Supplementary Material for:

Multi-membrane Hydrogel Fabricated by Facile Dynamic Self-assembly

Hongjun Dai, Xiaofeng Li, Yuhua Long, Junjie Wu, Songmiao Liang, Xiaoli Zhang, Ning Zhao,* Jian Xu*

State Key Laboratory of Polymer Physics and Chemistry, Institute of Chemistry and Graduate School, Chinese Academy of Sciences, Beijing, 100190, P. R. China

*To whom correspondence should be addressed.

e-mail: jxu@iccas.ac.cn; zhaoning@iccas.ac.cn

Preparation of the alginate multi-membrane hydrogel: Typically, we produced the spherical alginate gel core by dropping 1.5 *wt*% sodium alginate (Sigma) solution into 0.2 mol/L $CaCl_2$ solution and kept for 1 hour to get the gel completely crosslinked. After absorbing the water on the surface by a filter paper, we immersed the gel core into 0.75 *wt*% alginate sodium solution for 60 sec under gentle agitation. Then the gel cores were filtered through a 20 mesh sieve rapidly and absorbed the redundant solution on the surface before being dropped into the 0.2 mol/L $CaCl_2$ solution and cured for 5 min. By repeating the above process as many as necessary, we obtained the spherical multi-membrane hydrogel with inter-membrane space. Accordingly, if the curing time was as long as 30 min, we could produce the spherical multi-membrane hydrogel without inter-membrane space by the same process. Also, we prepared the rod-like multi-membrane hydrogel by the same approach by starting from a rod-like alginate hydrogel.

Photomacrograph acquisition and membrane thickness measurement: After preparing the multi-membrane hydrogel, we placed it in a cuboid quartz colorimetric utensil, and got it fully immersed in the deionized water. Then we captured the photomacrograph from a side of the utensil with WAT-2215 CCD (maximal magnification is 30 fold) coupled with the computer. The membrane thickness of the hydrogel was measured in the photomacrograph by a scaleplate (the minimal calibration is 50 μm) obtained under the same condition, and every membrane was measured at 3 different palaces to calculate the average value.

SEM characterization: We put the prepared 5 membranes alginate hydrogel into liquid nitrogen to fully frozen and cut it in half rapidly, then observe the sample by JEOL 6700F FE-SEM after freeze-drying (the accelerating voltage is 5.0 kV).

(Viscometry was carried out by Rotating Cylinder Method on an Advanced Rheometric Expansion System (ARES, Rheometric Scientific, NJ) at 25℃.)

Drug loading and release: According to the preparation of the spherical multi-membrane alginate hydrogel, we placed the alginate gel-core in the 0.75 *wt*% sodium alginate solution,containing 1.25 *wt*% Blue Dextran ($\overline{M}_w$ = 2×10^6) for 1.5 min, and transferred it into 0.2 mol/L $CaCl_2$ solution to get the membrane further cured for 10 min, and the first membrane entrapped drugs was accomplished. Then we put the hydrogel into the pure 0.75 *wt*% sodium alginate solution for another 1.5 min and cured it in 0.2 mol/L $CaCl_2$ solution for 10 min to form the second membrane without drugs. Repeating the above process, we loaded Blue Dextran in every odd membrane of the 6-membrane hydrogel. The drug release investigation was carried out in a diffusion cell with magnetic agitation. The media is deionized water or 11 mmol/L sodium citrate aqueous solution, and the accumulated release of Blue Dextran was monitored by Rayleigh UV-1600 spectrophotometer at λ = 259 nm under 25^{o}C.

