Anisotropically Fatigue-Resistant Hydrogels

Xiangyu Liang, Guangda Chen, Shaoting Lin, Jiajun Zhang, Liu Wang, Pei Zhang, Zeyu Wang, Zongbao Wang, Yang Lan, Qi Ge, Ji Liu

Nature builds biological materials from limited ingredients, however, with unparalleled mechanical performances compared to artificial materials, by harnessing inherent structures cross multi-length-scales. In contrast, synthetic material design overwhelmingly focuses on developing new compounds, and fails to reproduce the mechanical properties of natural counterparts, such as fatigue resistance. Here, we report a simple yet general strategy to engineer conventional hydrogels with a more than 100-fold increase in fatigue thresholds. This strategy is proven to be universally applicable to various species of hydrogel materials, including polysaccharides (i.e. alginate, cellulose), proteins (i.e. gelatin), synthetic polymers (i.e. polyvinyl alcohols), as well as corresponding polymer composites. Our fatigue-resistant hydrogels exhibit a record-high fatigue threshold than most synthetic soft materials, making them low-cost, high-performance and durable alternatives to soft materials used in those circumstances including robotics, artificial muscles, etc.

As a polymer network infiltrated with water, hydrogel has emerged as the critical engineering material for soft robotics, tissue engineering, bioelectronics, wearable and implantable electronics, etc. The past decades have witnessed the advancement in hydrogel innovation with unprecedented mechanical properties, for example, hydrogel materials could be facilely engineered with tissue-like toughness (i.e. 1,000 J m⁻²), thus capable to resist crack propagation under dramatic deformation. However, these tough hydrogels are still susceptible to fatigue fracture during multiple-cycle mechanical loads, exhibiting fatigue threshold (i.e. the minimal fracture energy required for crack propagation under cyclic loads) below 100 J m⁻². Therefore, the long-term reliability has substantially hampered the in practical utility of hydrogels and hydrogel-based devices, and remains a key challenge in these fields.

On the contrary, biological tissues, such as skeletal muscles, tendon and cartilage, are well known for not only their superior strength, modulus, toughness, but also long-term robustness. For example, skeletal muscles can sustain a high stress (i.e. 1 MPa) over millions cycles per year without fracture, exhibiting fatigue thresholds (i.e. the minimal fracture energy required for crack propagation under cyclic loads) over 1,000 J m⁻², despite their high water content (~80%). Such unrivalled fatigue-resistance originates from their hierarchically-arranged collagen fibrillar micro/nanostructures. Despite bioinspired construction of structural materials has been promising for the design of fatigue-resistant hydrogels, how to produce hydrogel materials with unprecedented fatigue-resistance in a universal and viable manner still remains an open issue. More recently, fatigue-resistant hydrogels have been fabricated by engineering the crystalline domains, fibir structures or mesoscale phase separation. Ice-templated freeze-casting strategy has been utilized as a powerful technology to impart hydrogel materials with preferentially-aligned microstructures, thus substantially improved fatigue-resistant performance.

Herein, we describe a simple yet general strategy to engineer conventional hydrogels with over 100-fold increase in fatigue thresholds. Our two-step process involves the formation of preferentially-aligned micro/nanostructures within a hydrogel material through the ice-templated freeze-casting process followed by thermal annealing. Crucial to the extraordinary fatigue resistance to crack propagation of these hydrogels is the synergetic integration of hierarchically-arranged structures and well-defined crystalline domains.
**Figure 1.** Fabrication of hydrogels with preferentially-aligned fibril structures. **A.** Schematic illustration for the hydrogel fabrication by freezing a polymer solution on a copper substrate, one side of which is submerged within liquid nitrogen. The ice crystals nucleate simultaneously over the surface of copper substrate, and grow perpendicularly, resulting in honeycomb-like structures with only a single domain. The anisotropic polymer scaffolds are further annealed at high temperature (i.e. 100 °C, 90 minutes), leading to polymer materials with higher degree of crystallinity and larger size of crystals. Afterwards, the annealed samples were soaked in water till equilibrium, resulting in the hydrogels with preferentially-aligned fibril structures. **B.** Presence of larger-size crystals and aligned fibril structures synergistically pin the crack, imparting them with astonished fatigue-resistance. **C.** Images of twisting, rolling and folding the as-prepared hydrogels, demonstrating their compliant, soft and flexible essence. **D.** Image demonstrating the remarkably high strength of the as-prepared hydrogels along the alignment direction, by sustaining a dumbbell (25 kg) with over 31,000× of its own weight.

