 hours in a nitrogen-only environment, broken out of the test tube, and rinsed.

NIPA/LAP(6.4)--NIPA/LAP(3.3) Hidden Message Gel. The hybrid gels in which a pattern is embedded (hidden) were made with NIPA as the monomer and Laponite of different concentrations as the crosslinker. A high-Laponite pre-gel was created with 6.4 wt% Laponite and a low-Laponite pre-gel was made with 3.3 wt% Laponite. In the case of the high-Laponite pre-gel, the particles had to be added to the monomer solution very

slowly along with vigorous mixing by magnetic stirring as well as using a vortex mixer. The resulting viscous mixture was then centrifuged to remove trapped bubbles. The mixture was then transferred to a cake pipetting bag in order to hand-write the pattern/message. After the message was written, the 3.3 wt% pre-gel was poured around until the message was just covered. The hybrid was then placed in an oxygen-free environment and polymerized for 20 hours.

NIPA/LAP(4.9)--NIPA/LAP(3.3) Hidden Message Gel. Another NIPA-based hybrid gel with a hidden pattern was made using Laponite of moderate concentration (4.9 wt%) to write the pattern/message. The corresponding pre-gel mixture was not as viscous as the 6.4 wt% and did not require a cake pipetting bag. Instead a simple disposable pipette was used to write the message. Once again, after the message was written, the low-Laponite (3.3 wt%) pre-gel was poured around it and the hybrid was polymerized as above.

NIPA/LAP(4.0)--DMAA/LAP(4.0)--AAm-SA/BIS-MONT Squid Gel. The squid gel was polymerized in a home-made glass mold, constructed by gluing several pipettes together for the tentacles, then epoxying the pipettes to a glass tube for the head and body. The pre-gel recipe for the tentacles was comprised of 4.0 wt% LAP/NIPA and was pipetted into the squid gel mold, flowing down into the tentacle region of the mold. Next, the pre-gel for the body was added, a 4.0 wt% LAP/DMAA solution. Finally, the pre-gel for the head was pipetted on top of the body, containing SA and AAm (in a 1:9 ratio) as comonomers and BIS (2.2 mol%) and Cloisite Na+ natural montmorillonite clay (1 wt%)

as co-crosslinkers. The hybrid was then left to polymerize for 20 hours in an oxygen-free environment before being extracted from the mold and rinsed.

DMAA/LAP(5.2)--DMAA/LAP(3.3) Spinal Disc Replacement Gel. The spinal disc replacement hybrid was created by combining the various pre-gels in a prescribed fashion in the bottom of a glass beaker. The pre-gel for the outer region consisted of 5.2 wt% LAP/NIPA. Since the pre-gel became quite viscous almost immediately after adding the KPS and TEMED, two-thirds of the mixture was scooped and then molded into the bottom of a beaker. The pre-gel for the inner core (3.3 wt% LAP/NIPA with a small amount of blue MB dye) was then gently poured into the "crater" left by the first pre-gel. After waiting a few minutes for the viscosity of the inner core pre-gel to increase, the remainder of the outer region pre-gel was then pipetted across the top in thin strips, continuing to add strips until a thick layer completely covered the core. The gel was then polymerized at room temperature for 20 hours in an oxygen-free environment before being taken out of the beaker and rinsed.

Rheology/Viscosity Measurements. Rheological and viscosity measurements were performed on an AR2000 (TA Instruments) stress-controlled rheometer. Dynamic rheology was conducted for gel samples (e.g. the spinal disc gels) using a 20 mm diameter parallel plate geometry with a solvent trap to minimize water loss. Dynamic frequency runs were conducted in the linear viscoelastic regime of the samples, as determined from dynamic stress sweep measurements. Viscosity measurements were

taken using the same rheometer with a couette (bob and cup) geometry for increased sensitivity/accuracy at low shear stresses, maintained at 20 °C.

3.3. RESULTS AND DISCUSSION

3.3.1. HYBRID METHOD

Our hybrid approach consists of combining gels when they are in the pre-gel state in order to allow them to polymerize together. The central idea arose out of the fact that adding a few weight percent of Laponite particles to a monomer solution (pre-gel) makes the mixture quite viscous. This is not surprising because Laponite is well-known for its ability to thicken and gel water by physical interactions of the particles[15] (as discussed in section 2.4.1). The viscous nature implies that when two Laponite-containing pre-gels are brought into contact, they will not mix at their interface. Shown in Figure 3.1 is the typical procedure for preparing a hybrid gel. In panels 1 and 2, viscous pre-gel A (4 wt% LAP, DMAA, and a small amount of methylene blue (MB) dye) was pipetted into a test tube. In panel 3, viscous pre-gel B (3.3 wt% LAP, DMAA, and a small amount of pink rhodamine B (RB) dye) was gently pipetted over top. It can be seen that since both mixtures were sufficiently viscous (consistency of honey) at the time of contact, the two zones of the hybrid did not undergo any convective mixing. There was still some weak diffusive mixing, however, (as seen by the purple region at the interface), which ensured that the zones of the hybrid were strongly melded. Panels 5, 6, and 7 reveal a single hybrid gel with two distinct regions that can be stretched to great extents without tearing apart at their interface.

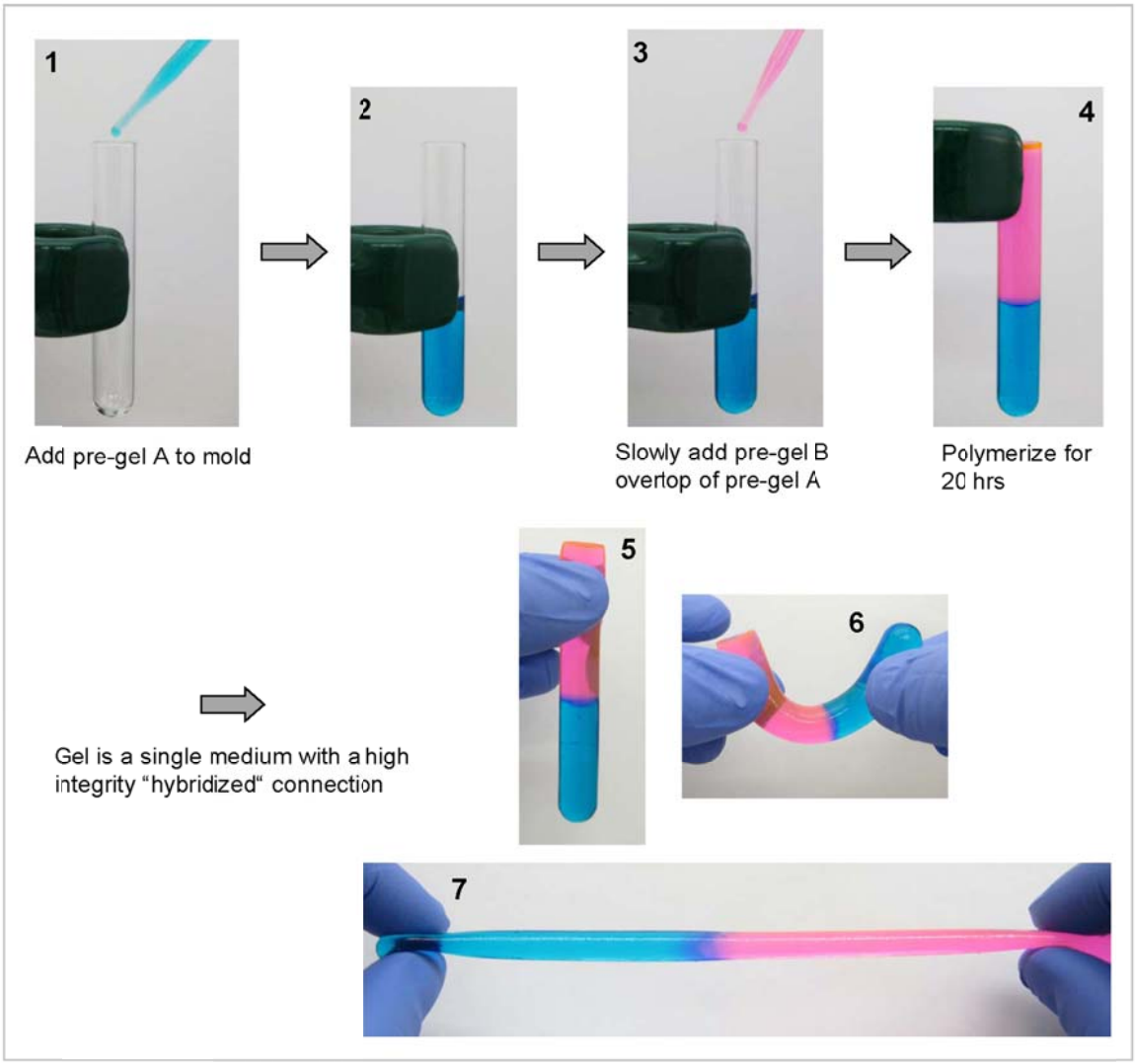

Figure 3.1. Standard procedure for preparing a hybrid gel. In panels 1 and 2, viscous pre-gel A (4 wt% LAP, DMAA, and a small amount of blue MB dye) is pipetted into a test tube. In panel 3, viscous pre-gel B (3.3 wt% LAP, DMAA, and a small amount of pink RB dye) is gently pipetted over top. While convective mixing is minimized, weak diffusive mixing ensures that the zones of the hybrid are strongly melded. Panels 5, 6, and 7 show a single gel that can be stretched to great extents without tearing apart at its interface.

This concept can be extended to pre-gels containing no Laponite by noting that the onset of gel polymerization causes the viscosity of the pre-gel to increase substantially. Such a hybrid is shown in Figure 3.2 and was prepared in a test tube

similarly to that of the previous figure. The AAm/BIS and RB dye pre-gel was added first and contained ~0.05 M TEMED (ten times higher than the usual amount) in order to produce an appropriate viscosity increase within about 10 minutes. As soon as the viscosity began to increase, the second pre-gel containing no RB dye and ~0.005 M TEMED was added over top. The hybrid was then left to polymerize overnight. As Figure 3.2 (b) shows, the hybrid method can be extended to pre-gels with no clay particles while still forming a high-integrity hybrid.

