

ABSTRACT

Title of Thesis: A NEW CLASS OF HYBRID HYDROGELS

Neville Justine Fernandes, Master of Science, 2013

Directed by: Professor Srinivasa R. Raghavan
Department of Chemical & Biomolecular Engineering

Hybrid hydrogels are a novel way of combining materials with different properties and retaining their individual functionalities within the same composite gel. Here we attempt to demonstrate how this approach can be used to create hydrogels whose morphologies can be altered depending on external stimuli. First we report the creation of hollow hybrid gels which are similar to the previously created solid hybrid gels but have the advantage of a faster and enhanced response to external stimuli. Two stimuli that we have specifically investigated are temperature and solvent composition. We show how to modify the type and extent of response of the gels, i.e. make them shrink or swell, by changing the composition of the polymer as well as the crosslinker within the gel. Thereafter, we also demonstrate how the responses can be manipulated to change the morphology of the hybrid gel itself.

A NEW CLASS OF HYBRID HYDROGELS

by

Neville Justine Fernandes

Thesis submitted to the Faculty of the Graduate School of the
University of Maryland, College Park, in partial fulfillment
Of the requirements for the degree of
Master of Science
2013

Advisory Committee:

Professor Srinivasa R. Raghavan, Dept. of Chemical & Biomolecular Engineering, Chair
Professor Panagiotis Dimitrakopoulos, Dept. of Chemical & Biomolecular Engineering
Professor Ganesh Sriram, Dept. of Chemical & Biomolecular Engineering

Dedication

To Apollo and Anesidora, Tyche and Heracles.

Acknowledgements

Firstly, I would like to thank my advisor, Dr. Srinivasa Raghavan, not only for his unparalleled guidance and expertise on the subject matter at hand, but also for his unstinting support of me through my tough times and for showing me how to approach research with the apt attitude.

I would like to thank all my lab-mates, past and present, for their help in all of my research problems and their support throughout my stint in the lab. I would like to thank Peter for his initial input in the field of hydrogels, Hee-Young, Veidhes and Matt for helping me find my feet in the lab, Vishal for his constant guiding and tweaking, Hyuntaek for his unflinching help and constant inputs, Anand for being a good sounding board, Steve for collaboration and work ethic, Bani for his calm advice on all things hydrogels as well as Charles, Kevin, Chanda, Kunqiang, Annie, Veena, Jasmine, Ankit Goyal, Ankit Gargava, Wonseok and all the others who helped me indirectly in my work. I also want to thank my three undergraduate students Jason, Majid and Nadia for their efforts and assistance at different times throughout my research.

I would like to thank Dr. Robert Briber for his ready help and advice on polymer strength testing.

I would like to thank all my friends, old and new, who have helped me go on and given me a release valve when I needed it.

Lastly, but most importantly, I would like to thank my family for their immense support and constant encouragement throughout the period of my thesis, without which it wouldn't have reached its culmination. My Mom for being the best life advisor without whom I wouldn't be here today, my sister for her tremendous drive and practicality among many other things, my brother for his unwavering and totally biased backing and Dad for being the shining light to which I aim – I am grateful for having all of them as my family. And of course, my soul mate, with whom I have traversed the entire journey that is this thesis and without whom I wouldn't have lasted the course – we made it!

TABLE OF CONTENTS

Dedication	ii
Acknowledgement	iii
List of Abbreviations	vi
Chapter 1. Introduction and Overview	1
Chapter 2. Background	5
2.1 Hydrogels formation by free-radical polymerization.....	5
2.2 Types of monomers used to create hydrogels	8
2.3 Stimuli-responsive swelling and shrinking of hydrogels	9
Chapter 3. Hollow Hybrid Gels: Synthesis and Properties	12
3.1 Introduction	12
3.2 Experimental Section	13
3.3 Results and Discussion	25
3.3.1 Solid Hybrid Gels (SHGs)	16
3.3.2 Hollow Hybrid Gels (HHGs)	18
3.3.3 Swelling kinetics of solid and hollow gels: comparison	19
3.3.4 Stimuli-responsive HHGs	24
3.4 Conclusions	31
Chapter 4. Conclusion	32
4.1 Conclusions	32
4.2 Future Work	33
References	35
Publications and Conference Presentations	39

LIST OF ABBREVIATIONS

AAm	Acrylamide
DMAA	N,N-dimethylacrylamide
NIPA	N-isopropylacrylamide
BIS	N,N'-methylenebisacrylamide
LAP	Laponite®
KPS	Potassium persulfate
TEMED	N,N,N',N'-tetramethylethylenediamine
DMEM	(2-dimethylamino)ethyl methacrylate
SA	Sodium acrylate
AA	Acrylic acid
DI	Deionized (water)
UCST	Upper critical solution temperature
LCST	Lower critical solution temperature
SHG	Solid hybrid gel
HHG	Hollow hybrid gel

Chapter 1: INTRODUCTION & OVERVIEW

Polymer hydrogels are three-dimensional networks of polymer chains cross-linked by chemical or physical bonds and swollen in water.¹ Hydrogels are ubiquitous in nature and serve many functions depending on properties such as water retention, mechanical strength and chemical functionality. Gels occur in various biological contexts, including in the interior (cytoplasm) of single biological cells.^{2,3} Biological tissues and the extracellular matrix are also examples of soft materials in the gel state.⁴ Current research in creating synthetic replacements for these biological gels has focused on using the suitable properties of polymer hydrogels to mimic these biological gels.⁵ Polymer gels can be conditioned to give responses to different stimuli like temperature,⁶ pH,⁷ solvent composition,⁸ ionic strength⁹ and light.¹⁰ Many of the changes induced result in changes in shape and surface morphology of the gel,¹¹ which can also find application as biomaterials in bioengineering in the form of replacements for various tissues.^{12,13}

In this thesis, we focus on hybrid gels that combine two or more gels with widely varying properties, joined through a robust interface. This approach builds on previous work by Banik et al.¹⁴ in our laboratory. The key element of the approach is to contact two pre-gel solutions containing crosslinkable monomers wherein at least one of the solutions has a high viscosity. The pre-gel solutions are then allowed to undergo gelation (crosslinking) by free-radical polymerization. The high viscosity prevents intermixing of the pre-gel solutions and allows us to control the spatial positioning of the gels within the overall hybrid. It is well-known that gels often exhibit large changes in volume in

response to changes in their environment. We are specifically interested in hybrids that contain two or more portions that show very different swelling ratios in a particular solvent of interest. Such hybrids could be engineered to undergo specific predetermined changes in shape under certain conditions.

The challenges in inducing large shape changes in bulk gels are two-fold: first, the rate of volume response of bulk gels can be quite slow; and second, at the high swelling ratios required for large shape changes, the hydrogels become mechanically weak and disintegrate easily. The simplest way to control the response time of gels is by manipulating the size of the gel. It is known from Fick's law that the kinetics of swelling or deswelling of the gel is inversely proportional to smallest dimension of the gel.¹⁵ It is still possible to prepare large gels that have fast response times as long as the controlling size scale of the gels is small. One example is in the case of superporous hydrogels;^{16,17} in this case, the pores interspersed throughout the gel reduce the size scale relevant to volume changes and thus result in rapid swelling and shrinking.

In this thesis, to improve the response time of hybrids, we report the creation of hollow hybrid gels wherein the overall size of the gel is still large but the effective size scale for diffusion is now much smaller, thus accelerating the rate at which the gel undergoes a change in shape. In our technique, we combine two pre-gel mixtures in a mold whose center is occupied by another smaller concentric container as shown in Figure 1.1. After polymerization is complete, we obtain a gel wherein the effective smallest dimension of the gel is smaller than in the solid case due to the hollow middle.

We compare the solid hybrid gel (SHG) to the hollow hybrid gel (HHG) by measuring the degree of swelling vs. time, and we are able to confirm the faster kinetics of the HHG.

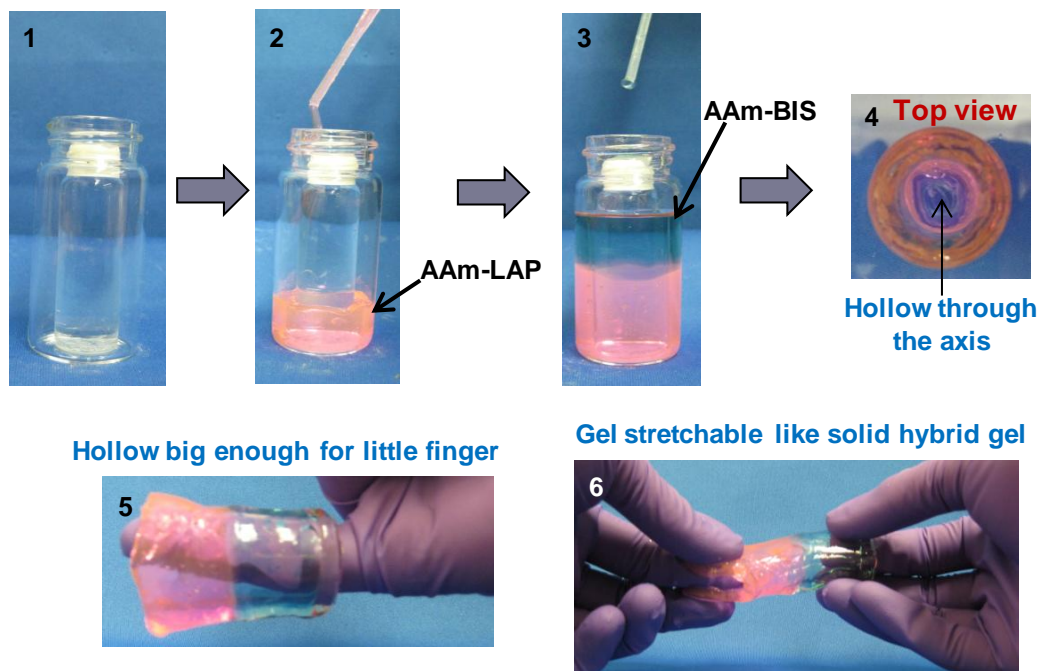


Figure 1.1. Procedure for making hollow hybrid gels (see Chapter 3). Here, two regions of the hybrid have the same monomer, acrylamide (AAm) but different crosslinkers, i.e., laponite particles (LAP) or bis-acrylamide (BIS). (1) A mold is created by placing or gluing a smaller glass cylinder within a bigger one. (2) A highly viscous pre-gel solution of AAm-LAP is pipetted into the space in the mold. (3) The second pre-gel solution of AAm-BIS is then gently pipetted over the first pre-gel so as not to induce convective mixing at the interface. (4) The hollow hybrid gel extracted in the shape of the cylindrical mold, shows two distinct and smooth surfaces. The hollow gel is strong enough that it can be held using one's fingers, as shown by (5) and stretched without breaking, as shown by (6).