**Fig. 1A** depicts our consecutive fabrication process to synergistically engineer the preferentially-aligned microstructures and nanocrystalline domains within a hydrogel system. This strategy is based on the freezecasting process, a well-established routine for endowing materials with anisotropic structures through unidirectional ice-templating [20-25]. To implement our design rationale, we choose poly(vinyl alcohol) (PVA) aqueous solution (146-186 kDa, 99% hydrolyzed) as the exemplary and starting material, due to its highly hydrophilic essence, well-documented strategies to engineer its crystalline structures, as well as biocompatible essence. [26] A PVA aqueous solution with weight fraction of 5 wt. % is used, whereas freeze-thawed PVA (referred as FT PVA) or chemically-crosslinked PVA (referred as Ch PVA) with the same weight fraction exhibits extremely low modulus, toughness and strength, making them difficult to be used as engineering materials. [13,26] Here, we transfer the PVA solution (5 wt. %) into a home-designed mold, which is placed directly in contact with the cold finger (copper plate, **Fig. 1A**). The vertical temperature gradient facilitates the ice nucleation and subsequent vertical growth in parallel. [25] During the subsequent lyophilization process, PVA polymer chains play a critical role as the scaffold to support the microstructures upon ice sublimation through strong hydrogen-bonding, leading to honeycomb-like porous structures, however, with an extremely low crystallinity of ca. 1.56 wt. % (referred as FC PVA, Supplementary **Fig. S1**). The PVA matrix is annealed afterwards at a temperature between its glass transition (ca. 70 °C) and melting temperature (ca. 200 °C), i.e. 100 °C for 90 minutes, in order to initiate further crystal growth. Final hydrogel material (referred as FC-A PVA) is obtained after swelling in deionized water till equilibrium. The FC-A PVA hydrogels possess a crystallinity of 36.6 wt. % (at its dry state) and water content of 90.8 wt. %, exhibiting outstanding softness yet high strength (**Fig. 1C-D**).

Scanning electron microscopic images (SEM, **Fig. 2A-C**) reveal unique micro/nanostructures of FC-A PVA hydrogels: undisrupted cellular structures with a compartmental size of 1-10 μm and wall thickness of 100-200 nm, as well as highly-ordered cellular arrays along the ice-template direction. The preferentially-aligned microstructures could
also be observed in the confocal microscopic image (Supplementary Fig. S2-3), similar to the mechanically-trained PVA hydrogels.\(^{[16]}\) Moreover, wide-angle X-ray scattering (WAXS) and small-angle X-ray scattering (SAXS) patterns (Fig. 2D and Supplementary Fig. S4-5) further verify that nanocrystalline domains orient during the freeze-casting and annealing treatment. Increase in the size of nanocrystalline domain (D), as well as decrease in the distance among nanocrystalline domains (L), corroborates the role of annealing in increasing crystal size and overall crystallinity (Fig. 2E). By contrast, FT or Ch PVA hydrogel possesses random pores, while freeze-casting (without annealing) can generate preferentially-aligned microstructured hydrogels (Supplementary Fig. S6), however, with extremely small crystals (Supplementary Fig. S5). Based on these analysis, a hierarchical network is built for the FC-A PVA hydrogel, as depicted in Fig. 1A, that is, at nanoscale, PVA nanocrystals form during the freeze-casting and annealing process (1\(^{st}\) order); the nanocrystalline domains generate along the ice-growth direction, and are connected by the amorphous chains forming the microwalls (2\(^{nd}\) order), while these microwalls further assemble the preferentially-aligned cellular arrays, leading to the anisotropic hydrogel network (3\(^{rd}\) order).