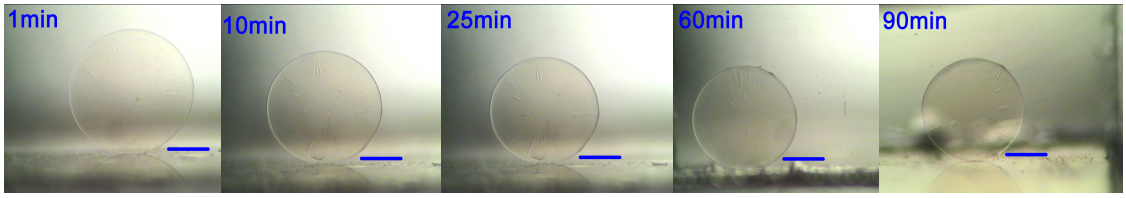


Figure S1. The macroscopic shrinkage of the alginate hydrogel. 1.5 *wt*% sodium alginate solution was dropped into 0.2 mol/L $CaCl_2$ solution, and the whole gelation process was captured by CCD instrument. The hydrogel shrinked with the curing time until the time reached 60 min (the scale bar is 1 mm).

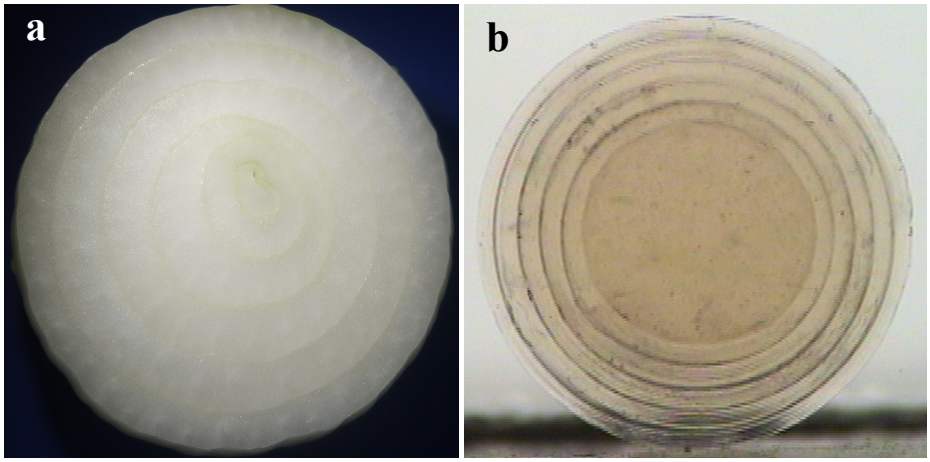
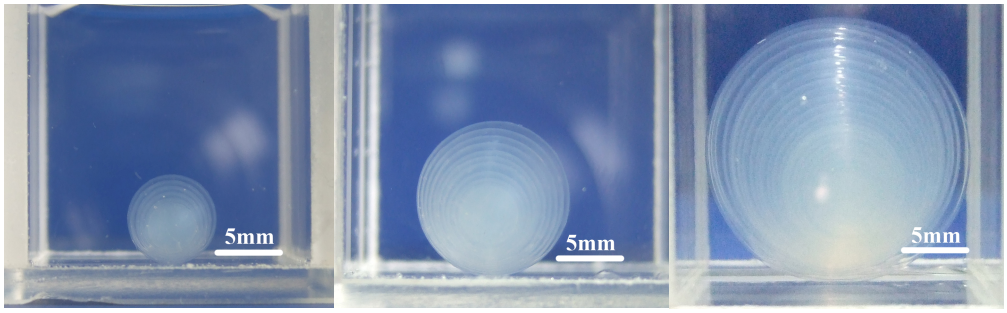


Figure S2. The similar inner structure between the onion and the multi-membrane alginate hydrogel. a) The digital photo of the onion's cross-section cut. b) The photomacrograph of alginate hydrogel with 5-membrane.



5 membranes 10 membranes 25 membranes

Figure S3. The digital photos of the multi-membrane hydrogel. The crosslinking time is 45 sec; $C_{Alg} = 0.75$ *wt*%; $C_{Ca^{2+}} = 0.2$ mol/L.

