Optimizing Double-Network Hydrogel for Biomedical Soft Robots

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Abstract

Double-network hydrogel with standardized chemical parameters demonstrates a reasonable and viable alternative to silicone in soft robotic fabrication due to its biocompatibility, comparable mechanical properties, and customizability through the alterations of key variables. The most viable hydrogel sample in our article shows tensile strain of 851% and maximum tensile strength of 0.273 MPa. The elasticity and strength range of this hydrogel can be customized according to application requirements by simple alterations in the recipe. Furthermore, we incorporated Agar/PAM hydrogel into our highly constrained soft pneumatic actuator (SPA) design and eventually produced SPAs with escalated capabilities, such as larger range of motion, higher force output, and power efficiency. Incorporating SPAs made of Agar/PAM hydrogel resulted in low viscosity, thermos-reversibility, and ultralow elasticity, which we believe can help to combine with the other functions of hydrogel, tailoring a better solution for fabricating biocompatible soft robots.

Keywords: biomedical soft robots, endoscopy, hydrogel

Introduction

The choice of materials envisioned for biomimetic soft robots poses a great challenge for organic material scientists to come up with novel, soft, flexible, yet robust, and resilient solutions. In this realm, silicone has extensively been regarded as the most viable material of choice for soft robots due to its flexibility and ease of fabrication. It can be seen commonly used in external (with respect to the human body) therapy and rehabilitation purposes. However, despite the ease of fabrication of silicone components, a gap in this current technology includes the inability of silicone to adapt to small-scale/delicate soft robotic structures as they cannot be cast and cured in small-scale molds due to their high viscosity (i.e., Ecoflex 00-30; Smooth-On viscosity 3000 cps). Moreover, the issue with utilizing silicone in medical applications is that silicone poses biocompatibility threats. With predominant exposure to the internal body environment, silicone has the tendency to rupture and release toxins, evoking the bodily immune response and leading to infection. Most notably, silicone-type soft robots are fabricated using pre-prepared silicone mixtures (e.g., Smooth-On, Inc.), which give them standard mechanical properties, making them noncustomizable to specific applications.

On the other hand, hydrogel has long been considered one of the most commonly used materials in bioengineering. The high water content of hydrogel makes it an ideal biocompatible material for tissue engineering and cell culture, while the nature of cross-linked hydrophilic porous structure of hydrogels also enables to absorb and release water easily to maintain structural regularity. Hydrogel in some cases has been utilized to construct millimeter-scale gel walkers that responded to electrical stimuli. With the inception and ever-increasing capabilities of the multivalve three-dimensional bioprinter, hydrogel fabrication can be scaled down to the micrometer scale comparable with cellular interactions. Although being a promising technology, some limiting factors of fabricating hydrogels are the cumbersome multiphase polymerization process, difficulty in achieving reproducibility due to the properties in swelling, diffusion processes, and softness recovery. Due to the high water content and cross-linking structure, commonly used hydrogels such as agarose and polyethylene glycol (PEG) usually yield very low stretchability and compressibility. Soft robotics, in contrast to their rigid, inflexible conventional counterparts, involves application of dexterous, soft, and compliant mechanical actuators. For example, pneumatic actuators in soft robotics are often designed for in vivo
applications, which require a flexible biocompatible material that can endure the pneumatic pressure in certain biological environments.18–21

In this study, a one-pot synthesis of highly stretchable hydrogel is shown and the product’s mechanical property has been characterized for its application in soft robotics.22 A similar one-pot synthesis of PEG-gelatin double-network (DN) hydrogel is also developed to reduce the potential toxicity of the agarose–acrylamide system.

In this article, the primary contributions include providing details on how DN hydrogels can be used as elastic material to fabricate soft robots, optimizing the soft robotic fabrication method while incorporating the DN hydrogel and translating to the related biomedical endoscopic soft robot application. We observed that changes in the method of DN hydrogel fabrication and variations in ingredient composition can alter their mechanical properties, suggesting that DN hydrogels can be tailored and customized according to specific soft robotic applications. We have further shown that bending and translational actuators, as well as small delicate structures, can be fabricated using this DN hydrogel. Due to its innate softness and biomimicry, high customizability DN hydrogel-based soft robots can further be introduced as an emerging field in bioinspired robotics.

