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Review

Hydrogel 3D Printing for Diverse Applications: A review

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Abstract: Hydrogels have emerged as a versatile and promising class of materials in the field of 3D printing, offering unique properties suitable for various applications. This review delves into the intersection of hydrogels and 3D printing, exploring current research, technological advancements, and future directions. It starts with an overview of hydrogel basics, including composition and properties, and details various hydrogel materials used in 3D printing. The review explores diverse 3D printing methods for hydrogels, discussing their advantages and limitations. It emphasizes the integration of hydrogel 3D printing in biomedical engineering, showcasing its role in tissue engineering, regenerative medicine, and drug delivery. Beyond healthcare, it examines applications in industries like food, cosmetics, and electronics. Challenges like resolution limitations and scalability are addressed. Looking ahead, the review predicts future trends in material development, printing techniques, and novel applications. In summary, this comprehensive review offers insights into the transformative potential of hydrogel 3D printing for diverse fields, serving as a valuable resource for researchers and innovators.

Keywords: Hydrogels; 3D printing; Biomedical applications; Natural hydrogels; Synthetic hydrogels

1. Introduction

The rapid advancement of additive manufacturing, commonly known as 3D printing, has revolutionized the way we conceive, design, and produce objects across a spectrum of industries. From aerospace to healthcare, 3D printing has ushered in an era of unparalleled customization, reduced lead times, and intricate geometries that were previously unattainable using traditional manufacturing methods [1]. By layering materials to construct three-dimensional objects directly from digital designs, 3D printing has transcended conventional limitations, allowing for unprecedented levels of innovation. Applications of 3D printing are extensive and span a myriad of sectors. In aerospace, the technology has enabled the production of complex lightweight components with enhanced performance characteristics. In the automotive industry, it has facilitated the rapid prototyping of parts and the creation of specialized tools on-demand. Similarly, healthcare has experienced transformative changes, with 3D printing being employed to craft patient-specific implants, anatomical models for surgical planning, and even bioengineered tissues [2,3].

Amidst this technological evolution, one class of materials has emerged as particularly intriguing for 3D printing: hydrogels. Hydrogels are three-dimensional networks of hydrophilic polymers that possess the remarkable ability to absorb and retain large amounts of water or biological fluids [4]. This unique property imbues hydrogels with an inherent compatibility with living systems, making them an ideal candidate for a range of applications that intersect with the life sciences. Hydrogels can be of several types including natural hydrogels, synthetic hydrogels, hybrid hydrogels, physically crosslinked hydrogels

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and chemically crosslinked ~~hydrogels~~. Notably, hydrogels' high water content and tunable mechanical properties render them an exceptional material for 3D printing. Various 3D printing technologies can be successfully employed for the printing of hydrogels including extrusion-based 3D printing [5], inkjet-based printing [6], stereolithography [7], laser-assisted bioprinting [8], digital light processing [9], etc. Naghieh et al. [10]., explored the printability of 3D hydrogel scaffolds, focusing on the influence of hydrogel composition and printing parameters and contributes to the optimization of 3D printing processes for creating intricate structures used in tissue engineering and other applications. Kalyan and Kumar [11]., provided insights into the broad spectrum of 3D printing applications, including tissue engineering, medical devices, and drug delivery and serves as a comprehensive overview of the current state of 3D printing technology in healthcare and biomedicine.

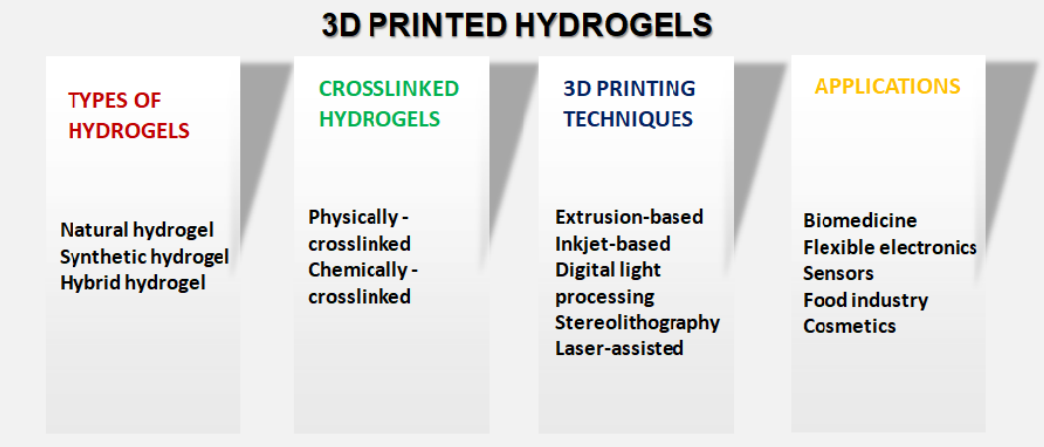

Figure 1. Schematic representation of the various types of hydrogels, and their printing techniques that can be employed several applications in various sectors including biomedicine, flexible electronics, sensors, food industries and cosmetics..

The capability to precisely engineer the stiffness, porosity, and degradation rate of hydrogels allows for tailoring constructs to match the specific requirements of the target application. This adaptability opens doors to advancements in tissue engineering, drug delivery, wound healing, and beyond. Moreover, the compatibility of hydrogels with cells and tissues offers the potential to create biomimetic structures that closely mimic natural physiological environments, thereby enhancing their utility in regenerative medicine and disease modeling. Figure 1 schematically represented the various types of hydrogels, and their printing techniques that can be employed several applications in various sectors. In a recent ~~concise~~ review, Kapusta and colleagues [12]., have delved into the utilization of antimicrobial natural hydrogels in the realm of biomedicine, offering an examination of their attributes, potential applications, and the challenges they present. This work sheds light on the manifold opportunities these hydrogels hold within various medical fields. Kaliaraj et al [13]., have directed their attention to the auspicious uses of hydrogels in the realm of 3D printing technology where the emphasis lies in highlighting the versatile nature of hydrogels as viable materials for 3D printing, underscoring their pivotal role in this innovative manufacturing technique.

Zhang et al [14]., have conducted an exhaustive review that encapsulates the latest advancements in the domain of 3D printing concerning sturdy hydrogels. Their in-depth exploration provides valuable insights into the evolution of resilient hydrogel materials and their applications, thereby contributing significantly to the burgeoning field of 3D printing.

As we embark on this journey through the realm of hydrogels in 3D printing, this review article aims to explore their multifaceted potential, discussing the diverse range of

hydrogel materials, printing techniques, and applications within which they play a pivotal role. By delving into the synergy between hydrogels and 3D printing, we seek to unravel the novel avenues for innovation that this convergence has unlocked, ultimately shaping the landscape of industries ranging from healthcare to consumer products.

2. Hydrogels: An Overview

Hydrogels are a class of materials with a three-dimensional network structure composed of hydrophilic polymers that can absorb and retain significant amounts of water or biological fluids. This unique property gives hydrogels a resemblance to natural soft tissues, making them valuable for a wide range of applications across various fields. This section will discuss the classification of hydrogels, their properties and applications.

2.1. Classification of hydrogels

The choice of hydrogel material significantly influences the printability, biocompatibility, and mechanical properties of 3D-printed constructs. Researchers need to carefully consider these factors when selecting a hydrogel material for their specific application to ensure optimal performance and desired outcomes. It should be noted here that the hydrogels can be classified based on their composition as well as crosslinking methods.

On the basis of composition, they can be natural hydrogels or synthetic hydrogels. Natural hydrogels can be derived from natural polymers such as alginate, collagen, chitosan, and hyaluronic acid and often possess inherent bioactivity and biocompatibility. These hydrogels can be challenging to 3D print due to their complex rheological properties, including viscosity and shear-thinning behavior. Modifications, such as optimizing gelation kinetics or mixing with other materials, might be necessary to enhance printability. Also, they tend to be biocompatible due to their similarity to the extracellular matrix of tissues and hence promote cell adhesion, proliferation, and differentiation, making them valuable for applications involving direct interaction with living cells. Başyiğit et al [15]., explored soy protein-based hydrogels enhanced with locust bean gum, conducting an investigation into their mechanical properties and release characteristics. This research advances our comprehension of the potential utility of these hydrogels in applications such as controlled drug delivery systems. In other work, Xin and colleagues [16]., developed a specialized okra-based hydrogel for addressing chronic diabetic wounds, addressing a significant healthcare challenge and underscoring the promise of natural hydrogels in wound care. In the same year, Haghbin et al [17]., embarked on the creation of a Persian gum-based hydrogel loaded with gentamicin-loaded natural zeolite, conducting a comprehensive study of its properties both in vitro and in silico. This investigation carries implications for drug delivery and infection management, underscoring the adaptability of natural hydrogels. Biodeterioration of stone monuments and its correlation with cyanobacterial biofilm growth was also investigated [18]. They also explored the use of essential oils in natural hydrogels. This study has practical applications in the preservation of cultural heritage and the environmentally friendly management of biofilms. Huang et al [19]., directed their efforts toward the biofabrication of a natural Au/bacterial cellulose hydrogel for bone tissue regeneration via in-situ fermentation. This research addresses the pressing need for biocompatible materials in regenerative medicine, underscoring the potential of natural hydrogels in the field of tissue engineering.