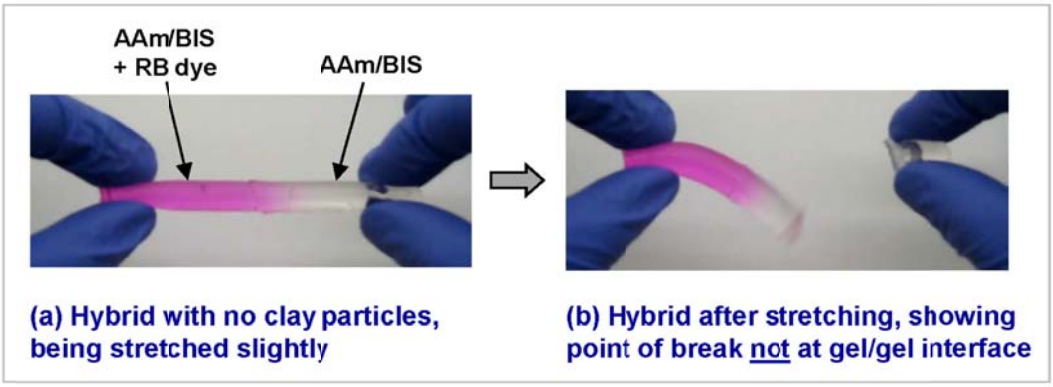

Figure 3.2. Hybrid method in which neither pre-gel contains Laponite clay particles. A few minutes after adding the first pre-gel to the gel mold, the onset of gel polymerization caused the viscosity of the pre-gel to increase substantially, preventing any convective mixing with the second pre-gel, which was added over top. As shown, the hybrid method can be extended to pre-gels with no clay particles while still forming a high-integrity hybrid.

Note that if instead of utilizing the hybrid technique, one of the two pre-gels were largely polymerized (i.e., converted to gel) at the time of contact, there would obviously be no convective mixing at the interface, and furthermore there would be negligible diffusive mixing at the interface. Thus, one would expect the interface would be very weak in this case. An example of such a "non-hybrid" gel--one that is polymerized

sequentially--can be seen in Figure 3.3. Panel 1 of the figure begins with gel A (4 wt% LAP, DMAA, and a small amount of pink RB dye) having already been polymerized. In panel 2, pre-gel B (3.3 wt% LAP, DMAA, and a small amount of blue MB dye) were poured over top of gel A and polymerized overnight. After polymerization and removal from the mold, panel 3 (which is actually a single frame taken from a video of the non-hybrid network being stretched) shows the gels as they are about to tear apart. It can be

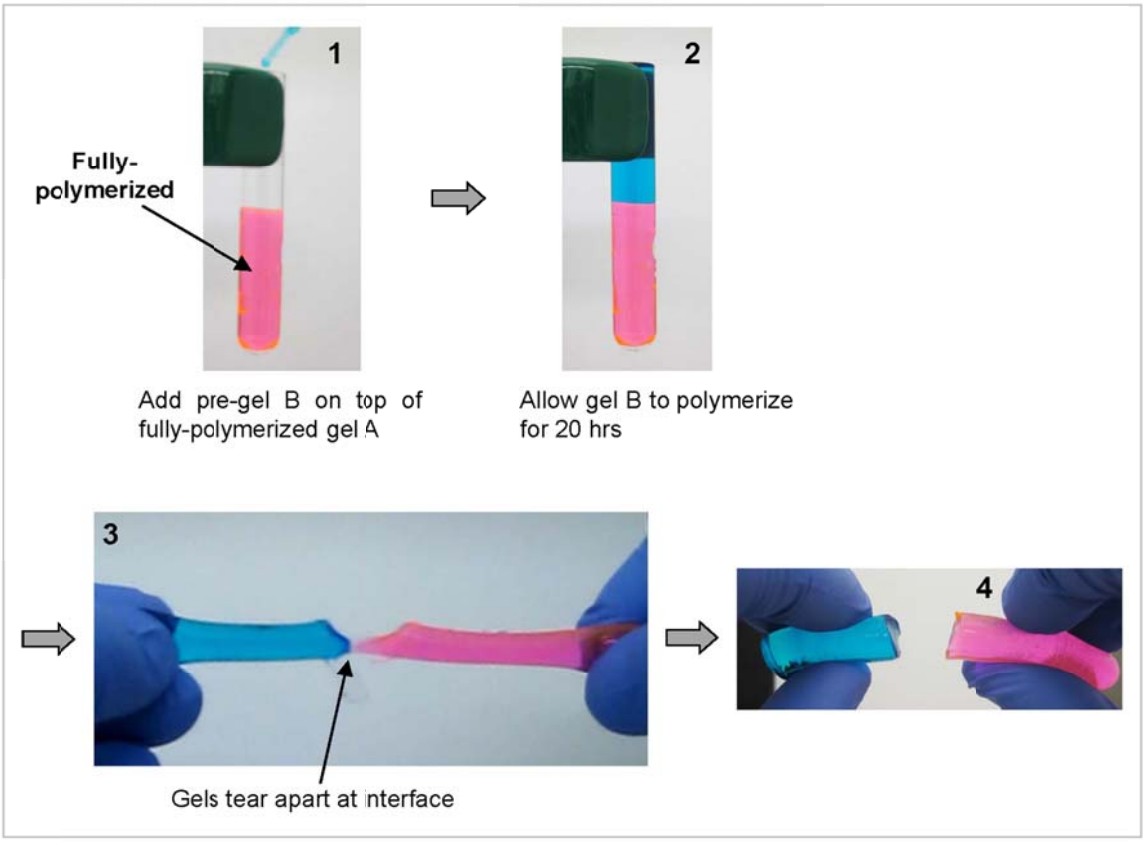

Figure 3.3. Non-hybrid approach, i.e. sequential polymerization. Panel 1 of the figure begins with polymerized gel A (4 wt% LAP, DMAA, and a small amount of pink RB dye). In panel 2, pre-gel B (3.3 wt% LAP, DMAA, and a small amount of blue MB dye) is poured over top of gel A and left to polymerize overnight. After polymerization and removal from the mold, panel 3 and 4 show that the two gels tear apart at their interface when stretched.

seen that the tearing appears to be at the interface of the two gels, and panel 4 indeed confirms this.

It is clear that the two networks are only weakly connected when prepared using consecutive polymerizations (i.e. the non-hybrid method), with a second pre-gel that had a moderate viscosity and/or was initiated immediately. The poorly connected interface of the non-hybrid gel from Figure 3.3 really highlights the significance of our hybrid method while also illustrating its improvement over traditional interpenetrated networks (see section 2.3). Two main limitations of interpenetrated networks are the fact that they are time consuming to make and have restrictions on the size and components of the gel networks that can be used. Thorough diffusion of one monomer into a fully-polymerized gel can require hours, depending on the size and shape of the gel to diffuse into. Thus, polymerization cannot be initiated at the time in which the gel and the second monomer are brought into contact. In this case, polymerization will begin to increase the viscosity of the second pre-gel, slowing down/ inhibiting further diffusion. Because of this, IPNs usually use low viscosity pre-gels for the second monomer and are initiated either thermally or with UV light, after sufficient time has been allowed for thorough diffusion. Yet this poses another limitation--thermal initiation is incompatible with a thermoresponsive polymer (as it will cause phase separation during the polymerization) and UV initiation is generally restricted to 2D patterns or thin 3D films (because of the limited penetration depth of the UV light). Therefore, our hybrid approach seems to stand out; in a single polymerization we can combine many different pre-gel solutions on a large scale and be confident that they will form a high-integrity connection with each other.

To reiterate one of the key points made earlier--in order to bring the two pre-gels into contact, at least one of the gels must have a "sufficiently high viscosity." Without such, convective mixing occurs (as shown in Figure 3.4), ultimately resulting in a single gel of a mixture of gels A and B.

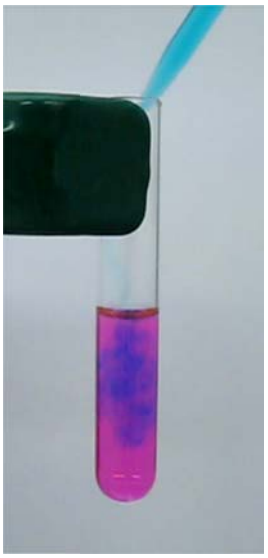

Figure 3.4. Convective mixing occurs if at least one of the pre-gels does not have a sufficiently high viscosity.

It then becomes necessary to identify what is "sufficiently high." It is difficult to offer a single viscosity value, as the goal is simply to prevent mixing and thus depends upon several factors (including how carefully one can layer the pre-gels, the complexity of the gel mold, and number of gels to be layered). We have, however, identified an order of magnitude estimate, as explained below.

Covered in section 2.4.1 was the mechanism by which clay particles form a "house-of-cards" gel-like structure under the appropriate conditions in water. Specifically, high clay concentrations, heat, and ions/salts accelerate the increase in

viscosity and "house-of-cards" formation. It was qualitatively observed from experimentation that for a 4 wt% LAP pre-gel, the viscosity became high enough to layer another gel on top of it after approximately 3-4 minutes. It was also noted that the viscosity at this point seemed to be somewhere between syrup and honey. To try to quantify this value, an AR2000 stress-controlled rheometer with a couette (bob and cup) geometry was used to apply a very small steady shear stress (0.2 Pa) and track the viscosity change with time. All of the pre-gel components were combined before time = 0, with the exception of the initiator and accelerant. (Note that at the level of clay used, it takes on the order of hours for substantial formation of the "house-of-cards" structure in pure water.) As soon as the initiator and accelerant are added (which act as salts/ions), the "house-of-cards" structure formation is greatly accelerated and the mixture starts to thicken, even before the onset of polymerization. As Figure 3.5 shows, the viscosity of the pre-gel increases very sharply over the first few minutes, keeping in mind that the y-axis is log-scale. (One may notice that after the data point at t = 0, there are a lack of data in the plot between time = 0 and ~75 s. This was the time it took for the bob geometry to descend into the pre-gel before it started acquiring data.) In addition to the pre-gel data, viscosity values were measured for Giant® brand Clover Honey and Original syrup in order to try to establish common reference points with what was noticed during the hybrid gel preparation. The zero-shear viscosity for the honey was ~27 Pa·s, and the syrup was ~2 Pa·s. It can be seen from the graph that the viscosity of the pre-gel reaches, then exceeds that of syrup shortly before 4 minutes, while it reaches that of honey at approximately 5 minutes. This roughly agrees with our experimental observations that the

