

Summary: A novel approach was developed to prepare a superporous hydrogel with superior mechanical and elastic properties. According to this method, a synthetic monomer was polymerized and crosslinked in the presence of a water-soluble alginate polymer. Later in the process, the alginate part of the synthesized hydrogel was treated with metal cations, which resulted in a hydrogel hybrid with an interpenetrating network structure. In this article, a hydrogel hybrid of acrylamide and alginate is highlighted because of its unique swelling and mechanical properties. This hydrogel hybrid shows resilience and a rubbery property in its fully water-swollen state, which not previously been reported. To help understand the underlying mechanism responsible for such unique properties with hydrogel hybrids, the ionotropic gelation of the alginate polymer was also studied in more detail.



The elastic nature of the prepared, water-swollen, acrylamide-alginate hybrid hydrogel.

Elastic, Superporous Hydrogel Hybrids of Polyacrylamide and Sodium Alginate

Hossein Omidian,*¹ Jose G. Rocca,¹ Kinam Park²

¹Kos Pharmaceuticals, Inc.; Hollywood, Florida 33020, United States

²Department of Pharmaceutics and Biomedical Engineering; Purdue University; West Lafayette, Indiana 47907, United States
E-mail: homidian@kospharm.com

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Introduction

Superporous hydrogels (SPHs) are a three-dimensional network of hydrophilic polymers that absorb a considerable amount of water in a very short period of time due to the presence of many pores with diameters on the micron to millimeter scale.^[1–3] These hydrogels are distinguished from other porous hydrogels in terms of their pore sizes and the methods used to generate the pores. If any portion of a superporous hydrogel is exposed to water or aqueous fluids, fluid is immediately absorbed through the open channels to fill the whole space. This capillary-driven absorption mechanism helps dried superporous hydrogels to swell very quickly into a very large size.

Superporous hydrogels can be made to possess mechanical or high mechanical strength properties after swelling. As previously reported, the SPH mechanical strength can be improved by adding crosslinked hydrophilic polymers into the SPH formulation.^[4] This modification essentially

increases the crosslink density of the hydrogel without making the SPHs too brittle. In other words, this approach results in a higher modulus SPH. As a new development, the mechanical properties of the SPHs can be significantly improved through a novel interpenetrating network formation. Before polymerization and crosslinking, a given solution of water-soluble alginate polymer was added into the mixture of monomer, crosslinker and other necessary ingredients for the SPH preparation. The mixture was polymerized and crosslinked at room temperature using redox initiator couples. The polymerized SPH was further treated with metal cations to induce the metal complexation of the alginate portion of the SPH structure. These products are very resilient and resistant to compression and elongation. In their water-swollen state, elastic superporous hydrogels can be repeatedly stretched to almost twice their original length without breaking. These novel products may find applications in the development of drug and protein delivery systems, fast-dissolving tablets, occlusion devices for

aneurysm treatment, scaffolding, cell culture, tissue engineering, water-absorbent pads, hygiene products (baby diapers, feminine pads) and many others.^[5] In this regard, a new development of elastic superporous hydrogel hybrids of polyacrylamide and sodium alginate is reviewed herein.

Properties of Sodium Alginate

Alginates are a family of linear, non-branched polysaccharides which contain varying amounts of 1,4'-linked β -D-mannuronic acid and α -L-guluronic acid residues.^[6–7] Alginates can make a gel in the presence of divalent and trivalent cations including Ca^{2+} and Al^{3+} . It has been shown that the exchange of the sodium ions from the guluronic acids with divalent ions, and the stacking of these guluronic groups, form a so-called egg-box structure. The divalent cations bind to the α -L-guluronic acid blocks in a highly cooperative manner. The alginate chains can then dimerize to form gel networks.^[7]

Sodium Alginate in Hydrogels

The metal-treated alginate hydrogels have been used as scaffolds in tissue engineering,^[8] as biomaterial,^[9] in cell culture/transplantation,^[10] and in cell immobilization.^[11] The internal bead structure,^[12] gelation models,^[13] and viscoelastic properties^[14] of the calcium alginates have been studied in detail. On the other hand, chemically-crosslinked alginate hydrogels have been used as a controlled release medium for drugs,^[15–19] pesticides,^[20] superabsorbent filament fibers,^[21] and flocculants.^[22] Similarly, the semi-interpenetrating (semi-IPN) membrane networks have been developed based on sodium alginate and synthetic polymers including polyacrylamide or poly(acrylic acid),^[23] polyacrylonitrile,^[24] and poly(vinyl alcohol).^[25] To the best of our knowledge, a fully-interpenetrated (fully-IPN) network of alginate and synthetic polymers is a new development in hydrogel industry. This development requires addition of the alginate polymer in solution form into the polymerizable mixture, followed by metal-complexation of the alginate portion of the SPH structure.