Volume changes in hydrogels, in response to suitable stimuli, are a result of its inherent polymer network structure which obviously depends on the monomers used in polymerization process as well as the type of crosslinker used in forming the network. We can assign different properties to gels within the same hybrid by changing the polymer network or by using different types of crosslinkers. In addition to crosslinkable

(multifunctional) monomers,^{18,19} we can also use clay particles²⁰ as crosslinkers. Specifically, particles of laponite, which is a type of synthetic layered silicate clay, can serve as crosslinker. Gels formed by crosslinking with laponite are highly extensible and tough.²¹ Such gels were reported by Haraguchi over a decade ago,²²⁻²⁴ and are now gaining popularity in the field. In our work, we have created hybrid gels with different monomers, both ionic and non-ionic and different crosslinkers, both multifunctional monomers as well as laponite. The use of laponite as crosslinker allows gels to undergo substantial changes in volume while preserving their mechanical integrity.

Finally, we report the creation of hybrid gels that change their three-dimensional shape on exposure to certain stimuli. The first is a two-gel hollow hybrid in which one of the gels responds to an external stimuli and contracts around an object in its interior, thereby being able to pick it up. The second sample is a hollow tube with ‘kinks’ that swell/shrink to induce bends; in turn, the tube changes its shape to a polygon. These experiments illustrate the ease of use of our technique and how it can be utilized to create gels with enhanced response to stimuli and control over shape and morphology.

Chapter 2: BACKGROUND

In this section we discuss the fundamentals of hydrogel formation via free-radical polymerization, some of the monomers used for forming the gels, and the swelling and shrinking of the gels in response to stimuli.

2.1. HYDROGEL FORMATION BY FREE RADICAL POLYMERIZATION

A polymer hydrogel consists of a crosslinked polymer network that is swollen in water. The large affinity of the polymer network for water prevents the latter from escaping the three dimensional network. Polymer gels can be formed *in situ* in water by the free radical polymerization of one or more water soluble monomers and a crosslinker. In the first step of the polymerization, the initiation step, polymerization is initiated by the decomposition of an initiator into free radicals. The monomer has a polymerizable group (e.g., a vinyl group) that is attacked by the free radicals generated by the initiator to form a radical which goes on to form covalent bonds with other monomers or crosslinkers. Conventional gels usually use tetrafunctional molecules like bisacrylamides or diacrylates as crosslinkers as they too could form free radicals and crosslink four propagating polymer chains at once. The initiator is the source of the free radicals which start the polymerization and they can be activated either by thermal decomposition (persulfates), photolysis (azoisobutylnitrile) or redox-mediated decomposition. Typically, an accelerant like tetramethylethylenediamine (TEMED) is used to start the initiation of a persulfate like potassium persulfate (KPS) in an aqueous solution. Figure 2.1 shows the

components typically used to form a typical hydrogel of polyacrylamide, which are the monomer, acrylamide (AAm), the crosslinker, N,N'-methylenebisacrylamide (BIS), the initiator KPS and the accelerant TEMED.¹⁸

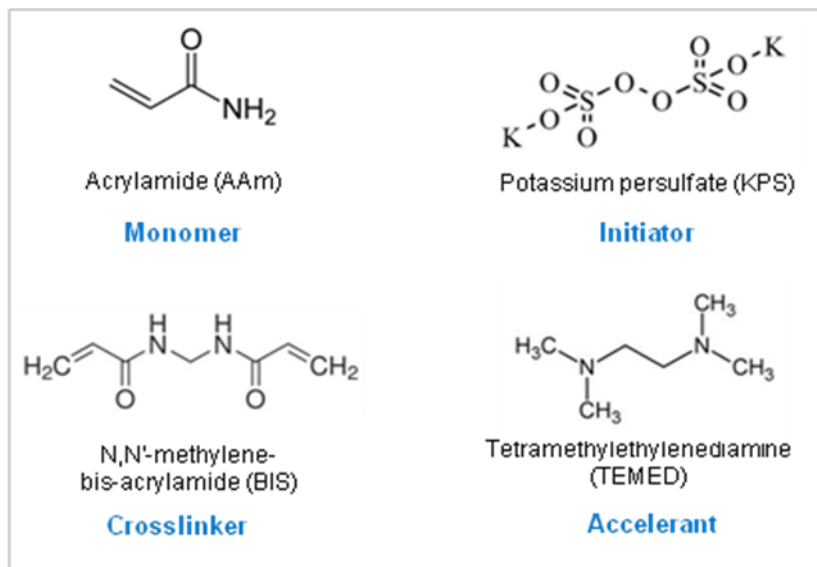


Figure 2.1. The basic constituents of an acrylamide-based polymer gel formed by free-radical polymerization.

In conventional hydrogels, the polymer chains grow in size till their growth is terminated by chain transfer or crosslinking with a crosslinker. As the crosslinker is usually $1/100^{\text{th}}$ the molar concentration of the monomers, the polymer grows to a considerable length before being crosslinked. This enables the formation of an intricate three-dimensional (3-D) network of polymer chains. Radical-scavenging impurities like oxygen can terminate the propagation reaction before all the monomers are used up, which results in the formation of a gel with little or no integrity. Because of this, a nitrogen atmosphere is generally used to promote a hypoxic environment.

A new class of hydrogels called nanocomposite hydrogels were created by Haraguchi and his group in 2002.²¹ These hydrogels used laponite clay particles to crosslink the polymer chains. Laponite is a synthetic layered silicate that has the empirical formula $\text{Na}_{0.7}^+ [(\text{Si}_8 \text{Mg}_{5.5} \text{Li}_{0.3}) \text{O}_{20} (\text{OH})_4]_{0.7}^-$. Each disc-shaped clay particle is approximately 25 nm in diameter and 1 nm in thickness (see Figure 2.2) with an abundance of hydroxyl and oxygen atoms on the flat surface giving it a net negative surface charge.²⁵ To form laponite-crosslinked gels, the monomer, laponite, and initiator are combined and a free-radical polymerization is conducted. During this process, polymer chains grow from the surface of the laponite, and thus the particles act as crosslinkers. Because of the particles' net negative charge, laponite-crosslinked gels retain a strong cation-absorption ability.^{26,27} But, at the same time, polymerization of acidic or ionic monomers in the presence of laponite is not possible as the ions precipitate out the particles. For this reason, we use BIS as the crosslinker in preparing hydrogels with ionic monomers, as reported in Chapter 3.

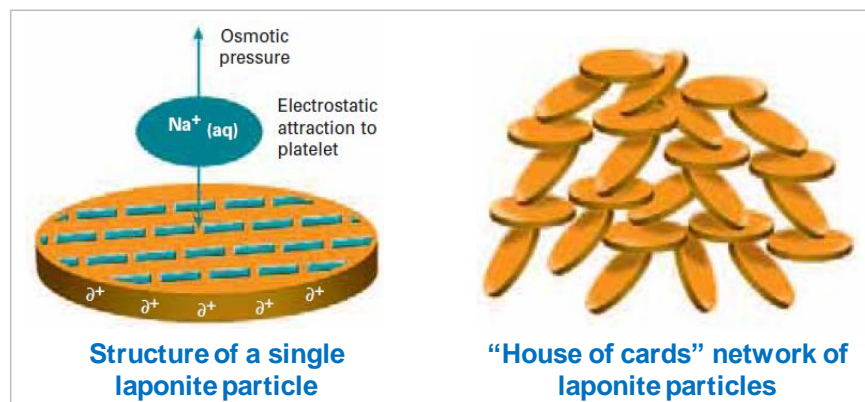


Figure 2.2. (Left) Laponite particles are discs of 25 nm diameter and 1 nm thickness. They have a net negative charge on their faces and positive charges along their edges. (Right) When added to water, attractive interactions between the edges and faces result in a house of cards network, which viscosifies the water.

Another important phenomenon to keep in mind with regard to laponite particles is the increase in viscosity of the pre-gel solution. This can be explained by the aggregation of particles into a physical network, also called a ‘house of cards’ structure (Figure 2.2).²⁸ In this case, the positively-charged edges of the particles are attracted to the negatively charged faces of other particles, resulting in the ‘house of cards’ network, and thus to a large increase in viscosity. Since the attractive bonds in the above network are weak, physical bonds, they can be destroyed by shear, i.e., the sample is shear-thinning.²⁹ The network is reformed when shear is stopped.

2.2. TYPES OF MONOMERS USED TO CREATE HYDROGELS

Common monomers used to form hydrogels are acrylamide (AAm), N-isopropylacrylamide (NIPA) and N,N-dimethylacrylamide (DMAA) (structures shown in Figure 2.3).³⁰ Acrylamide is a highly hydrophilic monomer as it has an uninhibited amide group with two hydrogen atoms attached to the nitrogen atom. These hydrogen atoms can easily participate in hydrogen-bonding with amide units on other polymer chains.^{31,32} Ionic monomers like sodium acrylate (SA) or acrylic acid (AA) can also be polymerized to form hydrogels, either in conjunction with acrylamide (or other acrylamide-based monomers) to impart some ionic character to the polymer backbone, or as standalone monomers to get completely ionic polymer chains. Ionic hydrogels swell greatly and can absorb water up to 2000 times their own weight. As mentioned above, these ionic polymers cannot be crosslinked with laponite particles; instead, they are usually crosslinked using nonionic chemical crosslinkers like BIS.

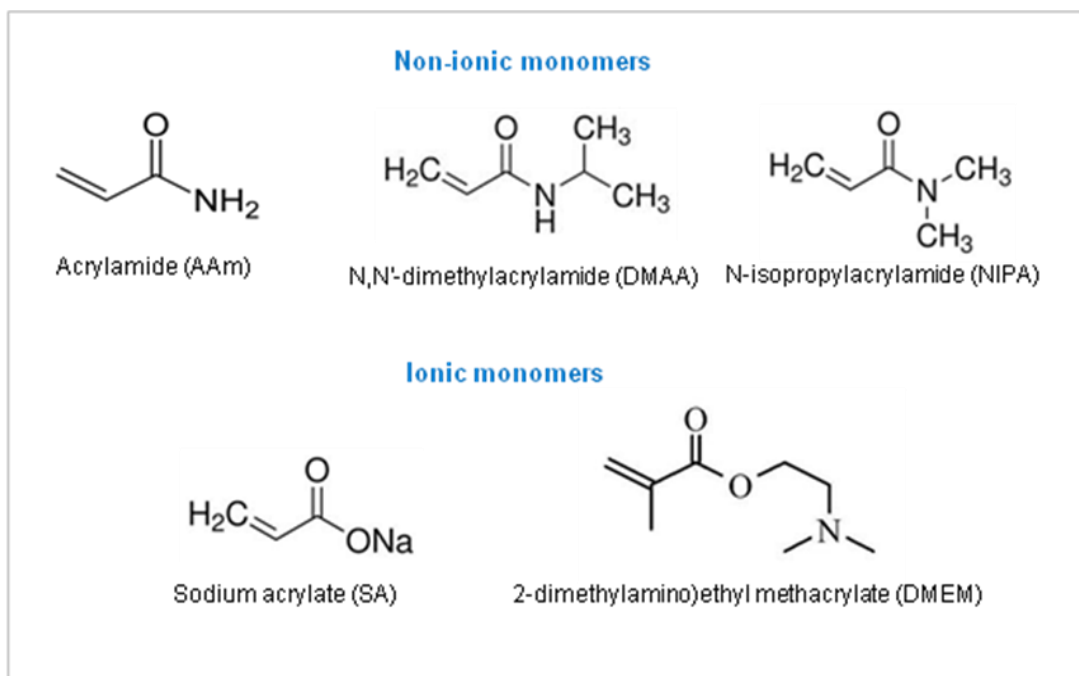


Figure 2.3. Chemical structures of different monomers used to make hydrogels. (Top) Nonionic monomers; (Bottom) Ionic monomers.