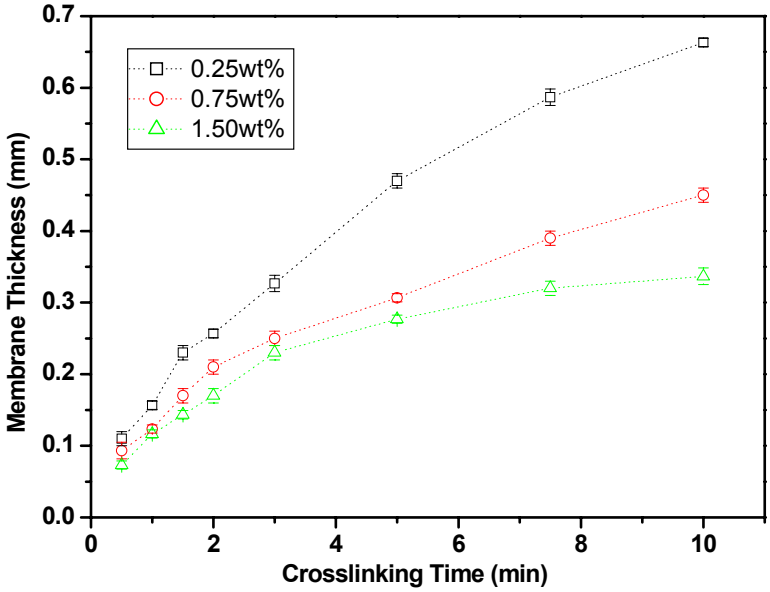


Figure S4. The influence of crosslinking time on the membrane thickness. C_{Alg} is 0.25 *wt*%, 0.75 *wt*% and 1.50 *wt*%, respectively; $C_{Ca^{2+}}$ = 0.2 mol/L.

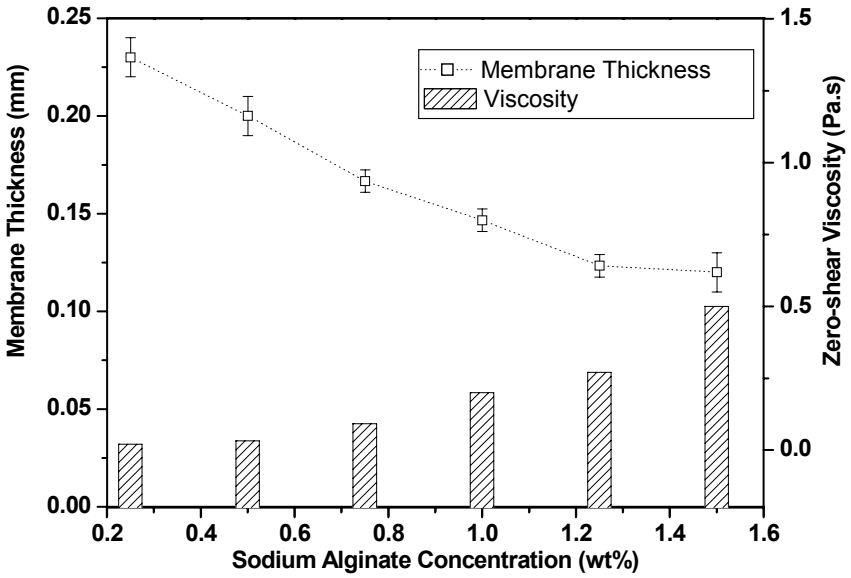


Figure S5. The relationship between the membrane thickness and the concentration or viscosity of the sodium alginate solution. The crosslinking time is 1.5 min; $C_{Ca^{2+}} = 0.2$ mol/L.

Table S1. The influence of $C_{Ca^{2+}}$ on the membrane thickness. The crosslinking time is 1.5 min; C_{Alg} = 0.75 *wt*%

C_{CaCl2}(mol/L)	0.01	0.02	0.05	0.1	0.2
Membrane Thickness (mm)	--	--	0.05±0.006	0.10±0.006	0.17±0.01

Notes: "--" represents that the membrane does not form or cannot be observed.

Table S2. The membrane thickness of different layers. The crosslinking time is 45 sec; C_{Alg} = 0.75 *wt*%, $C_{Ca^{2+}}$ = 0.2 mol/L.

Number of membrane	1	2	3	4
Membrane Thickness (mm)	0.13±0.006	0.14±0.01	0.14±0.006	0.13±0.006
Number of membrane	5	6	7	8
Membrane Thickness (mm)	0.14±0.01	0.15±0.01	0.14±0.01	0.15±0.01