Experimental Part

Materials and Methods

The following materials were used in this study: alginic acid, sodium salt (Sigma, LV (A 2158), MV (A 2033), HV (A 7128)); ammonium persulfate (Aldrich, 21,558-9); *N,N'*-methylenebisacrylamide (Sigma, M-7256); *N,N,N',N'*-tetramethylethylenediamine (Aldrich, 41,101-9); Pluronic[®] F127 (BASF, EO₁₀₀PO₆₅EO₁₀₀, $\bar{M}_w = 12\,600$, $\bar{M}_{PPO} = 3\,780$), poly(ethylene oxide), PEO (70 wt.-%, HLB 18-23); ethanol (Pharmco, 200 proof ACS/USP grade); acrylamide (Sigma, A-8887); calcium chloride (Mallinckrodt, 4225); acetic acid (Mallinckrodt, V194).

All materials were used as received and all solutions were prepared using deionized water.

Sodium Alginate Beads

Alginate Solution

The sodium salt of alginic acid (3.0 g) was poured, dispersed and homogenized into 97.0 g of nanopure water. The container was covered with aluminum foil and kept overnight in the dark with no agitation and mixing. It was then homogenized into a very smooth solution under very gentle mixing.

Ion Solution

Calcium chloride (20 g) was dissolved into 50 g of nanopure water under magnetic stirring. After cooling to room temperature and obtaining a clear solution, various aqueous solutions were accordingly prepared by diluting the original solution. Similar volumes of the ion solutions (ranging from 0.089 to 28.57 wt.-%) were used to prepare the alginate beads.

Bead Preparation

An as-prepared, 3 wt.-% aqueous solution of the alginate was dropped into individual ion solutions using a disposable polyethylene transfer pipette (2mm internal tip diameter). Under smooth magnetic stirring, beads were produced inside the glass vials each containing 16 ml of the ion solutions. Stable alginate beads were instantly formed in all crosslinker solutions except in the 0.089 wt.-% CaCl_2 solution.

Bead Size Measurements

A micrometer (AMES, Waltham, Mass, USA) was used to measure the bead size. At least 10 different measurements were made and averaged.

UV Absorbance

A UV detector (Gilson, Model 111B) was used to quantify the absorbance of the alginate at 280 nm. The corresponding absorbance figures were correlated to the water soluble (sol) fraction of the sodium alginate gel network. For this measurement, 2 to 3 ml supernatants of the individual ion solutions were filtered and examined. Neither water nor CaCl_2 showed absorption over this wavelength.

Bead Deformation Under Load

A Bench Comparator (AMES, Waltham, Mass, USA) was used. The bead deformation was measured under a 10 g load. At least 10 different beads were tested and the mean value was reported.

Synthesis of the Hydrogel Hybrids

Acrylamide solution (50 wt.-%, 500 μL) was poured into a glass test tube (11.0 mm internal diameter (I.D.), 100 mm height) containing 500 μL of deionized water. The *N,N'*-methylenebisacrylamide (100 μL of the 1 wt.-% aqueous solution) was added and the glass tube was shaken. To this

combined solution, 50 μL of Pluronic F127 (10 wt.-%) was added, and the mixture well-shaken. After combining acrylamide, bisacrylamide, Pluronic F-127 with acetic acid, 1 500 μL of an aqueous solution of sodium alginate (2 wt.-%) was added. To initiate the polymerization at room temperature of 26 °C, tetramethylethylenediamine (40 v/v) and ammonium persulfate (20 wt.-%) were used in an amount of 50 μL each. The sodium bicarbonate (35 mg) was added to the reaction mixture 45 s after addition of the APS. This addition was followed by foaming and gelation, which occurred over a period of 50 to 75 s. After treatment in ion solution (30 wt.-%) and purification with water, the SPH foam was dried out to a constant weight in an oven at 50 °C, overnight. Excluding the treatment step, a semi-interpenetrated network of sodium alginate-polyacrylamide was similarly prepared and used as control.

Results and Discussion

The non-treated, semi-interpenetrated network of polyacrylamide-sodium alginate swelled to about 100 $\text{g} \cdot \text{g}^{-1}$ of the active swellable material and was mechanically very weak in its fully-swollen state in water. On the other hand, its fully-IPN counterpart swelled to 40 to 50 $\text{g} \cdot \text{g}^{-1}$ and was mechanically very strong, and elastic in its fully-swollen state. The fully-IPN hybrid was found to be significantly resistant to various types of stresses including tension, compression and bending.