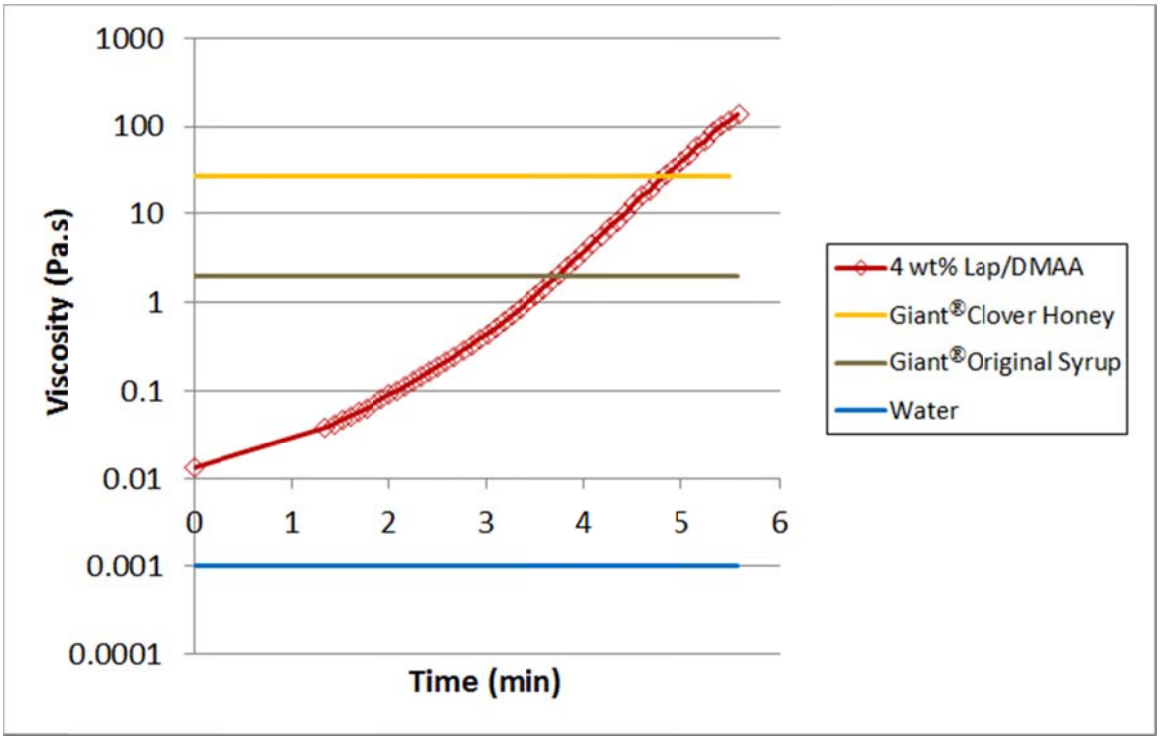

Figure 3.5. Viscosity of a 4 wt% LAP/DMAA pre-gel solution along with the viscosity of several other liquids for comparison (Data obtained at 20 °C using an AR2000 stress-controlled rheometer with a couette (bob and cup) geometry, applying 0.2 Pa steady shear stress and tracking with time.)

pre-gel viscosity was somewhere between syrup and honey by 3-4 minutes. Thus, we find it safe to say that two pre-gels can be combined when at least one of them reaches a viscosity on the order of 10 Pa·s.

It is worth mentioning why a more exact value for the viscosity cannot be obtained. As discussed in background section 2.4.1, the "house-of-cards" structure that clay particles form in water can be easily disrupted when shear stress is applied. Thus, simply using the rheometer to take measurements of the viscosity actually decreases the viscosity. Hence why a very small shear stress value, 0.2 Pa, was used for the time sweep. Stress values around this range produced similar data whereas values of 2 Pa and

greater started showing noticeably lower values. But even though the viscosity value is an approximation at best, it nonetheless provides useful insight for hybrid preparation--that pre-gel viscosities must be at least several orders of magnitude greater than water (0.001 Pa·s) in order to prevent convective mixing during layering.

3.3.2. HYBRIDS WITH DIFFERENT CROSSLINKING METHODS

3.3.2.1 CLAY GEL HYBRIDIZED TO BIS-ACRYLAMIDE GEL

Having developed a method for preparing high-integrity hybrids, we can now begin to create hybrids that combine gels of distinct properties with specific features and applications in mind. Figure 3.6 shows the DMAA/LAP--DMAA/BIS hybrid gel that was briefly mentioned in the introduction--a rod of diameter 5 mm and length 7 cm. The top half of the hybrid, termed DMAA/LAP, was crosslinked using Laponite nanoparticles, as shown schematically in the upper portion of Figure 3.6. As indicated in the schematic, the polymer chains are expected to extend from one face of the Laponite discs and terminate at another.[18,19] The bottom half of the hybrid, termed DMAA/BIS, was crosslinked using the conventional BIS crosslinker, shown as red dumbbells in the lower schematic. The polymer chains are covalently crosslinked by BIS molecules within this region. Note that the interface between the two regions of the hybrid gel is not discernible in the photograph. Thus, the overall gel looks to be a single, homogeneous mass.

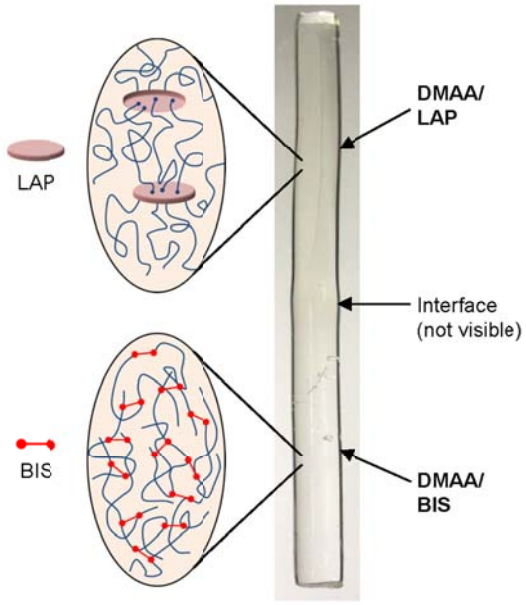

Figure 3.6. A hybrid gel rod (5 mm diam, 7 cm long) made from DMAA monomer with a LAP-crosslinked portion (top half) and a BIS-crosslinked portion (bottom half). Schematics of the two regions of the hybrid are shown on the left. Note that the interface between the regions is smooth and hence not visible.

We now contrast the properties of the two zones of the hybrid gel. First, we focus on the differences in ionic dye absorption from solution. For this, the cationic dye, MB and the anionic dye, CF were combined (Figure 3.7, panel 1), producing a dark blue/green solution (panel 2), with the final concentration of each dye in this solution being 50 μM. The hybrid gel (~ 2 g in mass) was placed in this solution (panel 3). After approximately 5 hours with no stirring, we note that the cationic MB dye is preferentially absorbed by the DMAA/LAP portion of the hybrid, due to which that portion assumes a blue color (panel 5). In contrast, the DMAA/BIS portion is seen to have absorbed some of both dyes and consequently has a light green color (panel 5). These differences are due to the anionic faces of Laponite discs having a strong affinity for cationic solutes.[15,21] As a result, Laponite-bearing gels can effectively separate a cationic dye from a mixture of

cationic and anionic dyes.[21,27] Indeed, the DMAA/LAP zone of the hybrid gel in the present case is able to extract much of the MB from the solution--thus, the final solution has a lower MB concentration (and a greener color, panel 4) compared to the original solution. Overall, Figure 3.7 shows that the zones of the hybrid have different chemical properties due to the crosslinkers chosen for the zones.

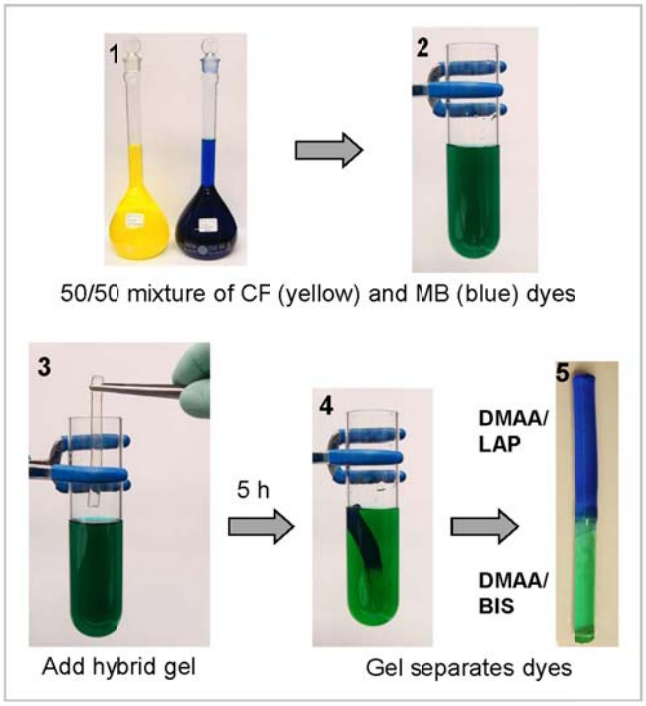

Figure 3.7. Chemical differences between zones of the hybrid gel. A mixture of the cationic dye, methylene blue (MB) and the anionic dye, carboxyfluorescein (CF) is made (panels 1, 2) and the gel is immersed in it (panel 3). Due to the affinity of Laponite particles for cationic solutes, the DMAA/LAP portion of the gel (top half) selectively absorbs the MB and separates it from solution (panels 4, 5). Some of the CF is absorbed by the DMAA/BIS portion (bottom half) of the gel.