2.3. STIMULI-RESPONSIVE SWELLING AND SHRINKING OF HYDROGELS

Polymer hydrogels either swell or shrink compared to their original volume when exposed to changes in temperature, solvent composition, pH or ionic strength. Tanaka reported that acrylamide (AAm) hydrogels are sensitive to acetone concentration in water. At acetone concentrations greater than $\sim 40\%$ v/v in water, the polymer chains collapse and the gel shrinks. Also, the collapse of AAm gels varies with temperature, with the gel remaining in the shrunken state below 23°C .⁸ Thus, AAm gels display an *upper critical solution temperature* (UCST) of 23°C in a 40% acetone/water solution.

In the case of acrylamide derivatives like DMAA and NIPA, other hydrophobic groups like methyl (in DMAA) and isopropyl (in NIPA) are also present along the

polymer. This increases the hydrophobicity of the polymer chains. In the case of NIPA gels, the hydrophobicity significantly affects its behavior in water. As temperature increases to $\sim 32^\circ\text{C}$, the hydrophobic groups tend to aggregate and limit the exposure of polymer chains to water. As a result, water is expelled out and there is a sharp decrease in volume of NIPA gels. This temperature is called the *lower critical solution temperature* (LCST) of NIPA.⁶ Figure 2.4 shows the degree of swelling of a NIPA gel undergoing a sharp transition in volume between 32 and 33°C.

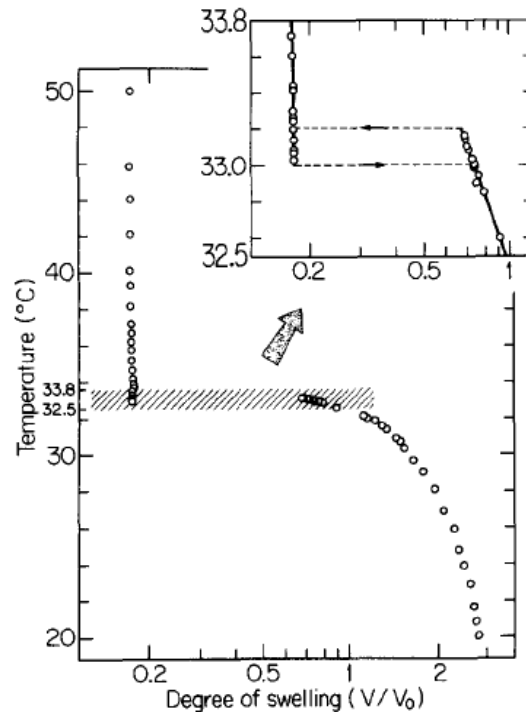


Figure 2.4. Plot of the degree of swelling of a NIPA gel in pure water as a function of temperature. Inset shows the slight hysteresis in the transition of PNIPA gels when going from a swollen state to a shrunken state and vice versa. Figure reproduced from Hirokawa et al.⁶

The gels discussed above are all composed of nonionic polymer chains. In comparison, ionic gels swell significantly more than nonionics. Tanaka was the first to

report on the effect of ionization of acrylamide (AAm) on the volume transition of AAm gels.³³ He found that hydrolysis of the amides on AAm to acrylic acid caused a 350-fold change in volume between the collapsed and swollen states of the gel. Beltran et al. studied the effects of ionizable comonomers SA and DMEM (structures in Figure 2.3) on the swelling behavior of NIPA (Figure 2.5).⁷ SA is an anionic monomer and imparts negative charges to the polymer chains whereas DMEM is a cationic monomer and imparts a basic character (positive charges) to the chains. Note from Figure 2.5 that the ionic gels swell much more than the nonionics and that their swelling is dependent on pH. This increase in swelling can be attributed to the repulsion between the ionized groups on the chains, which leads to expansion of the network due to the increased osmotic pressure within the gel.

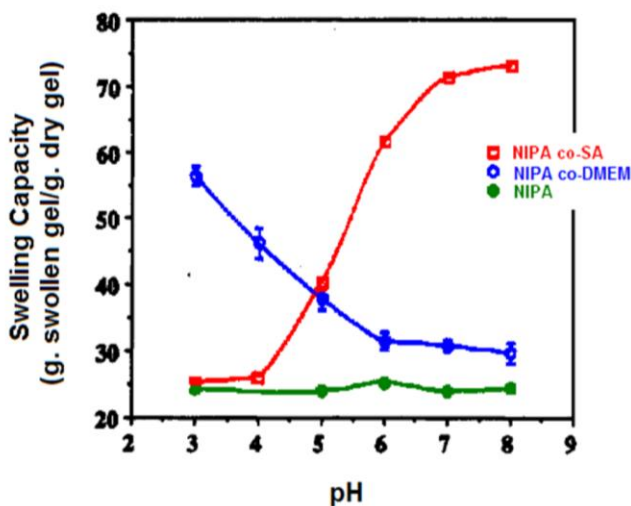


Figure 2.5. Swelling response curves as a function of pH for NIPA, NIPA-co-DMEM and NIPA-co-SA gels. Cationic NIPA-co-DMEM gels swell to their maximum extent in acidic pH whereas anionic NIPA-co-SA gels show the reverse behavior. Swelling of non-ionic NIPA gels remains unaffected by change in pH. Figure reproduced from Beltran et al.⁷

Chapter 3:

HOLLOW HYBRID GELS: SYNTHESIS AND PROPERTIES

3.1. INTRODUCTION

In this chapter, we will present our method for the creation of a new class of hybrid gels. The overall motivation for this work arises from the widespread interest in gels with new properties. Researchers have been looking to create gels with a combination of two or more properties (e.g., responsiveness to two or more stimuli). However, so far, this challenge has been mainly tackled from the viewpoint of polymer chemistry, i.e., researchers have focused on creating novel polymer backbones with more than one functional group, for example. Recently, in a paper by Banik et al.,¹⁴ our laboratory reported a new approach for combining dissimilar gels into one whole while preserving the character of each gel. The key to our approach was to bring two or more pre-gel mixtures into contact when their viscosities were sufficiently high, followed by polymerization of the whole system. Our approach allowed dissimilar gel components to be spatially placed next to each other in any desired fashion. Moreover, interfaces between the component gels in the hybrid were smooth and robust, i.e., not susceptible to mechanical failure.

The hybrid gels created by Banik et al. were solid gels. These solid gels showed the expected combination of properties, but their response was often quite slow. Our goal is to increase the response time of our hybrids and thereby to rapidly induce large

changes in gel volume and shape. It is known from Fick's law that the kinetics of swelling or deswelling of the gel is inversely proportional to smallest dimension of the gel.¹⁵ Towards this end, we report the creation of *hollow hybrid gels* wherein the overall size of the gel is still large but the effective size scale for diffusion is now much smaller, thus accelerating the response time of the gel. The procedure for making hollow hybrids is described below. We confirm the faster volume transition of hollow gels in comparison to solid gels of identical dimensions and composition. Finally, we use this procedure to create hybrid gels that undergo a significant change in overall shape upon exposure to an external stimulus.

3.2. EXPERIMENTAL SECTION

Materials: The monomers acrylamide (AAm), N,N-dimethylacrylamide (DMAA) and N-isopropylacrylamide (NIPA) were purchased from TCI America. The crosslinker N,N'-methylene-bis(acrylamide) (BIS) and the initiator potassium persulfate (KPS) were purchased from Sigma-Aldrich. The accelerant N,N,N',N'-tetramethylethylenediamine (TEMED) was purchased from J. T. Baker. The ionic monomers sodium acrylate (SA) and 2-(dimethylamino)ethyl methacrylate (DMEM) were purchased from Sigma-Aldrich. The inorganic clay laponite XLG (LAP) was obtained from Southern Clay Products. All chemicals were used as purchased without any further purification.

Sample Preparation: First, deionized (DI) water (Millipore) was degassed for 3 h by bubbling nitrogen gas through it. Monomers were dissolved in water to a total concentration of 1 M. The crosslinkers, either BIS or laponite particles, were then added.

BIS was usually added up to 0.5–1 mol% with respect to the concentration of monomer. Laponite content in the solution varied between 3–7.5 wt% with respect to the total weight of the solvent. In the case of laponite, to prevent particle clumping, it was important to add the particles very slowly while the solution was being vigorously stirred on a magnetic stirrer plate. Stirring was continued until the mixture appeared homogeneous and translucent. If the need arose, then these mixtures would be sonicated or centrifuged for a short time till any dispersed gas bubbles were removed. The initiator KPS and accelerant TEMED were then added in molar concentrations (with respect to total monomer) of 0.426 mol% and 0.735 mol% respectively. As soon as the initiator and accelerant were added, the polymerization reaction began and was allowed to continue in a nitrogen environment (or oxygen-free environment) at room temperature. Although the BIS-crosslinked gels would polymerize within 10–30 min, all gels were left to polymerize for about 20 h before extracting them from the vials/molds.

Solid Hybrid Gels: Solid hybrid gels were created by the following procedure, as typified for a hybrid of AAm-BIS (0.1%)/AAm-LAP (4%). The two pre-gel solutions were prepared in 10 g of water each to get a total gel volume of ~ 20 mL. The AAm-LAP pre-gel, which was already viscous, was added at the bottom of a vial. The AAm-BIS pre-gel was then added on top. The vial was sealed and allowed to polymerize for 20 h at room temperature. The vial was then broken and the hybrid gel was removed and washed.

Hollow Hybrid Gels: Hollow hybrid gels were created by the following procedure, as typified for a hybrid of AAm-BIS (0.1%) and AAm-LAP (4%). The hollow hybrid gel

had a total gel volume of ~ 10 mL with equal amounts of both pre-gel mixtures. To make the hollow hybrid, a 5 mL vial of 16 mm diameter and 50 mm length (with cap unscrewed) was filled with water, sealed off with parafilm, and placed inside a bigger 20 mL vial of 25 mm diameter and 55 mm length. The first pre-gel mixture (AAm-LAP) was poured carefully in the annulus around the smaller vial, with care taken to ensure that no air bubbles were formed. Then the same was done with the second pre-gel (AAm-BIS). The bigger vial was then allowed to polymerize for 20 h at room temperature. The vial was then carefully broken and the hollow hybrid gel was extracted and washed.