During the development of elastic hydrogel hybrids, a number of parameters were found to be more important, and

are summarized in Table 1. Although sodium alginate of medium viscosity grade was used in this experiment, there were other parameters, including the alginate grade (low to high viscosity), the alginate concentration, and the calcium chloride concentration (ratio of $\text{CaCl}_2/\text{alginate}$), that could potentially affect the properties of the final product. These parameters were evaluated in turn in order to obtain a superporous hydrogel with desirable physical and mechanical properties.

Structural homogeneity (pore size and its distribution) is the basic requirement to develop a mechanically strong SPH. This requirement can be met by proper optimization of the synthetic and processing steps involved in the SPH preparation. Nevertheless, the unique elastic property of these hybrid hydrogels can mainly be accounted for in terms of the gelation properties of sodium alginate at a high ion concentration. The physical and mechanical properties of this novel hybrid are shown in Figure 1 and 2.

The hydrogel hybrid of acrylamide and alginate in its water-swollen state could be stretched to about 2 to 3 times of its original length; it also recovered like a rubber. The loading/unloading cycle could be repeated for at least 20 times (Figure 2). The hybrid could also resist a static, mechanical pressure of at least 10 N as shown in Figure 3.

During the developmental process, the ion solutions of different concentrations were examined, which resulted in hybrids of different swelling and mechanical properties. With an increase in the ion concentration of the treatment medium, the mechanical properties of the hybrid were

Table 1. Variables and effects in the synthesis of superporous hydrogel hybrids.

Variables	Effects
Ratio of alginate to acrylamide, wt./wt.-%	Negligible strength enhancement at lower extreme (4%); SPH phase separation at higher extreme (20%); ratio of about 10% resulted in successful SPH preparation with significant mechanical properties; lower swelling rate and swelling capacity at higher concentration
Alginate grade, LV, MV, HV	Lower alginate viscosity promotes two phasing, better bicarbonate dispersion, more homogeneous foaming, and faster gelation
Post-crosslinker concentration	High mechanical and swelling properties, water-absorption rate of 0.8 to 5 min and swelling capacity of 33 to 50 $\text{g} \cdot \text{g}^{-1}$ under high ion concentration (10 to 50 wt.-%) and using a low viscosity grade of alginate; higher swelling rate and swelling capacity at higher ion concentration
Temperature of the ion solution (30 to 100 °C)	A higher treatment temperature resulted in a higher swelling capacity; thermal degradation of bisacrylamide is presumably accountable for the higher swelling
Foam height	Inferior swelling but superior mechanical properties when foam is short: 3.5 cm; moderate swelling and mechanical properties when foam height is about 6 cm; superior swelling but inferior mechanical properties when foam was tall: 8.5 cm; with a typical glass tube reactor (ID/H ratio of 0.11), the optimum foam volume is about 60% of the reactor volume
Bicarbonate, acid and F127	The bicarbonate concentration was as effective as the acid concentration on the foam volume. Increased foam volume resulted in better swelling properties; a more heterogeneous foam with high carbonate concentration is due to local bicarbonate aggregate formation (local bicarbonate aggregation favors gelation of the surrounding reacting system); better foam homogeneity at lower bicarbonate concentration; increased bicarbonate or acid components generally results in increased foam volume, swelling rate, swelling capacity, capillary absorption and decreased resiliency, diffusional absorption and foam homogeneity



Figure 1. The final, dried hydrogel hybrid of acrylamide and alginate is rigid and brittle (left); it swells to about 10 to 15 times of its own volume in water (right).

significantly increased, at the expense of the swelling properties. Therefore, a range of high-to-low-swelling polymers having poor-to-good mechanical properties (flexible, low modulus, high modulus and elastic) was achieved over the ion concentration studied. Since the elastic properties of the hydrogel hybrid were solely obtained at a very high cation concentration, the gelation properties of the alginate polymer were studied more in detail over a broad range of ion concentration. This study was intended to obtain a better understanding of the underlying mechanism controlling the elastic properties of the hybrid in its water-swollen state.

Gelation Properties of Sodium Alginate

Alginate beads were prepared in ion solutions containing 0.089 to 28.57 wt.-% CaCl_2 . During the bead preparation, all attempts to prepare beads in 0.089 wt.-% solution failed. The beads were loose and broke apart even under gentle mixing. On the other hand, the alginate beads were successfully formed in the other solutions, containing 0.17 to 28.57 wt.-% CaCl_2 . The size of the beads was measured after they were incubated in their corresponding crosslinker solutions for one week.