Next, we contrast the mechanical properties of the two zones of the hybrid gel. A typical mechanical test is illustrated in Figure 3.8 on the dye-soaked gel from Figure 3.7. The different colors of the two regions help in visualization. In the experiment, the hybrid gel was slowly stretched by hand until it broke. The key result is shown in Figure 3.8 (b),

where we see that the DMAA/BIS portion (green) does not elongate much on stretching, i.e., it is not very elastic or flexible. In comparison, the DMAA/LAP portion (blue) can be stretched to several times its original length. Ultimately, when the hybrid as a whole breaks in Figure 3.8 (c), it consistently does so in the middle of the DMAA/BIS region (this was seen in every experimental run). Note that the break does not occur at the

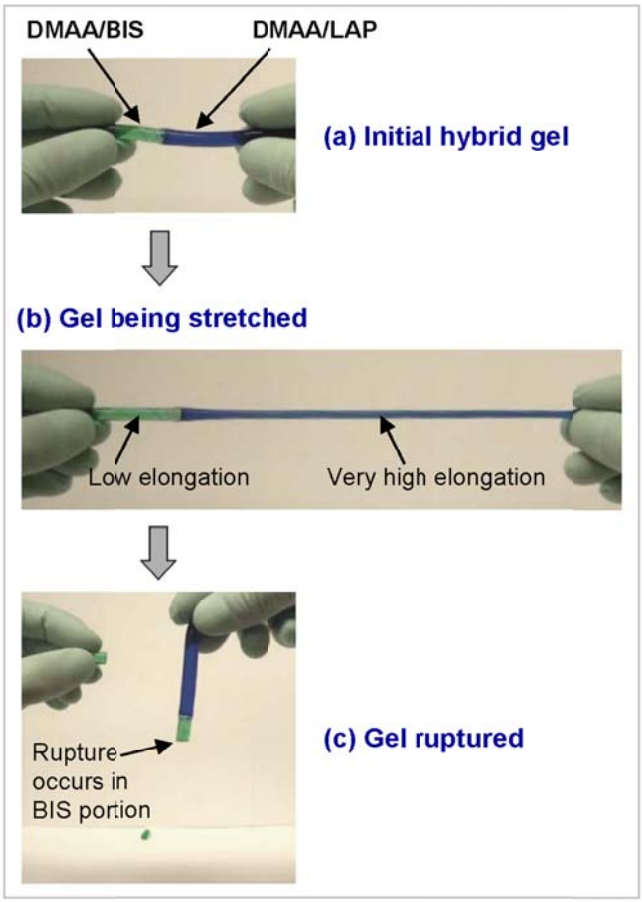

Figure 3.8. Mechanical differences between zones of the hybrid gel. (a) A hybrid gel with DMAA/BIS and DMAA/LAP regions is shown in its initial, unstretched state. The absorbed dyes from Figure 2 help to distinguish the two regions. (b) When stretched, the BIS region elongates slightly whereas the LAP region gets highly elongated. (c) With continued stretching, the gel eventually ruptures. The break point always occurs in the DMAA/BIS portion, showing that the gel strength is much higher for DMAA/LAP than for the DMAA/BIS. Also, the rupture does not occur at the interface between the LAP and BIS regions, which indicates that the gel/gel interface is highly robust.

interface between the two gel regions, which is usually assumed to be the weakest point in a composite or layered network. This indicates the high integrity and robustness of the gel/gel interface in our hybrid.

Overall, Figure 3.8 shows that the DMAA/LAP zone of our hybrid has very different mechanical properties (a much higher strength and extensibility) compared to the DMAA/BIS zone. The higher strength and extensibility of Laponite-crosslinked gels are well-known and are attributed to the fact that the polymer chains between junction points in these gels are longer and less polydisperse than those in a conventional gel (as discussed in section 2.4.2.[19,20] Incidentally, we performed the stretching by hand to ensure a gentle grip on the gel. When stretching was attempted with a clamp or vise, the hybrid would prematurely tear at the gripping point of the DMAA/BIS portion, which further shows its lower strength. Also, we should clarify that the same results were obtained on dye-free gels and so the dye has no influence on the mechanical tests.

3.3.2.2 CLAY GEL HYBRIDIZED TO NO-CROSSLINKER GEL

While Haraguchi's finding that clay particles can be used as substitutes for conventional crosslinkers was quite notable, a similarly interesting discovery was made long before by Needles et al. in 1965[28]. They found that growing chains of poly(DMAA) would crosslink with other poly(DMAA) chains in the absence of any external crosslinker as long as the free-radical polymerization had been initiated using a disulfate system (e.g. potassium persulfate, ammonium persulfate). The mechanism described by Needles is shown in Figure 3.9.

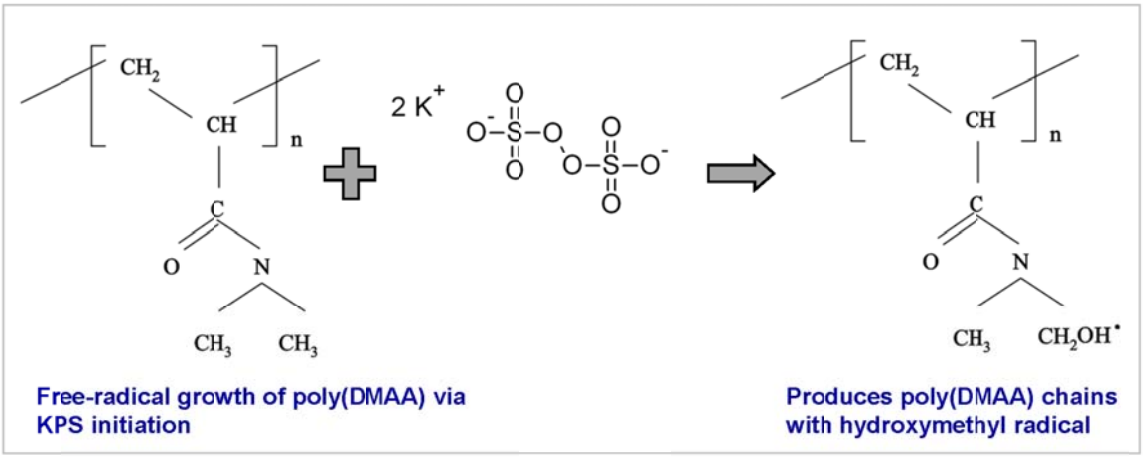

Figure 3.9. Formation of a hydroxymethyl radical on a growing poly(DMAA) chain when initiated using a disulfate system. The hydroxymethyl radical thus allows linear poly(DMAA) to self-crosslink and form a gel network without the presence of any external crosslinkers.[28]

Basically, initiation using a disulfate system causes the formation of a hydroxymethyl radical on one of the methyl end groups of the growing DMAA chain. This radical can then either continue reacting with DMAA monomers, or if it finds another poly(DMAA) chain, it reacts with it, forming a crosslink in the network. While most of the gels we have made thus far use 1 M monomer (~10 wt%), DMAA self-crosslinked gels typically require considerably more. This is due to the fact that the crosslinking density is directly tied to the monomer content. Thus, to form a stronger gel (i.e. higher crosslinking density) requires more monomer. Self-crosslinked DMAA gels of considerable strength usually require up to 50 wt% monomer, though they can be made with less if a softer (lower elastic modulus) gel is desired.

The interesting thing about this system (which seems to be very underutilized to date) is that it produces covalent crosslinks in the network (which are generally stronger and more permanent than physical), yet does not exhibit the same poor mechanical

properties of a traditional covalently-crosslinked network. As previously mentioned, BIS-crosslinked networks are quite fragile/brittle, cannot be elongated substantially without breaking, and have poor swelling properties. As we show in Figure 3.10, however, DMAA self-crosslinked gels are highly stretchable, very flexible, and show large and fast swelling characteristics.

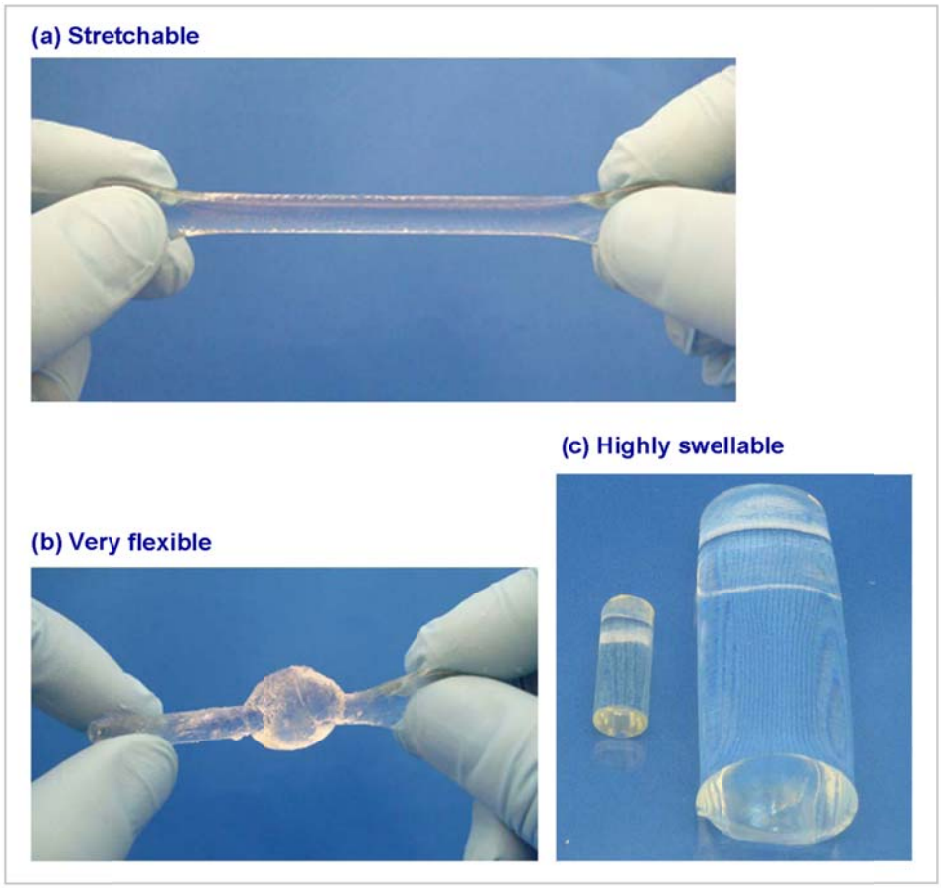

Figure 3.10. Impressive properties of a DMAA self-crosslinked gel. They are shown to be (a) highly stretchable, (b) very flexible, and (c) have large and fast swelling characteristics. This is unusual for a covalently-crosslinked gel, as BIS-crosslinked networks are known to be quite fragile/brittle, cannot be elongated substantially without breaking, and have poor swelling properties.

In the previous section, we showed that a LAP-crosslinked gel could by hybridized to a BIS-crosslinked gel. We now extend our technique to produce a hybrid where one of the gel regions is self-crosslinked using DMAA. As seen in Figure 3.11, we successfully hybridized a 4 wt% LAP/DMAA (with a small amount of blue MB dye) to a 50 wt% DMAA self-crosslinked gel (shown as transparent).

