ABSTRACT

Title of Document: POLYMER CAPSULES AS BUILDING BLOCKS FOR SOFT, CONNECTED MESOSTRUCTURES

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We show that polymer capsules can serve as soft building blocks for creating a range of mesoscale (0.1 to 10 mm) structures. The central innovation is a new approach for connecting spherical capsules by exploiting electrostatic complexation. Using this approach, connected structures with complex shapes can be easily assembled, and more importantly, a single connected structure can be made to have a diverse array of functions. The modular approach to shape and function is very much like using Lego bricks of different colors. The connected structures can be made responsive (capable of being actuated) by magnetic fields by including magnetic capsules within them. One motivation for creating these structures is to mimic the mechanics and motility of small creatures such as the earthworm or ant – this could eventually enable the design of autonomous biomimetic robots. In addition, soft connected structures could be employed to transport cargo such as drugs or proteins in blood vessels, or to construct valves, rotors, or mixers in microfluidic or lab-on-a-chip devices.

Polymer Capsules as Building Blocks for Soft Connected Mesostructures

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Dedication

This thesis is dedicated to my late parents who raised my siblings and me in a loving and God-fearing way. You will forever be missed. We will meet again in Glory.

Acknowledgements

I'm grateful to all who in one way or another selflessly offered their time, effort, prayers, counsel and resources at some point or the other towards this work.

First and foremost, I would like to thank my Heavenly Father. Baba, it starts with you and ends with you. It is your grace and mercy that kept me. I owe it all to You. Thank you Lord.

I would like to thank Dr. Raghavan for the precious opportunity to join his group and show what I could do. In addition, I'm grateful for the concern he showed not just for my work while in his lab but also for my overall career. He knew my potential and never ceased to encourage and inspire me. He did all to support my career goals and aspirations. Srini, I owe you a whole lot. Thanks.

Thanks to all my group members who continuously supported and inspired me in the course of this effort. In particular, I would like to acknowledge "Big Brother" Hee-Young who would never hesitate to take time out of his busy schedule to assist me with experiments in this work.

Perhaps the people I owe the most to are those that were not directly involved in the research efforts, but whom without their constant support (morally and otherwise) I would not have made it this far. Mama, thank you for the love you lavished on us. Thank you for never giving up on us. Thank you for the consistent prayers and the support you continue to show. I owe you the universe; Toyin (Hannah), I don't know where to begin: I owe you the world. Thanks for your love, patience, support and good cooking. I don't know what I would've done without you; Pastor Adebisi, thank you for everything.

You've been a father in every sense of the word. I couldn't have made it this far without you. You kept my dream alive. May the Almighty God continue to elevate you and bring all your dreams and aspirations to fruition; Fikayo, I've never had a friend like you. You're one-in-a-million. Thanks for your prayers, support, advice and help. Above all, thanks for being a brother.

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Chapter 1: INTRODUCTION & OVERVIEW

In the current age of micro- and nanotechnology, there is a lot of interest in making structures, machines, and robots at smaller scales. While processing techniques for metals or plastics are well-established at the macroscale (e.g., > 10 cm), the same techniques can be difficult to implement at smaller scales. For example, the machining or molding of a small (~ 5–10 mm) robot made of metal or plastic is not an easy task. In this context, it is useful to look to nature for inspiration. Nature's equivalent of crawling mini-robots are creatures such as geckos, earthworms, and ants. It is worth noting that these creatures are generally "soft", i.e., they are not hard like metal or plastic but gooey and pliable structures. Is it possible to build an artificial earthworm, and if so, what materials would need to be used?

In this Thesis, we describe the use of polymer capsules as soft mesoscale building blocks (0.1 to 10 mm) that can be linked into structures of arbitrary complexity. The central innovation will be a new procedure that we have developed to chemically connect or "glue" these capsules. We will also describe how to make the connected structures responsive (capable of being actuated) by magnetic fields – this is accomplished by using a combination of magnetic and non-magnetic capsules in the connected structures. The magnetic capsules, in turn, are made by including magnetic nanoparticles in the precursor mixture during capsule synthesis. This proposal builds on previous work in our lab on the construction of individual polymer capsules with embedded nanostructures, including

nanoparticles of various kinds. The focus in the present thesis is on connecting individual capsules into a variety of structures.

FIGURE 1.1. A biomimetic "earthworm"-like structure composed of linked capsules. The structure features a big green magnetic head linked to a chain of pink non-magnetic spheres. The big magnetic head allows for easy maneuverability by an external magnetic field in a liquid medium.

The potential of our approach is best described by making an analogy to Lego® bricks. As most children know, building a complex structure out of Lego® bricks involves interconnecting the bricks in a particular way. In much the same vein, Figure 1.1 shows an example of a linked capsule structure. The big green capsule contains magnetic nanoparticles and therefore has magnetic properties. The pink capsules are all non-magnetic. All these capsules are linked together to form a structure that resembles an artificial "earthworm". The magnetic head allows the "earthworm" to be actuated by a hand-held magnet. In effect, we can think of the green and pink capsules to be two kinds of mesoscale Lego® bricks – with the important difference being that the capsules are soft and pliable. Another point worth mentioning is that the capsules have nearly the same

density as water. Therefore, the above "earthworm" can be made to float in aqueous solutions. In other words, our "earthworm" has a very different character when compared to, say, a linked chain of ball bearings.

The focus of this thesis is on developing a procedure to build connected structures from capsules. As will be discussed in Chapter 2, our approach is considerably different from previous attempts at linking particles, magnetic or otherwise. The main advantage is in the extent of control that we can achieve – both to create unique shapes or three-dimensional structures, as well as in our ability to mix and match capsules with varying functionalities (e.g., magnetic next to non-magnetic etc.; also see below). With the procedure reasonably optimized, we have explored some of the many possibilities for interesting and/or useful structures. In addition to the "earthworm" in Figure 1.1, we have connected capsules into simple shapes (e.g, resembling various letters of the alphabet); into a rotor structure with rotating arms; and into a "circuit breaker" structure with two magnetic ends. These are all described in detail in Chapter 3. It should be noted that the size of individual capsules in a connected structure can be varied during the formation process from ~ 10 mm to ~ 50 μm, while still smaller sizes can be achieved using microfluidic methods. However, size control will not be the focus of this thesis – rather we will focus on demonstrating different kinds of connected structures.

As mentioned earlier, one motivation for creating soft structures from capsules is to be able to mimic the mechanics and motility of small creatures such as the earthworm or ant – this could eventually enable the design of autonomous biomimetic robots that

could one day be used, for instance, in endoscopic surgery. In addition to robotics, numerous other applications are possible for soft connected structures. For example, a scaled-down version of the earthworm structure shown in Figure 1.1 could be employed to transport cargo in fluidic devices or in blood vessels. The key to such applications will be the ability to integrate multiple functions into the same structure. In this context, previous work in our lab has shown that, by varying the cargo in polymer capsules, we can imbue them with sensing capabilities (e.g., the ability to change color in response to pH or temperature), or absorptive capabilities (the ability to selectively absorb molecules such as toxic metal ions or cationic dyes from solution), or delivery capabilities (e.g., the ability to slowly release encapsulated drug or protein molecules into solution).