The macroscopic mechanical behaviors of the PVA hydrogels are comparatively investigated with a tensile machine. As shown in Fig. 3A-B, before annealing, the FC PVA hydrogel displays unique anisotropic mechanical properties, such as 1.5 times difference in modulus, 3.2 times in strength and 1.8 times in stretchability between the parallel and perpendicular directions. However, the strength (32 kPa) and modulus (7.4 kPa) of the PVA hydrogels are still too low. Upon annealing, due to the substantial increase in crystallinity (from 1.56% to 36.6% in solid state, Fig. 2B, and Supplementary Fig. S7), the FC-A PVA hydrogel exhibits a remarkably-enhanced strength of 2.5 MPa along the ice-growth direction (S\(_{||}\)), 6.4 times that of FT PVA hydrogel (5 wt.%, 0.39 MPa) and 94 times that of Ch PVA hydrogel (0.027 MPa, Supplementary Fig. S8). Moreover, the anisotropic difference in mechanical performance, namely, ratio of specific parameter between the parallel and perpendicular directions, markedly increases, i.e. > 10 times in strength (S\(_{||}\)/S\(_{\perp}\), Fig. 3B).

We then investigate the fracture behaviors of the PVA hydrogel along different directions. When a precut crack is introduced in parallel with the ice-growth direction, the crack propagates promptly through the entire sample (Supplementary Fig. S9-11), resulting in a low toughness of 0.5 kJ m\(^{-2}\). On the contrary, crack perpendicular to ice-growth direction is effectively pinned before reaching a stretch of 2.6. The characteristic crack insensitivity originates from the inherently aligned fibril structures, similar to those fatigue-resistant biological prototypes, i.e. muscle and tendon,[9,10] as well as artificial materials with preferentially-aligned structures[16,17,19] Once the stretch further reaches 4.7, the crack branches near the interface, and rupture of the fibrils occurs afterwards. Further cross-sectioned SEM images reveal distinct fracture behaviors: delamination of fibrils for a crack propagating along the alignment direction, while both fibrils fracturing and fibrillar delamination for a crack propagating perpendicular to the alignment direction (Supplementary Fig. S10). A toughness of 116 kJ m\(^{-2}\) is quantified for the parallel direction, 224 times higher than that of the perpendicular direction (Supplementary Fig. S11). In the finite-element analysis simulation diagrams, crack perpendicular to the alignment is effectively pinned at the notched tip, featured with a large yielding zone and a butterfly-shaped cloud pattern (Fig. 3C, Supplementary Fig. S13 and Movie S1). Therefore, a higher energy is required to initiate the crack propagation, afterwards, the fracture energy decreases until the whole sample is completely fractured (Fig. 3D).

It is revealed that tough hydrogels, such as alg-
nate/PAAm or freeze-thawed PVA (Γ > 1,000 J m⁻²), are susceptible to fatigue fracture under cyclic mechanical loads, since the resistance to fatigue crack propagation after prolonged cyclic loading is the energy required to fracture a single-layer polymer chains, which is unaffected by additional dissipation mechanisms. However, introduction of well-defined nanocrystalline domains or preferentially aligned fibrillar architectures is capable of increasing the hydrogel’s fatigue threshold up to 1,000 J m⁻².³,¹⁶ We further quantify the fatigue threshold (i.e., minimal fracture energy required for crack propagation under cyclic mechanical loading, Γ₀) of these hydrogel samples employing the single-notch method (Fig. 4A). FT PVA (5 wt.%) exhibits a fatigue threshold of 20 J m⁻², comparable to the energy required to fracture a single-layer polymer chain (ca. 10 J m⁻²). On the contrary, FC PVA hydrogel is featured with anisotropic fatigue resistance (Supplementary Fig. S14), possessing a fatigue threshold of 24 J m⁻² in the parallel direction (Γ₀∥) and 5.9 J m⁻² in perpendicular direction (Γ₀⊥). These relatively low fatigue thresholds could also be interpreted by its extremely low crystallinity (1.56 wt.%) and high water content (95 wt.%). However, these values are still comparable to that of FT PVA hydrogel (20 J m⁻², 5 wt.%). Since crystallinity of PVA hydrogels could be facilely tuned through multiple freeze-thaw cycles and/or annealing process, we detect that after annealing, Γ₀ of FC-A PVA hydrogel remarkably increases up to 1,340 J m⁻², while 34 J m⁻² for Γ₀∥ (Fig. 4A-B). This record-high fatigue threshold of Γ₀ arises from the preferentially-aligned fibril structures and remarkably high crystallinity (36.6%). Whereas, low Γ₀⊥ value could be interpreted by the low polymer content among the fibrils, similar to previous report on mechanically-trained PVA hydrogels with aligned structures.¹⁶ Impressively, the water content of FC-A PVA hydrogel remains as high as 90.8 wt.% (Fig. 3B), while Γ₀ is orders of magnitude higher than that of existing tough hy-
Figure 4. Anisotropic mechanics of fatigue-resistant hydrogels. A. Schematic diagram of pre-notch model and crack extension per cycle dε/dN versus applied energy release rate G for FC-A PVA hydrogels in both parallel (||) and perpendicular (⊥) directions, while isotropic FT PVA hydrogel is used for comparison. B. Summary of fatigue threshold (Γθ) of the FT PVA, FC || PVA and FC-A PVA hydrogels in both parallel (||) and perpendicular (⊥) directions. C. Validation of fatigue threshold as high as 2,740 J m⁻² for FC-A PVA hydrogel sample (10 wt.%) using the single-notch test at the cycle number of 1, 15,000 and 30,000. D. Summary of tensile strength (Δ) and fatigue threshold (Γθ) of HEC (5 wt.%), alginate (3 wt.%), gelatin (2.5 wt.%) and PVA (10 wt.%) hydrogels, as well as PVA/GO composite hydrogels, in both parallel (||) and perpendicular (⊥) directions. E. Comparison chart by plotting the fatigue thresholds versus water contents among tough hydrogels, (i.e. PAAm-alginate, PAAm-poly(2-acrylamido-2-methylpropanesulfonic acid), polyanhydroylyle hydrogels, freeze-shaved PVA and nanocrystalline hydrogel (i.e. dry-annaled PVA), bios (i.e. biological tissue), composite hydrogels (i.e. PDMS filament-filled by drogels), mechanically-trained PVA by drogels, polyprotein-based by drogels, single network (i.e. polyacrylamide hydrogel) as well as hydrogel from nature polymers (i.e. HEC, gelatin, chitosan and sodium alginate). Without specification, the starting weight fraction PVA hydrogels is 5 wt.%. Data in B and D are means ± SD, n = 3.