Swelling Comparison of Solid and Hollow Gels: Gels of AAm-co-DMEM/BIS (0.1%) and AAm-co-SA/BIS (0.1%) were compared in their solid and hollow forms. Both sets of gels had 90 mol% of AAm and 10 mol% of the ionic DMEM or SA monomer. AAm-co-DMEM/BIS (0.1%) gels were created as two sets of solid and hollow hybrid gels with two different outer diameters. The first set of comparison had solid and hollow gels with outer diameter of 25 mm each, with the hollow gel thickness being 5 mm. The second set had one solid gel and two hollow gels of outer diameter of 15 mm each, with the hollow gels being 1.8 mm and 1.2 mm thick respectively. AAm-co-SA/BIS(0.1%) gels were also created in solid and hollow gel forms with outer diameters of 25 mm each, with the hollow gel having a thickness of 5 mm. The gels were washed thoroughly before being immersed in DI water for a week. The beakers in which the gels were immersed were constantly replenished with DI water because the water levels would go down as the gels swelled. Only the outer diameter of the gels were measured as a parameter to gauge the extent of swelling.

3.3. RESULTS AND DISCUSSION

3.3.1. SOLID HYBRID GELS (SHGs)

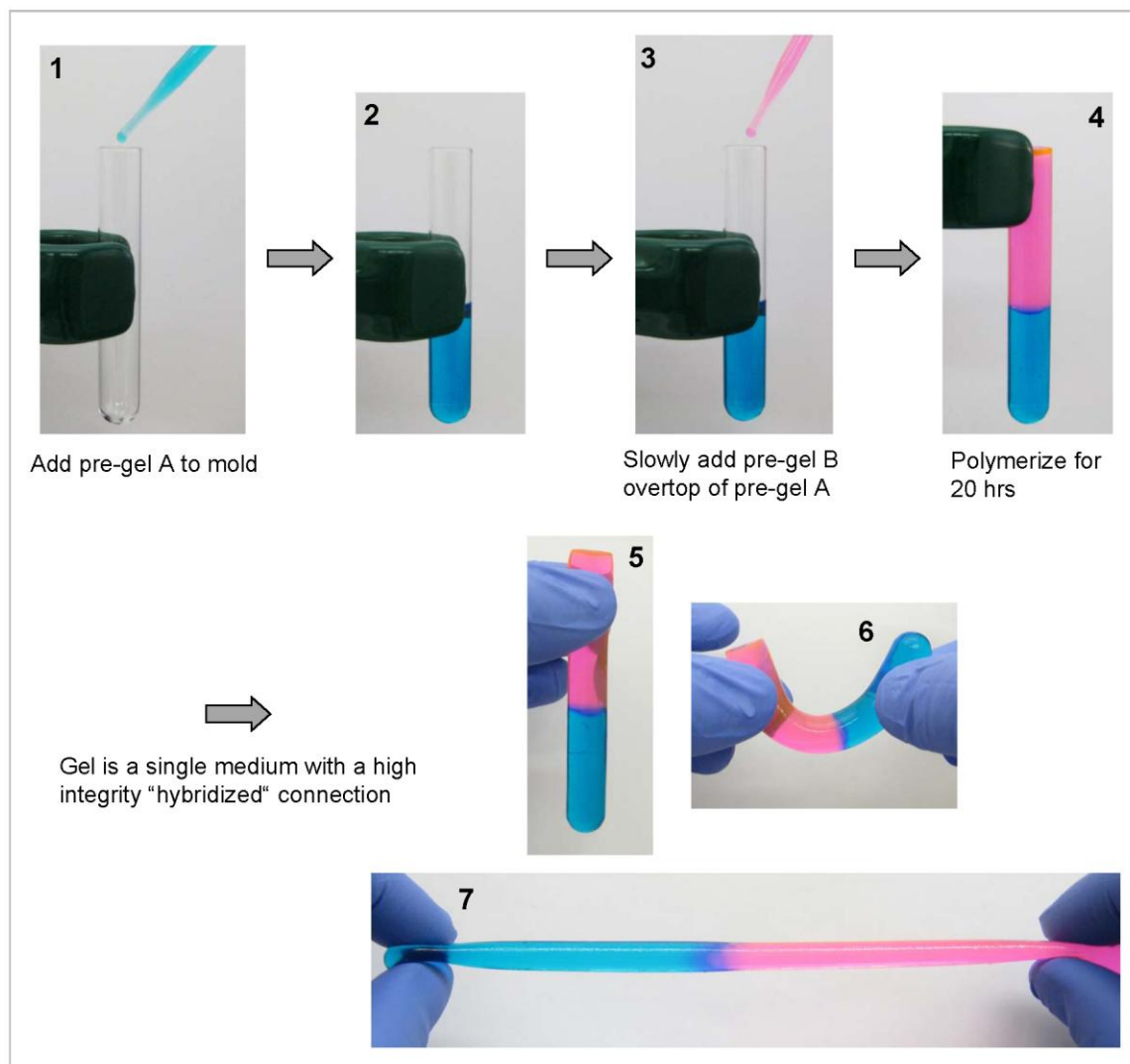


Figure 3.1. Procedure for preparing a solid hybrid gel. (1), (2) Viscous pre-gel solution A (dyed blue) is pipetted into a glass tube and (3) the other pre-gel solution B (dyed pink) is then gently pipetted over the first one. (5), (6), (7) After polymerization, the hybrid gel is a single mass that can be stretched to great extents without tearing apart at its interface. Figure reproduced from Banik, Fernandes et al.³⁴

The preparation of solid hybrid gels (SHGs) is illustrated in Figure 3.1. The key to the approach is to stack the two pre-gel solutions when their viscosities are sufficiently

high to prevent any convective mixing. For example, in the present study, the pre-gel A corresponding to Figure 3.1 is a mixture of AAm and 4% LAP. This is introduced first into the tube and it is already a viscous sample. Next, pre-gel B, a solution of AAm and 0.1% BIS is introduced on top of the pre-gel A. The high viscosity of pre-gel A prevents convective mixing at the interface between the two pre-gels. Upon polymerization of the whole system, we obtain a solid hybrid gel (SHG) that shows well-separated regions of the two different gels. The interface is strong and robust and the gel does not rupture on twisting or high stretching.

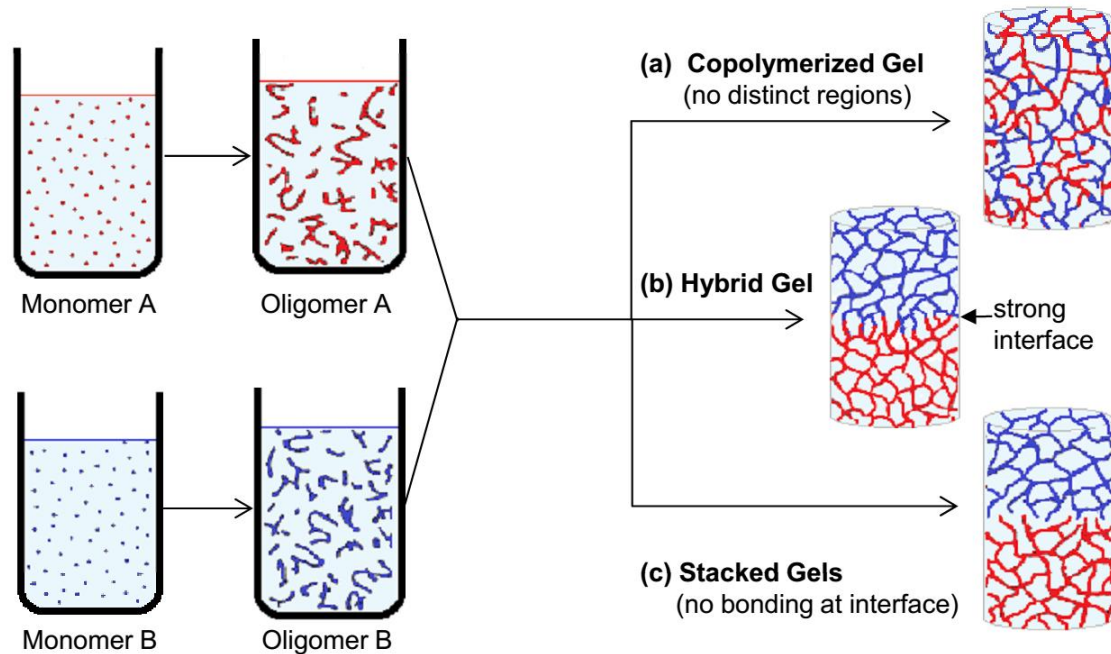


Figure 3.2. Sequential preparation of a hybrid gel of monomers A (red) and B (blue). The difference between our technique and other methods of preparing dual polymer network gels is the contacting of the two pre-gel solutions A and B when their viscosities are high. The high viscosities allow only for diffusive mixing at the interface while almost eliminating convective mixing. The result is a single hybrid gel that retains the constituent polymer networks in separate regions, giving it properties of both polymer gels, as shown by (b). In comparison, if monomers A and B are pre-mixed thoroughly, one ends up with a copolymerized gel, as shown in (a). On the other hand, if A and B are nearly completely polymerized and then contacted, there is very little bonding at the interface and one ends up with a stack of two gels, as shown in (c).

Figure 3.2 shows the difference between our technique and other methods of preparing dual polymer gels. Specifically, the key in our case is the high viscosity of the pre-gel solutions when they are brought into contact. At the same time, the polymers are not completely formed and therefore there is still some diffusion and thus some covalent bond formation at the interface between gel A and gel B. This ensures a robust interface. If the pre-gels are not viscous, they will undergo mixing and one will end up with a gel that is a copolymer of A and B, which will not retain the properties of gel A or of gel B. However, if the polymerizations of gel A and gel B are nearly complete, they cannot be joined at the interface in a robust way. Thus, the significance of our technique is that within the SHG, the component gels retain their distinctive character while also being bonded strongly at the interface.

3.3.2. HOLLOW HYBRID GELS (HHGs)

We now present a method to create a new class of gels that we call *hollow hybrid gels* (HHGs). The basic technique is the same as described above, except that we use a mold so that the center of the hybrid gel remains hollow. The simplest version of the mold is made by arranging a small vial or tube concentrically inside a bigger vial. The smaller vial is filled with water to increase its inertia. The pre-gel solutions are then pipetted in the annular space between the two vials, one on top of the other, and polymerization is conducted. As seen in Figure 3.3, the resulting HHG has a hollow center and a strong interface between the two gel portions, just like the SHGs. The vial diameters dictate the wall thickness of the HHG, which in this case was 5 mm.