Based on DN hydrogel’s biocompatibility, these hydrogel soft robots can make human–robot interactions inside the human body more patient-friendly and crucial to the innovation of new-age treatment. Therefore, incorporating the biocompatibility of hydrogels,8,9 in general with the improved mechanical properties of DN hydrogels, we believe that hydrogel potentially is a feasible alternative to silicone as a central material in soft robot fabrication.

Materials and Methods

DN hydrogel has two different networks within its structure, while in the Agar/PAM DN hydrogel, the agarose forms the first-network gel, which is physically linked by the agarose helix bundles, and then, by photoinitiation, the acrylamide turns into polyacrylamide gel as the second network. The final synthesized gel was tested to be not only rather soft in terms of its initial elasticity but also strong in terms of maximum stress and strain, which is desirable for soft pneumatic robotic applications (SPRAs) from a mechanical standpoint. In this study, we analyze DN hydrogel materials with methods of customizing chemical parameters to get desired output for SPRAs.

Experimental procedure for fabrication of hydrogel

Components and recipe. To produce Agar/PAM DN hydrogel, the required components are deionized water, agarose (Agar; Sigma-Aldrich), acrylamide (AM; Sigma-Aldrich), N,N’-methylene-bis-acrylamide (MBA; Sigma-Aldrich), and 2-hydroxy-4-(2-hydroxyethoxy)-2-methylpropioophenone (photoinitiator or PI; Sigma-Aldrich). The recipe that demonstrates the most desirable mechanical properties for our soft nasal endoscopic robot is listed in the table below (Table 1). This composition of chemicals shows most favorable recipe to fabricate DN hydrogels for soft robot applications based on the hydrogel’s ability to exhibit both load bearing (tensile strength) and elasticity.

Fabrication. On top of the toughness of this hydrogel, its synthesis method, called one-pot synthesis,22 renders it highly suitable for SPRA fabrication. Briefly, after mixing all the components in one falcon tube as per the recipe above, the mixture is heated to 90°C in an oven for 10 min until the agarose is fully dissolved (Fig. 1). What follows is to introduce

![FIG. 1. Adapted one-pot fabrication method for DN hydrogel synthesis. DN, double-network. Color images available online at www.liebertpub.com/soro](image-url)
the solution into the mold and cool it down for another 10 min so that the agarose gel can form. The mold with room temperature mixture is then exposed to UV light for polymerization of acrylamide as the second network for a couple of hours. After 2 h, the final Agar/PAM hydrogel is synthesized.

**Experimental procedure for dehydration and recoverability**

The hydrogels were observed to dehydrate when left to rest, completely drying out after a period of 2 weeks. After complete dehydration, hydrogels can be recovered by adding deionized water. To quantify dehydration and recoverability characteristics of the hydrogel, the following methods were adopted.

### Dehydration and preservation

To prevent dehydration of DN hydrogel in the first place, we preserved hydrogel soft robot and actuators at temperature below 0°C. According to the recipe, the concentration of water in Agar/PAM hydrogel was around 80%, accordingly the hydrogel can freeze below 0°C and the water loss can be prevented. Three samples were tested four times each on a weekly basis. In between the tests, the samples were packed in sealed sample bags and stored in a cold room (–20°C).

**Gravimetric analysis of dehydration and recoverability kinetics.** After initial measurements, the room temperature-dehydrated hydrogels were placed at a constant temperature of 21°C. Since it is optimal to determine dehydration kinetics gravimetrically, the weight of each hydrogel had to be recorded at a specific, predetermined time interval. For this hydrogel, it was observed that complete dehydration occurred at ~2 weeks, with the predetermined time interval for mass measurement set to 1 day. The calculation of dehydration of our DN hydrogel can be quantified with the percentage of water evaporated at a given time t. The amount of water evaporated from a given sample of DN hydrogel can be determined by the following simple equation:

\[
M_t = \frac{m(t) - m(0)}{M_\infty - m(0)}
\]

where
- \(M_t\) = total amount of water evaporated at a given time t;
- \(M_\infty\) = total water content in the freshly made DN hydrogel sample;
- \(m(0)\) = mass of custom-made DN hydrogel at initial state;
- \(m(t)\) = mass of custom-made DN hydrogel at a given time t; and
- \(m(\infty)\) = mass of custom-made DN hydrogel when completely dried.