Using such diverse capsules and our new connection procedure we can take a modular approach to building a composite device having an array of functions – this further extends the analogy to Lego® bricks. That is, for example, we can now combine some **capsules containing drugs or proteins** (the drug delivery module) with other **capsules containing a contrast agent for imaging** (the imaging module) and with a **magnetic capsule** at the head (the actuation module). Such composite capsules could be magnetically targeted to deliver their drug payload to the site of a tumor while also allowing the tumor to be imaged, say, by magnetic resonance imaging (MRI). To our knowledge there is no simple method to integrate such diverse functions into a single device at millimeter or smaller length scales. In addition to biomedical applications, connected capsules could also be used to construct valves, rotors, or mixers in microfluidic or lab-on-a-chip devices.

Chapter 2: BACKGROUND

In this chapter, we briefly discuss previous work documented in literature on the subjects of (a) linking spherical particles into chains or filaments; and (b) soft materials with crawling capabilities (earthworm mimics). We then describe the basics of polymer capsules made by electrostatic complexation using the polymer, chitosan, in conjunction with anionic surfactants or polymers.

2.1. PREVIOUS STUDIES ON LINKING PARTICLES

Previous work on linking of particles has been mostly done with magnetic particles. Typically these particles have been linked into one-particle-thick chains that contain 10 – 100 such particles. One motivation for building chains of magnetic particles has been in an attempt to mimic the flagella of micro-organisms such as bacteria. The term "flagella" refers to the flexible filament at the head of bacteria, which the organism uses to swim in water. Structures such as flagella are critical to enable swimming of microscopic structures, because at those length scales, their motion is dominated by viscous rather than inertial forces (i.e., the Reynolds number is low).

One attempt at magnetic flagella was reported by Dreyfus et al.[1] These authors linked superparamagnetic 1 μm particles using DNA strands (Figure 2.1a). To accomplish the linking, the particles had to be coated with the protein, streptatividin while the DNA had to be conjugated on each end with the biomolecule, biotin. This allowed the DNA to bind to adjacent particles via the strong non-covalent biomolecular

interaction between biotin and streptavidin. The resulting magnetic chains were quite flexible and they were capable of being actuated by a dynamic magnetic field in a manner similar to flagella. The chains were used to magnetically propel red blood cells (RBC) in water (Figure 2.1b).

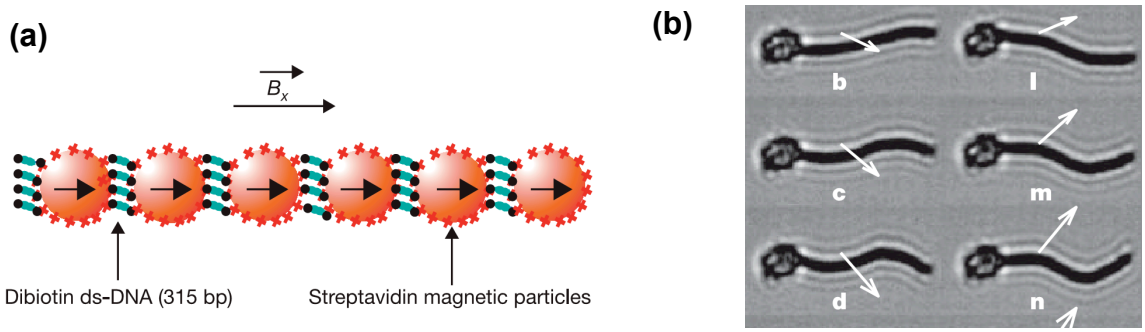

FIGURE 2.1. (a) Micron-sized magnetic particles linked into a flexible filament by DNA strands. (b) The above filament is attached to a red blood cell and used to propel it by mimicking the beating pattern of bacterial flagella.

In a similar approach, linked chains of magnetic microspheres were prepared by Biswal et al.[2,3,4] using bis-biotinylated polyethylene glycol (PEG) as a bifunctional linker. Similar to the work of Dreyfus et al., the microspheres in this case were also coated with streptavidin, and linking of adjacent microspheres was again accomplished by biotin-streptavidin interactions. The authors also showed that the flexibility of the chains could be altered by varying the molecular weight, and hence length, of the PEG linkers.[2] Specifically, chains formed by bis-biotin-PEG of molecular weight 3400 were more flexible than those formed using bis-biotin-PEG of molecular weight 733. Note that particle chains in the above system can be "assembled" by incubating the particles and the bis-biotin-PEG in the presence of an external magnetic field, as illustrated by

Figure 2.2.a The same authors were also able to estimate the bending and flexural rigidity of their chains using optical tweezer experiments.[2]

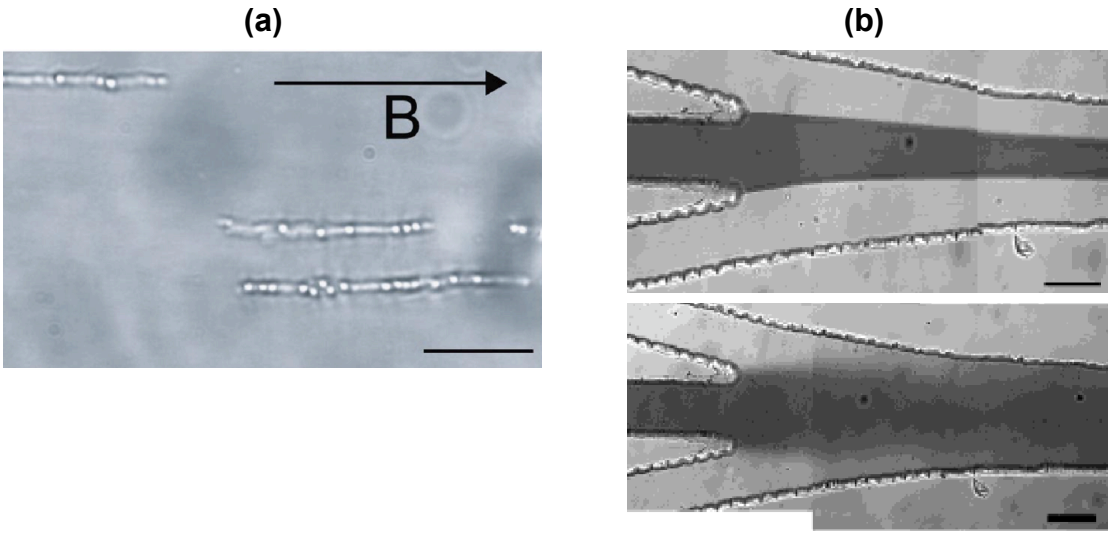

FIGURE 2.2. (a) Magnetic particles linked into chains using biotinylated PEG as a bifunctional linker. The scale bar is 5 μm. (b) The above chains are used to promote mixing in a microfluidic device. Here a clear buffer flows through the side channels while a dye solution (dark color) flows through the middle channel. The top panel shows that in the typical case of laminar flow, the streams do not mix. In the bottom panel, magnetic chains are included within the dye stream and a rotating magnetic field of frequency 0.5 Hz is applied. In this case, considerable mixing of the fluids in the different streams is seen. Scale bars are 100 μm.

