EDITORIAL

Bioinspired multiscale regulation for hydrogels with superior mechanics

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As humanity ventures deeper into the era of advanced materials, the need for versatile, high-performance systems that can excel in complex environments has become increasingly critical. With billions of years of evolutionary refinement, nature offers unparalleled examples of structural ingenuity—heart valves, muscles, and cartilage demonstrate extraordinary combinations of strength, toughness, flexibility, and durability through multiscale hierarchical architectures. These biological systems have served as blueprints for a new wave of materials innovation. Notably, these tissues can be regarded as natural hydrogels, composed of crosslinked polymer networks and high water content. This understanding has inspired the development of synthetic hydrogels to mimic and replace biological tissues.[1] Hydrogels, composed of crosslinked polymer networks and water, mimic the soft texture of biological tissues, making them highly promising for applications such as wound dressings, prosthetics, implants, and drug deliv-

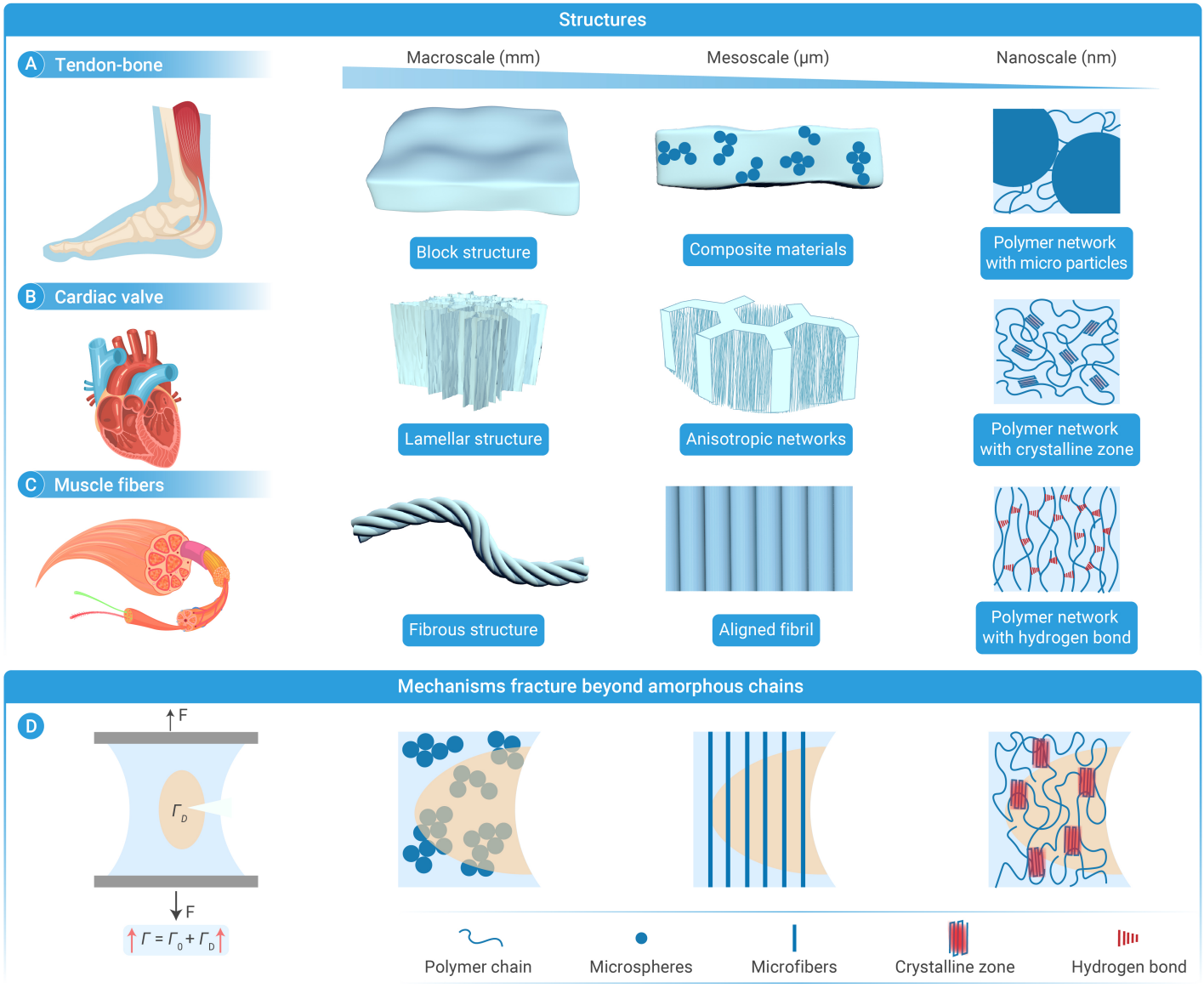

Figure 1. Bioinspired multiscale regulation to engineer hydrogels with unprecedented mechanics (A) By mimicking the interfacial architecture of the tendon-to-bone joint, a hydrogel is engineered with ultra-high stiffness and toughness by incorporating nanoscale minerals. (B) Similar to the tendons, hydrogels with preferentially aligned structures, together with the inter-/intra-chain hydrogen bonds, are imparted with anisotropic mechanics and superior fatigue resistance. (C) By engineering the fibrillar architecture, the twisted hydrogel fibers exhibit superior toughness, flexibility and also fatigue resistance. (D) Multiscale fracture mechanisms in hydrogels, highlighting the contribution of various structural elements such as micro/nano-scale phases, micro/nano-scale fibers and inter-/intra-chain hydrogen bonds. The modalities, across multiple length scales, synergistically contribute to improved mechanics. The equation shows the total fracture energy (Γ) as the sum of the intrinsic and extrinsic fracture energy ($\Gamma_0 + \Gamma_D$).

ery systems. Additionally, hydrogels have also been employed in a variety of emerging technologies, including wearable electronics, soft robotics, rechargeable batteries, and water treatment. Conventional hydrogels, formulated by a single network of hydrophilic polymer chains, exhibit inferior mechanics and are prone to damage, with fracture energies of approximately 10 J/m^2, which significantly limits their practical applications. Drawing inspiration from natural prototypes such as heart valves, muscles, and cartilage, significant breakthroughs have been achieved in imparting synthetic hydrogels with unprecedented mechanics —including strength, toughness, and long-term robustness —through the engineering of hierarchical structures (Figure 1).

