Sponge-Like Cryogels

Cellulose Nanofibers are used to overcome the Problem of Shape Fixing and Recovery in Biodegradable Chitosan Cryogel.

Soft matter, especially smart soft matter, can be developed as biomedical materials and used to repair human tissues.

In 2017, in the article[1] "I will be back: the return of rubber," Shan-Hui Hsu (National Taiwan University) shared the novel shape memory mechanism enlightened by using small-angle X-ray scattering (SAXS) technique at Taiwan Light Source. Elastomer (or rubber) is a type of soft matter that exhibits elasticity (*i.e.*, the ability to deform freely when an external force is applied and to return to its original shape after force removal). Elastomer without shape memory has formed only one permanent shape. Elastomer with shape memory, however, has formed two permanent shapes. In each permanent shape, it can be deformed freely and recovered upon force removal. The switch between the two permanent shapes is often triggered by a temperature change. In the earlier study,[2] the trigger was water at 37°C; a small-shaped elastomer was discovered to expand into a large-shaped elastomer when placed in 37°C water. This indicates that such elastomer is suitable for application in medical devices and can be used for minimally invasive surgery. The SAXS results revealed that the retention of a crystalline orientation during the integration of shape memory materials into elastomer could be considered a novel mechanism for creating such materials.

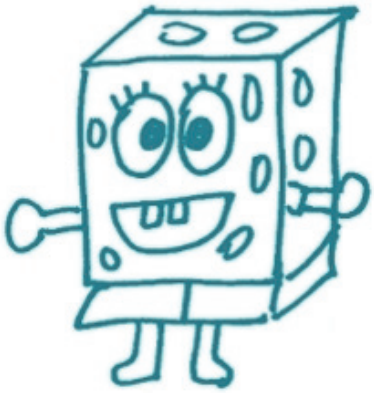

Fig. 1: Cryogel, a sponge-like soft matter, is generated from a polymer solution at freezing temperatures. This involves the use of a crosslinker to link the polymer chains and to form a network. Ice crystals fill the pores within the network. At room temperature, the ice melts and the remaining porous network forms the cryogel. [Figure drawn by Shan-Hui Hsu]

The present study[3] focused on cryogel, another type of soft matter. Cryogel is also elastic but exhibits properties more similar to those of a sponge (**Fig. 1**). It can be compressed by external forces and recovered upon force removal. Cryogel does not exhibit shape memory but forms only one permanent shape, as elastomer does. The high porosity of cryogel would be generated after polymer solution froze and then melted. At low temperatures, the polymer molecules form a network in which large pores are generated and left empty after the ice crystals melt within. As a highly compressive sponge, cryogel can be injected through a needle. It will be amazing if one can repair human tissue by injecting a cryogel instead of open-approach surgery. The difficulties of shape memory cryogel served as the biomaterial in minimally invasive surgery application includes (1) the highly compressive cryogel may clog the needle because the permanent shapes of cryogels are complicated; (2) a shape memory cryogel with two permanent shapes should have a smaller, rod-like shape for smooth injection and a larger, more complex shape after exposure to 37°C water (body temperature); (3) the cryogel is required to be biodegradable. Such kind of shape memory cryogel is rarely developed, but Hsu did it.

Hsu selected chitosan, which is derived from crab and oyster shells and is biodegradable, as the polymer matrix. Hsu used the shape memory elastomer from the previous research[2] and modified the end group to ensure it could crosslink with the chitosan in an aqueous solution at freezing temperatures to form a network. After the ice was melted, a cryogel that exhibited shape memory was formed because of the shape memory crosslinker. Although SAXS revealed that the crystalline orientation of the polymer network accounted for the shape memory mechanism, the interaction between the chitosan and the shape memory crosslinker deflected the SAXS signals. This first-generation shape memory cryogel was injectable and expanded in 37°C water. Moreover, the aqueous solution was able to be three-dimensionally printed and frozen to form custom-shaped memory cryogel (**Fig. 2**).[4]

Hsu developed the second generation of shape memory cryogel with an increased degree of shape memory. Instead of shape memory elastomer, Hsu used a simpler crosslinker, cellulose nanofiber, to form a chitosan network at low temperature. Cellulose nanofiber is from a green resource (obtained from trees) and can be modified to contain