One application investigated by Biswal et al. for their magnetic chains is in promoting mixing within microchannels. This is shown in Figure 2.2b, where three channels of diameter ~ 100 μm lead into a single wider channel. The middle stream has been colored with a dye for visualization. In the absence of any additional means to promote mixing, the three streams do not mix and each stream retains its individual identity throughout the wide channel (top panel of Figure 2.2b). In contrast, the bottom panel shows the effect of adding magnetic chains such as those in Figure 2.2a to the fluid,

followed by application of a rotating magnetic field. The chains undergo tumbling and rotation within the wide channel, causing the three streams to mix, as seen by the spread of dye molecules throughout this channel. Similar use of magnetic filaments as mixing aids has also been demonstrated within stagnant *microdroplets* instead of microchannels[5].

2.2. PREVIOUS STUDIES ON MOTILE FILAMENTS

Flexible soft filaments with motile capabilities (e.g., crawling) can be achieved by alternative routes that do not involve linking of spherical precursor particles. We broadly refer to these as "earthworm mimics" – a term often used in the relevant literature as well. In the specific case of the earthworm, it is known that motion occurs by peristalsis. That is, the earthworm has muscles that undergo successive waves of contraction, which in turn pushes the overall structure forward. Saga and Nakamura[6] make the case that peristaltic motion actually requires the least amount of "space" to generate the motion; see Figure 2.3a. To mimic the earthworm motion, they placed an aqueous magnetic fluid (suspension of magnetic nanoparticles) inside sacs made of rubber, which were then closed and sealed. These sacs, of diameter ~ 10 mm, were connected by elastic rods of rubber having a thickness ~ 5 mm, as shown in Figure 2.3b. The resulting structure showed peristaltic motion under an external magnetic field.

Other attempts at building earthworm mimics have used polymer hydrogels with temperature-responsive properties. For example, hydrogels of N-isopryopyl acrylamide (NIPAAm) are swollen at room temperature but shrink when heated to ca. 40°C.[7] Filaments of such gels were used along with precision-control of temperature at various

positions along the filament. The hot portions of the filament shrunk while the cold portions remained swollen and the net result was to mimic the peristaltic motion of the earthworm. Finally, we should mention the use of shape memory alloys to build an earthworm-like micro-robot with a built-in power supply.[8] The design of this robot is shown in Figure 2.3c and its key advantage is its ability to be controlled by wireless. Motion is achieved through the bellows, made out of silicone polymer, which acts as a biased spring – the retraction force of the spring drives the motion, as illustrated by Figure 2.3d.

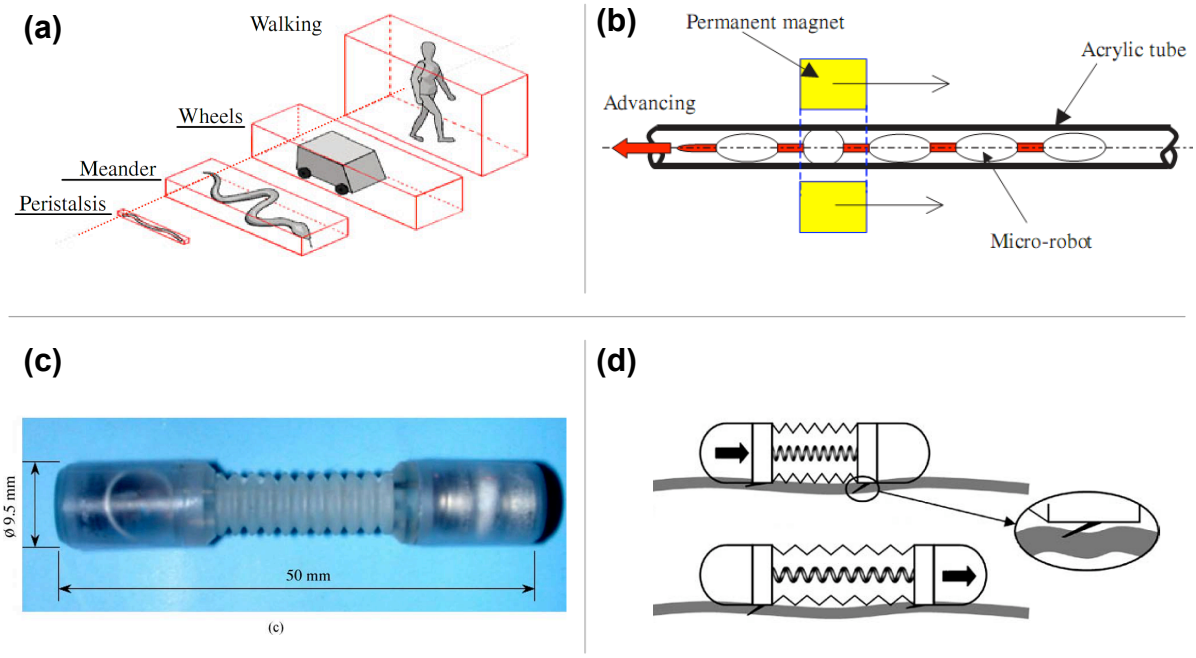

FIGURE 2.3. (a) Comparison of the space requirements for various motion mechanisms. (b) A magnetic earthworm built from polymer sacs filled with magnetic fluid, which are connected by rubber rods, shown in red. (c) A self-powered earthworm-mimic that can be controlled by wireless. The silicone bellows in the middle act like a loaded spring. As shown in (d), the force exerted by releasing the spring drives the motion of the structure.

2.3. BASICS OF POLYMER CAPSULES

We define a capsule as a structure that has a thin shell enclosing a liquid-filled core. Capsules ranging in size from a few microns to several millimeters can be prepared both from biopolymers as well as synthetic polymers. The method we will use to prepare capsules involves *polyelectrolyte complexation*. This process requires two species of opposite charge, of which at least one should be a polymer. We will use the cationic biopolymer, chitosan as the first species and the anionic surfactant, sodium dodecyl benzene sulfonate (SDBS) as the second one. The procedure for forming the capsules is illustrated by Figure 2.4 – here, the chitosan solution is added drop-wise to a solution of SDBS. Contact between the oppositely charged polymer and surfactant at the drop interface leads to electrostatic complexation, which results in a soft shell around the drop. Thus, polymer capsules of size equal to the size of the generating drop are created by a simple, mild process taking place at room temperature and without the need for volatile organic solvents. The capsules can be subsequently transferred to buffer solutions or deionized water, where they remain stable for long periods of time.

Previous studies in the Raghavan lab have investigated some issues related to capsule size, integrity, and stability. With regard to capsule size, the above process using pipettes or syringes leads to capsules with diameters between 1 to 10 mm. Smaller capsules can be created by a modified process where (instead of drop-wise addition) the chitosan is sprayed into the SDBS as a fine mist – this yields microcapsules having a size around 10 to 100 μm. Alternately, microcapsules can also be used by creating smaller

drops using different nozzle designs or by employing a microfluidic device to generate the drops.