To further process and characterize dehydration characteristics of the hydrogel, a mass transfer mechanism can be obtained. This is quantified by a power-law equation, demonstrating the time-reliant evaporation process as follows:

\[
\frac{M_t}{M_\infty} = K t^n
\]

where
- \(K\) = dehydration characteristic constant (can also be understood as dehydration rate) and
- \(n\) = classified diffusion factor, which decides Fickian/non-Fickian diffusion of our custom-made DN hydrogel.

It is possible that the dehydration characteristics vary for the different recipes of hydrogels that we have, meaning that the value of \(K\) and \(n\) can vary for different recipes. This is because hydrogels with higher gel fractions or stronger cross-linking have less free volume available for transporting water molecules. Therefore, separate measurements have to be taken for different recipes to obtain a clearer view of dehydration behavior. Dehydration kinetics was only performed for the best recipe in this report at 21°C.

**The method for recoverability testing is to add** \(M_\infty\) (initial amount of deionized water added during fabrication) to the hydrogel samples dropwise, ensuring that all exposed surfaces of the hydrogel are in contact with the water, allowing hydrogel to rest for 2–3 days at the same room temperature for final stress–strain behavior measurement.

**Experimental procedure for fabrication of soft robot**

In this study, we illustrate detailed steps of fabricating a miniaturized bending actuator using Agar/PAM hydrogel. Since curing process requires UV exposure, the mold that holds the hydrogel mixture must be transparent. In our case, we used acrylic tube as the crust of the mold (details in Supplementary Data; Supplementary Data are available online at www.liebertpub.com/soro) and a small opening is drilled near the bottom of the tube for hydrogel to enter. Due to low viscosity, the hydrogel mixture can be pumped up easily without trapping any air bubble.

In UV photopolymerization, the mold with hydrogel mixture is placed 10 cm away from the light source (Axend Pte Ltd) and rotated at 6 rpm for even distribution of UV light. After 2 h, the hydrogel is solidified and ready for demolding. The humidity of the hydrogel and the smooth surface of the acrylic tube ensure smooth demolding. The humidity of the hydrogel and the smooth surface of the acrylic tube ensure smooth demolding. When the main body of the soft pneumatic actuator (SPA) is constructed, the tubular hydrogel was wrapped densely wound threads using a winding machine tailored for winding threads with adjustable pitch.

The wound SPA was dipped into the hydrogel solution and underwent another curing process for an extra thin layer of hydrogel coating to secure exact position of the threads. By inserting air tube and side sealing using stretchable adhesive tape, the fabrication of this mini hydrogel bending actuator was completed. A dual-system soft robotic endoscope was designed with the aim of multiple degrees of pneumatic action. Details of information of design for fabrication of soft endoscopic robot and pneumatic actuation are given in Supplementary Table S1 and Supplementary Figures S1 and S2 (Supplementary Data are available online at www.liebertpub.com/soro).

**Results**

**Investigation of experimental variables on mechanical properties**

The synthesis of DN hydrogel normally follows a multistep, sequential, free radical polymerization method,^25,26^
which encounters a tedious time-consuming process associated with inflammation, evaporation, and two-stage polymerization technique that consume 1–2 days in general. Moreover, association of inflammation and evaporation posits increasing challenge to regulate precise molar ratio of the two networks for comparable mechanical properties. This, in practice, leads to a large amount of unrestored second-network monomers. Thus, in this section, we have tried to commensurate effects of three key variables on the mechanical properties of the acrylamide–agarose DN hydrogel system as (i) duration of UV exposure, (ii) MBA concentration, and (iii) resting time for manufacturing optimized soft robots.