Although the alginate beads were uniform and well shaped, they were obtained in different sizes ranging from

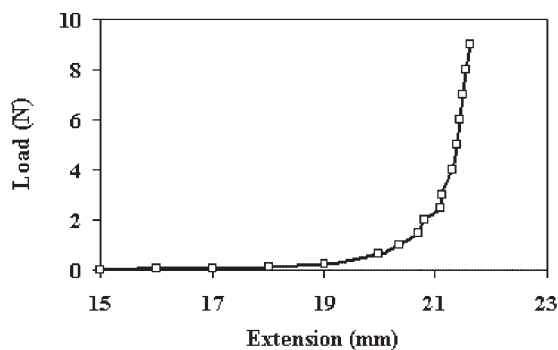


Figure 3. The static mechanical strength of the acrylamide-alginate hydrogel hybrid obtained using a Chatillon TCD-200 Digital Mechanical Tester.

1.91 to 3.68 mm, as is shown in Table 2. The smallest and the largest beads were respectively obtained at higher and lower extremes of the crosslinker concentrations. The bead size decreased in a non-linear trend as the ion concentration increased.

A UV detector was used to evaluate the extractable (sol) fraction of the beads. As a common observation, the cross-linked systems always contain a gel and a sol fraction. The gel and sol fractions of the alginate network were semi-quantitatively determined through monitoring the UV absorbance of the alginate polymer (sol fraction) at 280 nm.

The alginate bead size and the sol fraction of the alginate network are displayed in Figure 4 over the range of the ion concentrations studied. A correlation was found between the bead size and the values of the UV absorbance as the ion concentration increased. Over a very broad range of ion concentrations, the UV absorbance remained at a plateau value, except at very low crosslinker concentrations. As a result, the efficiency of the ionotropic gelation for the calcium alginate system was found to be critically dependent on the amount of ions at the lower concentration extreme. On the other hand, the ionotropic gelation is almost independent of the crosslinker amount at the higher extreme of the ion concentration range. Although there is no

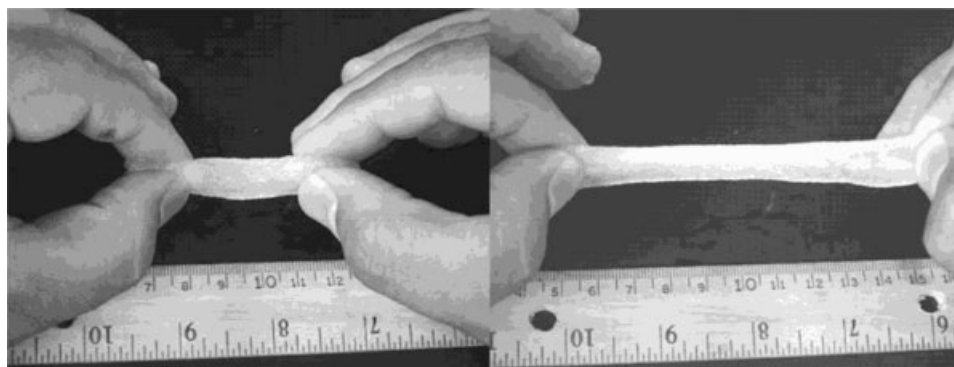


Figure 2. A water-swollen acrylamide-alginate hybrid with elastic, rubbery properties.

Table 2. Gelation features of alginate beads; bead size and sol fraction dependence on ion concentration.

CaCl ₂ concentration	Range of bead sizes ^{a)}	Mean bead size	UV Absorbance at 280 nm
wt.-%	mm	mm	
0.17	2.88 to 3.50	3.18	0.080
0.44	3.05 to 3.42	3.21	0.011
0.89	3.12 to 3.68	3.36	0.012
1.78	2.79 to 3.61	3.13	0.012
3.57	2.82 to 3.18	3.01	0.013
7.14	2.73 to 3.05	2.86	0.012
14.28	2.37 to 2.90	2.65	0.012
28.57	1.91 to 2.40	2.21	0.019

^{a)} Number of beads tested = 10.

sol fraction detected by UV in the concentration range of 0.44 to 28.57 wt.-%, the bead size decreased with an increase in the crosslinker amount.