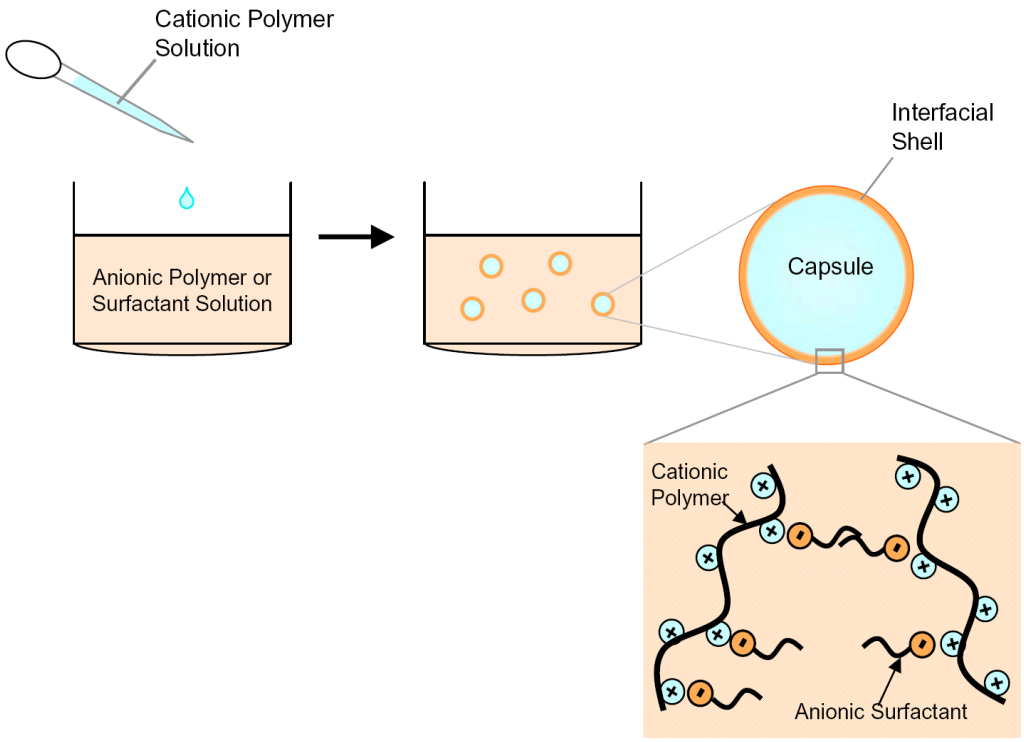

FIGURE 2.4. Creation of chitosan capsules by electrostatic complexation. A drop of chitosan is added to a solution of anionic biopolymer or surfactant. The resulting capsules have a shell consisting of chitosan complexed with the anionic moiety.

Tiwari studied the effects of three key variables that impact the properties of the capsules: the concentration of chitosan, the concentration of SDBS, and the incubation time, i.e., the time that the drop stays in the SDBS solution. Her results (Figure 2.5) showed that, with increasing incubation time, the capsules shrank in overall diameter while their shell thickness increased. The shrinking with time was especially apparent at the lower chitosan concentration (1 wt%). Note that if the incubation time was too low

(< 3 min), the capsules were not strong because their shells were too thin. Increasing the chitosan concentration to 2 wt% improved the integrity of the capsules and reduced the shrinking; however, the capsule diameters were larger than at 1 wt% – this was because the higher viscosity of 2% chitosan gave rise to bigger drops. Indeed, concentrations greater than 2 wt% chitosan could not be handled easily due to their high viscosity. Also, with regard to SDBS, a concentration around 5 wt% was found to be required to produce strong capsules. Taken together, Tiwari's results give us an optimal composition window for chitosan-SDBS capsule formation: which is to use 1.5–2 wt% chitosan and 5 wt% SDBS, with an incubation time of about 3–4 min.

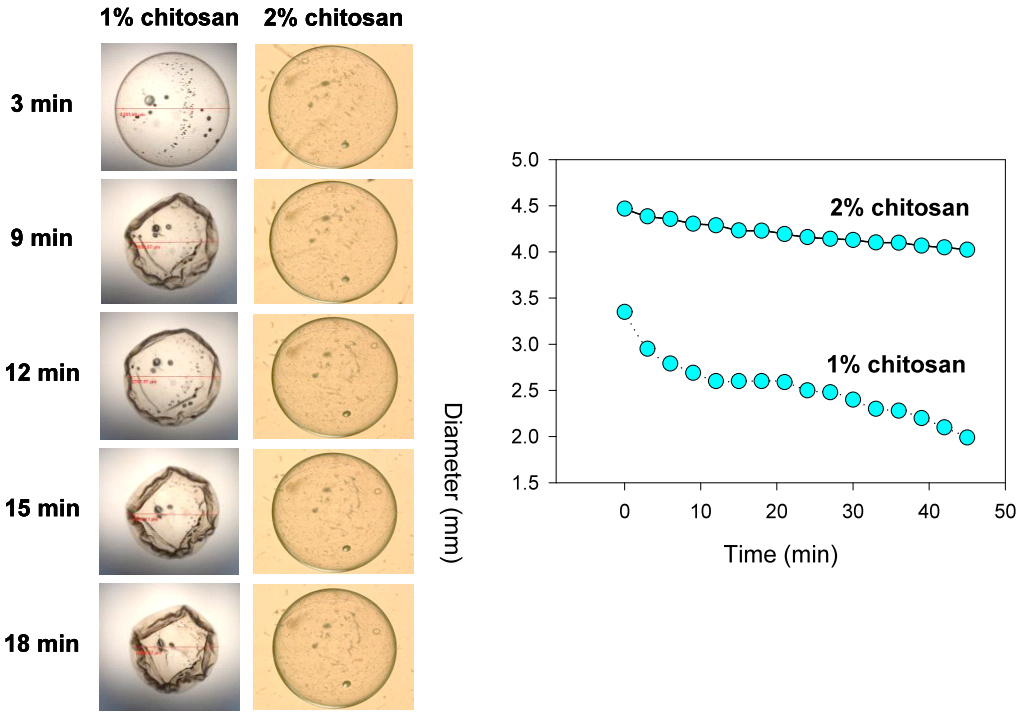

FIGURE 2.5. Typical optical microscope images of chitosan-SDBS capsules at various incubation times. For these experiments, the chitosan concentration was varied while the SDBS concentration was fixed at 5 wt%. The capsule diameter extracted from these images is shown as a function of time on the plot.

The Raghavan lab has also investigated the encapsulation of different types of materials in polymer capsules. Note that encapsulation is quite straightforward – it only involves mixing the chitosan with the material to be encapsulated and then bringing drops of this mixture in contact with the SDBS solution. A few examples of materials encapsulated are listed below:

1. **Magnetic Nanoparticles:** Lee et al. and Tiwari have shown that ferromagnetic nanoparticles could be encapsulated in chitosan-SDBS capsules. The resulting capsules could be actuated using an external magnet. This thesis builds on their previous work – we will use such magnetic capsules as building blocks for making connected chains.