The construction and properties of physically cross-linked hydrogels based on natural polymers was carried out by Yang et al [20]. Their work bears wide-ranging implications in the field of biomedicine, including applications in drug delivery, wound healing, and tissue engineering. Xu et al [21]., delved into the examination of chitosan-based high-strength supramolecular hydrogels intended for 3D bioprinting which not only advances the bioprinting field but also highlights the promise of natural hydrogels as bioink materials. Cai and colleagues [22]., reported on the potential of Laponite®-incorporated oxidized alginate–gelatin composite hydrogels for use in extrusion-based 3D printing which

holds grweat significance within the realm of 3D printing technology, illustrating how natural hydrogels can be seamlessly integrated into advanced manufacturing processes. These collective studies contribute to the growing domain of natural hydrogels, showcasing their adaptability and potential across diverse applications, spanning from healthcare to cultural preservation and beyond. It should be noted that the mechanical strength and stability of these hydrogels may be relatively lower, which can limit their use in load-bearing applications. However, they excel in creating biomimetic environments for cell growth.

Contrary to this, synthetic hydrogels can be obtained from synthetic polymers like polyethylene glycol (PEG), polyacrylamide, and polyvinyl alcohol (PVA) and hence the properties of synthetic hydrogels can be precisely controlled through chemical synthesis. These hydrogels generally exhibit more consistent and predictable printing behavior and their properties can be finely tuned to match the desired viscosity and flow characteristics for different printing techniques. The biocompatibility of such hydrogels depends on the specific polymer and crosslinking chemistry used. Modifications can be made to enhance biocompatibility, and biofunctionalization can be applied to improve cell interactions. Apart from this, they also offer superior control over mechanical properties which can be engineered to mimic a wide range of tissue stiffness, making them suitable for applications where mechanical support is crucial. Van Velthoven et al. [23]., conducted a study focused on the entrapment of growth factors within synthetic hydrogels, specifically examining the bioactive bFGF-functionalized polyisocyanide hydrogels. Their goal was to enhance the controlled release and biological activity of growth factors, potentially benefiting biomedical applications.

Saccone et al [24]., have pioneered a novel additive manufacturing (AM) technique based on visible light photopolymerization, called Hydrogel Infusion Additive Manufacturing (HIAM), which allows for the creation of a wide range of micro-architected metals and alloys using a single photoresin composition. In this process, 3D architected hydrogel scaffolds are employed as platforms for in situ material synthesis reactions, as depicted schematically in Figure 2(a). To produce metal microlattices, the first step involves using DLP to print architected organogels based on N,N-dimethylformamide (DMF) and polyethylene glycol diacrylate (PEGda). The DLP printing phase determines the final shape of the part and following printing, a solvent exchange replaces DMF with water, transforming the organogels into hydrogels. These hydrogel structures are then soaked in a solution containing metal salt precursors, allowing the metal ions to infiltrate and expand the hydrogel scaffold. Calcination in an air environment converts the metal-salt-swollen hydrogels into metal oxides, and subsequent reduction in a forming gas mixture (95% N_2, 5% H_2) yields metal or alloy replicas that match the initially designed architecture. Throughout this process, the shape of the part, defined during DLP printing, is retained, with each dimension experiencing approximately 60-70% linear shrinkage, accompanied by an approximate mass loss of 65-90% during calcination. To illustrate the versatility of HIAM when compared to previous visible light photopolymerization AM techniques, they employed HIAM to create octet lattice structures using various materials such as copper (as shown in process steps in Figure 2(b-e)), nickel, silver, their alloys, and more complex materials like the high-entropy alloy CuNiCoFe and the refractory alloy W-Ni (Figure 2(f)) . Additionally, they demonstrated the fabrication of multimaterial structures, such as Cu/Co (Figure 2(g-h)). HIAM stands out for its capacity for parallelization, allowing multiple organogels to be printed simultaneously, swelled in distinct solutions, and subsequently calcined/reduced collectively. In Figure 2(i), one can observe the simultaneous calcination of eight hydrogel lattices (precursors for Cu, CuNi, CuNiCoFe, and CuNiCoFeCr), resulting in the formation of oxides. The scale bars shown in figures 2(b,c) is 5 mm; figures 2(d–f) 1 mm; figure 2(g) is 1 cm; figure 2(h) 2 mm; and figure 2(i) is 2 cm. Figures 2(j-m) represents the SEM image of Cu and CuNi samples from an overhead view (figure 2(j, l)), and a single junction node (figure 2(k, m)), respectively, and revealed that the Cu

and CuNi samples retained their octet lattice shape throughout the thermal treatment, with beam diameters approximately around 40 μm.

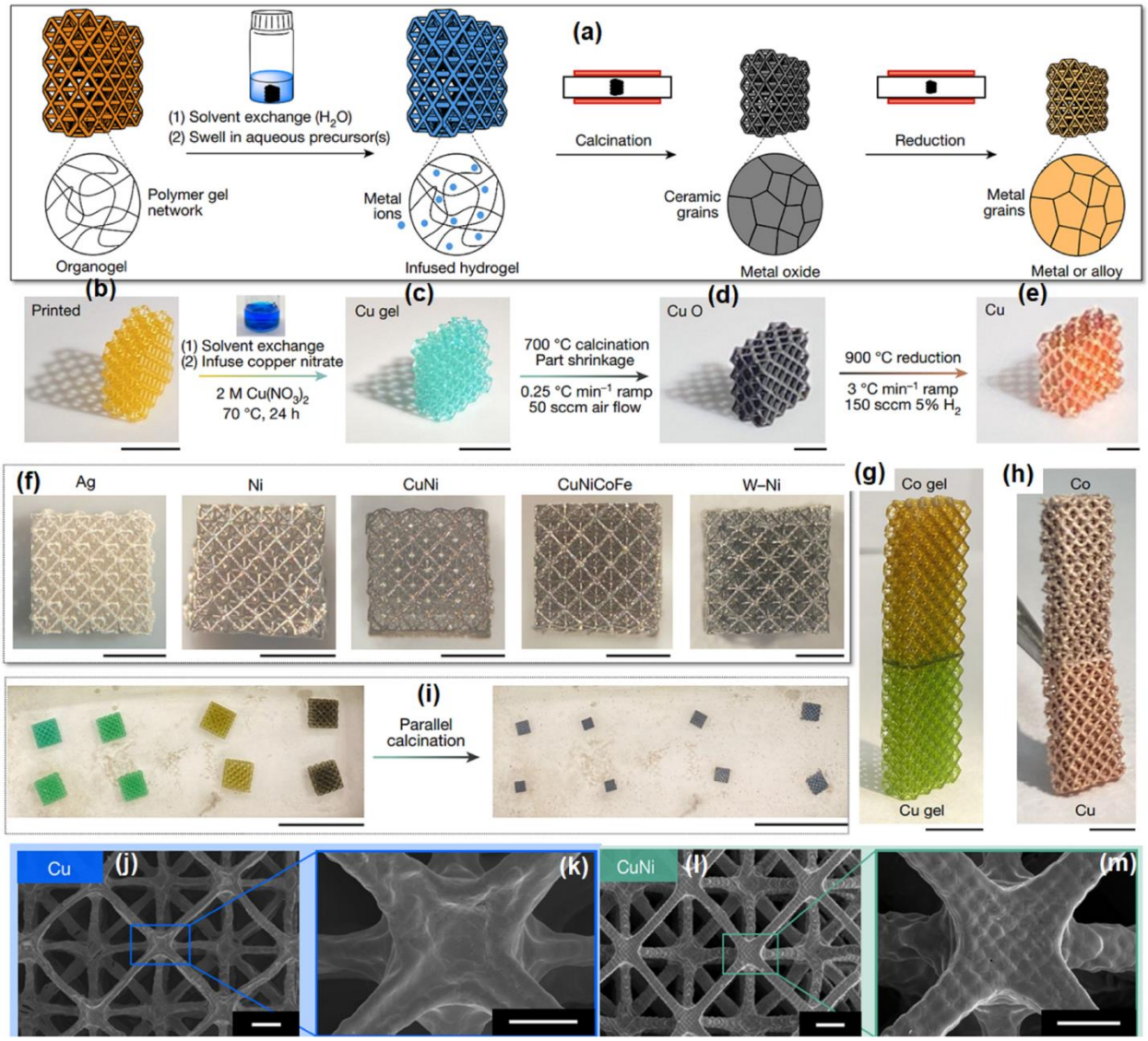

Figure 2. Hydrogel-Infused Additive Manufacturing process and materials. (a) Illustration of the HIAM process. A 3D-printed organogel structure, composed of DMF/PEGda, undergoes a transformation into an infused hydrogel replica through the sequential steps of photoactive compound removal, solvent exchange, and infusion with a suitable aqueous precursor. Subsequent calcination in an oxygen environment leads to the formation of metal oxide structures, which are subsequently reduced to metals in a forming gas. (b–e) Visual representations of the HIAM process for Cu metal: the printed organogel (b), the infused hydrogel (c), the calcined metal oxide (d) and the reduced metal (e). (f) Diverse metals and alloys fabricated using HIAM, including Ag, Ni, a binary CuNi alloy, a high-entropy CuNiCoFe alloy, and a refractory W–Ni alloy. (g) An octet lattice infused with $Cu(NO_3)_2$ on one end and $Co(NO_3)_2$ on the other. (h) After calcination and reduction, the Cu/Co gel transforms into a Cu/Co multimaterial. (i) Simultaneous calcination of various infused gels. (j, k) and (l, m) SEM micrographs of Cu and CuNi octet lattices, depicting several unit cells from an overhead view (j, l), and a single junction node (k, m), respectively. (Scale bars: j,l, 100 μm; k,m, 50 μm). Reprinted from [24] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