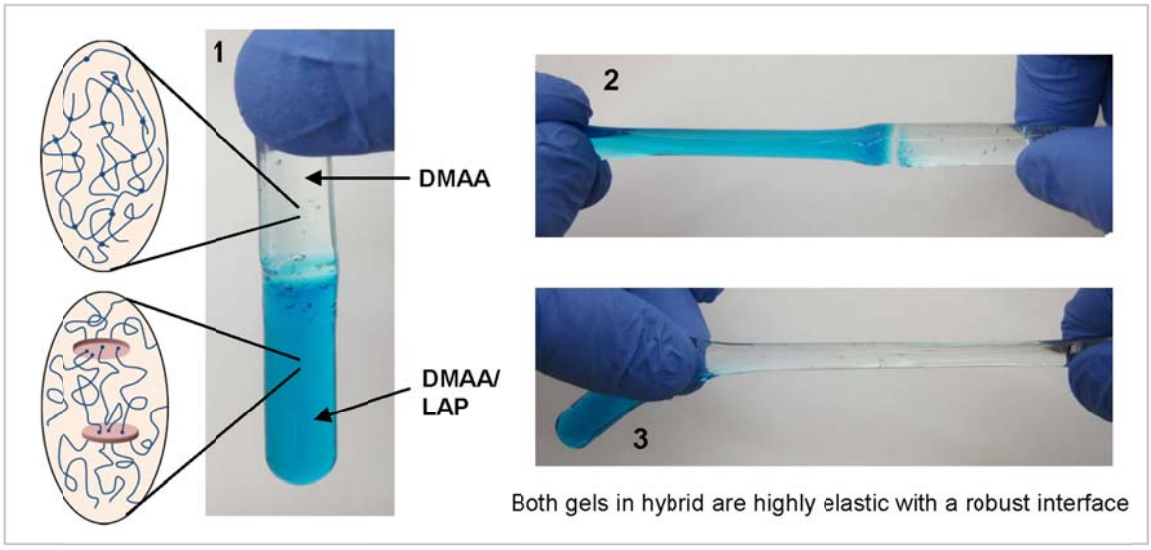

Figure 3.11. Hybrid gel rod with the bottom half comprised of 4 wt% LAP/DMAA (with a small amount of blue MB dye) and the top half consisting of a 50 wt% DMAA self-crosslinked gel (shown as transparent).

As the figure shows, the interface between the two gels is quite robust. Panels 2 and 3 show the hybrid being stretched, first as a whole (2), and then just in the DMAA region (3). These panels illustrate that while each region has different firmness (corresponding to different elastic moduli), both are still highly stretchable.

3.3.3. HYBRIDS CROSSLINKED WITH DIFFERENT LEVELS OF CLAY

Haraguchi, Murata, and others have shown that the level of clay in a polymer hydrogel can affect a number of its characteristics.[17,29] In this section, we explore two specific hybrids, the gels in each containing different levels of clay-crosslinking.

3.3.3.1 LOW-CLAY HYBRIDIZED TO HIGH-CLAY

It is known that Laponite nanodiscs impart optical anisotropy to clay-crosslinked gels.[29,30] Isotropy implies uniformity in all orientations, whereas anisotropy describes something as being directionally dependent. For example, sodium chloride is comprised of sodium and chloride ions that are ordered with uniform spacing along all three axes, resulting in an isotropic material. Contrast this to calcite, a very anisotropic crystal, which is highly ordered, but its structure in perpendicular planes is quite different (as shown in Figure 3.12).

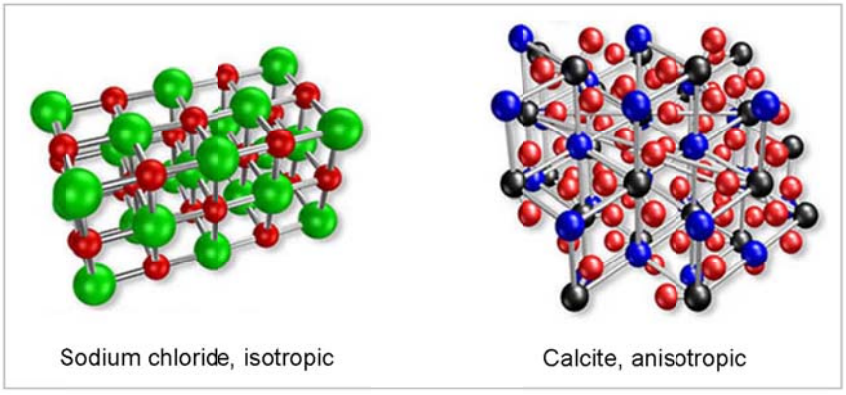

Figure 3.12. Examples of molecules showing isotropic (left) and anisotropic (right) crystalline structures.[31]

Light entering an isotropic material is refracted at a constant angle and passes through the crystal at a single velocity without being polarized. When a ray of light enters an optically anisotropic material, however, it is refracted into two rays, each polarized and traveling at different velocities. Thus, anisotropic materials will have more than one index of refraction (measure of the speed of light in that substance). The quantification of the difference between these indices of refraction is defined as birefringence. When viewed under a pair of polarizers (crossed with respect to each other), birefringence can be observed as streaks of light (which would normally be blocked by the crossed polarizers, but instead comes through, ranging in colors corresponding to the extent of birefringence).[31]

As mentioned, clay particles impart optical anisotropy to clay gels, as they are discs, not spheres and thus are not symmetrical in all dimensions. Furthermore, the birefringence in clay-crosslinked gels is concentration-dependent.[29,30] At low Laponite concentrations, the nanodiscs are oriented randomly and the gel is not birefringent at rest, as shown in Figure 3.13 (b). However, above a critical Laponite concentration (C_{crit} > 6 wt%), the nanodiscs stack together into columns and the resulting alignment of the particles causes the gel to be birefringent at rest.[30] We used this property to engineer hybrid gels with birefringent regions. For these experiments, we worked with NIPA as the monomer because its thermoresponsive property also prove useful in the experiments (shown later). We created the hybrid by first forming a pattern or "message" consisting of the letters "UMD" using a pre-gel mixture of NIPA/LAP with 6.4 wt% Laponite (above C_{crit}), as shown in Figure 3.13 (a). Thereafter, a pre-gel mixture of NIPA/LAP with 3.3

wt% Laponite (below C_{crit}) was poured around and over the message. The hybrid was then polymerized, and the photograph in Figure 3.13 (b) shows the material after polymerization. Note that the hybrid gel is smooth, transparent, and homogeneous, and the message is not discernible. To reveal the hidden message, the hybrid is viewed under crossed polarizer plates, as shown in Figure 3.13 (c). The regions corresponding to the

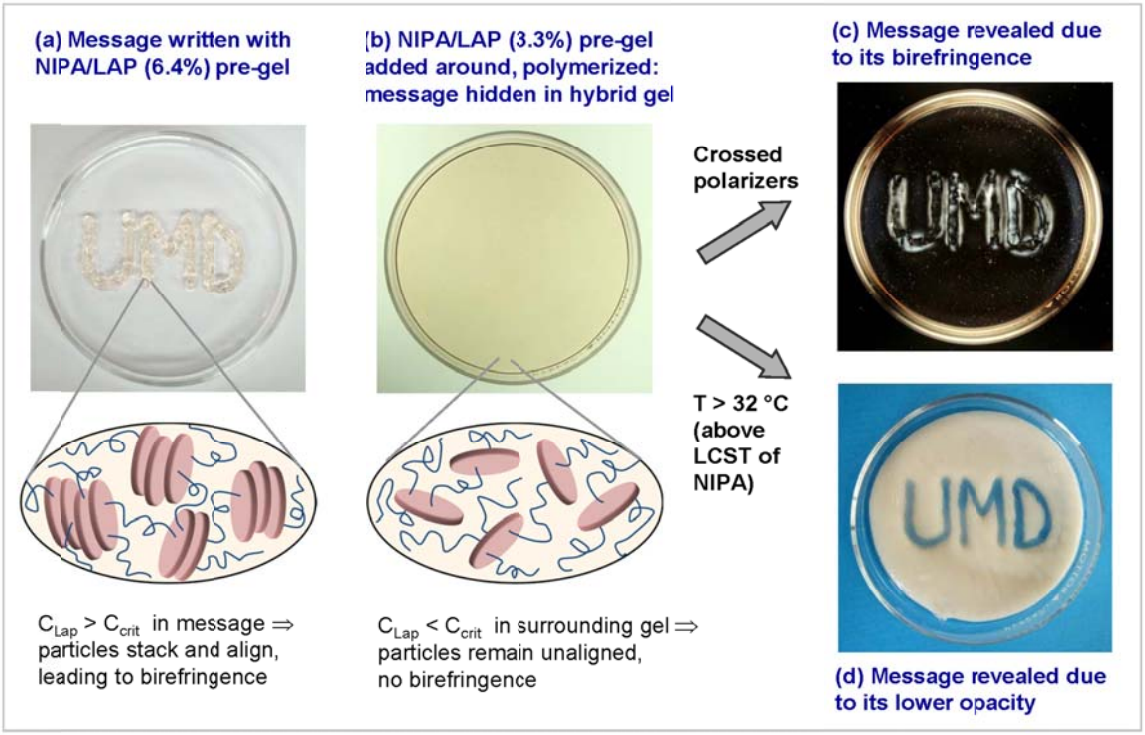

Figure 3.13. Embedding a hidden pattern or "message" in a hybrid gel. (a) The message "UMD" is written with a pre-gel of NIPA/LAP (6.4 wt%). At this higher concentration, the Laponite particles stack and align, leading to birefringence. The message is surrounded by a pre-gel of NIPA/LAP (3.3 wt%). At this lower concentration of Laponite, the particles are unaligned and there is no birefringence. (b) After the entire system is polymerized, the gel appears homogeneous in the Petri dish and the message cannot be seen under normal light. (c) When the gel is viewed under crossed polarizers, the message region lights up due to its birefringence. (d) The message can also be revealed under normal light if the gel is heated above the LCST of NIPA. In this case, the message region is relatively transparent while the surrounding gel is opaque (the underlying blue background beneath the Petri dish can be seen through the message).

message are strongly birefringent compared to the background, allowing the message to be easily read off.