2. **Drugs, Enzymes, Proteins:** Lee et al. and Dowling et al. have investigated the encapsulation of biologically relevant molecules such as drugs, enzymes, and proteins in capsules of chitosan-SDBS or chitosan-gellan (gellan is an anionic biopolymer). Small molecules such as drugs could be released slowly from the capsules while large macromolecules such as enzymes remained entrapped. In other words, the capsule shell is permeable to small, but not large molecules.

3. **Colorimetric Vesicles:** Tiwari was able to encapsulate vesicles of a diacetylenic surfactant in chitosan-SDBS capsules. These vesicles had the ability to change color in response to changes in the pH of the solution or the temperature. Their encapsulation thereby conferred the same properties to the capsules itself. For example, the capsules turned color from blue to orange as the pH was increased.

Chapter 3: RESULTS AND DISCUSSION: CAPSULES AS BUILDING BLOCKS FOR SOFT CONNECTED STRUCTURES

3.1. INTRODUCTION

In the previous Chapter, we discussed previous attempts at linking spherical particles into chains. The connections between particles were accomplished using complicated molecules such as dibiotinylated DNA or PEG (as shown in Figures 2.1 and 2.2). These molecules usually have to be synthesized for a given project – i.e., they may not be available commercially (or if they are, they would be very expensive). Also, the magnetic particles that were used in these attempts were also of a special and expensive type – since they were coated with the protein, streptavidin. All in all, it is clear that the materials used in previous studies were expensive and complex. These aspects would deter many researchers who were more interested in applications for the magnetic chains rather than in the synthesis details. Another factor with these previous methods is their lack of control of the final structures. For example, the number of particles forming a chain in Figure 2.2a is an aribitrary value – this cannot be adjusted within the synthesis procedure. Moreover, once the chains are formed and the biotin-streptavidin links are in place, the chains cannot be altered any further.

We also discussed the earthworm mimics in Chapter 2 – these are soft structures that can mimic the peristaltic motion of earthworms. A much better degree of control over the final structure is possible using the designs in Figure 2.3b and c; however, it should be noted that the cross-sectional diameters of both structures is ~ 10 mm. It is

unlikely that the size of these "earthworms" could be reduced by much relative to these values. In other words, the manufacturing of the structures in Figure 2.3c is still essentially a conventional approach involving plastic objects and physically gluing them together. While such approaches may be adequate for some applications, the push towards micro- and nano-manufacturing demands alternatives.

In this Chapter, we describe our approach to chemically connecting spherical polymer capsules of chitosan-SDBS. This approach should have some clear advantages over the ones discussed above. In particular, we use inexpensive and readily available chemicals and magnetic particles – hence our method can be easily replicated by researchers as well as scaled-up for commercial applications. Moreover, our modular design approach will allow exquisite control over the shape, orientation, and arrangement of sub-units within the final connected structures. Using magnetic capsules, we will show that our structures can be moved along by an external magnetic field – this will be a primitive earthworm-mimic. In addition, we have connected capsules into simple shapes (e.g, resembling various letters of the alphabet); into a rotor structure with rotating arms; and into a "circuit breaker" structure with two magnetic ends. We hope our approach to soft, connected structures will prove to be a worthy alternative over a range of length scales – from 1 mm to 1 cm (robotics) as well as from 0.1 mm to 1 mm (micro/nano-manufacturing). In addition, we will describe applications for specific structures: for example, as fluidic mixers, fluidic valves, and in targeted drug delivery.

3.2. EXPERIMENTAL SECTION

Materials

Chitosan (from Sigma-Aldrich) was of medium molecular weight (190–310K), with a Brookfield viscosity of 286 cps and a degree of deacetylation around 80%. The anionic surfactant, sodium dodecyl benzene sulfonate (hard type) was obtained from TCI America. The magnetic nanoparticles (γ-Fe_2O_3) were purchased from Alfa Aesar. Their size was specified to be 32 ± 18 nm, and their average surface area was 42 m^2/g. Magnets were obtained from United Nuclear. Dyes (methylene blue, rhodamine B) were purchased from Sigma-Aldrich.

Solution Preparation

Chitosan is soluble only under acidic conditions, i.e., at a pH < 6.5. Therefore, a 0.2 M acetic acid solution was used and the chitosan was dissolved in this at a concentration of 1.5 wt%. The mixture was stirred for 1 h at room temperature until a homogeneous solution was obtained. The SDBS solution was prepared at a concentration of 5 wt% using deionized water. For preparing magnetic capsules, the magnetic nanoparticles were added to a homogenous chitosan solution, and a vortex mixer was used to disperse the particles uniformly.

Optical Microscopy

The Zeiss Axiovert 135 TV inverted microscope equipped with the Motic Image Plus imaging system has been used for optical microscopy (bright-field). Capsules were imaged with a 2.5X objective.

3.3. RESULTS AND DISCUSSION

3.3.1. PROCEDURE FOR LINKING CAPSULES

The procedure we have developed to link chitosan-SDBS capsules utilizes the same electrostatic interactions responsible for forming the capsules in the first place. That is, the electrostatic complexation tendency between the cationic chitosan chains and the anionic SDBS molecules is exploited as chemical glue. We start with a Petri dish lined with parafilm to provide a non-stick surface for capsule connection (Figure 3.1). The 5 wt% aqueous solution of SDBS is then added to the Petri dish to a height of less than half of the desired diameter of the capsule. To begin the chain formation process, a droplet of 1.5 wt% chitosan is added to the Petri dish using a drop dispenser appropriate for the desired capsule diameter (Step 1). SDBS solution from within the dish is then applied to the entire surface of this capsule to allow for its full complexation (Step 2). The next droplet of chitosan is then added so that it is in contact with the first capsule (Step 3). Again, SDBS solution from within the dish is applied to the entire surface of the second capsule to complete the complexation, which takes a few minutes (Step 4). The extent of contact between the capsules will determine the stiffness of their link. The process is repeated to add additional capsules to the chain. Once the chain is formed, it can be transferred to a solution of deionized water and stored for several weeks. The key to the success of this technique can be summarized as the following "rule": *at the moment that capsule linking is initiated, the first capsule must be fully complexed, while the second capsule must be "fresh", i.e., incompletely complexed*. This point is elaborated below.