Adjuik et al [25]., have presented an extensive review that delves into the degradability of both bio-based and synthetic hydrogels, with a particular emphasis on their potential as sustainable soil amendments. This comprehensive review explores the

environmental implications and ecological consequences of using hydrogels in agriculture, shedding light on the sustainability and compatibility of these materials when applied to soil enhancement practices. 3D printable synthetic hydrogel designed as an immobilization matrix for continuous synthesis involving fungal peroxygenases has also been reported [26]. This innovative approach holds promise in the field of biocatalysis, enabling efficient and uninterrupted production of valuable compounds. The synthetic hydrogel matrix offers a stable and controlled environment for enzyme activity, facilitating the development of sustainable and efficient biochemical processes. Yuk et al [27]., have created a high-performance 3D printable ink utilizing one of the most commonly used conducting polymers, poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS), to harness the capabilities of advanced 3D printing in producing conducting polymer structures. To ensure suitable rheological properties for 3D printing, they have developed a paste-like conducting polymer ink which is is derived from cryogenically freezing an aqueous PEDOT:PSS solution 3(a), followed by lyophilization and controlled re-dispersion in a mixture of water and dimethyl sulfoxide (DMSO) (as shown in figure 3(b)). The resulting conducting polymer ink demonstrates exceptional 3D printing capabilities, enabling high-resolution printing (with a resolution of over 30 μm), the creation of structures with a high aspect ratio (exceeding 20 layers), and consistent fabrication of conducting polymers. These structures can also be seamlessly integrated with other 3D printable materials, such as insulating elastomers, using multi-material 3D printing. By subjecting the 3D-printed conducting polymers to dry annealing, they have achieved highly conductive microstructures that remain flexible in their dry state which can be easily transformed into a soft, highly conductive PEDOT:PSS hydrogel through subsequent swelling in a wet environment (figure 3(c)). To showcase the achievement of high-resolution microscale printing, they have used 7wt% PEDOT:PSS nanofibril-based conducting polymer ink to create intricate mesh patterns through nozzles of various diameters: 200 μm, 100 μm, 50 μm, and 30 μm (referred to as figures 3(d-g)). The conducting polymer ink's favorable rheological properties also facilitate the construction of multi-layered microstructures with high aspect ratios, using a 100 μm nozzle and incorporating up to 20 layers.

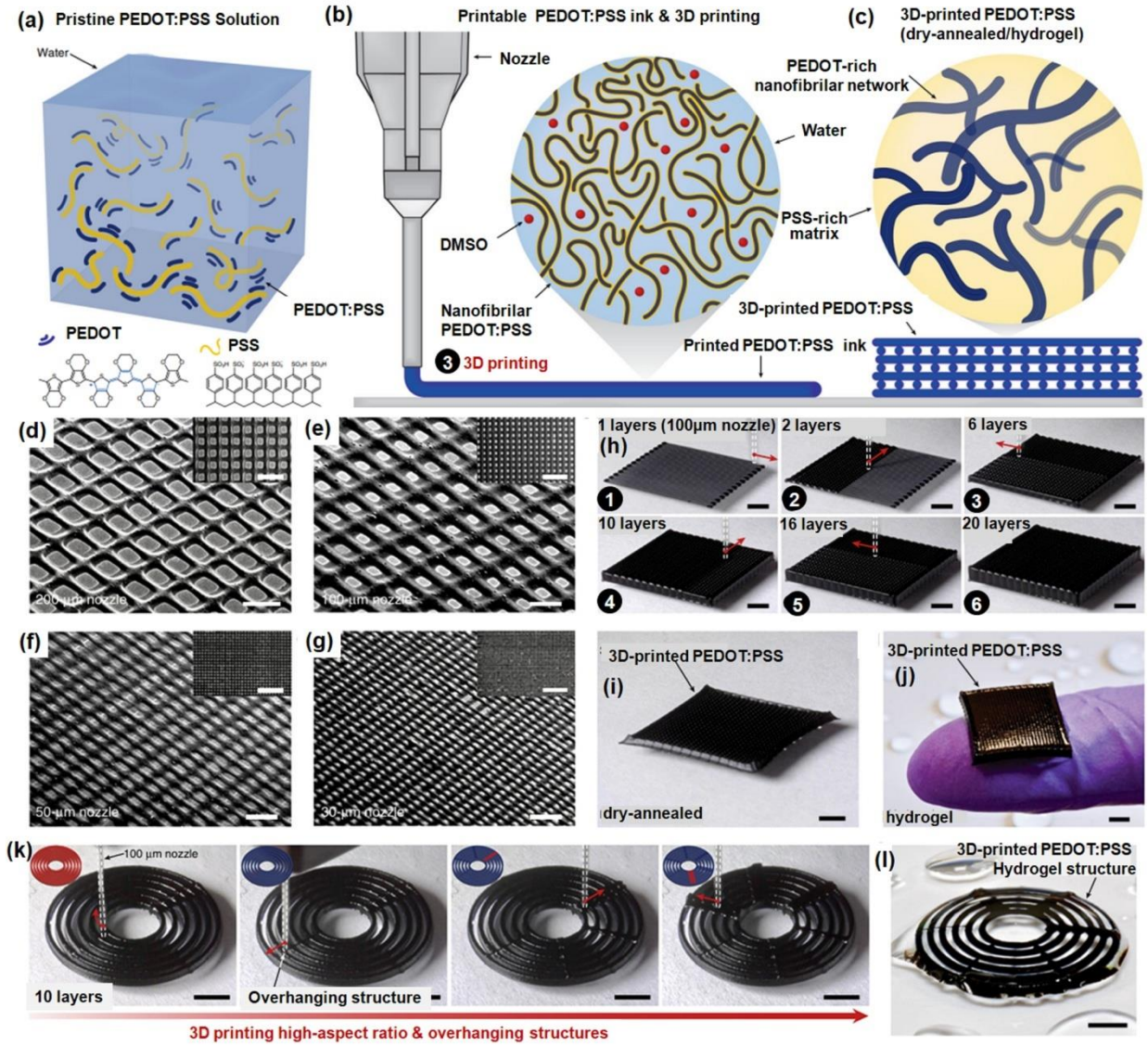

Figure 3. Development of a 3D printable conductive polymer ink design. a, b, The initial pristine PEDOT:PSS solution (a) can undergo a transformation into a 3D printable conductive polymer ink (b) through lyophilization under cryogenic conditions followed by re-dispersion using an appropriate solvent. (c) 3D-printed conductive polymers can be transformed into pure PEDOT:PSS, whether in their dry state or hydrogel state, through a process involving dry annealing and subsequent expansion in a wet environment, respectively. (d-g) SEM micrographs of 3D-printed conducting polymer meshes. (h) Step-by-step progression of creating a 20-layered meshed structure using the conducting polymer ink. (i) 3D-printed conducting polymer mesh after undergoing a dry-annealing process, crucial for enhancing its conductivity. (j) 3D-printed conducting polymer mesh in its hydrogel state, highlighting its adaptability to different environmental conditions. (k) Sequential snapshots for 3D printing overhanging features across high aspect ratio structures using the conducting polymer ink, demonstrating its ability to maintain structural integrity during complex printing. (l) 3D-printed conducting polymer structure with overhanging features, transformed into a hydrogel state. Reprinted from [27] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

Figure 3(h) illustrates step-by-step progression of creating a 20-layered meshed structure using the conducting polymer ink. Following the printing, figure 3(i) displays the 3D-printed conducting polymer mesh after undergoing a dry-annealing process, which is crucial for enhancing its conductivity. In contrast, figure 3(j) showcases the same 3D-printed conducting polymer mesh, but in its hydrogel state, highlighting the adaptability of this

material to different environmental conditions. Figure 3(k) provides a visual representation of the sequential snapshots for 3D printing overhanging features across high aspect ratio structures using the conducting polymer ink, demonstrating the ink's ability to maintain structural integrity during complex printing. Finally, figure 3(l) reveals the 3D-printed conducting polymer structure with overhanging features, which has been transformed into a hydrogel state. These figures collectively demonstrate the versatility, resilience, and transformative capabilities of conducting polymer inks in advanced 3D printing applications.