It is observed that altering the parameters of these key variables directly affects the mechanical properties of the hydrogel, allowing it to be customizable for specific applications. Three samples of acrylamide–agarose hydrogel were tested four times each, varying each variable and each parameter for robust and optimized solution to counteract reproducibility issues. Mean and standard deviation (SD) of mechanical testing, for example, stress–strain analysis to incorporate each of these variables, were obtained via universal testing machine (UTM). These graphs were then curve fit to nearest polynomial degrees, and SDs recorded as error bars in all figures.

Customization by UV exposure. UV exposure time is defined by the amount of time the hydrogel is exposed under the UV lamp during the curing process. Figure 2 shows the effect of changing UV exposure time while hydrogel is cured. The following UV exposure times were investigated: 60, 90, 120, 150, and 180 min.

It is observed that UV exposure time of 120 min is the most optimum as it displays both maximum tensile strain of 851% and maximum tensile stress of 0.273 MPa. In addition, as can be seen from Figure 2, lower exposure times lead to an increase in load-bearing ability (quantified by Young’s modulus, which is the slope of the graph) of the hydrogel and decrease in strain, whereas increasing exposure time past the optimum results reveals an eventual decrease in overall load-bearing ability and increase in elasticity (Table 2).

When the UV exposure time is decreased, an increase in initial Young’s modulus is observed, seen by the steep initial gradient in the 60-min sample. However, tensile strain of the hydrogel is greatly compromised, exhibiting a maximum strain much lower than the hydrogel that was cured for 120 min, 851%. When the UV exposure time is increased, average tensile strain of the hydrogel is observed to marginally increase to 864%. However, the shape of the stress–strain graph changes greatly, exhibiting a high initial Young’s modulus, thus leading to a plateau effect.

It is presumed that the plateau effect signifies a change of material properties from elastic deformation to plastic deformation (i.e., the deformation caused is permanent, and the hydrogel is unable to withstand high loads at larger tensile strain). This shows that hydrogels exposed for 150 and 180 min under the UV lamp are less able to withstand load bearing compared with the hydrogel cured at 120 min. Table 2 summarizes the essential data obtained from stress–strain graphs.

Young’s modulus of all hydrogel samples is observed to vary till their point of break, although in different ways. Less-exposed hydrogels are observed to have overall Young’s modulus almost constant to their initial Young’s modulus.

<table>
<thead>
<tr>
<th>UV exposure time/min</th>
<th>Average initial Young’s modulus/kPa</th>
<th>Average maximum tensile strain/%</th>
<th>Average maximum tensile stress/MPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>92.869</td>
<td>467.51</td>
<td>0.151</td>
</tr>
<tr>
<td>90</td>
<td>83.880</td>
<td>433.58</td>
<td>0.122</td>
</tr>
<tr>
<td>120</td>
<td>60.585</td>
<td>851.09</td>
<td>0.273</td>
</tr>
<tr>
<td>150</td>
<td>72.891</td>
<td>864.19</td>
<td>0.223</td>
</tr>
<tr>
<td>180</td>
<td>83.730</td>
<td>895.45</td>
<td>0.159</td>
</tr>
</tbody>
</table>

FIG. 2. Customization by UV exposure. Effects of varying UV exposure times on stress and strain values of acrylamide–agarose hydrogel. Color images available online at www.liebertpub.com/soro

FIG. 3. Customization by MBA concentration. Effects of varying MBA concentrations on stress and strain values of acrylamide–agarose hydrogel. Color images available online at www.liebertpub.com/soro
Customization by MBA concentration. MBA concentration is defined as the concentration of the cross-linker that was added during fabrication of the DN hydrogel. It is depicted in Figure 3 that changing the concentration of MBA (cross-linker) (e.g., 3, 4, 5, and 6 mg/mL) also affects the resulting mechanical properties of the hydrogel. As per analysis, DN hydrogel made using 5 mg/mL MBA concentration yields the most favorable results, with 851% tensile strain and 0.251 MPa tensile strength.