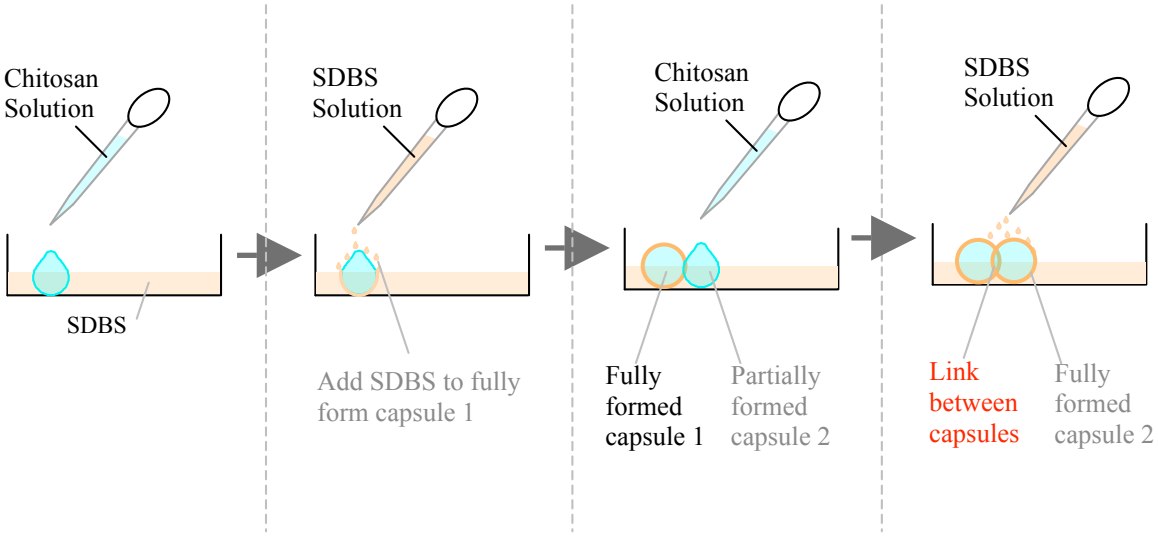

FIGURE 3.1. Schematic depiction of the procedure for linking adjacent chitosan-SDBS capsules. Details are described in the text.

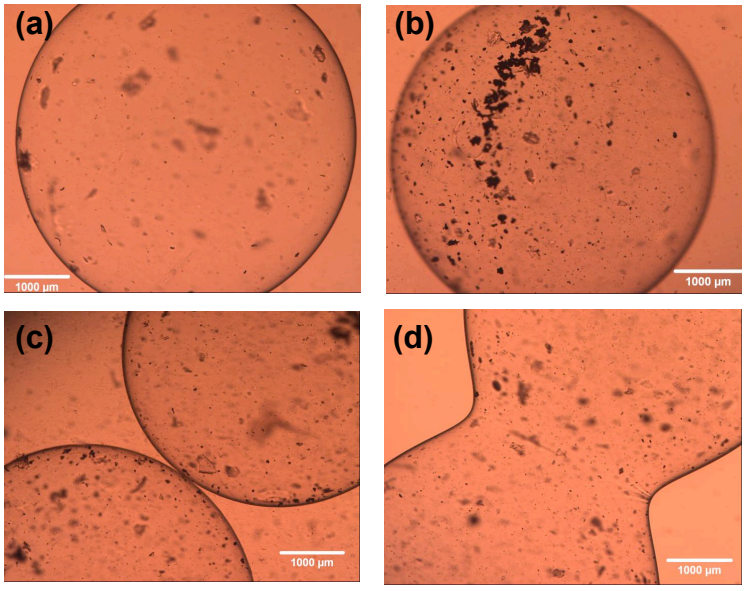

FIGURE 3.2. Optical microscope images of (a) a chitosan-SDBS capsule; (b) a chitosan-SDBS capsule containing magnetic particles; (c) two capsules with an underformed link; (d) two linked capsules. Scale bar is 1000 µm in each case. See text for further details.

We have characterized the linkage between capsules using optical microscopy, and this gives further insight into the key "rule" mentioned above, which is that ONE and ONLY ONE of the two capsules being linked should be fully formed. Figure 3.2a shows an image of a single capsule while Figure 3.2c shows two capsules brought next to each other that have failed to form a strong link. The latter scenario arises when the capsules are *both* fully formed when brought into contact. If, on the other hand, both capsules are "fresh", i.e., incompletely formed when contacted, then the two will fuse and the individual capsules will lose their identity (image not shown). The fused structure will then act like a rigid rod rather than a flexible chain. The optimal scenario is when a fully formed capsule is contacted with a fresh one: in this case, a neck region is induced between the two capsules and this implies a strong bond (Figure 3.2d).

We have found that the concentration of chitosan strongly affects capsule linkability. If a low chitosan concentration of 1 wt% is used, adjacent capsules do not form links, or if the links do form, they are easily broken by slight agitation. This is reasonable because chitosan chains are the major component of the "glue" between capsules. On the other hand, concentrations higher than 2 wt% chitosan are difficult to handle because of the high solution viscosity, as mentioned in Chapter 2. The optimal concentration is thus between 1.5 to 2 wt% and in such cases, mechanically stable links are formed between adjacent capsules.

Another variable that affects capsule linkability is the extent of overlap between the capsules when they are brought into contact. If the capsules overlap considerably, the

neck region (Figure 3.2d) would be a large fraction of the capsule diameter. In this case, the capsules would be linked strongly (considerable interpenetration of chitosan chains from each capsule), but the individual capsules would have lost some of their identity. Also, such links will lead to a rigid chain (see below). In the other extreme, if the extent of overlap between capsules is minimal, the neck region would be very thin and correspondingly, the link between the capsules may be weak. In sum, the overlap region between capsules needs to be controlled precisely to ensure optimal linkage.

With regard to the mechanics of a stable chain of capsules, the main parameters of interest are the strength of the chain under tension and the flexibility of the chain. These can be quantified in terms of the Young's modulus and tensile strength and the bending rigidity. We have not measured these parameters as part of the work done under this thesis, but we can still discern certain qualitative trends. The chain flexibility seems to be affected by three main factors: (i) extent of overlap when contacted; (ii) incubation time; and (iii) size of capsules in chain. The extent of overlap was discussed above – it is clear that a high extent of overlap makes the chain more rigid. The incubation time refers to the amount of time spent by the capsules in the SDBS solution after formation. Longer incubation time tends to stiffen the capsule chain. This is presumably because the shell surrounding each capsule in the chain becomes thicker as the SDBS diffuses inward. The third variable is the capsule size, and smaller sizes imply more flexible capsule chains. This is a well-known result in mechanics since the bending modulus of a filament scales with the filament radius to the fourth power.

We should mention that at the typical sizes we have used for our capsules (diameters ~ 2–3 mm), our capsule chains are rather rigid and not quite flexible. Improving the flexibility is one topic for future work. Nevertheless, it is worth noting that flexibility is essential only in some applications. For example, a swimming earthworm-mimic does require flexibility, whereas in the case of a microfluidic stirrer or gear pump, a rigid structure may be preferred.