Apart from these two types, hybrid hydrogels can also be prepared by combining the components from both natural and synthetic sources, leveraging the advantages of each material type. Hybrid hydrogels often strike a balance between natural and synthetic hydrogels, aiming to improve printability by combining the advantages of both material types. They can also harness the biocompatibility of natural components while introducing controlled synthetic elements to enhance mechanical properties and stability. Also, these hydrogels aim to combine the mechanical advantages of synthetic materials with the biocompatibility of natural materials, offering a balanced approach for applications requiring both properties. Tang et al [28]., delved into the domain of hybrid hydrogels for three-dimensional cell culture and employed stereolithography to craft nanocellulose/PEGDA aerogel scaffolds, thereby introducing tunability to the modulus of these structures. This investigation is of notable significance within the realms of tissue engineering and regenerative medicine as it provides a platform for 3D cell cultivation, effectively emulating natural tissue environments. Cao and their collaborators [29]., have also explored the potential of antibacterial hybrid hydrogels as a robust tool for combatting microbial infections. This research represents a vital area of study with broad-reaching implications in the field of medicine, where the development of infection-resistant materials can significantly elevate patient care and mitigate the transmission of infectious diseases.

Palmese et al [30]., have provided a comprehensive investigation and multifaceted applications of hybrid hydrogels within the biomedical field which underscores their versatility and potential, showcasing the diverse ways they can be applied to address various medical challenges, from developing drug delivery systems to advancing tissue engineering. Incorporation of natural polymers into hybrid hydrogels for medical applications was also examined by Vasile and his research team [31]. Their study sheds light on the diverse utility of these materials in healthcare, indicating their roles in drug delivery, wound healing, and various other medical interventions. This research emphasizes the increasing interest in harnessing the properties of natural polymers within medical contexts. Liao et al [32]., introduced a unique hybrid hydrogel with the specific aim of preventing bone tumor recurrence and promoting bone regeneration. This specialized hydrogel incorporates gold nanorods and nanohydroxyapatite and utilizes photothermal therapy. This innovative approach holds great promise for addressing bone-related health concerns and managing bone tumors, offering a novel and effective treatment strategy. Anisotropic hybrid hydrogels with mechanical properties reminiscent of tendons or ligaments was also explored [33] for tissue engineering, providing the potential to mimic the mechanical characteristics of specific tissues. This development offers a valuable resource for the creation of artificial ligaments and tendons. Yang et al [34]., introduced 3D macroporous oxidation-resistant Ti_3C_2Tx MXene hybrid hydrogels which demonstrate remarkable supercapacitive performance with an extraordinarily long cycle life. This research holds significant implications for energy storage applications, particularly in supercapacitors, where long-term stability and performance are imperative. Collectively, these studies contribute to the expanding field of hybrid hydrogels, underscoring their potential and versatility in a wide range of biomedical and materials science applications. These applications span from healthcare to advanced materials used in sustainable technologies. Table 1 comparatively summarizes the various properties of natural, synthetic and hybrid hydrogels in terms of preparation, printability, biocompatibility and mechanical properties.

Depending upon crosslinking, hydrogels can be classified as physically crosslinked hydrogels and chemically crosslinked hydrogels. Physically crosslinked hydrogels are formed through non-covalent interactions, such as hydrogen bonding or physical entanglements and are reversible and responsive to environmental changes, while the chemically crosslinked hydrogels are formed by covalent bonds between polymer chains, resulting in higher stability and mechanical strength. Examples include photopolymerization and chemical crosslinking agents. Iwanaga et al [35]., focused their efforts on the design and production of fully developed engineered pre-cardiac tissue using 3D bioprinting techniques, coupled with enzymatic crosslinking hydrogels. This pioneering investigation shows great potential in the fields of regenerative medicine and cardiac tissue engineering, addressing the significant hurdle of generating functional heart tissues. Recently, Ianchis et al. [36]., also delved into the creation of innovative green crosslinked hydrogels derived from Salecan and initiated their preliminary exploration of these hydrogels in the context of 3D printing. The prospects of utilizing sustainable and environmentally friendly hydrogel materials in additive manufacturing processes has been highlighted in this research, with implications spanning drug delivery and tissue engineering. Another groundbreaking work by Farsheed and his collaborators has been witnessed in the realm of 3D printing of self-assembling nanofibrous multidomain peptide hydrogels [37]. This research has the potential to revolutionize the fabrication of intricate and adaptable nanofibrous structures through 3D printing, introducing novel applications in regenerative medicine, drug delivery, and tissue engineering.

Table 1. Comparative summary of the properties of natural, synthetic and hybrid hydrogels in terms of preparation, printability, biocompatibility and mechanical properties.

Property	Natural Hydrogels	Synthetic Hydrogels	Hybrid Hydrogels
Preparation	-Derived from biological sources like alginate, collagen, or agarose. -Typically requires minimal chemical modification.	-Chemically synthesized with precise control over composition. -Tailored to specific requirements through chemical synthesis.	-Combination of natural and synthetic components. -Utilizes the advantages of both natural and synthetic components.
Printability	-Varies depending on source material. -May require additional modifications for 3D printing.	-Generally good printability due to controlled composition. -Compatible with various 3D printing techniques.	-Printability depends on the combination and ratio of components. -Printability can be customized for specific applications.
Biocompatibility	- Generally biocompatible due to natural origin. - Often suitable for cell encapsulation and tissue engineering.	- Biocompatibility can vary based on the polymer used. - Careful selection of synthetic components can enhance biocompatibility.	- Biocompatibility influenced by natural components. - Potential for improved biocompatibility through hybridization.
Mechanical Properties	- Mechanical properties can vary widely depending on the source. - May have lower mechanical strength compared to synthetics.	- Can be precisely tuned for specific applications. - Offers a wide range of mechanical properties (soft to stiff).	- Mechanical properties can be tailored to desired levels. - Balances natural properties with synthetic enhancements.

2.2. Properties and applications of hydrogels

They have several fascinating properties including high water content, tunable mechanical properties, swelling behavior, biocompatibility, permeability, etc. Hydrogels can consist of up to 90% water, conducive to interactions with biological systems and their

mechanical characteristics such as stiffness, elasticity, and resilience, etc. can be tailored by adjusting factors such as polymer type, crosslinking density, and composition. They also exhibit swelling and deswelling responses to changes in environmental conditions, such as pH and temperature which makes them suitable for controlled drug delivery systems. Several hydrogels are biologically inert and non-toxic, enabling their use in medical applications without adverse effects on cells and tissues and can also allow the diffusion of small molecules while restricting the movement of larger molecules, offering potential applications in separation and filtration processes. Hydrogels' unique properties, diverse composition, and tunable crosslinking methods make them invaluable materials with far-reaching applications. Their importance spans biomedical, pharmaceutical, and various other industries, fostering innovation and impacting multiple facets of modern life. However, the biomedical and pharmaceutical applications of hydrogel materials are more popular. Hydrogels hold immense promise in the biomedical field due to their biocompatibility and resemblance to natural tissues and are utilized as scaffolds for tissue engineering, enabling the regeneration of damaged tissues and organs. Additionally, hydrogels play a critical role in drug delivery systems, enabling controlled release of therapeutic agents over time. Their ability to encapsulate drugs and proteins ensures targeted delivery, minimizing side effects and improving treatment outcomes. In the pharmaceutical industry, hydrogels can be utilized for drug formulation and delivery. They can encapsulate and protect sensitive drugs, allowing for improved stability and sustained release. Hydrogel-based drug delivery systems can enhance the bioavailability of poorly soluble drugs and provide controlled release profiles, leading to better patient compliance and therapeutic efficacy. Hydrogels have also found use in diverse industries beyond biomedical and pharmaceutical domains. They are employed in agriculture for controlled nutrient release to plants, in cosmetics for sustained release of skincare ingredients, and in environmental engineering for water purification and pollutant removal.

2.3. Designing Hydrogel Formulations for 3D Printing

Designing hydrogel formulations for 3D printing involves optimizing various parameters to ensure proper printability, structural integrity, and compatibility with the chosen printing method. A delicate balance between rheological properties, gelation kinetics, and print fidelity is highly imperative for designing hydrogel formulations for 3D printing [38]. Additives also play a critical role in tailoring hydrogel properties to meet specific application requirements, enabling the creation of structures with optimized mechanical, biological, and functional characteristics.

2.2.1. Rheology gelation kinetics and print fidelity

Hydrogels must have a suitable viscosity to ensure proper extrusion or jetting during printing. Rheological modifiers, such as thickeners or viscosity enhancers, can be added to adjust the hydrogel's flow behavior. Hydrogels that exhibit shear-thinning behavior become less viscous under shear, allowing for smoother extrusion through nozzles or print heads. This property improves printability and fidelity.

It should be noted here that the gelation kinetics of the hydrogel should align with the printing process. Rapid gelation can impede material flow, while slow gelation may result in shape distortion. Formulations with tunable gelation kinetics can be adjusted to match printing speed. Some hydrogels can undergo gelation post-printing due to environmental factors such as temperature or pH changes which allows for improved print fidelity during deposition.

Moreover, hydrogel formulations should maintain their shape during printing and post-processing steps. Considerations for gel stiffness, crosslinking density, and curing parameters influence print fidelity and structural stability. Minimizing shrinkage upon gelation is crucial to maintaining the integrity of printed structures. Balancing crosslinking density and material swelling properties can help achieve minimal distortion.