Another way to reveal the hidden message is by heating the hybrid gel above ~ 32 °C, which is the lower critical solution temperature (LCST) of NIPA.[3] For example, Figure 3.13 (d) shows the above hybrid immersed in water at 50°C for ~30 seconds, then immediately photographed. In this case, the message can be seen even under direct light as the contrast is apparent between the message region of the gel (6.4 wt% Laponite), which is transparent, and the adjoining gel (3.3 wt% Laponite), which is white and opaque. These differences in opacity arise because Laponite content affects the thermoresponsive character of NIPA gels, as illustrated in Figure 3.14.

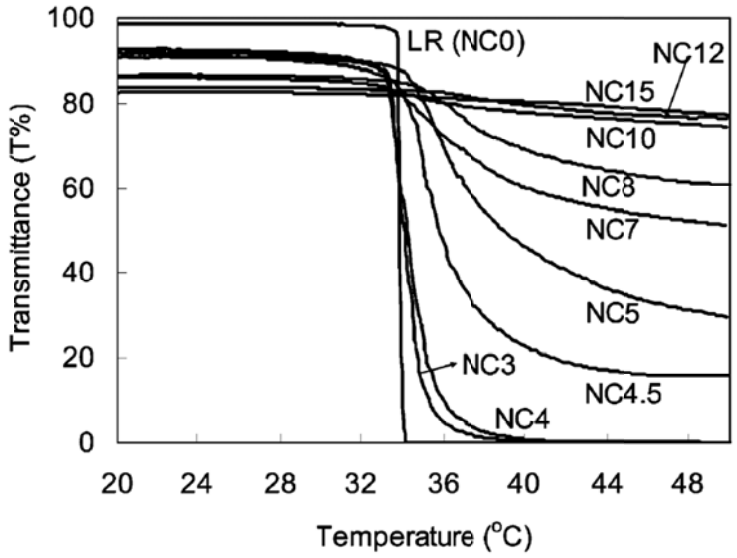

Figure 3.14. Effect of clay content on the change in transmittance upon heating above the LCST of NIPA.[30]

When a NIPA gel is heated above its LCST, the polymer segments between crosslinking points tend to aggregate and form large clusters, which strongly scatter light

and hence lead to opacity.[4] In the case of NIPA crosslinked with a large concentration of Laponite, the segments between adjacent Laponite particles are quite short.[18,19] As a result, there is less aggregation above the LCST and thus less opacity for a gel with 6.4 wt% Laponite.[19]

3.3.3.2 LOW-CLAY HYBRIDIZED TO MODERATE-CLAY

In a variation of the above approach, we created a hybrid gel that reveals its hidden message only when it is subjected to a substantial uniaxial stress. Murata et al. have shown that the birefringence of clay based gels increases as a function of strain. Furthermore, they found that the birefringence increases more sharply for higher clay content as compared to lower content (at lower levels of strain as seen in Figure 3.15).

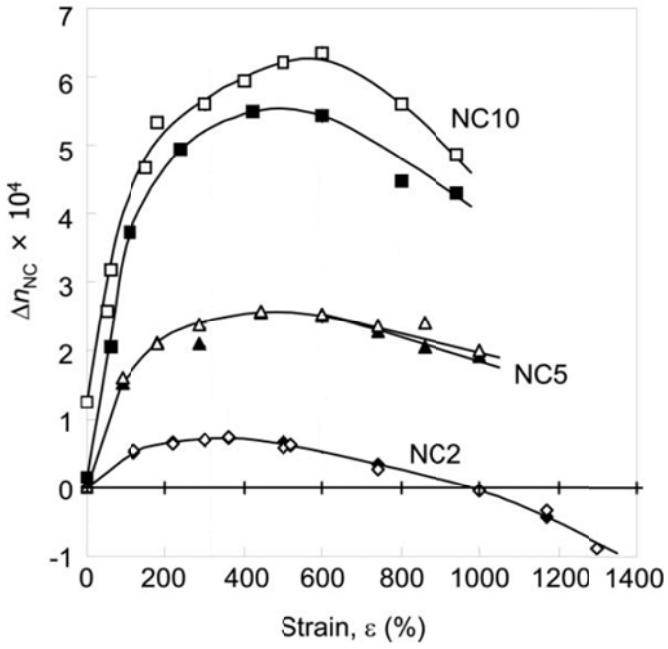

Figure 3.15. Effect of strain and clay content on the birefringence of NIPA/LAP hydrogels. $\Delta n_{NC} \times 10^4$ is the notation for birefringence, and NC2, 5, and 10 correspond to Laponite concentrations of ~ 1.3 wt%, 3.3 wt%, and 6.4 wt%, respectively.[29]

In the hybrid in Figure 3.16, the message "UMD" was formed by a NIPA/LAP pre-gel mixture with 4.9 wt% Laponite. This was surrounded as before by a pre-gel of NIPA/LAP with 3.3 wt% Laponite. Both these Laponite concentrations are below C_{crit}, and thus there is negligible birefringence anywhere in the gel at rest. Hence, the message is not visible under crossed-polarizers, as seen in the left panel of Figure 3.16 (a). However, when subjected to a uniaxial stress, the polymer segments tend to align parallel to the direction of the stress while the Laponite discs align perpendicular to it, as shown by the schematic in Figure 3.16 (b).[19,30] This causes stress-induced birefringence, which again is higher in gels with higher Laponite content. Figure 3.16 (b) shows a photograph of the hybrid gel while it is stretched uniaxially by hand. Both the message region as well as the surrounding gel show the stress-induced birefringence. Since the message portion has a higher Laponite content, it is more birefringent than the surrounding portion, allowing the message to be read off.

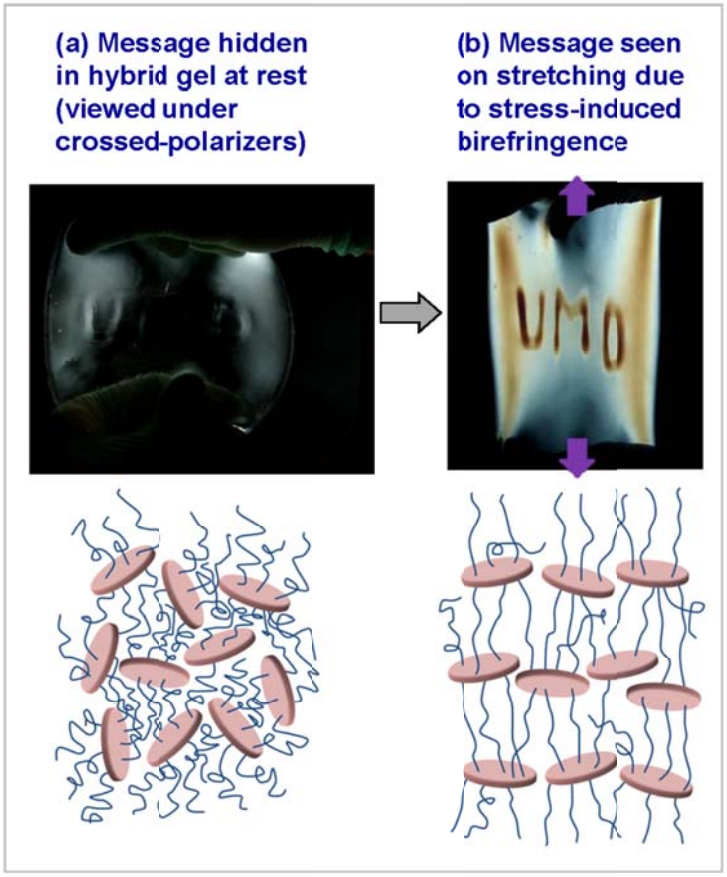

Figure 3.16. A second example of embedding a hidden pattern or "message" in a hybrid gel. In this case, the message is created with NIPA/LAP (4.9 wt%) and it is surrounded by NIPA/LAP (3.3 wt%). When the hybrid is viewed under crossed polarizers, the message is not visible when the gel is at rest, as shown in (a); instead, it is revealed when the gel is uniaxially stretched, as shown in (b). This result exploits the stress-induced birefringence of Laponite systems. At rest, the particles are unaligned, as indicated by the schematic in (a). When the gel is stretched, the particles align, as shown by the schematic in (b), which causes birefringence.[32] The message region is more birefringent than the surrounding gel in (b) due to the higher Laponite content in the former.

3.3.3. HYBRIDS OF DIFFERENT MONOMERS

All of the hybrids covered up to this point have consisted of gel regions with the same monomer and different crosslinkers. To fully utilize the application potential of our hybrid technique, it is necessary to be able to construct hybrids with regions of different

monomers as well. In this section, we create a hybrid of three different gels, each of a different monomer or comonomer combination selected to impart specific properties to each section of the hybrid. For inspiration, we look to nature, finding that the squid is a great example of a macroscale combination of several soft materials, each serving a specific purpose, yet melded together into one seamless body (as shown in Figure 3.17).

Figure 3.17. *Histioteuthis* squid.[33]

For our squid hybrid, we started with a glass mold which we created by gluing several pipettes together for the tentacles, then epoxying the pipettes to a glass tube for the head and body. Figure 3.18 (a) shows the assembled squid glass mold. The pre-gel recipe for the tentacles was comprised of NIPA monomer with 4 wt% Laponite crosslinker. This gave the tentacles thermoresponsive properties, causing them to turn opaque and begin to deswell when exposed to temperatures in excess of 32 °C. After pipetting the tentacle pre-gel into the mold (while oriented vertically), the pre-gel for the

body was then added, consisting of DMAA monomer, again with 4 wt% Laponite crosslinker. With this composition, the body would be unresponsive to temperature, yet would be highly extensible. Finally, the pre-gel for the head was pipetted on top of the body. The pre-gel for the head was the most elaborate, containing sodium acrylate (SA) and acrylamide (AAm) as comonomers and BIS and Cloisite Na+ natural montmorillonite clay (MONT) as co-crosslinkers. Sodium acrylate was chosen to cause the head to swell to a greater extent than the rest of the squid. As discussed in section 2.2, a gel with an ionic monomer such as sodium acrylate will swell greatly under certain conditions. Only 10% of the total monomer amount used was SA, the remainder being AAm (total monomer content being ~1 M). Had it consisted of 100% sodium acrylate monomer, the head would have swelled to an extremely large size, giving the squid an undesired top-heaviness. The choice for crosslinker composition corresponded to the monomers used. Laponite clay particles are not stable in solutions of high ionic content. At very low ionic levels, the clay particles quickly gel, forming the "house-of-cards" structure. As the ionic levels increase, however, the clay particles flocculate, clumping together and falling out of suspension. Thus, since Laponite could not be used, BIS was used as a crosslinker at 2.2 mol%. We have found from experience that the strength and elasticity of BIS-crosslinked gels is generally improved through the addition of small amounts of clay. While our SA-co-AAm pre-gel was too ionic for Laponite clay particles, the natural montmorillonite, Cloisite Na+, (which is more tolerant to ions than Laponite) was added, and at the level used (1 wt%), the pre-gel remained a low-viscosity solution able to be pipetted on top of the body pre-gel. Figure 3.18 (b) shows the squid hybrid after polymerization, having taken it out of its mold.