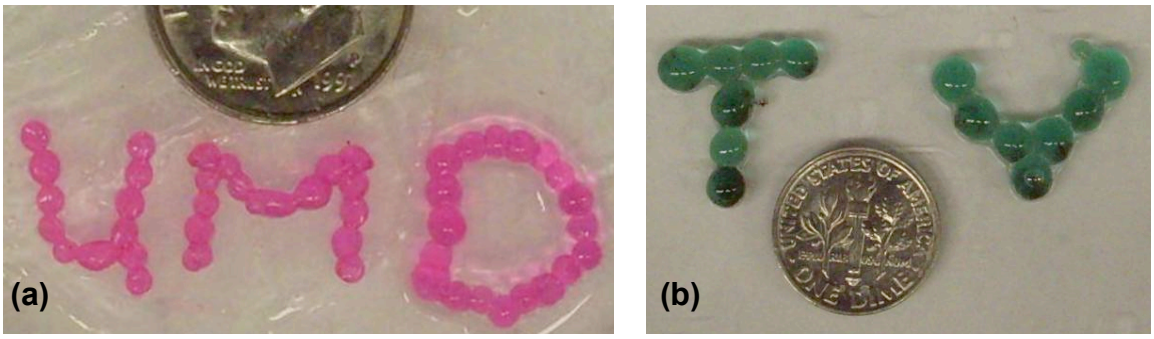

FIGURE 3.3. Examples of complex shapes obtained by linking chitosan-SDBS capsules. The letters (a) UMD and (b) TV are created.

3.3.2. EXAMPLES OF STRUCTURES DEVELOPED

Having established a procedure to connect capsules we then used it to make shapes or structures of interest. One point to note is that a single capsule can be linked at multiple locations with other capsules. For example, consider the letter T (Figure 3.3b). To create this, we can first form the top bar of the letter. Thereafter, the middle capsule can be linked to a second fresh capsule in the perpendicular direction to form the stem of the letter. As long as the key rule is followed (one fully formed, one fresh) linking can be done. (As a counter-example, we cannot first form two straight chains and link them

perpendicularly to form the letter T.) By extending the above approach, it is straightforward to form any desired letter of the alphabet. As examples, Figure 3.3a shows the letters UMD and Figure 3.3b shows TV. Note that this Figure underscores our ability to treat the capsules as mesoscale Lego® bricks.

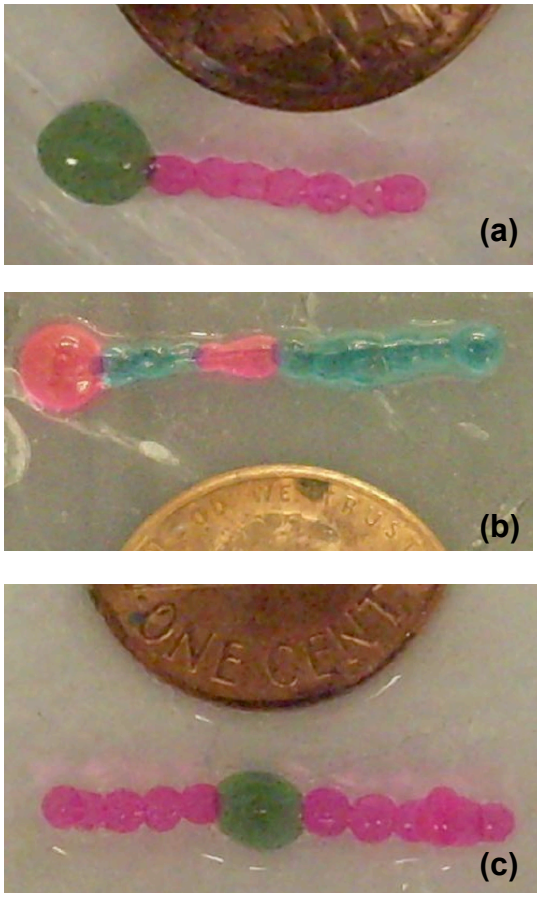

FIGURE 3.4. Biomimetic "earthworm"-like structures composed of linked magnetic and non-magnetic capsules. (a) magnetic head (green) linked to non-magnetic capsules (pink). (b) magnetic (pink) and non-magnetic (blue) segments alternate. (c) magnetic center (green) flanked by non-magnetic capsules (pink).

The next challenge we tackled was to combine capsules of varying functionalities in the same connected structure (Figure 3.4). For this, we started with magnetic capsules,

which are formed by combining the chitosan solution with magnetic nanoparticles and then adding it to the SDBS. Figure 3.2b shows an optical micrograph of a magnetic chitosan-SDBS capsule – note that the nanoparticles are seen to be considerably aggregated into large clusters. For our purpose, we ignore the issue of nanoparticle aggregation because it only takes place within the confines of the capsule.

Our focus was to see whether we could combine magnetic and non-magnetic capsules into the same linked structure in precise arrangements. Figure 3.4 shows that this is indeed possible using our linking technique. Note that we have colored the magnetic and non-magnetic capsules with different dyes for easy identification. In Figure 3.4a, the magnetic capsule (green) is at the head of the chain, while the succeeding capsules (pink) are all non-magnetic. Figure 3.4c shows the opposite structure, with the magnetic capsule at the center of a non-magnetic chain. Figure 3.4b is an intermediate case, where segments of magnetic (pink) and non-magnetic (blue) capsules alternate along the length of the chain. It is worth emphasizing that earlier studies on linking magnetic particles did not demonstrate the same level of control as we have shown. In those earlier studies, all the linked particles had to be magnetic. Here, we can vary the proportion of magnetic vs. non-magnetic capsules, and we can also control the precise arrangement of the two.

We suggest that mixing and matching of magnetic and non-magnetic particles within a chain could be useful in optimizing the magnetic response for different applications. One direct illustration is in the motility of the chains. When all the particles

in a chain are magnetic, the chain can undergo translation as well as rotation under a directed magnetic field. However, when only the head of the chain is magnetic, the chain will not rotate and will move along a straight path. The motion of the latter is shown in Figure 3.5 – this is the same structure shown in Figure 3.4a, with a green magnetic head and a pink, non-magnetic tail. We note from this figure that the chain can be moved linearly by the magnet. Regardless of the location of the magnet, this chain will always move head-first. Lastly, as an aside, we should mention that when all the capsules contain magnetic particles, the entire chain tends to substantially stiffen under an external magnetic field. This is presumably because the particles align themselves with the field.