2.2.2. Role of Additives in Tailoring Hydrogel Properties

Several additives can be employed to tailor the properties of hydrogels including crosslinkers, initiators, bioactive agents, fillers and reinforcements, etc., depending upon the requirement of specific application. Crosslinkers are essential additives that form covalent bonds between polymer chains, giving hydrogels their structure and mechanical stability. The type and concentration of crosslinkers also influence hydrogel stiffness, degradation rate, and swelling behavior. For example, higher crosslinking density leads to stiffer hydrogels suitable for load-bearing applications, while lower crosslinking density results in softer materials for tissue engineering. Initiators are used in photopolymerization-based printing methods to trigger the curing process upon exposure to light. Initiators control the speed and completeness of gelation, affecting printing accuracy and resolution. Bioactive agents, such as growth factors, enzymes, and drugs, can be incorporated into hydrogel formulations to confer specific functionalities and hence bioactive hydrogels find applications in tissue engineering, drug delivery, and wound healing. The controlled release of bioactive agents from hydrogels enhances their therapeutic potential. Additives like nanoparticles, fibers, or microstructures can be included to enhance mechanical properties, stability, and printability. These reinforcements improve the overall performance of the printed hydrogel constructs.

3. 3D Printing Methods for Hydrogels

Several 3D printing methods are employed to create hydrogel-based structures, each with its own set of advantages and limitations. In selecting a 3D printing method for hydrogel-based projects, the trade-offs between resolution, speed, and material compatibility should be carefully considered to align with the desired application and project requirements. The various 3D printing technologies includes extrusion-based 3D printing, inkjet-based printing, stereolithography, laser-assisted bioprinting, digital light processing, etc [5-9]. Figure 4 schematically illustrates the various 3D printing technologies that can be successfully employed for hydrogels printing. Kantaros et al [39]., have explored the technologies and resources employed in 3D printing within the realm of regenerative medicine and sheds light on the instrumental tools and methodologies used to propel the field forward, facilitating the generation of intricate tissue constructs for transplantation and mending. Bedell and colleagues [40]., investigated human gelatin-based composite hydrogels tailored for osteochondral tissue engineering, adapting them into bioinks suitable for a variety of 3D printing techniques. Their investigation contributes to the advancement of novel materials and printing methodologies aimed at the restoration of damaged joints and cartilage. Emerging domain of 3D printing for the immobilization of biocatalysts has also been reported [41]. This study underscores the immense potential of 3D printing in biotechnology, enabling the efficient immobilization of enzymes for diverse applications, spanning bioprocessing and biofuel production.

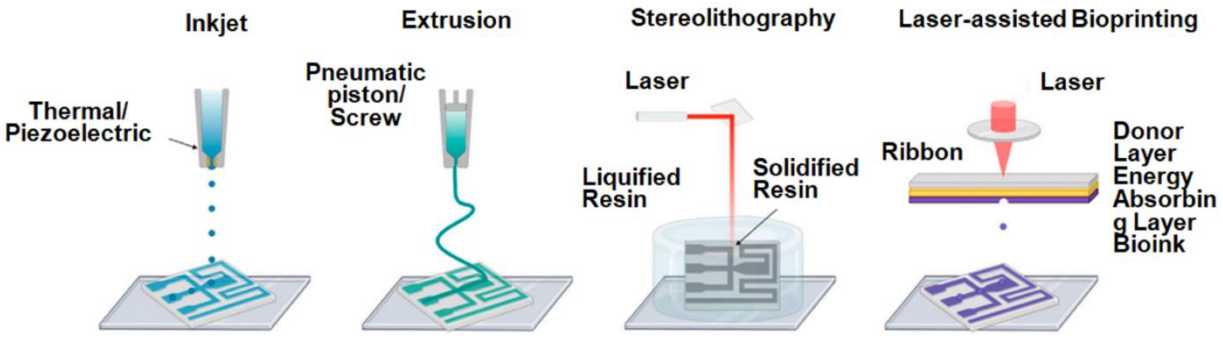

Figure 4. Illustration depicting diverse 3D printing techniques. Reprinted from [42] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

3.1. Extrusion-Based Printing

Extrusion-based 3D printing for hydrogels is a sophisticated additive manufacturing process that holds immense potential in various fields, particularly in biomedicine. This method harnesses the unique properties of hydrogel materials, which consist of a water-based gel with a polymer network, making them suitable for extrusion. In this process, a hydrogel material is meticulously prepared, often as a viscous bioink, customized with specific additives like cells or therapeutic agents. A specialized extruder nozzle is employed in a 3D printer, precisely depositing the hydrogel layer by layer to construct intricate three-dimensional structures. Each layer is carefully deposited and, if needed, undergoes a crosslinking process to solidify and stabilize the structure. This technique is widely used in biomedicine to fabricate tissue scaffolds, organ models, and drug delivery systems, as well as in other industries such as food and cosmetics for creating customized products. In recent years, a series of notable studies have significantly advanced the field of extrusion-based 3D printing, introducing innovative materials and technologies that broaden its application horizon. Cheng et al. [43]., delved into the printability of a cellulose derivative for 3D printing, with a specific focus on its use as a biodegradable support material and marks a vital step toward more sustainable and versatile 3D printing processes, which can contribute to environmentally friendly manufacturing. Zhou et al. [44]., explored the potential of gelatin-oxidized nanocellulose hydrogels in extrusion-based 3D bioprinting for tissue engineering and regenerative medicine, introducing a novel avenue in the quest for innovative and regenerative biomaterials.

Dong et al. [45]., have demonstrated the extrusion 3D printing of a gelatine methacrylate/Laponite nanocomposite hydrogel, emphasizing its promise for applications in the realm of bone tissue regeneration. A unique approach by exploring advanced printable hydrogels derived from pre-crosslinked alginate was demonstrated by Falcone et al [46]. This study highlights the suitability of these materials for semi-solid extrusion 3D printing, effectively extending the capabilities of this technology in creating intricate and complex structures for a wide array of applications, from tissue engineering to drug delivery systems. The work of Murphy et al. [47]., introduced a fascinating twist by focusing on 3D extrusion printing of stable constructs composed of photoresponsive polypeptide hydrogels. This innovative approach allows for the creation of responsive and tunable 3D-printed materials, paving the way for a variety of applications where dynamic, light-responsive materials are required. Hu et al. [48]., explored extrusion 3D printing of a cellulose hydrogel skeleton, which opens new possibilities for creating eco-friendly and sustainable materials through 3D printing. Their work aligns with the growing demand for more environmentally responsible manufacturing practices. Substantial progress in advancing extrusion 3D bioprinting, with a specific focus on multicomponent hydrogel-based bioinks was also demonstrated [49]. By pushing the boundaries of complexity and functionality in 3D-printed constructs, their research directly contributes to the development of cutting-edge biomedical applications, from tissue engineering to personalized medicine.

Apart from experimental works, simulations for extrusion 3D printing of chitosan hydrogels have also been reported [50]. Their research provides valuable insights into the virtual design and optimization of bioprinted structures, streamlining the development of precise and complex geometries for tissue engineering and other biomedical applications. Extrusion-based 3D printing for hydrogels offers versatility, cost-effectiveness, and the ability to work with various hydrogel formulations, making it a valuable tool for research, development, and manufacturing applications. However, moderate to lower resolution compared to other methods, potential nozzle clogging, and slower printing speeds due to layer-by-layer deposition limits its utility.

3.2. Inkjet-Based Printing

Inkjet-based 3D printing for hydrogels is a cutting-edge additive manufacturing technique that harnesses the precision of inkjet printing to construct three-dimensional structures using hydrogel materials. This innovative method is particularly well-suited for hydrogels, which often possess high water content and distinct rheological properties. The process commences with the preparation of a hydrogel ink, tailored to the specific application and often containing crosslinking agents, water, and additives like cells or therapeutic compounds. Specialized inkjet 3D printers are equipped with printheads designed to accommodate these hydrogel inks. These printheads feature micro-sized nozzles that dispense minute droplets of the hydrogel ink onto a build platform. Each droplet represents a pixel, and layer-by-layer, these droplets create the desired three-dimensional object. Following deposition, the hydrogel droplets are solidified, typically through methods such as UV light exposure or temperature adjustment. The technology is versatile, finding applications in biomedicine for creating tissue constructs, implants, and precise drug delivery systems. Additionally, it extends to various industries, enabling the customization of products with hydrogel components. In the field of 3D bioprinting, Suntornnond and colleagues [51]., focused on improving the printability of hydrogel-based bio-inks for thermal inkjet bioprinting applications and employed saponification and heat treatment processes to enhance the performance of these bio-inks, aiming to optimize their application in creating complex biological structures.