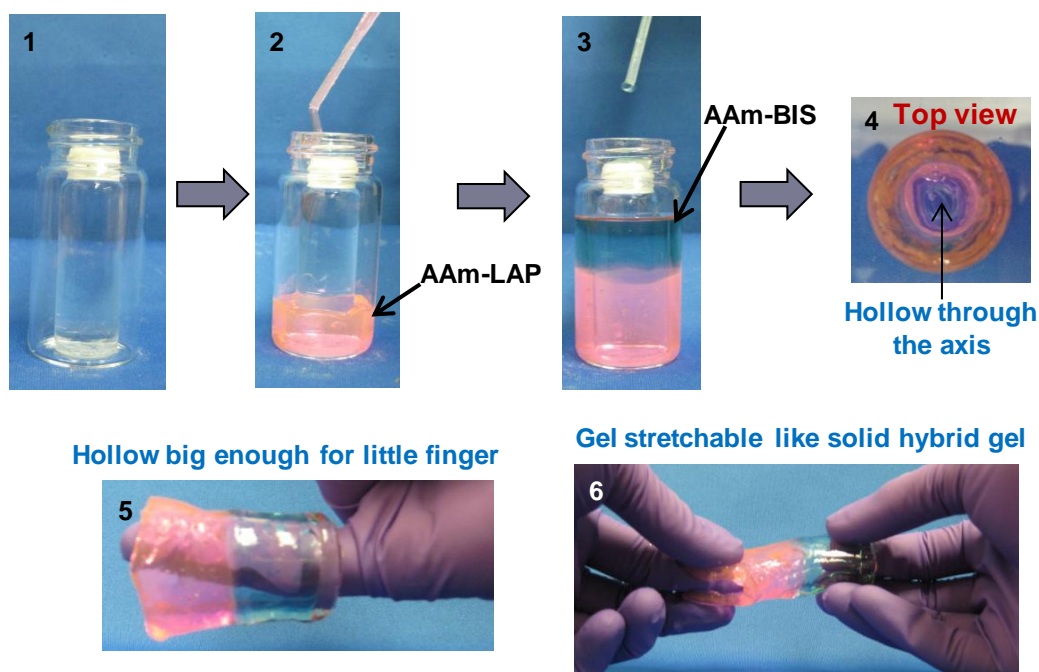


Figure 3.3. Procedure for making hollow hybrid gels. Here, two regions of the hybrid have the same monomer, acrylamide (AAm) but different crosslinkers, i.e., laponite particles (LAP) or bis-acrylamide (BIS). (1) A mold is created by placing or gluing a smaller glass cylinder within a bigger one. (2) A highly viscous pre-gel solution of AAm-LAP is pipetted into the space in the mold. (3) The second pre-gel solution of AAm-BIS is then gently pipetted over the first pre-gel so as not to induce convective mixing at the interface. (4) The hollow hybrid gel extracted in the shape of the cylindrical mold, shows two distinct and smooth surfaces. The hollow gel is strong enough that it can be held using one's fingers, as shown by (5) and stretched without breaking, as shown by (6).

3.3.3. SWELLING KINETICS OF SOLID AND HOLLOW GELS: COMPARISON

We made two sets of gels, one set of solid gels and the other set of hollow gels, each in the form of cylinders with the same outer diameter (25 mm) and length (40 mm) and with the thickness of the hollow gel being 5 mm. The rates of swelling of the two in water (at pH 7) were then compared by measuring their outer diameters over a period of time. Measurements were continued till equilibrium was attained, i.e., the diameters reached a constant value. For these comparisons, we focused on ionic gels because these

swell much more than nonionics. Note that the gels being compared are not hybrids, i.e., they had the same monomer composition over the entire gel.

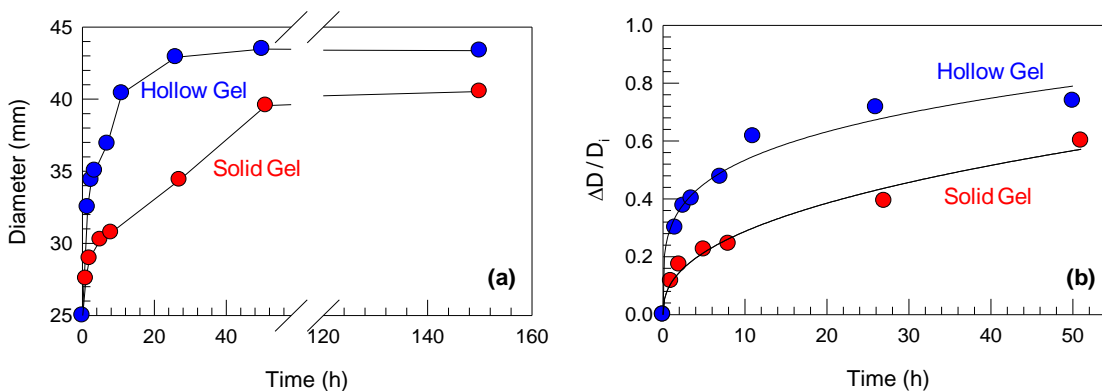


Figure 3.4. (a) Outer diameter of AAm-co-DMEM gels as a function of time for both solid and hollow gels. Both swell to almost the same extent at equilibrium, but the hollow gel swells much faster. (b) Data in (a) replotted for the fractional change in diameter ($\Delta D/D_i$) vs. time. At short time scales, the plots can be fitted by a power law relation, as given by eq (1).

The first comparison of solid and hollow gels was for AAm-co-DMEM (90% AAm, 10% DMEM), polymerized with 0.1% BIS. Note that DMEM is a cationic monomer. Data for the swelling of these gels in water at pH 7 is compared in Figure 3.4a. The solid gel (initial diameter $D_i = 25$ mm) swelled up to a maximum extent of 40.5 mm in about 150 h. The hollow gel with the same D_i and with a thickness of 5 mm swelled up to a diameter of 43.4 mm (slightly more than the solid gel), but more importantly in only about 50 h, i.e., in one-third the time. This clearly shows the faster swelling of the hollow gel compared to its solid counterpart. The same data are replotted in Figure 3.4b for the fractional change in diameter ($\Delta D/D_i$) vs. time t , where $\Delta D = D(t) - D_i$. The initial portion of these plots can be fitted to the following power-law expression^{35,36}:

$$\frac{\Delta D}{D_i} = kt^n \quad (1)$$

where k is a constant incorporating characteristics of the polymer network and the solvent in the gel and n is the diffusional exponent indicative of the transport mechanism. For the present data, we obtained n as 0.42 and 0.24 and k as 0.11 and 0.31 for the solid and hybrid AAM-co-DMEM gels respectively.

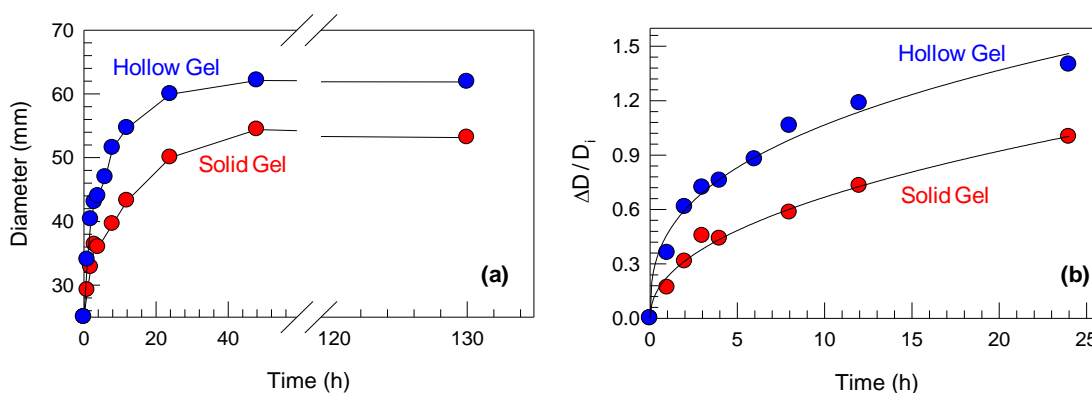


Figure 3.5. (a) Outer diameter of AAm-co-SA gels as a function of time for both solid and hollow gels. Again, the hollow gel swells much faster. (b) Data in (a) replotted for the fractional change in diameter ($\Delta D/D_i$) vs. time. At short time scales, the plots can be fitted by a power law relation, as given by eq 1.

The next comparison of solid and hollow gels was for AAm-co-SA (90% AAm, 10% SA), polymerized with 0.1% BIS. Data for these anionic gels in water at pH 7 are shown in Figure 3.5a. This time, the solid gel ($D_i = 25$ mm) swelled up to a maximum of 52.9 mm in ~ 50 h. The hollow gel with the same D_i and with a thickness of 5 mm swelled up to a higher maximum of 62.7 mm in a shorter time of about 30 h. Once again, the hollow gel is seen to swell much faster than its solid counterpart. Also, note that the maximum extents of swelling of the AAM-co-SA gels (both solid and hollow) are higher

than those for gels of AAm-co-DMEM. This is reasonable because the data are for swelling in water at pH 7, which is much closer to the optimum pH for the AAm-co-SA than for AAm-co-DMEM (see Figure 2.5, Chapter 2). The data in Figure 3.5a are again replotted in Figure 3.5b for the fractional change in diameter ($\Delta D/D_i$) vs. t , and the plots are fitted to eq 1. In this case, we obtained n as 0.46 and 0.36 and k as 0.23 and 0.47 for the solid and hollow AAm-co-SA gels respectively. The fit parameters for the fits of eq 1 to the swelling plots of AAm-co-DMEM and AAm-co-SA are shown in Table 1 (the quality of fits in all cases was very good, with $R^2 > 0.97$).

Table 1. Parameters Obtained by Fitting Eq 2 to Dye Release Curves in Figure 7

Polymer gel		n	k
AAm-co-DMEM	Solid gel	0.42	0.11
	Hollow gel	0.24	0.31
AAm-co-SA	Solid gel	0.46	0.23
	Hollow gel	0.36	0.47

On the whole, the data in Figures 3.4 and 3.5 confirm the faster swelling of hollow gels compared to solid gels. This is due to the fact that the smallest dimension pertinent to swelling in the hollow gels is the wall thickness, which is ~ 5 mm. The relevant counterpart for the solid gels is the outer diameter of the cylinder, which is about 25 mm, i.e., a much larger dimension. Diffusion in the main mode of mass transport into the gel, and diffusive processes scale with the smallest dimension of the gel. This is clear from the equation derived by Einstein in his treatment of diffusion due to Brownian motion. From the solution to the problem of motion of a single Brownian particle, we get,

$$\lambda_x = \sqrt{\bar{x}^2} = \sqrt{2Dt}$$

which shows that the mean displacement of a diffusing particle is proportional to the square root of time. Hence, the smaller the length to be diffused through, the lesser is the time taken for the diffusion.

This explains the faster swelling of the hollow gels. In addition, we note that the extent of swelling may also be slightly larger for the hollow gels. This can be explained by modifying the Fick's second law of diffusion in a thin film of thickness δ at short time scales³⁷:

$$\frac{M_t}{M_\infty} = 4 \left(\frac{Dt}{\pi\delta} \right)^{1/2} = k' t^{1/2} \quad (2)$$

where M_t and M_∞ are the amount of species diffused at time t and at infinity respectively and D is the diffusivity of the species. We see that the constant k' is in turn proportional to the diffusivity of the species and inversely proportional to the critical length (thickness δ) of the film. Peppas et al. modified equation (2) to reflect diffusion in a polymeric system as given in equation (1). Thus, we can infer that the constant k in equation (1) must depend on the inverse of the critical length scale of the gel, or in other words, k will be larger for smaller values of thickness of the gel and hence, result in enhanced swelling. This is indeed the trend observed in both sets of hollow gels when compared to their solid gel counterparts, as shown in Table 1.