Droplets (~ 50 J m⁻²). The high water content could also be attributed to the microporous structures within the FC-A PVA hydrogels, which can trap more free water molecules, despite the high crystallinity of the polymer walls (see more discussion in Supplementary Fig. S16).

Given its excellent flexibility and versatility of freeze-casting technique, our strategy to design and fabricate anisotropic hydrogels provides a new and powerful routine to engineer conventional hydrogel materials with highly anisotropic structures and mechanics. We envision that other water-soluble polymers and their nanocomposites could be engineered with similar aligned structures, giving distinct fatigue-resistant performance. To validate this predictable generality, we also fabricate freeze-casted hydrogels from other polymer systems, such as aqueous solutions of hydroxyethyl cellulose (HEC, 5 wt.%), sodium alginate (SA, 3 wt.%), gelatin (2.5 wt.%), polyvinyl alcohol (10 wt.%) or PVA/graphene oxide mixture (5 wt.% PVA and 0.1 wt.% GO). It is widely-recognized that pristine random hydrogels of HEC, alginate or gelatin are generally brittle and fragile, exhibiting fatigue thresholds below 10 J m⁻² (Supplementary Fig. S17). Surprisingly, thanks to the characteristically-
aligned fibril structures inherited from the freeze-casting technique (Supplementary Fig. S20), these freeze-casted hydrogels are also endowed with remarkably high fatigue thresholds (compared to their random analogues) and high anisotropic ratio ($\Gamma_{0,1}/\Gamma_{0,1}$, Fig. 3F and Supplementary Fig. S21-24).

A long-standing challenge in engineering hydrogel design is the conflict between superior mechanical performances (i.e., high strength, modulus and fatigue threshold) and low solid content, since these attributes are in general mutually exclusive. For example, in our previous report, once a freeze-thawed PVA hydrogel (10 wt.%) is exposed to air-dry and annealing, crystallinity increases up to 47.3%, the fatigue threshold reaches 1,000 J m$^{-2}$, on the cost of low water content of 60 wt.%. Here, we also fabricate FC-A PVA hydrogel from a PVA precursor solution of 10 wt. % (146-186 kDa, 99% hydrolyzed), and a record-high fatigue threshold of 2,740 J m$^{-2}$ (Supplementary Fig. S18) is quantified (crystallinity of 46.8%), while the water content is as high as 82 wt. % (Supplementary Fig. S25-26). To validate this extremely high fatigue threshold, we apply $G_c$ of 2,740 J m$^{-2}$ to a notched sample over 30,000 cycles (to approximate infinite cycles of loads) and observe no crack extension (Fig. 3D, Supplementary Fig. S27 and Movie S2). Accordingly, we show here that the unprecedented high fatigue threshold of a hydrogel system is not always accompanied with substantially-decreased water content, highlighting the attractive merits of our strategy in constructing fatigue-resistant soft materials.