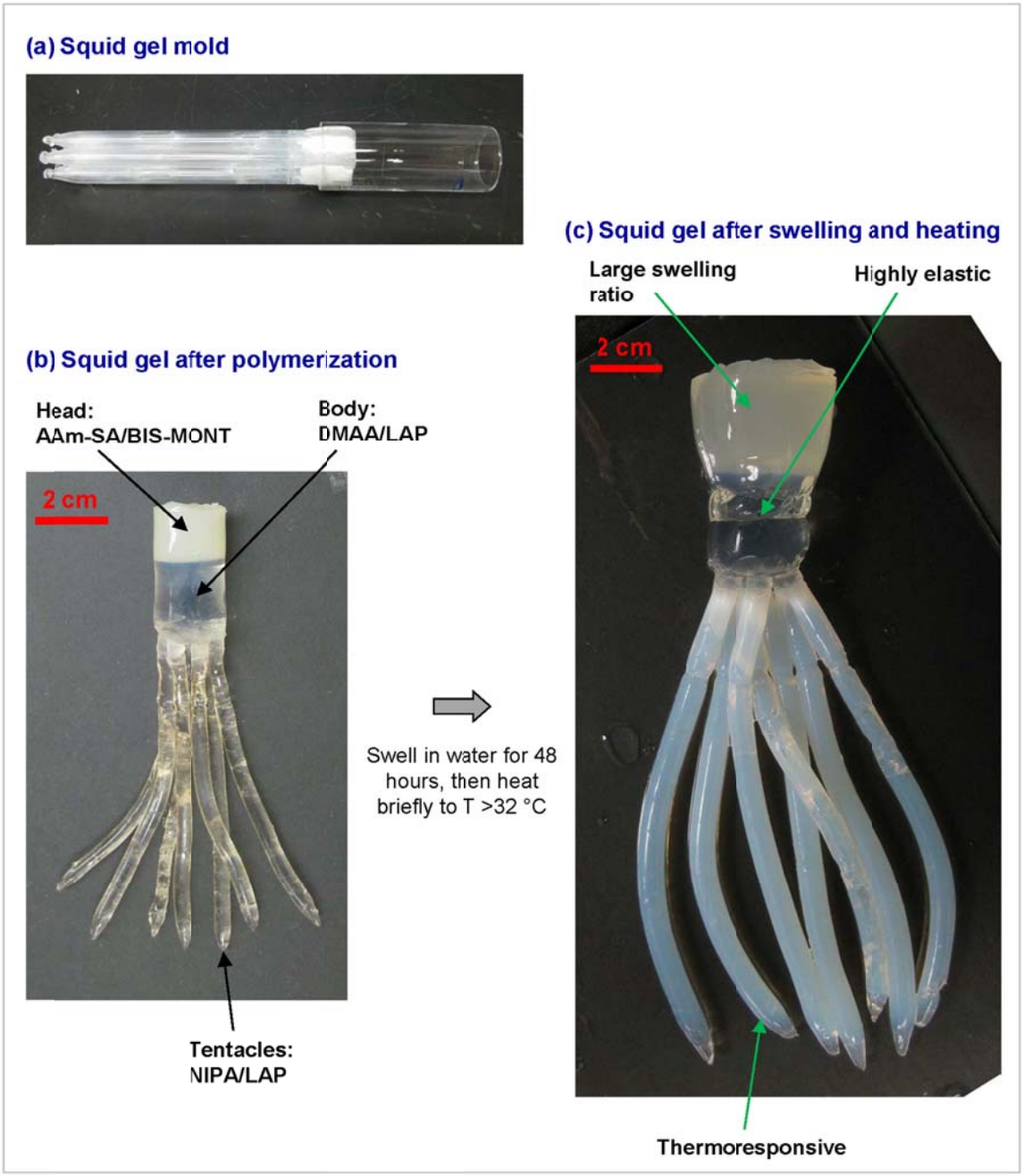

Figure 3.18. Squid gel hybrid comprised of three distinct regions: head, body, and tentacles. The tentacles were comprised of 4 wt% Laponite/NIPA gel to give them thermoresponsive properties (causing them to turn opaque and begin to deswell when exposed to temperatures in excess of 32 °C). The squid body consisting of 4 wt% Laponite/DMAA to give it high strength and extensibility. The head contained sodium acrylate and acrylamide (in a 1:9 ratio) as comonomers and BIS (2.2 mol%) and Cloisite Na+ natural montmorillonite clay (1 wt%) as co-crosslinkers. Including ionic sodium acrylate as comonomer causes the head to swell to a greater extent than the rest of the squid. The small amount of montmorillonite was added to improve the strength and elasticity of the usually brittle BIS-crosslinked gel.

The difference between the head and body can be seen in the figure, as the head is yellow and opaque. This is due to the montmorillonite, whose color and opacity are the result of the size of the clay particles and the presence of naturally occurring impurities. A clear interface between the tentacles and body cannot be readily discerned as both have similar color and transparency. Figure 3.18 (c) shows the squid after swelling in water for 48 hours, then briefly heating in 50 °C water for ~30 seconds to reveal the thermoresponsive character of the tentacles. Notice that the scale bars between Figure 3.18 (b) and (c) are the same--the gel hybrid has swollen to about one and a half times its original size in only a 48 hour period. Also notice that the head has become more bulbous than the body, due to its high degree and fast rate of swelling (imparted by the ionic comonomer). Because of the brief heating, the tentacles can now be readily differentiated from the body as they have turned opaque.

Placing the squid hybrid into a vigorously circulating 50 °C water bath (Figure 3.19) demonstrates the integrity of the connection between each hybrid section. Though the actual video is more revealing than the still photo, the squid survives being tossed around in a “swimming”-like fashion, with all sections of the hybrid firmly intact.

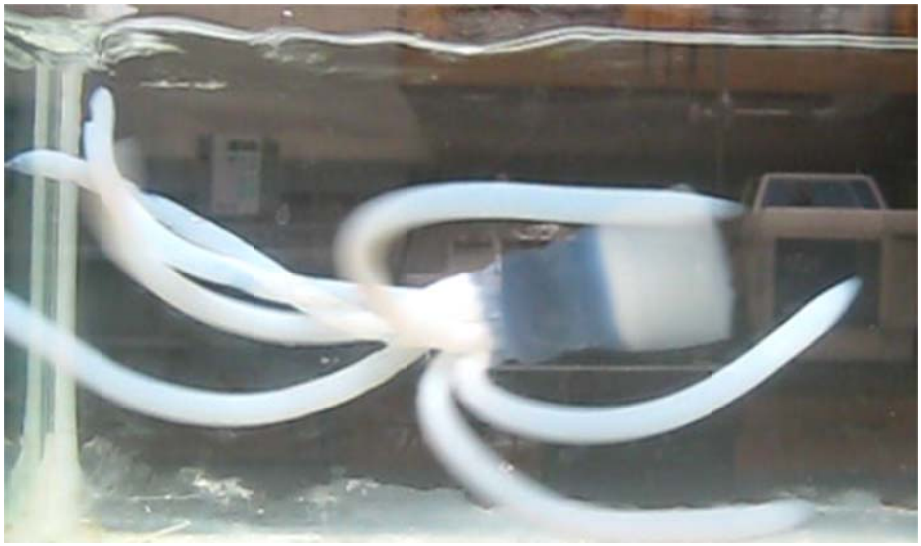

Figure 3.19. Squid hybrid "swimming" in a 50 °C circulating water bath.

While the specific characteristics given to each region of the squid have no relevance to the functions actually required by a living squid, they nonetheless provide an example of how various stimuli-responsive gels with both differing monomers and crosslinkers can be combined into one seamless hybrid. Moreover, the hybrid demonstrates that large scale soft material hybrids can be constructed and can endure the wear-and-tear that biological applications require.

3.3.4. SPINAL DISC REPLACEMENT HYBRID

In a more practical application of the previous section, we again recall the fact that many soft materials in biology and nature are actually hybrids. For example, the spinal disc consists of a soft gel-like core (*nucleus pulposus*) surrounded by a firmer outer layer (*annulus fibrosus*), yet the two are integrated into a single, fused material.[34,35]

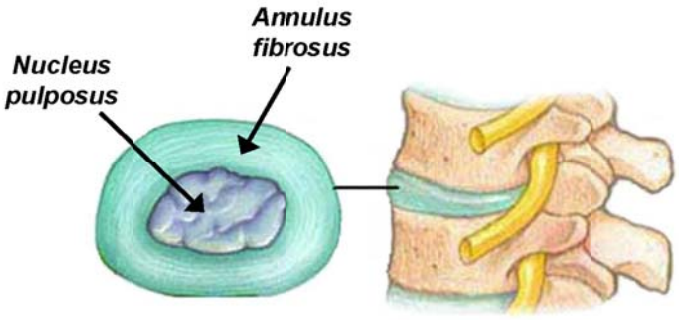

Figure 3.20. Schematic of spinal disc showing the soft inner core (*nucleus pulposus*) and the firm outer region (*annulus fibrosus*).[36]

It is clear that a single polymeric gel cannot provide an adequate model for the entire spinal disc.[35] However, a hybrid gel created by our approach may allow for the first time a faithful replication of the mechanical heterogeneity inherent in a spinal disc. We begin by making a pre-gel for the *annulus fibrosus* consisting of 5.2 wt% LAP/NIPA.