Also, the values of n obtained for solid gels are close to the ideal value of 0.45 established for Fickian transport in cylindrical polymer systems.³⁷ On the other hand, if

$0.45 < n < 0.89$, then the transport mechanism is said to be non-Fickian or anomalous transport, and if $n = 0.89$, then it is Case-II transport, which is independent of time.³⁸ Peppas also discusses that although n is equal to or higher than the threshold value in case of Fickian diffusion, it is possible to get a lower value in case of swollen polymer systems, as shown in Table 1.³⁹ The lower values of n obtained in case of the hollow gels affirms that their swelling behavior cannot be modeled after either cylindrical or slab-like templates.

It should be noted that the plots of fractional change in diameter ($\Delta D/D_i$) vs. t in Figure 3.4b and 3.5b were done when the gels were swelling from a lower content of water. If the fully swollen gels were subjected to conditions averse to their swelling (opposite pH or dry conditions), they would then shrink because of the polymer network expelling water out of the gels. As a result, they would retain their original shapes that they started from before swelling. Then, a plot of *fractional decrease in diameter* vs. time would be one of exponential decay, with the bulk of the decrease in diameter occurring in the initial time frames but slowing down as the water content reached its equilibrium level in the gel.

3.3.4. STIMULI-RESPONSIVE HHGs

We proceeded to create hollow hybrid gels (HHGs) having two zones with different stimuli-responsive properties. The first HHG had a zone of NIPA crosslinked with LAP (3%) and another zone of DMAA crosslinked with LAP (4%). As noted in Section 2.3, NIPA is thermoresponsive (shrinks above its LCST) whereas DMAA is not.

Also, we used a higher LAP concentration in the DMAA portion to inhibit its changes in volume. Figure 3.6 shows the result of placing this gel in hot water ($\sim 45^{\circ}\text{C}$), which is above the LCST of NIPA gels (32°C). As expected, the NIPA portion of the gel turns turbid and shrinks due to the temperature being above the LCST. In contrast, the DMAA portion remains clear and expands slightly due to swelling. Thus, the initial tubular hybrid is transformed into a funnel shape with a different diameter for the top portion and the bottom portion. On placing the gel back in water at room temperature (23°C , below the LCST of NIPA), the NIPA portion reverts to its initial clear and swollen state and the gel recovers its symmetric tubular shape.

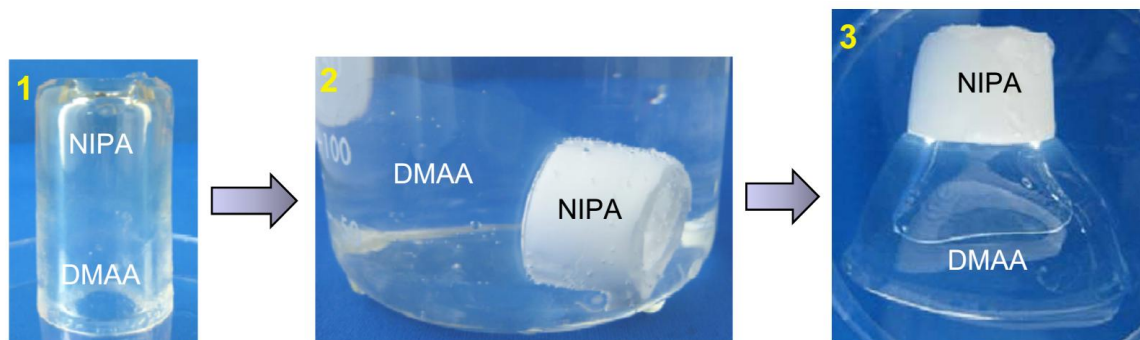


Figure 3.6. Behavior of a NIPA/DMAA hollow hybrid gel in water at 45°C . (1) The as-made gel before it is immersed in water. (2) As soon as it is immersed, the NIPA zone of the gel starts shrinking and turns turbid whereas the DMAA zone remains clear and swells slightly. (3) After 1 h, the NIPA zone has shrunk appreciably whereas the DMAA zone has expanded a bit more.

Another such HHG was made with one zone of AAm crosslinked with 3% LAP and another zone of DMAA crosslinked with LAP (4%). As noted in Section 2.3, AAm shrinks in water containing acetone above a critical level whereas DMAA is not sensitive to acetone. We placed the AAm/DMAA hybrid in a 50% acetone solution in water at room temperature (22°C). As shown by Figure 3.7, the AAm zone shrinks and turns

opaque, while the DMAA zone slowly starts swelling to absorb the solvent. After a day, the AAm portion of the gel has shrunken appreciably while the DMAA portion has swollen appreciably. Thus, once again, the initial tube is transformed into a funnel shape with a significant difference in diameter between the two zones, and this shape change can also be reversed by placing the gel back in water.

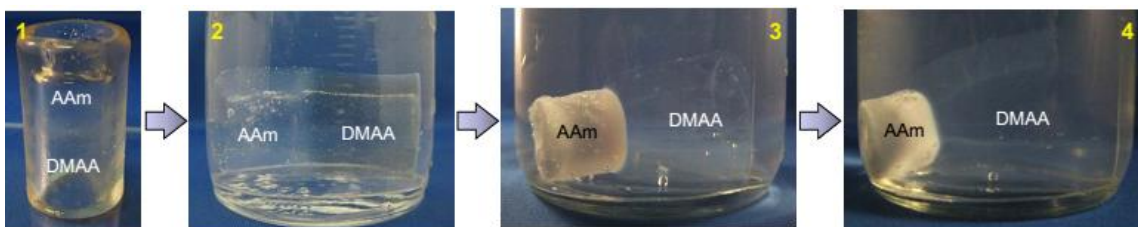


Figure 3.7. Behavior of a DMAA/AAm hollow gel in a 50/50 solution of acetone/water at room temperature. (1) The initial gel. (2) Soon after immersion, the AAm zone starts showing turbidity. (3) Within 1 h, the AAm zone begins to shrink. (4) After 1 day, the AAm zone has shrunken to half its original size, whereas the DMAA zone has swelled up. The overall gel has a funnel shape due to the different diameters in the two zones.

Next, we created HHGs with one ionic and one nonionic zone. The first such HHG had a zone of nonionic DMAA crosslinked with 7.5% LAP and the other of AAm-co-DMEM (90% AAm, 10% DMEM) crosslinked with 0.1% BIS. Note that DMEM is a cationic monomer, and for its zone, we used BIS instead of LAP as the crosslinker because laponite particles are incompatible with ionic monomers. Also, for the DMAA zone, we used a high LAP concentration to inhibit its swelling. The above HHG was placed in excess water at ambient pH and temperature, and the results are shown in Figure 3.8. We observe substantial swelling in the ionic zone of the gel whereas the nonionic DMAA zone swells only a little. After 4 days, the ionic zone has increased to about 4 times its original diameter whereas the nonionic zone is only slightly larger than

its original diameter. The overall gel thus has the shape of a bottle with a small neck relative to its body. Similar results were also obtained for a different HHG where we used the anionic monomer SA instead of the cationic DMEM. This gel consisted of the same DMAA/LAP zone and a zone of AAm-co-SA (90% AAm, 10% SA) crosslinked with 0.1% BIS. In water at ambient pH and temperature, this gel also shows substantial swelling of its ionic zone relative to its nonionic zone (Figure 3.9). In this case, the diameter of the ionic zone reaches about 3 times relative to its original diameter.

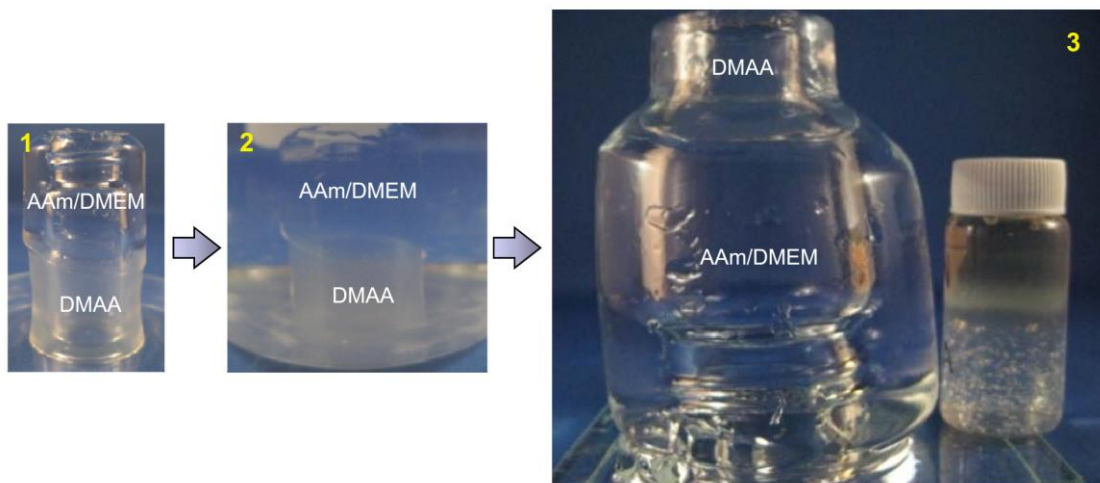


Figure 3.8. Behavior of DMAA/AAm-co-DMEM hollow hybrid gel in water at ambient pH and temperature. (1) The initial as-made gel. (2) Gel immersed in water. (3) After 4 days, the gel is removed from water and photographed next to the vial for size comparison. The DMEM-containing (cationic) zone of the gel has swollen appreciably whereas the DMAA zone (nonionic) has swollen just a little. The overall gel has a bottle-like shape due to the different diameters in the two zones.

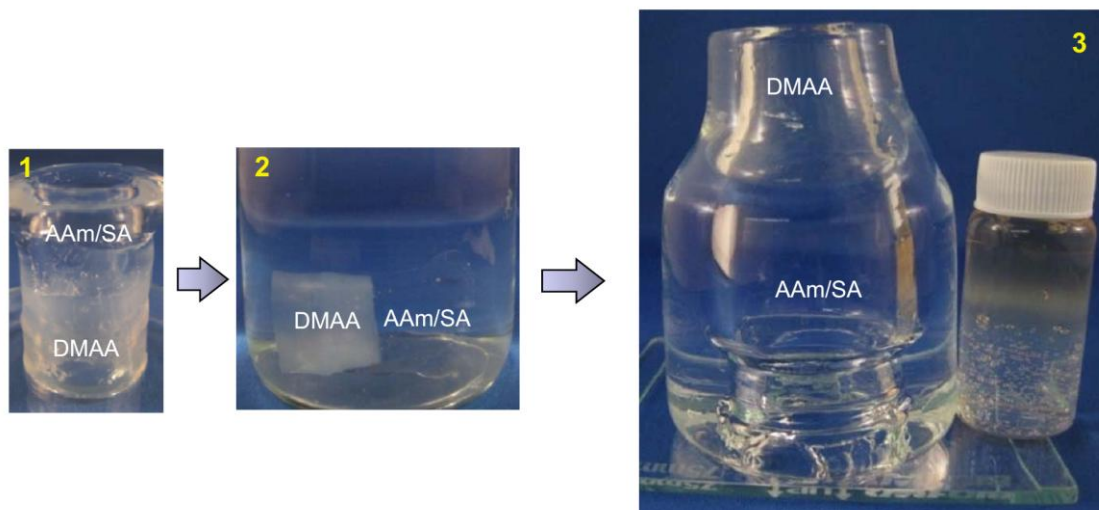


Figure 3.9. Behavior of DMAA/AAm-co-SA hollow hybrid gel in water at ambient pH and temperature. (1) The initial as-made gel. (2) Gel immersed in water. (3) After 4 days, the gel is removed from water and photographed next to the vial for size comparison. The SA-containing (anionic) zone of the gel has swollen appreciably whereas the DMAA zone (nonionic) has swollen just a little. The overall gel has a bottle-like shape due to the different diameters in the two zones.