The equilibrium bead size is a measure of the equilibrium swelling capacity of the beads in their corresponding swelling solutions. Hence, small or large bead sizes display low and high swelling systems respectively. The data for bead size and crosslinker concentration are consistent with the swelling capacities of the beads. To exclude the effect of the ionic strength of the crosslinker solution, all beads obtained in individual crosslinker solutions were thoroughly washed several times with nanopure water and then soaked in fresh nanopure water for another week. Although the alginate beads were uniform, white in color, and well shaped, they were obtained in different sizes to their original sizes in the crosslinker solution. They were whiter in color than when they were directly obtained in the ion solution. Table 3 shows that the size of the alginate beads varies from 1.35 to 2.54 mm as opposed to their typical original sizes in the range of 1.91 to 3.68 mm.

The mean size of the beads obtained from different ion solutions decreases with an increase in the ion concentration in both cases, that is, beads in the ion solution and

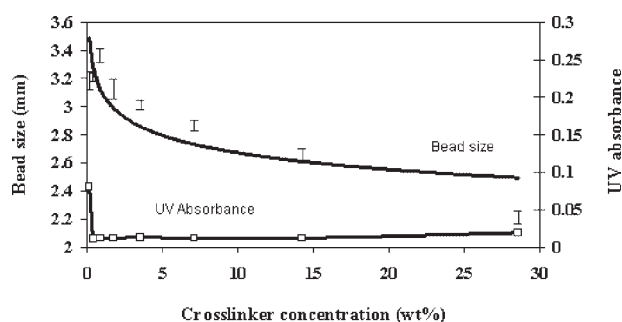


Figure 4. Bead size and sol fraction of the alginate network versus ion concentration.

Table 3. Size of the alginate beads crosslinked at different ion concentrations after soaking in nanopure water for 1 week.

CaCl ₂ concentration	Range of bead sizes ^{a)}	Mean bead size
wt.-%	mm	mm
0.17	2.02 to 2.35	2.197
0.44	1.79 to 2.29	2.001
0.89	1.88 to 2.28	2.083
1.78	1.92 to 2.25	2.049
3.57	1.85 to 2.20	2.012
7.14	1.81 to 2.02	1.897
14.28	1.57 to 1.87	1.776
28.57	1.53 to 1.74	1.605

^{a)} The number of beads tested was 22 for the 0.17 wt.-% CaCl₂ concentration beads, 27 for the 0.44 wt.-% CaCl₂ concentration, and 10 in all of the other cases.

beads in nanopure water. A similar trend was observed in both cases, except that the beads incubated in nanopure water displayed an approximate 30% loss in bead size. Figure 5 clearly shows that the bead size is strongly dependent on the ion and not on the ionic strength. The reduced size of the beads in water can be related to the observation that the beads were whiter than their counterparts in the ion solutions. The white color of the beads can be attributed to the precipitation of the calcium alginate in water or in a medium of zero ionic strength.

The mechanical properties of the beads were also measured under a fixed compressive load of 10 g. Ten different beads were loaded and the values were averaged. The results are shown in Table 4 and Figure 6.

The beads were placed one by one under the mechanical tester and loaded with a 10 g weight. Since the bead deformation is a measure of the bead modulus, the higher modulus beads were expected to deform less under certain compressive loads. In this study, the beads obtained at high and low ion concentration deformed up to 1.14 and 2.15 mm respectively.

As found in the UV study, there is a range of ion concentration, (0.89 to 14.28 wt.-%) at which the bead deformation was found to be nearly at plateau value. This

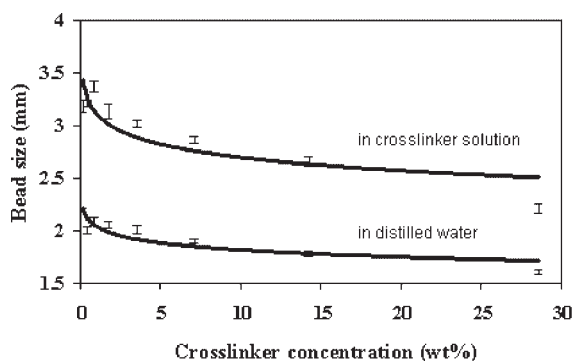


Figure 5. Alginate bead size dependence on ion concentration after swelling in ion solution and in pure water.

Table 4. Amount of deformation (mm) for different alginate beads, crosslinked in various ion media.

CaCl ₂ concentration	Range of bead sizes ^{a)}	Mean bead deformation
wt.-%	mm	mm
0.17	1.90 to 2.15	2.034
0.89	1.86 to 2.13	1.947
1.78	1.84 to 2.04	1.947
7.14	1.80 to 2.02	1.899
14.28	1.65 to 2.01	1.898
28.57	1.40 to 1.82	1.635

^{a)} Number of beads tested = 10.

shows that the dependence of the mechanical strength on the ion concentration is minor in the ion concentration range from 0.89 to 14.28 wt.-%. A more accurate evaluation requires beads with almost similar mean sizes. Given the fact that the smaller beads experience a higher pressure (force/area) under a certain load, the applied pressure is expected to be higher on smaller beads and hence they are expected to deform more under a given load. However, the reverse was the case as the smaller beads deformed less. It can be concluded that smaller beads are stronger as they were obtained at a high ion concentration.