At the nanoscale, interactions between polymer chains play a critical role in determining the mechanics of hydrogel materials. Optimizing the crosslinking density, incorporating nanocrystalline domains, and/or tailoring the physical entanglements can significantly enhance the strength and toughness. Similar to the fatigue resistance observed in biological tissues, which stems from the preferential alignment of nanocrystalline structures within collagen fibers. Since the energy required to fracture nanocrystals is much higher than that for amorphous chains, increasing the crystallinity (18.9% in the swollen state) of polyvinyl alcohol (PVA) hydrogels can significantly raise the fatigue threshold to as much as 1000 J/m^2.[2] In addition to the overall crystallinity, the size and spacing of crystalline domains also dominate the mechanical properties of hydrogels. In a recent work, Chen et al. introduced a strategy combining solvent exchange with dry annealing to produce PVA hydrogels with enlarged crystalline domains, while maintaining unparalleled structural uniformity.[3] This produced PVA hydrogels with a strength of 34.15 MPa, toughness of 95.21 MJ/m^3, and a fracture energy of 99.2 kJ/m^2. These findings underscore the importance of controlling nanocrystalline domains to optimize the nanostructure and, consequently, the mechanical performance.

At the mesoscale, designing composite structures for hydrogels provides an alternative approach to enhance their mechanics. By incorporating micro- or nano-scale fibers or spheres, hydrogels can achieve superior strength without compromising flexibility. The strong polymer-particle interactions enable stress to transfer from the polymer to the particles. Since the particles are rigid, the stress is dispersed across multiple particle-to-particle gaps within the cluster. This composite formulation not only significantly increases the fatigue threshold (1000 J/m^2), but also maintains a high modulus and excellent crack resistance. In a recent work by Wang et al., cellulose nanofibers (CNFs) were incorporated into a PVA hydrogel matrix using a salting-out process,[4] resulting in a highly oriented supramolecular hydrogel network during stretching. This structure exhibited exceptional stretchability (up to 7400%) and a true tensile strength of up to 420 MPa. It was also reported that the introduction of microspheres into hydrogels, combined with multiscale stress deconcentration mechanisms, significantly increased the fatigue threshold (up to 1000 J/m^2), while maintaining a high modulus. These properties make the material well-suited for applications that require high load-bearing under cyclic loading, such as tires, dampers, conveyor belts, and soft robotics.

Various macro-architectures, such as blocks, fibrous, and lamellar structures, can be employed to tailor the mechanics, including strength, toughness and fatigue resistance.[5] For instance, fibrous structures-particularly aligned or woven fibers-represent a classic strategy for macroscopic reinforcement. Hydrogels embedded with fibers, such as PDMS elastomer or synthetic fibers, exhibit superior tensile strength and toughness along fiber orientation. Lamellar structures, such as the nacre-inspired lamellar designs, are particularly effective for enhancing both toughness and impact resistance. Block structures, such as cartilage, exhibit high water content, collagen networks, and specialized molecules, including hyaluronic acid, lubricin, and phospholipids. These components work synergistically across multiple scales, enabling cartilage to possess exceptional durability and ultra-low friction under pressure.[1] It is important to note that these strategies are illustrative rather than exhaustive, and there is no absolute correspondence to specific scales. For example, fibrous structures can be constructed at various scales, functioning as nanowires, microfibers, or even larger fibers, each contributing uniquely to the mechanical properties. Similarly, particle doping can involve microspheres or nanoparticles, depending on the desired function and scale of reinforcement. This flexibility and scalability in applying different structural strategies across scales provide a comprehensive approach to optimizing hydrogel properties for diverse applications. In summary, the regulation of macroscopic structures enables precise tuning of hydrogel mechanics, including strength, toughness, and fatigue resistance, making them suitable for a wide range of high-performance applications.

Multiscale synergistic regulation has demonstrated great potential in enhancing the mechanical properties of hydrogels, providing innovative solutions to challenges in soft materials. This strategy recognizes that structural features at the nano-, meso-, and macro-scales can complement one another, working in concert to deliver superior performances, including enhanced strength, toughness, and fatigue resistance. Looking ahead, artificial intelligence (AI) is expected to further accelerate advancements in hydrogel design. AI algorithms, like machine learning and deep learning, analyze biological structures and simulate hydrogel behavior. Convolutional neural networks (CNN) process microscopic images to extract features such as porosity, while recurrent neural networks (RNN) analyze stress-strain data to predict performance under tension or fatigue. Inverse design with AI-driven databases streamlines material selection and performance prediction, reducing development time. Generative adversarial networks (GAN) optimize material configurations, and reinforcement learning (RL) adjusts compositions based on feedback. AI also optimizes hydrogel applications by monitoring fatigue in soft robotics, customizing implants for personalized medicine, and enhancing conductivity in wearable electronics. As AI integrates with multiscale strategies, hydrogels will become smarter and more adaptive, transforming future developments in biomedicine, flexible electronics, robotics, energy storage and conversion, environment remediation, smart agriculture, and beyond.

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AUTHOR CONTRIBUTIONS

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DECLARATION OF INTERESTS

The authors declare no competing interests.