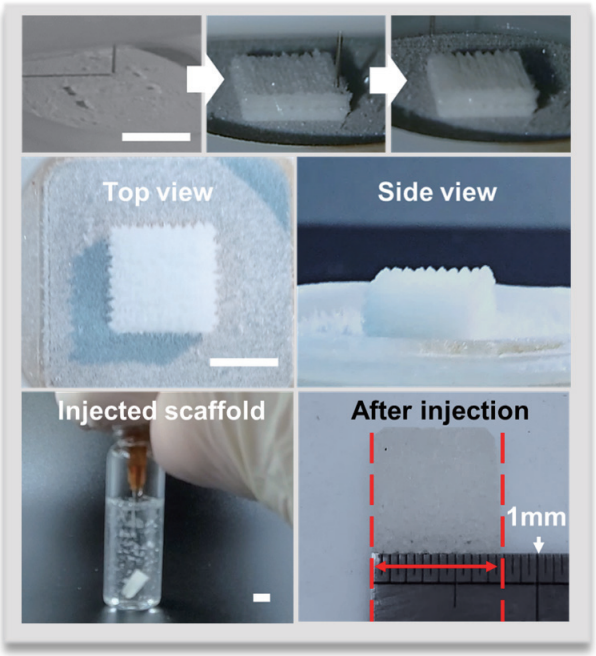

Fig. 2: Custom-shaped memory cryogel obtained through 3D printing. [Reproduced from Ref. 4]

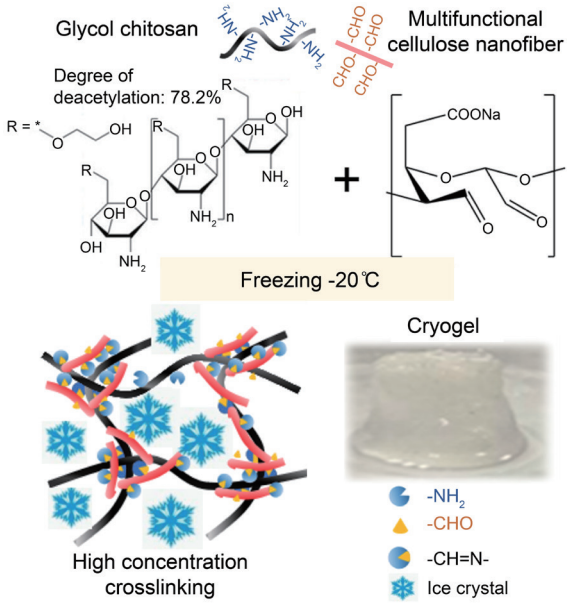

Fig. 3: Second-generation shape memory cryogel made from chitosan and cellulose nanofibers. [Reproduced from Ref. 3]

multiple aldehyde groups, rendering it a highly efficient crosslinker for chitosan network formation. The addition of nanofiber helps to reinforce the network, rendering the cryogel more durable (**Fig. 3**).

In situ SAXS can be used to monitor the structural changes of shape memory cryogel under the formation process in **TLS 23A1**. The initial chitosan–cellulose nanofiber cryogel exhibited a circular pattern (**Fig. 4(a)**). This indicated that the cryogel had no specific orientation in its crystalline domain. When the cryogel was heated to 70°C and deformed to the second permanent shape, shape memory was incorporated into the cryogel. This involved the specific orientation of the nanofibers, which was demonstrated by the rhombus shape of the resulting 2D SAXS pattern (**Fig. 4(b)**). The cryogel retained its second permanent shape until its shape memory was triggered by 37°C water. The cryogel recovered its first permanent shape and preserved its rhombus crystalline orientation. A sharp peak at 10.9° in the wide-angle X-ray scattering profile demonstrated the crystalline changes in the cellulose nanofibers (**Fig. 4(c)**). The cellulose nanofibers were thus critical to the cryogel having shape memory.