Fig. 4E compares the fatigue thresholds and water contents of reported hydrogels in literatures, biological tissues and our freeze-casted hydrogels. It is shown that the FC-A hydrogel outperforms existing synthetic hydrogels, such as PAAm-alginate,[7] PAAm-poly(2-acrylamido-2-methylpropanesulfonic acid),[27] polyampholyte hydrogels,[18] freeze-thawed PVA,[13] and dry-annealed PVA[12] biogels (i.e., biological tissue),[8] composite hydrogels,[28] mechanically-trained PVA hydrogels,[16] polyprotein-based hydrogels,[25] single network i.e. and polyacrylamide hydrogel),[6,27] in terms of fatigue thresholds, without sacrificing their high water contents (Fig. 3C). Moreover, as far as known to us, this is the first work which successfully fabricates hydrogel materials with record-high fatigue threshold (2,740 J m$^{-2}$) and high anisotropic ratio ($\Gamma_{0,1}/\Gamma_{0,1}$) over 40, at a high water content over 82 wt. %.

The capability to engineer conventional hydrogel materials with unprecedented resistance to crack propagation during long-term cyclic loads enables applications such as load-bearing components in underwater robotics. As shown in Fig. 5A, we design and fabricate an underwater swimming robot, employing an electrically-driven motor to expand the arms, while our load-bearing FC-A PVA hydrogel belts contract and generate the propulsive thrust by pushing the surrounding water rearward, thus this robot could continuously swim underwater (See detailed robot design in Experimental, Fig. 5B, Supplementary Fig. S28 and
Movie S3). During the long-term swimming, soft materials as the load-bearing components are experiencing cyclic stretching-and-contracting, similar to tendons, thus superior fatigue resistance is necessary. As a control, we employ FT PVA hydrogels, which are promising candidates for artificial tendons and cartilages thanks to its excellent elasticity and toughness. By introducing a small pre-crack (ca. 1/5 of the overall width) perpendicular to the stretching direction, we observe that after swimming for over 40 hours, approximately 197,630 stretching-and-contracting cycles at an energy release rate of 90 J m⁻², fatigue-induced fracture occurs (Fig. 5C, and Supplementary Fig. S29A). On the contrary, when the FC-A PVA hydrogels are loaded with pre-crack (ca. 1/5 of the overall width), no crack propagation is observed over 1,000,000 stretching-and-contracting cycles at an energy release rate of 1,340 J m⁻² over 250 hours, showing unprecedented fatigue-resistant performance in real application circumstances (Fig. 5D, Supplementary Fig. S29B and Supplementary Movie S4).

In this study, we have reported a general design rationale, through freeze-casting strategy, to engineer conventional soft materials with unprecedented either anisotropic fatigue-resistance. These hydrogel materials offer advantages over existing analogues, including fatigue thresholds, ease of manufacturing, versatility in material choices, allowance for both isotropic and anisotropic design, etc. These fatigue resistant hydrogel materials provide new opportunities for making them low-cost, high-performance and durable alternatives for soft materials used in those circumstances including robotics, artificial muscles, etc.

References

Hydrogels with Unprecedented Mechanical Properties

Xiangyu Liang¹, Guangda Chen¹, Shaoting Lin², Jiajun Zhang³, Liu Wang³, Pei Zhang³, Zeyu Wang⁴, Zongbao Wang⁴, Yang Lan⁵, Qi Ge¹, Ji Liu¹, 6, 7, *

Anisotropically Fatigue-Resistant Hydrogels

Hydrogels with Unprecedented Fatigue Resistance: Fatigue-resistant hydrogels are fabricated through synergistically engineering the preferentially-aligned microstructures and nanocrystalline domains, enabling the application as load-bearing components in underwater robots.