The alginate study shows that the bead size, the extractable fraction and the mechanical properties of the Ca-alginate networks are significantly affected by the calcium concentration. An increase in the calcium concentration results in smaller and stronger networks, in which the majority of the alginate chains are incorporated into the alginate network. These observations can explain why hydrogel hybrids of alginate/Acrylamide, treated at high calcium concentrations, show elastic properties in their water-swollen state.

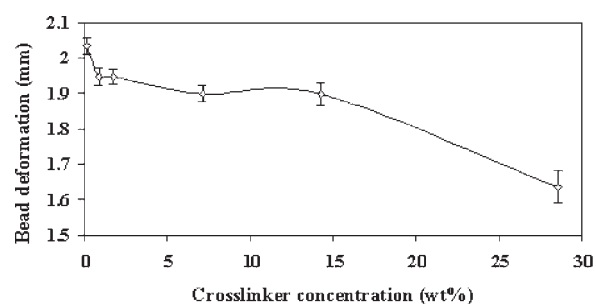


Figure 6. Bead deformation dependence on ion concentration.

Suggested Mechanism

The elastic properties of a fully-swollen hydrogel hybrid are an interesting phenomenon, which can potentially be utilized in applications in which a fast-swelling elastic substrate is required. With this type of hybrid, the crosslinked polyacrylamide controls the fast, swelling property. On the other hand, the interaction of the Ca²⁺-alginate and the synthetic polymer chains is presumably responsible for the highly elastic property in the swollen state. Although elastic properties are a common feature of solid, crosslinked rubbers, this behavior is rare for fully water-swollen, porous hydrogels. Given the fact that a hydrogel with an absorption capacity of 40 to 50 g · g⁻¹ contain quite a large amount of water in between the synthetic polymer chains, there should be a specific mechanism by which the hybrid shows elasticity in its swollen state. In the case of hydrogel hybrids containing alginate, a tight entanglement with synthetic polymer chains is assumed if the alginate chains are highly crosslinked, as is the case with the current hybrid. As highlighted in the previous section and shown in Figure 7, a high crosslink density, low amount of extractable fraction and low deformability are features of highly crosslinked Ca-alginate systems. Therefore, for an SPH hybrid in its water-

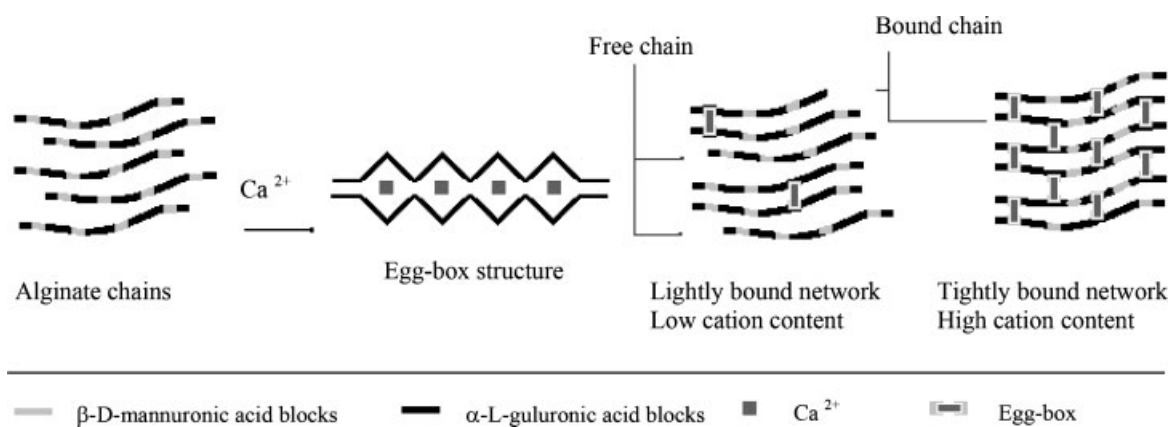


Figure 7. Features of calcium-treated alginate networks at low/high ion concentrations.