Overall, low MBA concentrations result in increased load-bearing ability. It was hypothesized that MBA concentration is a key factor in conversion of material properties in hydrogel from plastic to elastic. Lower MBA concentration follows the transition from plastic to elastic in hydrogel characteristics, while high concentrations of MBA are shown to revert back into brittle plastic deformation. The key data are displayed in Table 3 below of varying MBA concentration hydrogels.

A high Young’s modulus is observed at the lowest MBA concentration of 3 mg/mL at 87.8 kPa. Again, Young’s modulus is determined by the gradient of the stress–strain graph in Figure 3. However, at 3 mg/mL, plastic deformation begins to set in at ~150% strain, indicating a change in the trend in tensile strain. At 4 mg/mL, the stress–strain behavior of the hydrogel is reliable; there is an increasing trend in Young’s modulus as the strain increases, as seen by the increasing gradient. The hydrogel fabricated with 5 mg/mL MBA concentration closely represents the ideal characteristics required by soft robotic applications, with an increasing Young’s modulus as strain increases.

However, when the MBA concentration is further increased to 6 mg/mL, the behavior reverts back to a high initial Young’s modulus at 110.1 kPa with it continuing to decrease as the strain increases. Experiments were conducted for hydrogels fabricated at 7 mg/mL as well; however, these hydrogels were extremely pliable and not stable enough to be gripped by the UTM gripper.

Therefore, it can be seen that at both extremes—high and low MBA concentrations—Young’s modulus behavior is similar: both have an initial spike, followed by a plateau effect. This could be due to the fact that at low MBA concentrations, there is not enough cross-linker to complete primary network formation, that is, cross-linker thus forms the limiting factor. Henceforth, the initial cross-linked networks that were formed have strong chemical bonds, reflected by large initial Young’s modulus. However, there is an eventual lack of cross-linker, resulting in the drop of Young’s modulus. At high MBA concentrations, there are similar strong network formations, resulting in high initial Young’s modulus. However, this hydrogel can be overcross-linked, which makes it more brittle, resulting in the premature fracture of the hydrogel.

### Table 3. Customization by MBA Concentration: Effects of MBA Concentration on Mechanical Properties

<table>
<thead>
<tr>
<th>MBA concentration/mg/mL</th>
<th>Average Young’s modulus/kPa</th>
<th>Average Young’s maximum tensile strain/%</th>
<th>Average Young’s maximum tensile stress/MPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>87.843</td>
<td>775.50</td>
<td>0.192</td>
</tr>
<tr>
<td>4</td>
<td>70.314</td>
<td>452.31</td>
<td>0.146</td>
</tr>
<tr>
<td>5</td>
<td>60.585</td>
<td>851.09</td>
<td>0.273</td>
</tr>
<tr>
<td>6</td>
<td>110.072</td>
<td>368.39</td>
<td>0.122</td>
</tr>
</tbody>
</table>

Customization by resting time. Resting time is defined as the time the DN hydrogel sample is left to stabilize after its fabrication and it was observed how it affects the final mechanical properties. When freshly fabricated, the cross-link is weak and needs some time to set, while long resting durations (>7 days) lead to dehydration of the hydrogel by evaporation. Therefore, an optimum resting time is crucial for the best performance of the hydrogel. Table 4 summarizes key data for the variable, resting time, and Figure 4 shows stress–strain behavior of the hydrogels with varying resting times.

Experimental investigation has shown that resting time does play a role in changing the mechanical properties of the hydrogel and the following resting times were investigated—14, 10, 7, and 3 days—with immediate sample. As seen from Figure 4, the most optimum resting time is 3–7 days after fabrication.