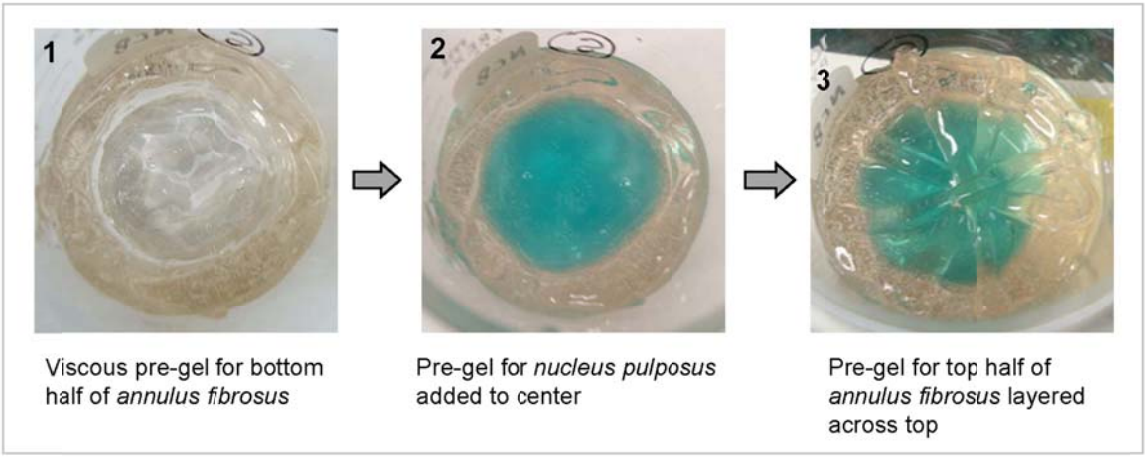

Figure 3.21. Method for creating spinal disc hybrid. In panel 1, two-thirds of the viscous pre-gel for the *annulus fibrosus*, consisting of 5.2 wt% LAP/NIPA, is scooped and then molded into the bottom of a beaker The pre-gel for the *nucleus pulposus* (3.3 wt% LAP/NIPA with a small amount of blue MB dye) is then gently poured into the "crater" left by the first pre-gel in panel 2. After a few minutes, the remainder of the *annulus fibrosus* pre-gel is then pipetted across the top in thin strips (as shown in panel 3), continuing to add strips until a thick layer completely covers the core. The gel is then polymerized at room temperature for 20 hours.

Since the pre-gel becomes quite viscous almost immediately after adding the KPS and TEMED, two-thirds of the mixture was scooped and then molded into the bottom of a beaker as shown in panel 1 of Figure 3.21.

The pre-gel for the *nucleus pulposus* (3.3 wt% LAP/NIPA with a small amount of blue MB dye) was then gently poured into the "crater" left by the first pre-gel (see panel 2 of Figure 3.21). After waiting a few minutes for the viscosity of the *nucleus pulposus* pre-gel to increase, the remainder of the *annulus fibrosus* pre-gel was then pipetted across the top in thin strips (as shown in panel 3 of Figure 3.21), continuing to add strips until a thick layer completely covered the core. The gel was then polymerized at room temperature for 20 hours before being taken out of the mold and rinsed.

Once polymerized, the spinal disc hybrid could be handled quite forcefully (Figure 3.22), demonstrating the toughness of the hybridized connection between the two gel regions. The differences in compressive behaviors were readily discernible when pinching various portions of the disc (softer in the center and firmer at its edges).

To attempt to quantify the differences in mechanical properties between the two regions, we utilized dynamic rheology. Though basic dynamic rheology cannot truly reflect how accurately our spinal disc hybrid would perform when placed between two vertebrae in a real spine, it can however illustrate how different the two regions of our hybrid are--the first step in creating a faithful replica. To analyze the gel regions individually, the spinal disc hybrid was cut up to obtain thin slices of both the outer ring

and inner core. A frequency sweep was then conducted on each gel slice using an AR2000 (TA Instruments) stress-controlled rheometer with a 20 mm diameter parallel plate geometry and solvent trap to minimize water loss. Before the frequency spectra was investigated, a dynamic stress sweep was performed to ensure that the frequency sweeps were conducted in the linear viscoelastic regime of the samples. As Figure 3.22 shows, the outer shell (*annulus fibrosus*) of our spinal disc hybrid has an elastic modulus value that is significantly larger than that of the inner core (*nucleus pulposus*)--with average values of 22,000 Pa and 7,600 Pa, respectively.

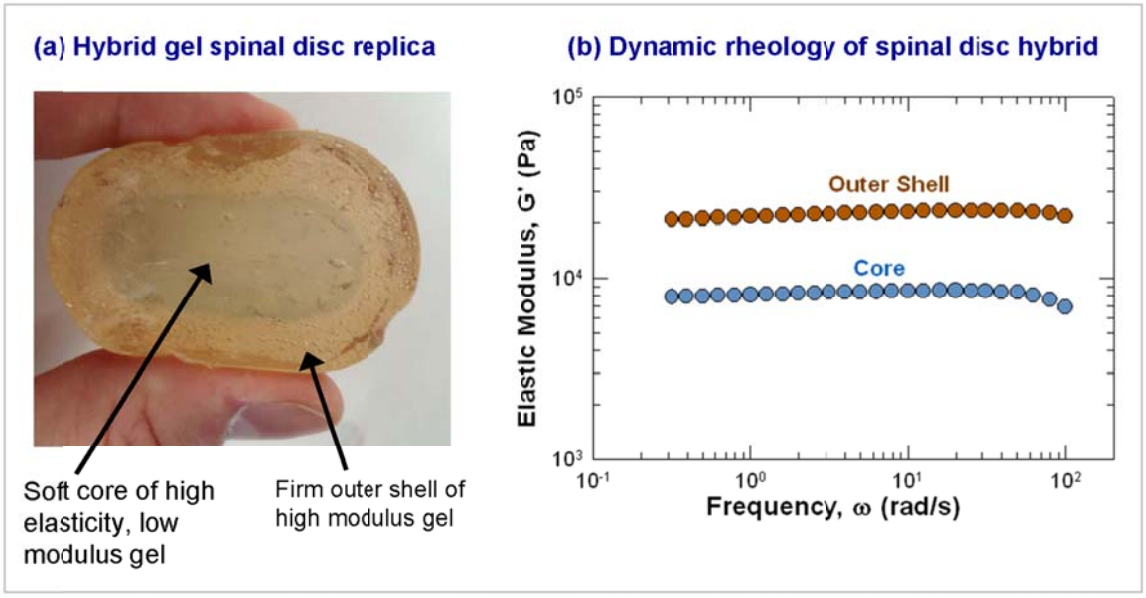

Figure 3.22. (a) Spinal disc hybrid gel replica consisting of a soft inner core gel (*nucleus pulposus*) and a firm outer region (*annulus fibrosus*), strongly melded into a single, complex hybrid. (b) Using an AR2000 stress-controlled rheometer with a 20 mm diameter parallel plate geometry, a dynamic frequency sweep was used to obtain values for the elastic modulus of each region of the gel. The outer shell is shown to have an elastic modulus value significantly larger than that of the inner core--with averages of 22,000 Pa and 7,600 Pa, respectively.

An actual human spinal disc is very complex, compressing and distributing loads on the spine in a multitude of directions. Though our spinal disc is fairly primitive, it can still be seen as the first step towards a fully-functional replacement. Future visions of a spinal disc replica utilizing our hybrid method involve enhancing the complexity and components of each region. For example, adding a collagen fiber mesh to the *annulus fibrosus* pre-gel can help mimic the radial-tire-like lamellae of an actual spinal disc.

3.4. CONCLUSIONS

In this chapter, we presented a new approach for combining dissimilar gels into a single material while fully preserving the unique character of each individual gel. We began by describing our hybrid method, and then demonstrated the utility of our approach through multiple examples utilizing the chemical, mechanical, and optical heterogeneity of various gel formulations. We created hybrids with regions that have different affinities for cationic dyes as well as distinct mechanical properties. We generated hybrids with regions of distinct optical characteristics that were revealed under crossed polarizers or in response to heat or stress. Finally, we designed several macroscale gels (squid gel and spinal disc gel) which combined a variety of monomers and crosslinkers in a manner which demonstrates the practicality of our hybrid technique.

Chapter 4: CONCLUSIONS AND RECOMMENDATIONS

4.1. CONCLUSIONS

In this thesis, we have demonstrated that hybrid hydrogels can be easily created in which individual components retain their identities in a single continuous matrix. We engineered hybrids with regions or patterns of one gel juxtaposed with another. Our method to assemble these hybrids is quicker, easier, and has fewer limitations than those used to make traditional interpenetrated networks. Moreover, the gel/gel interfaces in our hybrids have high mechanical integrity and are not the failure points during mechanical testing.

To demonstrate the utility of our method, we developed hybrids of multiple gels made with both different monomers and crosslinkers. Regions of our hybrids that were crosslinked by Laponite particles had distinct chemical properties (ability to selectively absorb a cationic dye), mechanical properties (higher strength and extensibility) and optical properties (birefringence). We also showed hybrids could be embedded with a message or pattern that remained hidden until it was revealed by viewing the material under crossed polarizers, heated, or subjected to a uniaxial stress. We also created some interesting macroscale gels. Our squid-like gel (which combines three gel types of various crosslinkers and monomers) is an example of large-scale construction of soft matter in a robustly-connected, highly malleable, functional fashion. We then extend this macroscale assembly to one very practical application as a hybrid gel for spinal disc replacement. In closing, we note that our overall approach is simple and versatile; it can

be easily extended in a variety of ways to create new gels with unusual and unique properties.

4.2. FUTURE DIRECTIONS

Our approach can be extended to create a range of new hybrid gels by varying the monomer and/or the crosslinker for different zones of the gel and also by forming hybrids of numerous gels (i.e. more than just two and three). Because our approach is relatively straightforward, its real utility is revealed with the conception of unique, novel hybrids with direct applications. Accordingly, time spent in the future to further explore how gel hybrids could be used in biological and soft matter applications would be very worthwhile.

Some of the more promising leads for hybrids include applications in separations, mechanical-optical sensors, biomaterials, drug delivery, and many other areas. For example, currently, gels can be used as scaffolds for stem cells to differentiate into specific cell types or tissues.[8,10] It is known that the differentiation is triggered by the physical and chemical nature of the scaffold. Thus, hybrid gels may be useful to induce stem cells to simultaneously differentiate into several different cell types within adjacent regions of a continuous matrix--this would be a step towards the bottom-up assembly of a tissue.[10]

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