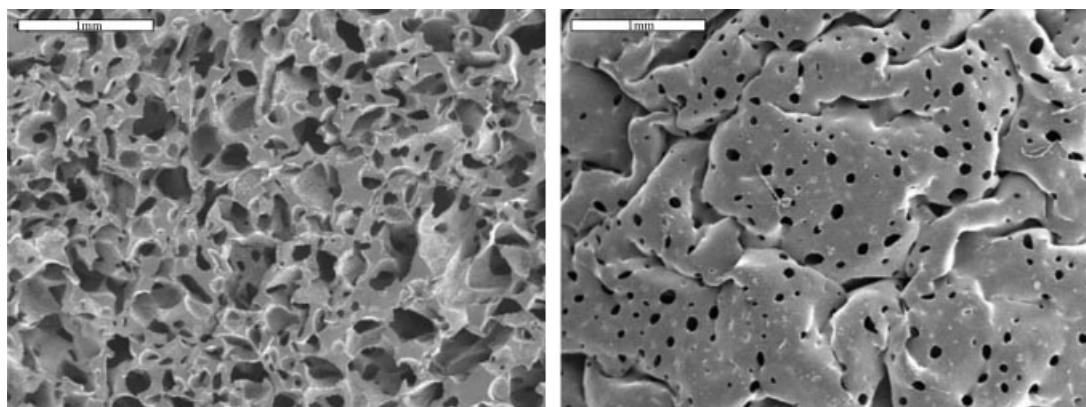


Figure 8. SEM micrographs of a typical, elastic, superporous hydrogel, hydrogel surface (right), and hydrogel cross-section (left); scale bar = 1 mm.

swollen state, the high crosslink density of the alginate part prevents the alginate chains from swelling in water. In this way, a strong tie between the two polymer systems will be maintained. Secondly, a minimal alginate extractable fraction provides a network with more stable physical and mechanical properties over the period of swelling in aqueous medium. Thirdly, the low deformation of the highly-crosslinked alginate network ensures that the ties between the two polymer systems at the different junction points are maintained. Figure 8 shows SEM micrographs of a typical, elastic, superporous hydrogel.

Examples of elastic superporous hydrogels have been fully described elsewhere and are summarized in Table 5.^[26]

Conclusion

We report an innovative approach for the preparation of a strong and elastic superporous hydrogel in its swollen state. According to this method, a synthetic monomer was polymerized and crosslinked in the presence of a water-soluble alginate polymer. The as-synthesized polymer was further post-crosslinked in the presence of calcium cations. This results in metal complexation of the polysaccharide content of the hydrogel. In this way, a hydrogel hybrid with an interpenetrated network structure was formed. While the synthetic acrylamide polymer controls the fast- and high-swelling properties, the interaction of Ca-crosslinked

Table 5. Examples of elastic superporous hydrogels.

Hydrogel Hybrid ^{a)}	Features ^{a)}
PAAm/Chitosan treated via ionotropic gelation	Materials: AAm, Bisacrylamide, Chitosan solution (2 wt.-%), acetic acid, diamine, persulfate, bicarbonate. Reaction at room temperature of 25 °C. Treated in 10 wt.-% aqueous pentasodium tripolyphosphate (pH = 1) for 20 min; water washed, dehydrated in ethyl alcohol, dried out in the oven at 60 °C overnight.
PAAm/NaCMC treated via ionotropic gelation	Materials: AAm, Bisacrylamide, CMC solution (2 wt.-%), acetic acid, diamine, persulfate, bicarbonate. Reaction at room temperature of 25 °C. Treated in 10 wt.-% aqueous ferric chloride (pH = 2) for 1 h; water washed, dehydrated in ethyl alcohol, dried out in the oven at 60 °C overnight.
PAAm/PVOH treated via cryogelation	Optimized ratio of sodium carboxymethylcellulose to acrylamide of about 3 to 4 wt.-%. Materials: AAm, Bisacrylamide, PVOH solution (10 wt.-%, MW 124 000 – to 186 000, 99% hydrolyzed), acetic acid, diamine, persulfate, bicarbonate. Reaction at room temperature of 25 °C. Samples frozen at –12 °C for 24 h, thawed at temperature of 8 °C for 12 h. Optimized ratio of poly(vinyl alcohol) to acrylamide of about 17 wt.-%. <i>General properties:</i> All of these SPHs showed a swelling rate of 10 to 30 s and swelling capacity of 35 to 45 g·g ⁻¹ (equivalent to about a 2 times increase in each dimension). They were extensible and very resistant to tear, tensile and compressive stresses even after a 1 week retention in water.