As shown above, juxtaposing different polymer gels next to each other in a hybrid gel can result in unique shapes after exposure to an external stimulus. This can be potentially exploited for certain applications. We illustrate two such applications of shape-changing gels below. First, we attempted to create a hollow hybrid gel capable of holding on to a object and exerting enough ‘grasping’ force to be able to pick up the said object. For this, we created a hybrid with one zone of DMAA crosslinked with 7.5% LAP and the other of NIPA crosslinked with 3% LAP. The inner diameter of the HHG was designed to be slightly more than 15 mm. A vial of 15 mm outer diameter was inserted into the hollow region of the hybrid. In this case, the HHG is not able to grasp the vial in its unaltered state, as shown in Figure 3.10a. But when the hybrid gel with the vial is immersed in hot water at 50°C, the shrinking of the NIPA zone allows this portion to

contract around the vial, grasping it tightly. When the HHG is now lifted by its DMAA portion, it is able to lift up the grasped vial off the ground cleanly and without any slippage (Figure 3.10b). Thus, we have successfully demonstrated a practical application of a stimuli-induced shape change in a gel. Such applications could become useful in soft robotics or related areas.

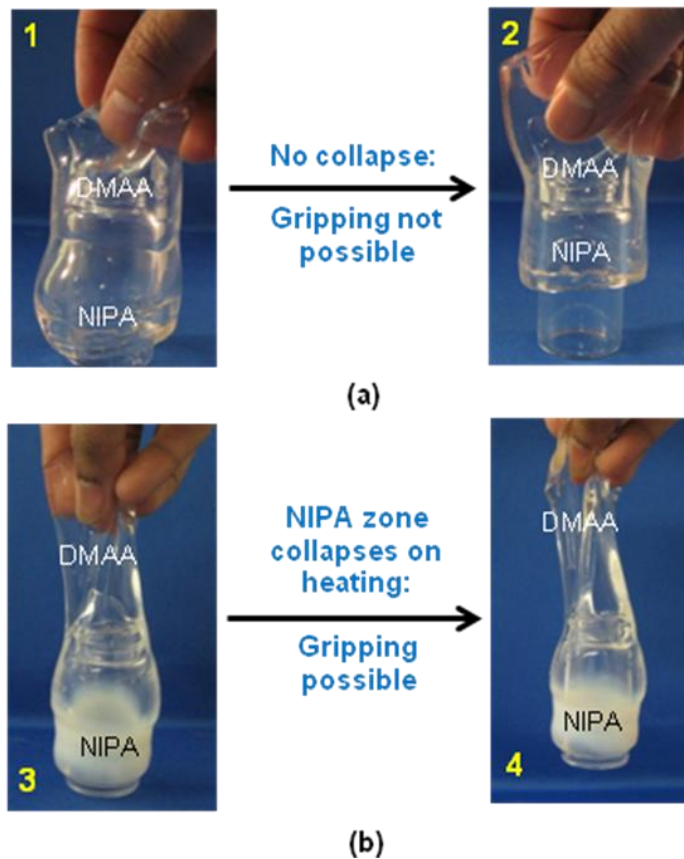


Figure 3.10. ‘Grasping’ application using a shape-changing DMAA/NIPA hollow hybrid gel. (a) A vial is inserted into the middle of the hollow gel. The vial diameter is slightly less than the diameter of the hollow region, and in this case, the gel is not able to grasp and pick the vial up. (b) When the vial/gel combination is immersed in hot (50°C) water, the NIPA portion of the HHG collapses around the vial and thereby grasps the vial. Upon lifting the HHG by its DMAA portion, the vial can now be lifted off the ground.

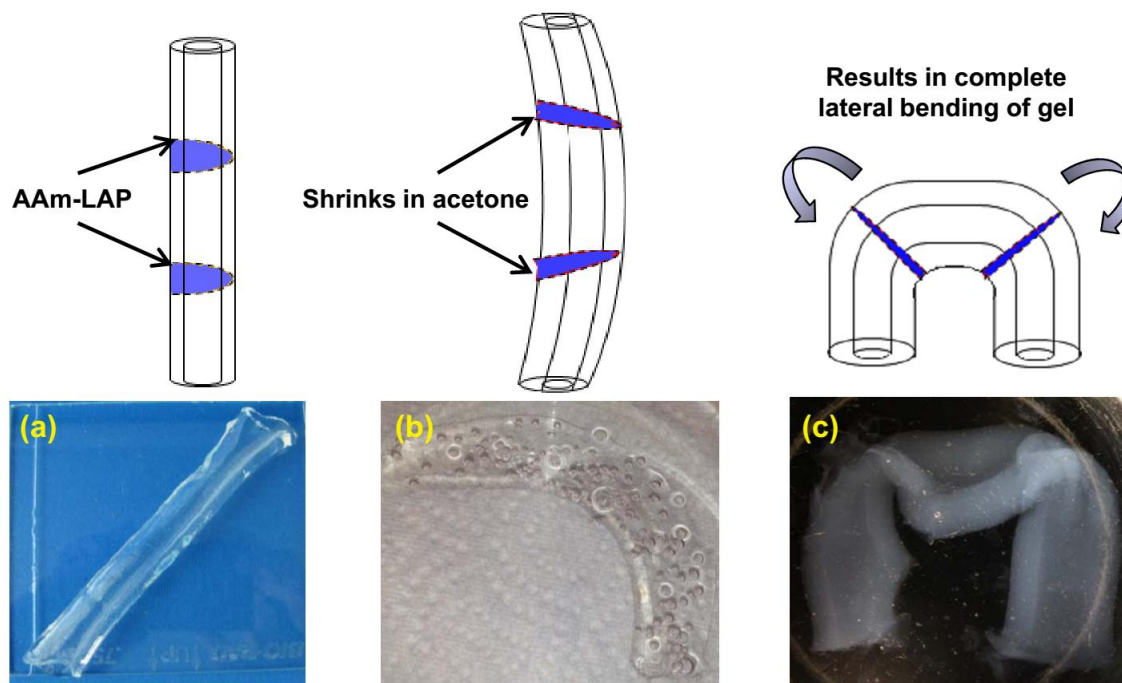


Figure 3.11. Kink-induced shape change in DMAA/AAm hollow hybrid gel. (a) Gel is prepared with a DMAA body and two AAm ‘kinks’ at specific locations. (2) When immersed in a 50-50 acetone-water mixture, the gel bends into a boomerang-like shape. (3) When returned to pure water, the gel is bent completely at the points where the kinks are present.

Our next attempt was to induce a change in three-dimensional (3-D) shape of a gel. For this, we made an HHG in the shape of a tube but with two kinks at specific positions, as shown in Figure 3.11a. The body of the tube was composed of DMAA crosslinked with 4% LAP. The kinks were triangular pie-like sections and were made of AAm crosslinked with 3% LAP. This HHG was placed in a 50/50 solution of acetone and water. As expected, the AAm-filled kinks of the tubular HHG shrink in the acetone environment. After 4 h, the shrinking at the two kinks triggers the bending of the tubular gel along its length into a boomerang shape (Figure 3.11b). Note that the body of the gel (DMAA) is insensitive to the acetone. Interestingly, when the gel is immersed back in

pure water, the boomerang shape gets accentuated more into a right-angled bent shape (Figure 3.11c). Further work is necessary to determine if the original shape can be recovered under some conditions or if the shape change is completely irreversible. In any case, our work shows that it is possible to create hybrid gels that show significant and unprecedented changes in shape in response to various stimuli. In particular, changes in the shapes of soft objects in 3-D are not accessible by previous methods and so that is our key contribution.

3.4. CONCLUSIONS

In this chapter, we have showcased a new approach for making hollow hybrid gels (HHGs) that combine different polymer gels in one whole gel and yet have them retain their unique properties individually. We demonstrated that these hollow hybrid gels are superior to their predecessors (i.e., solid hybrid gels) with respect to their rate of swelling and thereby in the expression of their response to various stimuli. We further showed that we can combine different monomers and crosslinkers in the same gel to control their response to stimuli and utilize these transitions to change the shape of our HHGs. Lastly, we were able to direct the responses of these gels towards changing their shape in a controlled and desired fashion.

Chapter 4: CONCLUSIONS AND RECOMMENDATIONS

4.1. CONCLUSIONS

In this thesis, we were able to expand the approach of making hybrid gels by combining polymer gels of distinct and dissimilar properties towards making hollow hybrid gels. Hollow hybrid gels have a unique advantage over solid hybrid gels in that they have a faster expression of their response to stimuli because of their smaller effective dimension (i.e., the thickness of the wall), which in turn enhances diffusion rates. At the same time, their form allows them to retain much of the mechanical strength and integrity of the solid gels.

We were able to demonstrate the effectiveness of this new technique by the many experiments conducted with hollow hybrid gels. We were successfully able to show the efficiency of hollow hybrid gels over solid hybrid gels in response times and swelling rates. We also created gels that could change their morphology in response to stimuli by exploiting the many different volumetric transition behaviors of acrylamide-based polymers. Such controlled expression gels can be of tremendous use in applications where such functionalities are highly desirable, like gastric retention devices and macroscale drug delivery. We also showed that we could not only change the shapes of the gels but also control the change to make controlled transitions between different shapes. This subtle advantage of hollow hybrid gels over regular gels makes them ideal candidates for use in applications like sensor technology.

Lastly, we would like to note that hollow hybrid gels can serve as a template for making gels of many different morphologies. While we have demonstrated only a cylindrical hollow through the center, other shapes can be easily incorporated. Along with the existing advantage of the hybrid gel technology, this improved approach can be used to create gels with myriad possible shapes, properties and applications.

4.2. FUTURE DIRECTIONS

Hybrid gels technology as demonstrated by Banik et al. holds a lot of promise in the creation of new hydrogels with increased and diverse functionalities within the same material. Hollow hybrid gels can expand the scope of these novel gels by being able to incorporate different morphologies. It can be thought of as adding another degree of freedom to the design of hydrogels. Coupled with the ease of preparing them – lack of sophisticated molds – they make ideal candidates for research in biomedical devices, drug delivery and sensor technologies.