Adamski et al [52]., have introduced an innovative technique for DNA analysis employing a lab-on-a-chip (LOC) system created through inkjet printing and on-chip gel electrophoresis. This novel capillary gel electrophoresis method is designed for the separation of genetic materials, primarily DNA and RNA, by examining the migration velocities of their fractions. The electrophoretic chip itself was produced using inkjet 3D printing. Two methods for fabricating the microfluidic electrophoretic chip are schematically depicted in Figures 5(a) and 5(b). In the glass microengineering approach (Figure 5(a)), two glass substrates were bonded together to create the structure, including the injector and separation microchannels. Conversely, in the inkjet 3D printing method (Figure 5(b)), the entire structure was created in a single printing process on a chip. The LOC structure, as fabricated, encompasses an injection microchannel, two separation microchannels with lengths of 20 mm and 50 mm, and integrated buffer and sample reservoir components. The chip's CAD design is presented in Figure 5(c), which was then exported to a geometric file (Figure 5(d)), leading to the final structure illustrated in Figure 5(e). To analyze DNA, the electrophoretic gel was injected into the chip's injection microchannel, subsequently entering the separation microchannel (Figures 5(f)-(h)). Finally, it underwent optical detection employing fluorescence modulation, accomplished with laser light and a CCD mini-camera, as shown in Figure 5(i).

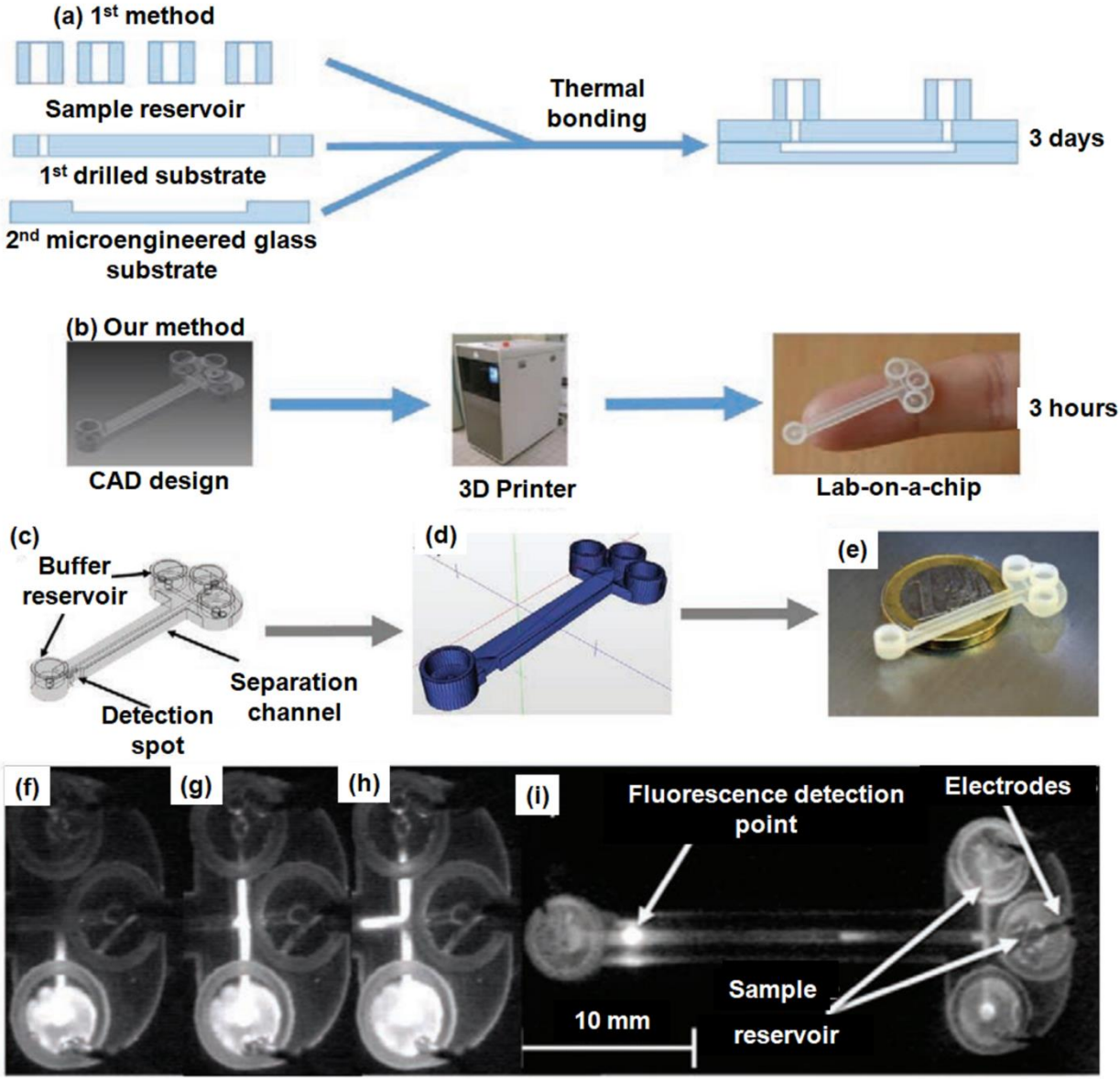

Figure 5. Sequential Steps in the Development and Application of a Microfluidics Chip for Gel Electrophoresis. (a) Schematic presentation of the microfluidics chip manufacturing process through glass microengineering. (b) CAD design and the subsequent inkjet 3D printing of the Lab-on-a-chip. (c) The original CAD design. (d) The exportation process leading to the creation of a geometric file. (e) The final structure, offering a size comparison to a coin. In the investigation of DNA samples, (f-h) delineate the process of introducing electrophoretic gel into the chip's injection microchannel and subsequently injecting it into the separation microchannel. (i) Depicts the optical detection method, involving fluorescence modulation via laser light and a CCD mini camera. Reprinted from [52] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

A comparative study involving hyaluronic acid hydrogel exquisite micropatterns using two distinct methods, photolithography and light-cured inkjet printing, to create intricate and precise microstructures has been reported by Chen et al [53]. This research contributes to the development of advanced techniques for fabricating microscale patterns with hyaluronic acid hydrogels, which have relevance in various biomedical and tissue engineering applications. While inkjet-based 3D printing for hydrogels offers high resolution and intricate control, it also presents challenges related to material viscosity and

nozzle maintenance. Nonetheless, it holds great promise for advancing research and development in fields demanding precise, biocompatible structures.

3.3. Stereolithography (SLA)

Stereolithography-based 3D printing for hydrogels represents a cutting-edge additive manufacturing technique that harnesses the power of light to create intricate three-dimensional structures using hydrogel materials. This technology builds upon the principles of traditional stereolithography but adapts them to accommodate the unique properties of hydrogels, which typically consist of water-based polymer networks. The process begins with a hydrogel resin that may contain photo-initiators, crosslinkers, and other additives. In this method, a precisely controlled light source, often in the form of a laser or projector, is used to selectively solidify specific regions of the hydrogel resin. As each layer is solidified, the build platform descends incrementally, allowing for the gradual construction of the 3D object. Stereolithography offers exceptional precision and fine detail, making it well-suited for applications in tissue engineering, biomedical devices, and microfluidic systems. Post-printing, additional steps such as rinsing and curing may be required to enhance structural stability. In the realm of 3D printing, various studies have explored the application of stereolithography to create hydrogels with unique properties and capabilities. Kalossaka and colleagues [54]., delved into the creation of 3D nanocomposite hydrogels featuring lattice vascular networks, demonstrating the potential for engineering intricate structures using this technique. Karakurt et al. [55]., focused on SLA 3D printing of hydrogels loaded with ascorbic acid, investigating their controlled release properties. The study sheds light on the use of SLA in drug delivery systems.

Impact of SLA 3D printing on the properties of PEGDMA hydrogels, contributing insights into the interactions between the printing process and hydrogel characteristics has also been discussed [56]. Magalhães et al. [57]., explored the use of low-cost stereolithography technology to create 3D hydrogel structures, offering potential applications in biomedicine and biomaterials. Effects of PEGDA photopolymerization in micro-stereolithography on 3D printed hydrogel structures, addressing aspects of structural integrity and swelling behavior has been reported by Alketbi et al [58]. Sun et al. [59]., introduced a new stereolithographic 3D printing strategy for hydrogels, focusing on achieving a large mechanical tunability and self-weldability which opens doors to more versatile and functional hydrogel applications.

Stereolithography-based 3D printing for hydrogels is celebrated for its ability to create complex, high-resolution structures, but challenges such as limited material options and the need for specialized equipment are considerations in its implementation. Nevertheless, it remains a powerful tool in the field of hydrogel-based additive manufacturing, enabling the fabrication of advanced, biomimetic structures for a wide range of applications.

3.4. Digital Light Processing (DLP)

DLP-based 3D printing for hydrogels is an innovative and precise additive manufacturing technique that harnesses digital light projection to construct intricate 3D structures using hydrogel materials. This method builds upon the principles of photopolymerization, where a liquid resin containing hydrogel components is selectively cured by a digital light source, typically a projector or UV LED. This process proceeds layer by layer, with each layer being solidified by the precise projection of light patterns, forming the desired object. DLP 3D printing for hydrogels is celebrated for its remarkable speed, high resolution, and ability to create complex geometries with fine detail. It finds particular utility in biomedical applications, including tissue engineering and the fabrication of customized implants and drug delivery systems. After printing, post-processing steps may include rinsing and additional curing to enhance structural stability. However, it's important to note that material selection and compatibility with the photopolymerization process are key

considerations. Despite these challenges, DLP-based 3D printing stands as a powerful tool for the creation of intricate hydrogel structures, pushing the boundaries of precision and complexity in various scientific and medical fields.