^{a)} PAAm = polyacrylamide; NaCMC = sodium salt of carboxymethyl cellulose; PVOH = poly(vinyl alcohol).

alginate and the synthetic polymer is presumably responsible for the elastic properties of the hybrid. The gelation properties of the sodium alginate were studied over a broad range of calcium concentrations in order to find the mechanisms for the elasticity and resiliency of the hydrogel hybrid. The high network density, the minimum amount of extractable fraction, and the good mechanical properties of the crosslinked alginate were found to be responsible for the elasticity of the water-swollen hydrogel hybrid. The hydrogel hybrid in this study can swell up to about 40 to $50 \text{ g} \cdot \text{g}^{-1}$, while it is very elastic in its swollen state and in its fully swollen state, it can be stretched up to 2 to 3 times of its original length. The cycle of stretching/unloading of the swollen elastic hydrogel hybrid can be repeated numerous times. This unique property can potentially be exploited in the development of fast- and high-swelling elastic hydrogels for a variety of pharmaceutical, biomedical and industrial applications.

- [1] US 6, 271, 278 (2001), Purdue Research Foundation, invs.: K. Park, J. Chen, H. Park.
- [2] J. Chen, H. Park, K. Park, *Trans. Soc. Biomater.* **1994**, *17*, 158.
- [3] J. Chen, H. Park, K. Park, *J. Biomed. Mater. Res.* **1999**, *44*, 53.
- [4] J. Chen, W. E. Blevins, H. Park, K. Park, *J. Controlled Release* **2000**, *64*, 39.
- [5] K. Park, *Drug Delivery Technol.* **2002**, *2*, 38.
- [6] M. Glicksman, "Gum Technology in the Food Industry", Academic Press, New York 1969, p. 163.
- [7] W. R. Gombotz, S. F. Wee, *Adv. Drug Delivery Rev.* **1998**, *31*, 267.
- [8] C. K. Kuo, P. X. Ma, *Biomaterials* **2001**, *22*, 511.
- [9] P. Eiselt, J. Yeh, R. K. Latvala, L. D. Shea, D. J. Mooney, *Biomaterials* **2000**, *21*, 1921.
- [10] L. Shapiro, S. Cohen, *Biomaterials* **1997**, *18*, 583.
- [11] K. D. Vorlop, H. J. Steinert, J. Klein, *Ann. N.Y. Acad. Sci.* **1987**, *501*, 339.
- [12] B. P. Hills, J. Godward, M. Debatty, L. Barras, C. P. Satrio, C. Ouwerx, *Magn. Reson. Chem.* **2000**, *38*, 719.
- [13] J. M. Duez, M. Mestdagh, R. Demeure, J.-F. Goudemant, B. P. Hills, J. Godward, *Magn. Reson. Chem.* **2000**, *38*, 324.
- [14] M. A. LeRoux, F. Guilak, L. A. Setton, *J. Biomed. Mater. Res.* **1999**, *47*, 46.
- [15] A. R. Kulkarni, K. S. Soppimath, T. M. Aminabhavi, *Pharm. Acta Helv.* **1999**, *74*, 29.
- [16] T. Ostberg, L. Vesterhus, C. Graffner, *Int. J. Pharm.* **1993**, *97*, 183.
- [17] V. Pillay, C. M. Dangor, T. Govender, K. R. Moopanar, N. Hurbans, *Drug Delivery* **1998**, *5*, 35.
- [18] V. Pillay, C. M. Dangor, T. Govender, K. R. Moopanar, N. Hurbans, *J. Microencapsulation* **1998**, *15*, 215.
- [19] V. Pillay, R. Fassihi, *J. Controlled Release* **1999**, *59*, 229.
- [20] A. R. Kulkarni, K. S. Soppimath, T. M. Aminabhavi, A. M. Dave, M. H. Mehta, *J. Controlled Release* **2000**, *63*, 97.
- [21] Y. J. Kim, K. J. Yoon, S. W. Ko, *J. Appl. Polym. Sci.* **2000**, *78*, 1797.
- [22] T. Tripathy, S. R. Pandey, N. C. Karmakar, R. P. Bhagat, R. P. Singh, *Eur. Polym. J.* **1999**, *35*, 2057.
- [23] S. R. Kim, S. H. Yuk, M. S. Jhon, *Eur. Polym. J.* **1997**, *33*, 1009.
- [24] X. P. Wang, *J. Appl. Polym. Sci.* **2000**, *77*, 3054.
- [25] S. Hertzberg, E. Moen, C. Vogelsang, K. Ostgaard, *Appl. Microbiol. Biotechnol.* **1995**, *43*, 10.
- [26] US 6,960,617 (2005), Purdue Research Foundation, invs.: H. Omidian, Y. Qiu, D. J. Kim, S. C. Yang, H. Park, K. Park.