### Table 4. Customization by Resting Time: Effects of Resting Time on Mechanical Properties

<table>
<thead>
<tr>
<th>Resting time/days</th>
<th>Average Young’s modulus/kPa</th>
<th>Average Young’s maximum tensile strain/%</th>
<th>Average Young’s maximum tensile stress/MPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>61.034</td>
<td>368.09</td>
<td>0.121</td>
</tr>
<tr>
<td>3</td>
<td>91.980</td>
<td>680.81</td>
<td>0.138</td>
</tr>
<tr>
<td>7</td>
<td>60.585</td>
<td>851.09</td>
<td>0.273</td>
</tr>
<tr>
<td>10</td>
<td>100.082</td>
<td>330.67</td>
<td>0.148</td>
</tr>
<tr>
<td>14</td>
<td>174.273</td>
<td>464.88</td>
<td>0.163</td>
</tr>
</tbody>
</table>

Acrylamide and agarose concentration variations. Acrylamide–agarose concentration recipe based on one-pot analysis adopted by Chen et al. was used for all previous experiments. In addition to this, experiments varying the acrylamide and agarose concentrations in hydrogel have also been conducted in an attempt to characterize a trend in behavior with respect to acrylamide/agarose concentrations. However, these experiments lead to inconclusive results, which further call for modifications to test and fabricate apparatus to realize these trends. These trends will serve to further complement existing understanding of the effect of primary ingredient concentrations on overall hydrogel characteristics.

As shown in Figure 5A, varying acrylamide concentrations lead to changing hydrogel behavior. These results show that both lower and higher concentrations of acrylamide result in presumably plastic deformation characteristics of the hydrogel. The probable reasons could be due to the following: (i) in low concentrations of acrylamide, acrylamide is the limiting factor, resulting in poor secondary network formation; and (ii) excess acrylamide results in weaker bond formation. In Figure 5B, varying agarose concentrations lead to an even more irregular trend in hydrogel behavior. It is perceived that high agarose concentrations will greatly disrupt network formation due to the large size of agarose molecule and its gelation abilities. Hence, the reason as to why
maximum tensile strength and load-bearing ability vary is not yet fully understood and summons future research investigations.

Material property: comparison test

To find out plastic flow behavior, strength, and ductility, a comparison platform has been established to interpret differences between commonly used silicone and custom-made DN hydrogel. The compression and tensile test results of Agar/PAM hydrogel with silicone samples (Ecoflex 0030; Smooth-On) are depicted in Figure 6 for comparison.

Custom-made DN hydrogel is seen to achieve dramatic extension of around 1800% strain, while compression test reveals similar behavior. Meanwhile, from 0% to 1000% of strain, the average elastic modulus is nearly 100 kPa, indicating its ultrasoftness. The corresponding property of silicone sample is only around 500% of strain at around 700 kPa. The difference in the properties implies their different fitness for various applications. We believe that for occasions demanding extreme deformation or higher power/energy efficiency, the Agar/PAM hydrogel stands out. Although the fracture stress is only about 300 kPa, it is still strong enough as a candidate for SPRA material. Moreover, our fabrication methods contain further reinforcement, leaving this shortcoming negligible.

Dehydration kinetics and recoverability

Dehydration kinetics and recoverability are key factors to understand the preservation and shelf life of hydrogels. This section realizes the dehydration mechanism of the hydrogels and how to effectively recover their properties after complete dehydration.

Dehydration kinetics. Dehydration kinetics refers to the mechanism in which water content of the hydrogel decreases at a particular temperature over a period of time. The standard condition of storage for this hydrogel was at 21°C. Figure 7 shows the changes in weight of three identical samples over the days gravimetrically.
Referring to the equation:

\[ \frac{M_t}{M_\infty} = Kt^n \]

From Figure 7, it can be calculated that at 21°C, the best hydrogel recipe has the following constant values: \( K = 0.187 \) and \( n = 0.720 \). This means that the rate of dehydration (dehydration characteristic constant) for this hydrogel is 0.187. Since the value of \( n \) is between 0.5 and 1, this hydrogel is therefore characterized to behave in a non-Fickian manner. Therefore, the final dehydration mechanism equation for the best hydrogel is

\[ \frac{M_t}{M_\infty} = (0.187)t^{0.720} \]

Figure 7 also shows the rate of water loss from the hydrogel and the above equation helps to calculate the rate of water loss by the dehydration mechanism.