Recent advancements in DLP 3D printing of hydrogels have ushered in a new era of possibilities and applications. Several research groups have made significant contributions to this evolving field. Hosseinabadi and collaborators [60]., have delved into the critical aspects of ink material selection and optical design in DLP 3D printing, underlining the importance of precision and performance in hydrogel printing. A concise review summarizing the key developments and prospects of this technology, providing an overview of the current state of DLP 3D printing for hydrogels has been presented by Ding et al [61]. Sun et al. [62]., have introduced a novel approach to DLP 3D printing by presenting hydrogels with hierarchical structures, enhanced through lyophilization and ionic locking, offering new possibilities for tailored hydrogel properties. In a different direction, Dong and colleagues [63]., have focused on creating tough supramolecular hydrogels using DLP 3D printing, emphasizing their potential application as impact-absorption elements. An effective DLP 3D printing strategy was also introduced for cellulose hydrogels with high strength and toughness, well-suited for strain sensing applications [64]. Cafiso et al. [65]., have explored 3D printing of fully cellulose-based hydrogels through DLP, highlighting the sustainability and versatility of this approach. On the biomedical front, Wang et al. [66]., have successfully fabricated antimicrobial hydrogels using DLP 3D printing, leveraging sustainable resin and hybrid nanospheres for potential applications in healthcare.

Caproili and colleagues [67]., have introduced a novel 3D-printed hydrogel imbued with self-healing properties, employing readily available materials and a DLP printer commonly found in the market. The ingenious design of this system involved creating a sequential semi-interpenetrated network by introducing chemical covalent network precursors into a solution containing a linear polymer. Following polymerization, this linear polymer is effectively encapsulated within the cross-linked matrix. The photocurable ink formulation involved the blending of an aqueous solution of unmodified, non-crosslinked Poly (vinyl alcohol) (PVA) with acrylic acid (AAc), the cross-linking agent Poly (ethylene glycol) diacrylate (PEGDA), and a water-compatible photoinitiator based on diphenyl (2,4,6-trimethylbenzoyl)phosphine oxide (TPO). Figure 6(a) provides a visual representation of the chemical structures of the initiator, monomer, cross-linker, and mending agent within the photocurable resin. Figure 6(b) illustrates the creation of the semi-interpenetrated network: a physical network is blended with the precursors of the chemical network, which materializes during exposure to light. The outcome is a hydrogel composed of PVA chains that are uniformly distributed and incorporated into a cross-linked acrylic matrix. For tensile testing, two distinct specimens were produced, each featuring a different color, one printed with methyl red sodium salt dye and the other with brilliant green dye. These samples demonstrated their capacity to endure bending deformation immediately upon rejoining, as depicted in figure 6(c). Figure 6(d) showcases a perforated cylindrical structure printed with methyl red sodium salt dye, clearly demonstrating that the reconnected sample could withstand stretching deformation after a 2-hour healing process. Figure 6(e) reveals body-centered cubic lattice-like structures printed with both methyl red sodium salt dye and brilliant green dye, enhancing visual comprehension. The inset in this figure vividly portrays diffusion at the interface after 12 hours of contact, owing to the gradient of the dye. Figures 6(f) and 6(g) display 3D fabricated samples with a PVA 0.8 formulation, featuring a body-centered cubic lattice-like structure printed with methyl red sodium salt dye and an axis-symmetric structure with a central pillar printed with brilliant green dye, respectively. Finally, figure 6(h) offers insight into the stress-strain curves of the self-healed hydrogels, showcasing their performance over increasing healing durations.

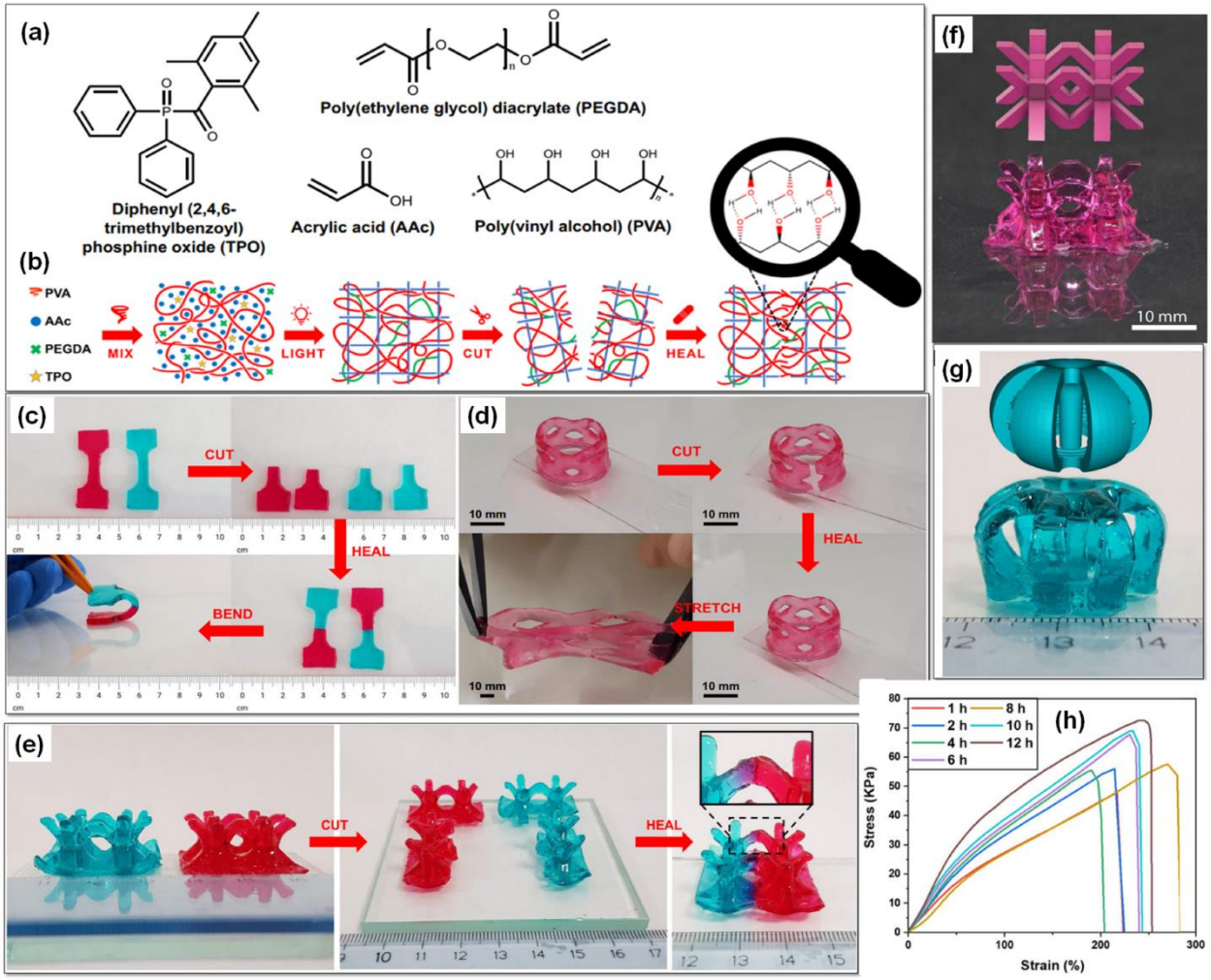

Figure 6. Composition Formulation and Network Formation. (a) Molecular structure of initiator, monomer, cross-linker, and mending agent within the photocurable resin. (b) Schematic depiction of semi-IPN and the healing process. Illustrated recovery of cut and rejoined objects printed with an AAc/PVA ratio of 0.8. (c) Tensile test samples featuring methyl red sodium salt and brilliant green dye. These specimens exhibited immediate bending deformation upon rejoining. (d) A cylindrical structure with holes printed using methyl red sodium salt dye. The reconnected sample demonstrated stretching deformation endurance after a 2-hour healing process. (e) Lattice-like structures with a body-centered cubic pattern, printed with methyl red sodium salt and brilliant green dye. Noticeable dye diffusion at the interface is visible after 12 hours (inset) due to the dye concentration gradient. (f, g) 3D printed samples with the PVA 0.8 formulation: (f) Body-centered cubic lattice-like structure printed with methyl red sodium salt dye. (g) Axisymmetric structure featuring a central pillar, printed with brilliant green dye. (h) Stress–strain curves of self-healed hydrogels over rising healing periods. Reprinted from [67] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

Zhang et al. [68]., have experimented with Antheraea pernyi silk fibroin bioinks for DLP 3D printing, offering new opportunities in bioprinting and regenerative medicine. In another innovative stride, Xiang et al [69]., have focused on creating 3D-printed high-toughness double network hydrogels via DLP, contributing to the development of mechanically robust hydrogel materials. Lopez-Larrea et al. [70]., have explored the application of PEDOT-based photopolymerizable inks for biosensing through DLP 3D printing, marking the potential for enhanced biosensor development. **Table 2** summarizes the various properties of 3D printing technologies including Extrusion-based, inkjet-based, SLA, DLP.