One possible avenue along which research can be performed with these hollow hybrid gels is in the topic of gastric retention devices. These devices basically stop the outflow of digested food from the pylorus of the stomach. The challenge is to get a gastric retention device into the stomach through the small opening of the esophagus while at the same time be big enough to act as a stopper at the pylorus. Hollow hybrid gels can be ideal in these situations and can be made so as to have one part swell to great volumes in the acidic pH of the stomach while have the other part relatively unswollen and act to block the opening to the duodenum.

Another application can be to create automatic flow systems in which the direction of flow of a fluid can be changed depending on the fluid that flows through the tube. A hollow hybrid gel tube, similar to the bending HHG described in Figure 3.11, can be created which can respond to a certain liquid that will trigger its shape change to create a bend that can direct flow to a different target.

The elastic properties of polymer hydrogels and their capacity to act as tissue scaffolds can be utilized in creating vascular grafts as replacements for diseased blood vessels in the human body. An obvious example of such a blood vessel is the human aorta, which has similar dimensions to the 25 mm diameter and 5 mm thickness HHGs demonstrated here.⁴⁰ In what is known as aortic dissection, blood can penetrate between the innermost (intima) and middle (media) layers of the aorta due to a tear in the intima. In such cases, the high blood pressure from the heart will make blood flow in between the two layers of the aorta resulting in death from decreased blood supply to the critical organs. As aortic dissection in most cases leads to sudden death, quick replacement of the affected area becomes a big priority.⁴¹ Hollow hybrid gels can be used to create aortic tissue scaffolds, as the tri-layer structure of the aorta and its curvature can be perfectly reproduced through the hollow hybrid technique.

REFERENCES

- [1] Tanaka, T. "Gels." *Scientific American* **1981**, *244*, 124-138.
- [2] Yin, H.; Stossel, T. "Control of cytoplasmic actin gel–sol transformation by gelsolin, a calcium-dependent regulatory protein." *Nature* **1979**, *281*, 583-586.
- [3] Stossel, T. P. "The Structure of Cortical Cytoplasm." *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences* **1982**, *299*, 275-&.
- [4] Cooper, G. M. *The Cell: A Molecular Approach*, 2 ed.; Sinauer Associates: Sunderland, MA, 2000.
- [5] Ye, Q.; Zünd, G.; Benedikt, P.; Jockenhoevel, S.; Hoerstrup, S. P.; Sakyama, S.; Hubbell, J. A.; Turina, M. "Fibrin gel as a three dimensional matrix in cardiovascular tissue engineering." *European Journal of Cardio-thoracic Surgery* **2000**, *17*, 587-591.
- [6] Hirokawa, Y.; Tanaka, T. "Volume Phase-Transition in a Nonionic Gel." *Journal of Chemical Physics* **1984**, *81*, 6379-6380.
- [7] Beltran, S.; Baker, J. P.; Hooper, H. H.; Blanch, H. W.; Prausnitz, J. M. "Swelling Equilibria for Weakly Ionizable, Temperature-Sensitive Hydrogels." *Macromolecules* **1991**, *24*, 549-551.
- [8] Tanaka, T. "Collapse of Gels and the Critical Endpoint." *Physical Review Letters* **1978**, *40*, 820-823.
- [9] Ricka, J.; Tanaka, T. "Swelling of Ionic Gels - Quantitative Performance of the Donnan Theory." *Macromolecules* **1984**, *17*, 2916-2921.
- [10] Mamada, A.; Tanaka, T.; Kungwatchakun, D.; Irie, M. "Photoinduced Phase-Transition of Gels." *Macromolecules* **1990**, *23*, 1517-1519.
- [11] Sharon, E. "Swell Approaches for Changing Polymer Shapes." *Science* **2012**, *335*, 1179-1180.
- [12] Peppas, N. A.; Langer, R. "New Challenges in Biomaterials." *Science* **1994**, *263*, 1715-1720.
- [13] Ramamurthi, A.; Vesely, I. "Evaluation of the matrix-synthesis potential of crosslinked hyaluronan gels for tissue engineering of aortic heart valves." *Biomaterials* **2005**, *26*, 999-1010.

- [14] Banik, S. J.; Fernandes, N. J.; Thomas, P. C.; Raghavan, S. R. "A New Approach for Creating Polymer Hydrogels with Regions of Distinct Chemical, Mechanical, and Optical Properties." *Macromolecules* **2012**, *45*, 5712-5717.
- [15] Lauffer, M. A. "Theory of Diffusion in Gels." *Biophysical Journal* **1961**, *1*, 205-&.
- [16] Chen, J.; Park, H.; Park, K. "Synthesis of superporous hydrogels: Hydrogels with fast swelling and superabsorbent properties." *Journal of Biomedical Materials Research* **1999**, *44*, 53-62.
- [17] Omidian, H.; Park, K.; Rocca, J. G. "Recent developments in superporous hydrogels." *Journal of Pharmacy and Pharmacology* **2007**, *59*, 317-327.
- [18] Raymond, S.; Weintraub, L. "Acrylamide Gel as a Supporting Medium for Zone Electrophoresis." *Science* **1959**, *130*, 711-711.
- [19] Wichterle, O.; Lim, D. "Hydrophilic Gels for Biological Use." *Nature* **1960**, *185*, 117-118.
- [20] Haraguchi, K. "Nanocomposite hydrogels." *Current Opinion in Solid State & Materials Science* **2007**, *11*, 47-54.
- [21] Haraguchi, K.; Takehisa, T. "Nanocomposite hydrogels: A unique organic-inorganic network structure with extraordinary mechanical, optical, and swelling/de-swelling properties." *Advanced Materials* **2002**, *14*, 1120-1124.
- [22] Haraguchi, K.; Takehisa, T.; Fan, S. "Effects of clay content on the properties of nanocomposite hydrogels composed of poly(N-isopropylacrylamide) and clay." *Macromolecules* **2002**, *35*, 10162-10171.
- [23] Haraguchi, K.; Farnworth, R.; Ohbayashi, A.; Takehisa, T. "Compositional effects on mechanical properties of nanocomposite hydrogels composed of poly(N,N-dimethylacrylamide) and clay." *Macromolecules* **2003**, *36*, 5732-5741.
- [24] Haraguchi, K.; Li, H. J. "Mechanical properties and structure of polymer-clay nanocomposite gels with high clay content." *Macromolecules* **2006**, *39*, 1898-1905.
- [25] Joshi, Y. M.; Reddy, G. R. K.; Kulkarni, A. L.; Kumar, N.; Chhabra, R. P. "Rheological behaviour of aqueous suspensions of laponite: new insights into the ageing phenomena." *Proceedings of the Royal Society a-Mathematical Physical and Engineering Sciences* **2008**, *464*, 469-489.
- [26] Li, P.; Siddaramaiah; Kim, N. H.; Yoo, G. H.; Lee, J. H. "Poly(Acrylamide/Laponite) Nanocomposite Hydrogels: Swelling and Cationic

- Dye Adsorption Properties." *Journal of Applied Polymer Science* **2009**, *111*, 1786-1798.
- [27] Thomas, P. C.; Cipriano, B. H.; Raghavan, S. R. "Nanoparticle-crosslinked hydrogels as a class of efficient materials for separation and ion exchange." *Soft Matter* **2011**, *7*, 8192-8197.
- [28] Cummins, H. Z. "Liquid, glass, gel: The phases of colloidal Laponite." *Journal of Non-Crystalline Solids* **2007**, *353*, 3891-3905.
- [29] Bonn, D.; Tanaka, H.; Wegdam, G.; Kellay, H.; Meunier, J. "Aging of a colloidal "Wigner" glass." *Europhysics Letters* **1999**, *45*, 52-57.
- [30] Hoffman, A. S. "Hydrogels for biomedical applications." *Advanced Drug Delivery Reviews* **2012**, *64*, 18-23.
- [31] Haraguchi, K.; Li, H. J.; Matsuda, K.; Takehisa, T.; Elliott, E. "Mechanism of forming organic/inorganic network structures during in-situ free-radical polymerization in PNIPAA-clay nanocomposite hydrogels." *Macromolecules* **2005**, *38*, 3482-3490.
- [32] Miyazaki, S.; Endo, H.; Karino, T.; Haraguchi, K.; Shibayama, M. "Gelation mechanism of poly(N-isopropylacrylamide)-clay nanocomposite gels." *Macromolecules* **2007**, *40*, 4287-4295.
- [33] Tanaka, T.; Fillmore, D.; Sun, S. T.; Nishio, I.; Swislow, G.; Shah, A. "Phase-Transitions in Ionic Gels." *Physical Review Letters* **1980**, *45*, 1636-1639.
- [34] Banik, S. J. Hybrid Polymer Hydrogels with Regions of Distinct Properties, University of Maryland, College Park, 2012.
- [35] Ritger, P. L.; Peppas, N. A. "A simple equation for description of solute release I. Fickian and non-fickian release from non-swellable devices in the form of slabs, spheres, cylinders or discs." *Journal of Controlled Release* **1987**, *5*, 23-36.
- [36] Ritger, P. L.; Peppas, N. A. "A simple equation for description of solute release II. Fickian and anomalous release from swellable devices." *Journal of Controlled Release* **1987**, *5*, 37-42.
- [37] Siepmann, J.; Peppas, N. A. "Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC)." *Advanced Drug Delivery Reviews* **2001**, *48*, 139-157.
- [38] Peppas, N. A.; Sahlin, J. J. "A Simple Equation for the Description of Solute Release .3. Coupling of Diffusion and Relaxation." *International Journal of Pharmaceutics* **1989**, *57*, 169-172.

- [39] Peppas, N. A. "Analysis of Fickian and non-Fickian drug release from polymers." *Pharmaceutica Acta Helvetiae* **1985**, *60*, 110-111.
- [40] Erbel, R.; Eggebrecht, H. "Aortic dimensions and the risk of dissection." *Heart* **2006**, *92*, 137-42.
- [41] Bentall, H.; De Bono, A. "A technique for complete replacement of the ascending aorta." *Thorax* **1968**, *23*, 338-9.

PUBLICATIONS AND CONFERENCE PRESENTATIONS

List of publications:

- (1) Banik, S. J.; Fernandes, N. J.; Thomas, P. C.; Raghavan, S. R. "A New Approach for Creating Polymer Hydrogels with Regions of Distinct Chemical, Mechanical, and Optical Properties." *Macromolecules* **2012**, *45*, 5712-5717.
- (2) Fernandes, N. J.; Raghavan, S. R. "A New Class of Hybrid Gels." In Preparation, **2014**.

List of conference presentations:

- (1) Banik S. J.; Fernandes N. J.; Thomas P. C.; Raghavan S. R. "A New Approach for Creating Polymer Hydrogels with Regions of Distinct Chemical, Mechanical, and Optical Properties." *ACS Colloids & Surface Science Symposium*, Baltimore, MD, **2012** (Speaker: Stephen Banik)
- (2) Fernandes N. J.; Banik S. J.; Raghavan S. R. "Creating Polymer Hydrogel 'Hybrids' Combining Gels of Distinct Properties." *ResearchFest*, University of Maryland, College Park, MD, **2012** (Speaker: Neville Fernandes)