Recoverability of hydrogel after dehydration. These DN hydrogels were observed to dehydrate completely within days, which lead to recovery and reservation crucial to extend their shelf life. Adding initial amount of water and allowing them to rest for 2–3 days recovered three samples of completely dehydrated hydrogels. These recovered hydrogels were tested through INSTRON UTM to analyze whether their mechanical properties can be recovered. Figure 8 demonstrates elastic recoverability of dehydrated hydrogels that reaches an average value of tensile strain of 747.6% and tensile strength of 0.159 MPa with elastic deformation. This shows promising recoverability values of the hydrogels after they have been fully dehydrated. Measurements of the recovered samples were also compared with original measurements of the sample. It was observed that the recovered samples are able to return to their original configuration, with an SD of 0.707 mm.

Microscopic analysis (AFM) of different hydrogel layers will be investigated in future to further improve the recoverability procedure to ensure equal water diffusion throughout the hydrogel. This recoverability result thus promises that hydrogel soft robots can be stored and reused, increasing their potential to be commercialized. However, future research will inculcate freezing the hydrogels at low temperatures to
retain their water content during storage to prevent dehydration. In this regime, Yuk et al. recently devised a method to robustly bind hydrogels to elastomers—a water-trapping barrier that kept the hydrogel moist, flexible, and robust, which is believed to reinforce our findings even more in future.

Discussion

**Stiffness modulation and methods of achieving impedance matching**

Soft materials such as human skin and cartilage possess Young’s modulus, \( E \), of much smaller magnitude (\( E \approx 10^7–10^9 \) Pa) than rigid materials (\( E \approx 10^9–10^{12} \) Pa) such as metals and hard plastics. Characterizing the transition from hard to soft material, and *vice versa*, is crucial as almost all living organisms come with a combination of both.\(^{28}\) Therefore, stiffness modulation is an important aspect for biomedical engineering applications. Hence, a clear understanding of elastic properties, yield point behavior, and mechanical impedance matching with internal organs can provide indispensable knowledge to further instigate our custom-made DN hydrogel for soft biomedical robots in healthcare application.

Experimental observation depicted in the previous section customizing different parameters, such as UV curing time, composition, and resting time, shows the most viable hydrogel sample to have tensile strain of 851% and maximum strength of 0.273 MPa, that is, Young’s modulus of \( 3.2 \times 10^4 \) Pa. The range of Young’s moduli of our custom-made DN hydrogel with various classes of materials is portrayed in Figure 9, and the gap between rigid and soft material is outlaid clearly.

It clearly shows a nice match between living cells and human skin, tailoring a viable alternative for future biomedical soft robots. On the other hand, the relationship between deformation kinematics (generalized displacement/velocity) and the resulting dynamics (generalized force/torque) is termed mechanical impedance and defines the linear or rotational stiffness and damping characteristics of the system under consideration.\(^{29}\) In our custom-made DN hydrogel, stiffness modulation depends on the polymer molecular weight distribution composition and stoichiometry of the Agar/PAM with agarose/acrylamide variations.\(^{30}\) So, to further tune the mechanical properties such as stiffness and swelling for more accurate impedance matching between the actuators and internal organs, physical factors such as cross-linking density (i.e., MBA concentration) and molecular weight distribution, as well as some chemical modification in polymer, are necessary.\(^{31,32}\)

**Preliminary soft robotic bending actuator using fabricated hydrogel**

The DN hydrogel was used to successfully fabricate an air pump-controlled bending actuator. This bending actuator is
controlled by three airways, which were placed 120° away from each other, providing three degrees of freedom (DOF) of movement. The amount and rate of bending are controlled by speed and pressure of the air that is pumped into the channels. A prototype of bending actuator contains a 3-mm cylinder with 1-mm hollow cavity, as shown in Figure 10. A video of the successful bending actuator is available in Supplementary Data (Supplementary Movie S1).

According to the design described in the Supplementary Data section, both components (main and distal sections) of the soft endoscopic robot were successfully fabricated. Both components of varying diameter were threaded to restrict radial expansion of the robot. Three flexible tubes were attached to each of the cavities in both components for actuation of the robot.