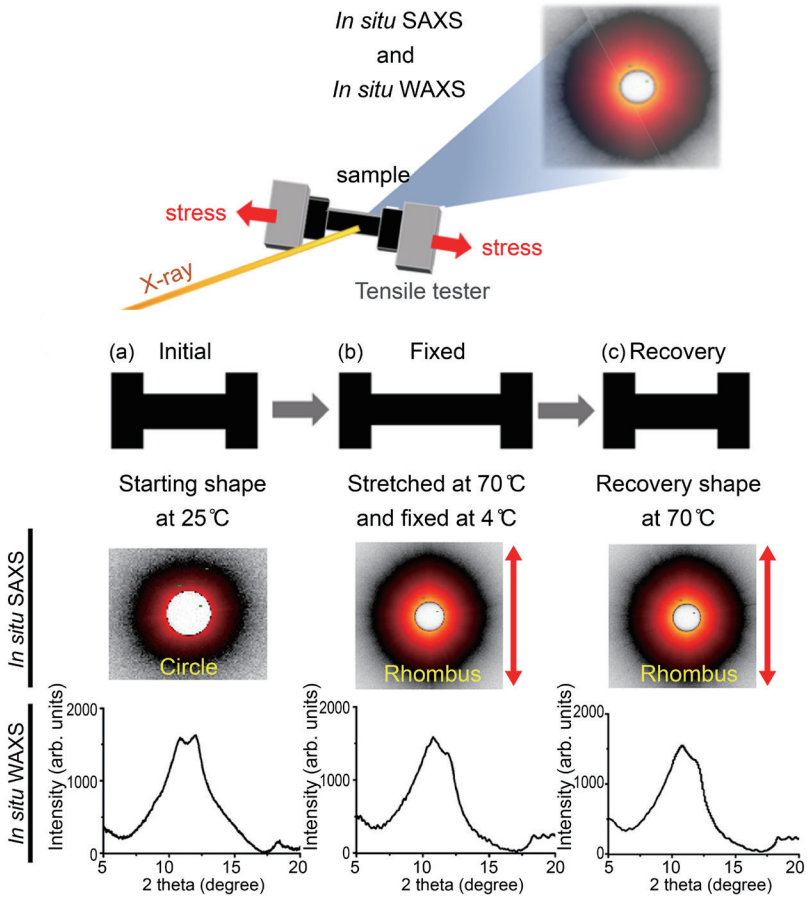

Fig. 4: *In situ* 2D SAXS pattern for cryogel during shape memory incorporation. (a) Initial cryogel; (b) cryogel in the second permanent shape; (c) cryogel returning to the initial shape. [Reproduced from Ref. 3]

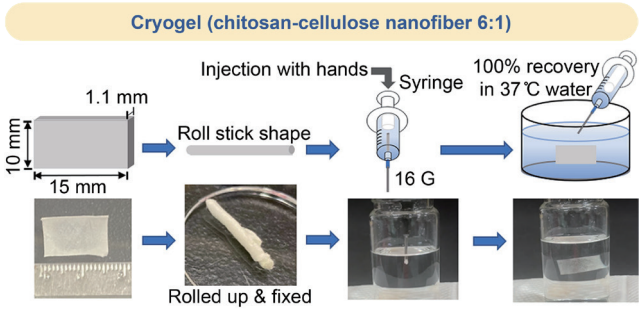

Fig. 5: Injected rod cryogel forms a large sheet of cryogel. [Reproduced from Ref. 3]

Because of the small proportion of nanofibers in the cryogel (1:7), the cryogel could be fixed into a rod shape and injected to form a large sheet in 37°C water (**Fig. 5**). The greatest volume of the second generation sponge that could be injected through a 16-gauge needle was 150% that of the first-generation shape memory cryogel and 260% that of the cryogel without shape memory. This biodegradable shape memory cryogel with a high injected volume and complex shape can be valuable for designing medical devices and tissue regeneration templates for minimally invasive surgery. (Reported by Shan-Hui Hsu, National Taiwan University)

*This report features the work of Shan-Hui Hsu and her co-workers published in ACS Appl. Mater. Interfaces **14**, 36353 (2022).*

TLS 23A1 Small/Wide Angle X-ray Scattering

- *In situ* SAXS and WAXS
- Soft Matter

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Skin Tactile Sensor / Electronic Skin

How sensor can mimic human skin? High-stretching and self-healing polymers can be the answer in skin tactile sensors.

Recently, stretchable and simultaneously self-healable elastomers have attracted considerable attention due to their prolonged service time and their potential in human motion sensing. The self-healing ability usually originates from the reversible bonds incorporated in the polymer matrix, including hydrogen bonding, π–π stacking, ionic interactions, and metal-ligand (ML) interactions. Among them, ML coordination bonds with their highly dynamic nature and easily-fabricated properties are usually incorporated into intrinsic self-healing materials. However, despite the prosperous structural designs and several attempts to combine different metal ions and their host materials, the mechanisms behind the ML interactions remain unsolved.

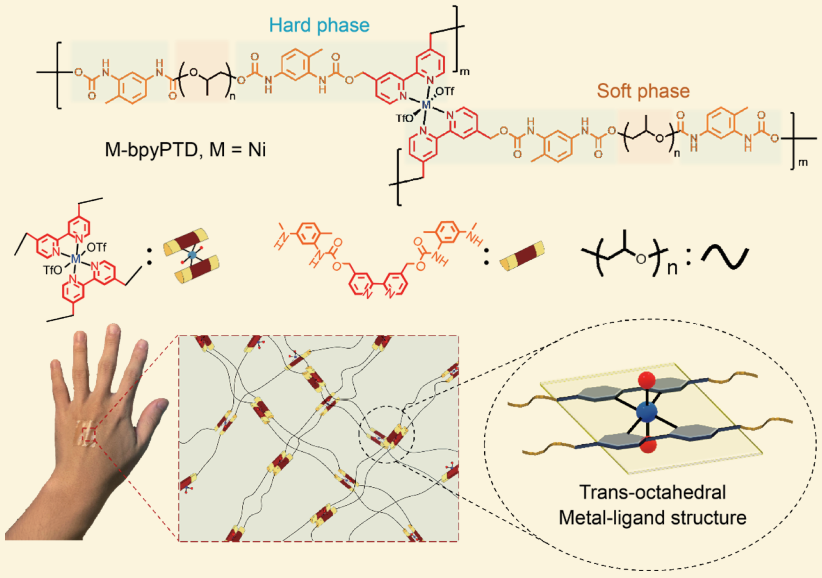

Fig. 1: A schematic illustration of the design concept and chemical structures of Ni-bpyPTD. [Reproduced from Ref. 1]