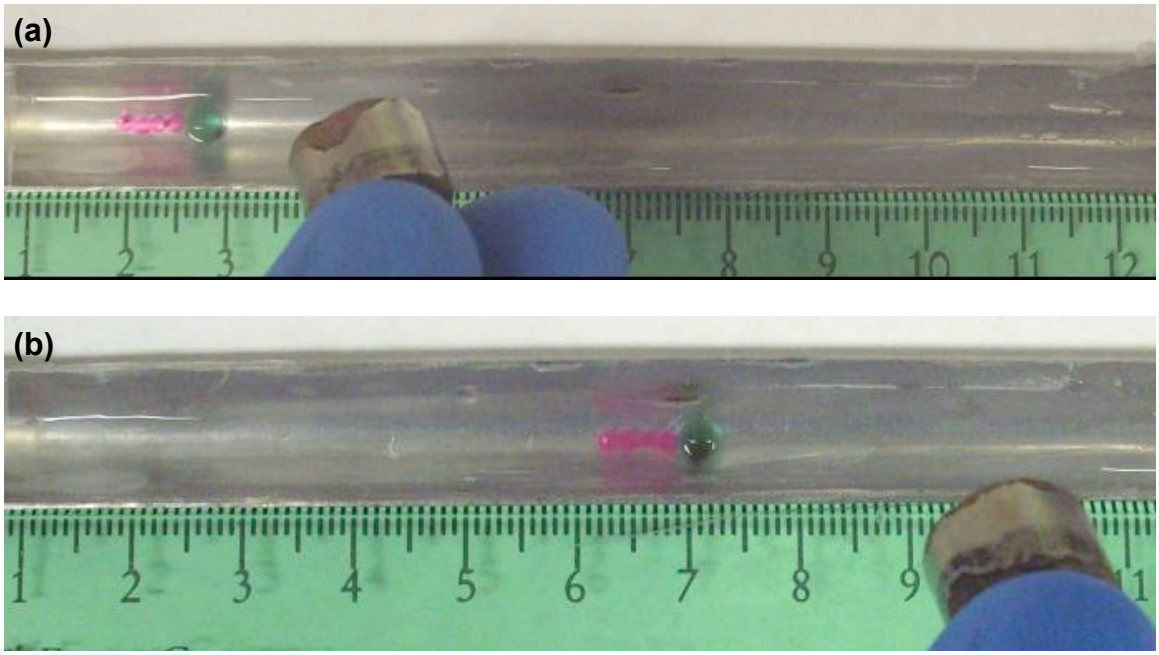

FIGURE 3.5. Motion of the earthworm-like chain shown earlier in Figure 3.4a under the action of an external magnet. Since only the head of the chain is magnetic, the chain will always move head-first.

The ability to combine various functionalities in the same connected structure is indeed a powerful concept. We can combine capsules containing drugs, imaging capsules, sensing capsules etc. into a single structure. Capsule chains with multiple functions may find use in robotics, drug delivery, microfluidics etc.

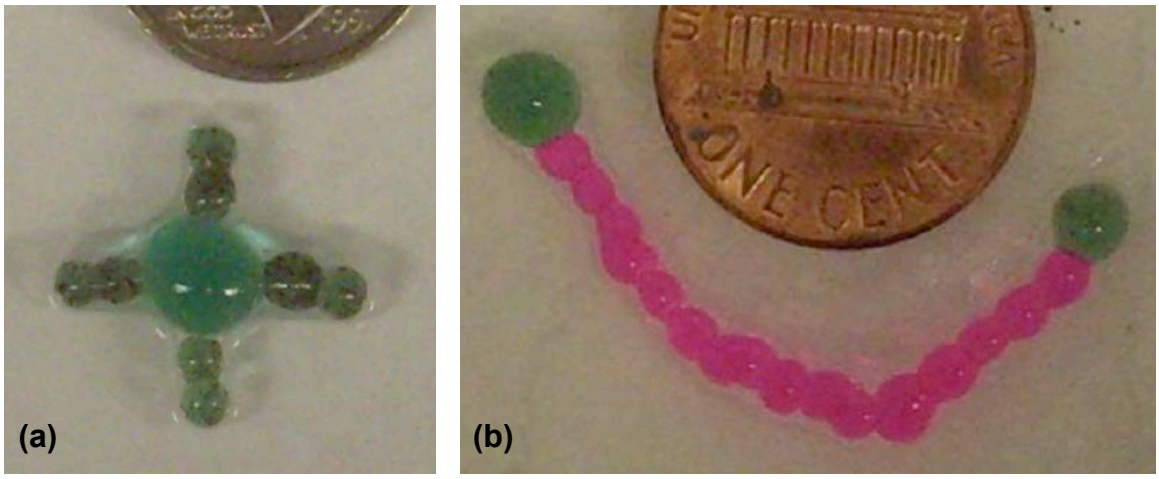

FIGURE 3.6. (a) A star-shaped device inspired by a gear pump. It features a large magnetic core and rigid fins comprising of smaller magnetic capsules. Under a rotating magnetic field, this device can be made to drive liquid flow. (b) A "circuit breaker" device that features a flexible non-magnetic chain with magnetic ends. Under a magnetic field, the two ends can be made to touch or the entire structure can curl up.

As a final aspect, we also conceptualize two other structures that could find use in fluidic devices (Figure 3.6). Figure 3.6a shows a gear-like structure that can rotate about its large magnetic core. When in combination with an identical gear structure, the actuation can be made to drive liquid flow. In the inlet side of the flow, the fins separate creating suction. The fluid is carried by the gears to the discharge side of the pump, where the meshing of the gears displaces the fluid. Figure 3.6b show a "circuit breaker"

like structure that can make contact with its two magnetic ends under the influence of an external magnetic field. This can be employed as a valve-type device that can cut off or reduce flow simply by making contact with its two ends in order to block a flow channel.

Chapter 4: CONCLUSIONS & RECOMMENDATIONS

4.1. CONCLUSIONS

Our research thus far has provided a way to fabricate a number of complex connected structures using soft chitosan capsules. This is made possible by an innovative technique that allows us to link these capsules without the aid of any linking agent. This novel technique of linking allows the flexibility of being able to link capsules in any desired configuration or pattern, very similar to the concept of building with Lego® blocks. Also, the added capability of being able to encapsulate magnetic particles provides a means for the capsules and the structures they comprise to be moved or actuated by a moving external magnetic field. By employing this technique, we can device a number of unique soft "robot" structures including a swimming earthworm, magnetically actuated gear, propeller like structure, etc. We have also been able to assemble shapes that resemble various letters of the alphabet. The studies have also showed that we can control a number of properties in these capsule comprised structures such as chain strength, chain flexibility and ductility by altering simple variables in the building process.

The findings of this work will be particularly useful in the area of biomimetics and nature inspired robotics where these structures can be used to create "soft" duplicates of parts or even entire living organisms. These devices could in addition be useful in fabricating a number of biomedical applications where there is a need for soft biocompatible devices that can respond to external stimuli such as the presence of an

external magnetic field, and can also bear "cargo" (e.g. drugs and protein) that would need to be transported to a certain site for delivery.

4.2. FUTURE DIRECTIONS

Future work in this effort would involve the quantitative study of such properties as chain strength and flexibility and how they relate to variables such as incubation time and chitosan concentration. For example, a proposed experiment to quantify the flexibility of a chain of capsules would involve measuring the radius of curvature when a chain such as the one shown in fig 3.6b is exposed to an external magnetic field. Both of the magnetic ends would be forced to respond to the magnetic field causing the chain to bend or curve. A lower radius of curvature would mean a more flexible chain and vice versa. Another proposed experiment to measure the strength of a capsule-capsule link would involve fixing or immobilizing one capsule in a two-capsule chain and applying a measured force on the adjoining capsule in the direction away from the fixed capsule. The force required to break the link would be a measure of the link strength. Success in experimentally measuring these quantities (flexibility and link strength) can ultimately allow for their optimization in terms of such variables as chitosan concentration and incubation time. Also, a number of these devices would be most impactful if they were scaled down to the micro scale. In this regard, it would become necessary to study how to replicate the fabrication process at smaller scales. Finally, it would be necessary to better stabilize the magnetic nanoparticles contained in the capsules such that they can be dispersed homogenously. This may involve functionalizing the surface of the magnetic

particles with a hydrophilic molecule. This should ultimately aid better actuation by magnetic fields.

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