Our solution offers a hydrogel-made soft robotic system that is easily customizable, delicate in small millimeter scales, and biocompatible. This makes it a better choice of biocompatible material for soft biomedical robotic fabrication compared with the current silicone method. Moreover, since the majority of rehabilitative or surgical robots are fabricated with hard materials, which are not naturally compliant with human soft tissue, these fabricated soft hydrogel robots and actuators can be a promising alternative for future biomedical robots.

**Soft endoscopic robot**

Clinical background and motivation. Nasopharyngeal carcinoma (NPC) is the most common tumor that originates in the nasopharynx, which is located at the uppermost area of the throat that lies behind the nose. There is also a high recurrence rate of NPC of 70% after remission. Therefore, it is important to regularly monitor the recurrence of NPC apart from early diagnosis. Due to the high recurrence rate of NPC in the patients, frequent checkup of the nasopharyngeal region is required so as to prevent the NPC from developing into distant metastasis.

The process of conducting a transnasal routine check has been a challenging task even for skilled ENT (ear–nose–throat) clinicians. Thus, there is a need to develop a robotic endoscopic device that is home based so that NPC can be regularly monitored. The device is to be inserted into the nasopharynx through the nostrils. To facilitate the usage of the device at home, it is designed to be easily operated by patients after special training on the use of the device so that patients would not have to periodically visit the medical centers for consultations.

Passive rigid or flexible endoscopes have been widely used for centuries in clinics, but not dedicated for the purpose of home-based monitoring with patient–administration capability. Therefore, this soft robotic fabrication approach in this article can facilitate the development of a multi-DOF and compact, soft, flexible endoscopic robot with safe, biocompatible soft materials.

DN hydrogel-based soft endoscopic robot: an initial trial. In this section, we discussed our DN hydrogel-based preliminary soft endoscopic robot, which is believed to overcome the shortcomings of endoscopes with active bending capabilities, as mentioned in the preceding section. Our soft endoscopic robot was actuated at varying air pressures and displayed bending of up to ~145° in each of the three directions (DOF) of actuating/pumping individual channel.

More sophisticated motion can be accomplished by cooperatively pumping the three air channels, and by simultaneously pumping all three channels, we can accomplish elongation axially of the manipulator. A minicamera module and LED lights were attached to the distal end of the soft endoscope and tested on a human phantom skull model (Fig. 9). The endoscope displayed easy passing through the nasal passageway. By controlling the air pressure through the pressure valves in each of the three chambers, movement and control of the position in the XYZ axes can be achieved. Videos of movement and pneumatic actuation are available (Supplementary Movie S1).
Summary of Obtained Results

Custom-made DN hydrogel for soft robotic application in our article shows tensile strain of 851% and maximum strength of 0.273 MPa. The key points we validated through this article are that mechanical stiffness, elasticity, and strength range of this hydrogel can be adjusted according to application requirements by altering key variables, for example, (i) duration of UV exposure, (ii) MBA concentration, and (iii) resting time for manufacturing optimized soft robots. The increasingly nontrivial challenge we faced was dehydration and evaporation of our DN hydrogel. In this realm, we have come up with a solution to recover the dehydration and regain tensile strain of 747.6% and tensile strength of 0.159 MPa with elastic deformation.

Furthermore, we have undergone mechanical testing for our custom-made DN hydrogel with commonly used silicone samples (Ecoflex 0030; Smooth-On). INSTRON UTM compression test resulted in a similar trend, while in tensile test, DN hydrogel outperformed silicone. DN hydrogel is shown to bear 1800% tensile strain and 300 kPa tensile stress, while silicone snapped through within 500% strain regime.

The results prove to have an immense potential on choosing next-generation active material for tailoring a better solution for fabricating biocompatible soft robots. Finally, in the last part of the article, we have successfully demonstrated our initial prototype for soft endoscopic robot, which further opened up a new avenue to rediscover biomedical robotics.

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Author Disclosure Statement

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