Table 2. Comparative summary of various aspects of 3D printing technologies in terms of principle, resolution, material compatibility, speed, post-processing, advantages and limitations..

	Extrusion-Based	**Inkjet-Based**	**SLA**	**DLP**
Principle	Layer-by-layer extrusion	Droplet deposition	Photopolymerization	Photopolymerization
Resolution	Moderate	High	Very High	Very High
Material Compatibility	Wide range of hydrogel materials	Limited to specific hydrogel formulations	Limited choice due to compatibility	Limited choice due to compatibility
Speed	Moderate	Moderate to Fast	Moderate to Fast	Very Fast
Post-Processing	Often minimal	May require curing	Minimal	Minimal
Advantages	-Versatile for various hydrogels. -Cost-effective and simple. -Well-suited for large-scale objects. -Handles high-viscosity inks well.	-Precise control. -Multi-material printing capabilities. -Suitable for biomedicine and research. -Excellent for fine-detail structures.	-Exceptional resolution and surface finish. -Complex and intricate geometries possible. -Fast printing speed for high-detail objects.	-Fast printing speed, suitable for large-scale production. -Capable of intricate geometries with precision.
Limitations	-Viscosity can lead to nozzle clogging. -Challenges with intricate structures. -Limited in applications requiring high precision.	-Prone to nozzle clogging, especially with viscous inks. -May require crosslinking. -Limited in creating large-scale objects.	-UV light exposure may affect cell viability -Specialized equipment with high upfront cost. -Potential resin waste if not fully used.	-UV light exposure may affect cell viability. -Requires specialized equipment and UV light source. -Potential resin waste if not fully used.

4. Applications of 3D printed hydrogels

4.1. Role of Hydrogel 3D printing in biomedical applications

Hydrogel 3D printing has emerged as a groundbreaking technology in the field of biomedical engineering, offering innovative solutions in tissue engineering, regenerative medicine, and drug delivery. By harnessing the unique properties of hydrogels, this approach enables the creation of precise and complex structures that closely mimic the natural extracellular matrix. By creating intricate structures with tailored properties, this technology opens avenues for personalized medicine, faster wound healing, and the development of advanced organ-on-a-chip systems, ultimately reshaping the landscape of biomedical research and healthcare. Hydrogel 3D printing plays a pivotal role in fabricating scaffolds and constructs for tissue engineering and regenerative medicine. These constructs provide a supportive framework for cells to adhere, proliferate, and differentiate, ultimately aiding in the regeneration of damaged tissues or organs. Lan et al. [71]., provides a comprehensive review of progress in 3D printing for bone tissue engineering, highlighting the potential for personalized and effective solutions in orthopedics. Varaprasad et al. [72]., underscore the importance of alginate as a biomacromolecule for 3D printing hydrogels in biomedical applications, focusing on its potential for creating bioactive scaffolds. Tajik et al. [73]., critically review the 3D printing of hybrid-hydrogel materials for tissue engineering, underlining the significance of this approach in advancing regenerative medicine.

Hydrogel-based scaffolds with patient-specific geometries can be 3D printed to replace damaged bone, cartilage, or skin tissues. The scaffolds provide mechanical support, promote cell infiltration, and guide tissue regeneration. Xu et al. [74]., presented a novel

glucose-responsive antioxidant hybrid hydrogel designed to enhance diabetic wound repair, highlighting its potential in addressing critical healthcare challenges. Tsegay and colleagues [75]., provide a review on smart 3D printed hydrogel skin wound bandages, emphasizing the potential of these advanced wound dressings for improved patient care and recovery. Hydrogel 3D printing is also used to create microfluidic devices that mimic the structure and function of human organs, allowing researchers to study diseases and drug responses in a controlled environment. These systems provide insights into organ-level behavior and drug efficacy without the need for animal testing. Hydrogel-based constructs can be engineered with vascular networks, enabling the perfusion of nutrients and oxygen to cells deep within the tissue. This advancement is crucial for creating thicker tissues and organs, addressing one of the challenges in tissue engineering.

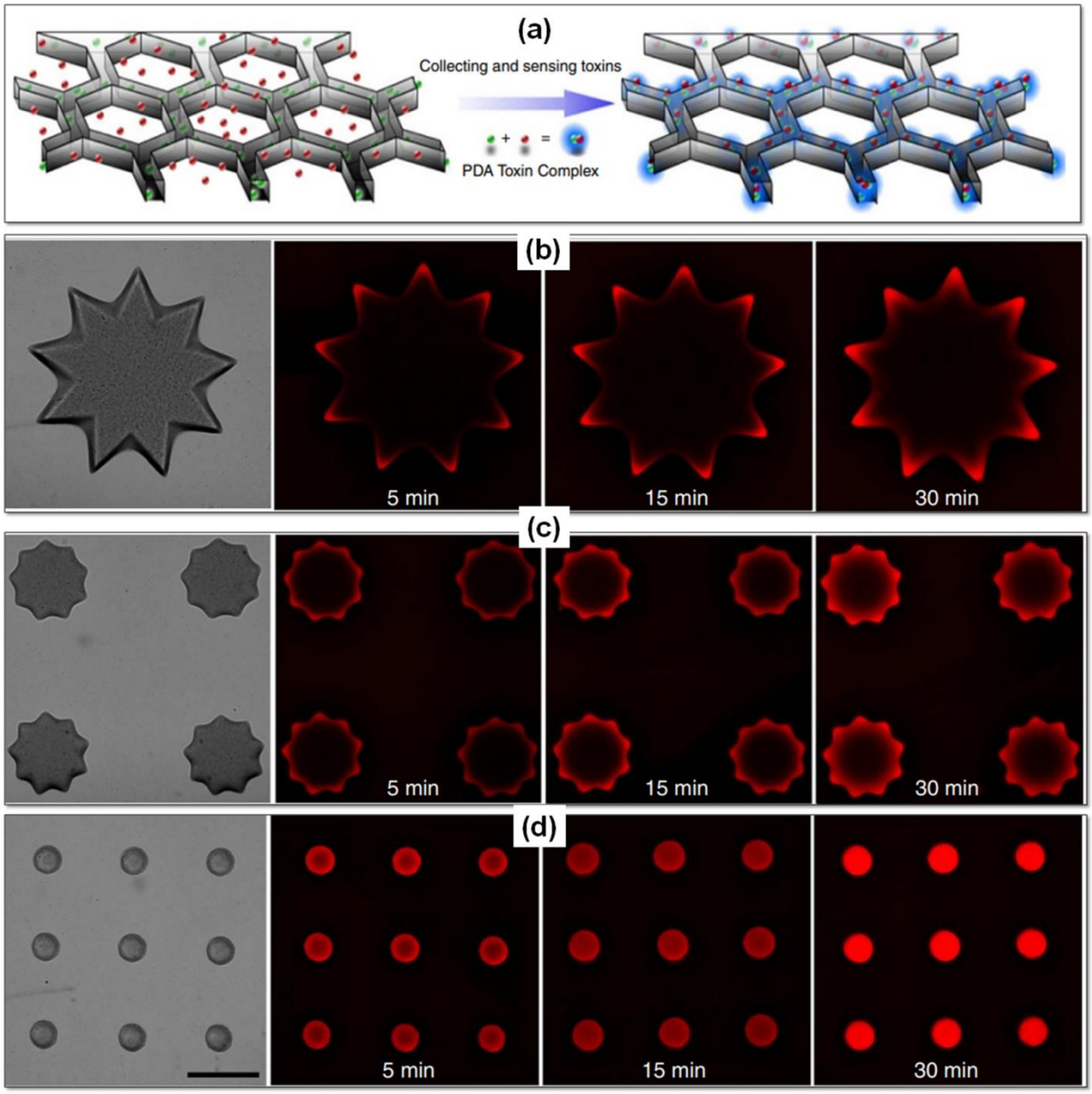

Figure 7. (a) PDA nanoparticles (green) embedded within a PEGDA hydrogel matrix (grey) to create a liver-mimetic 3D structure through 3D printing. Nanoparticles possess the capability to attract, capture, and sense toxins (red), while the modified liver lobule structure within the 3D matrix allows for efficient toxin entrapment. (b-d) Toxin capture within 3D-printed hydrogel nanocomposites featuring various surface patterns. Three distinct types of 3D structural posts, sharing a similar flower-like form and length but differing in diameters, undergo incubation at 37°C with a melittin solution

(50 mg/ml). (b) Demonstrates a post with a large diameter. (c) Represents the medium-diameter post. (d) Features the narrow-diameter post. The red fluorescence highlights the interactions between PDA and melittin, marking the toxic region. A scale bar of 200 mm is provided for reference. Reprinted from [76] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

Guo et al [76]., have introduced a groundbreaking 3D liver-inspired detox device. It's made by 3D printing hydrogels with special nanoparticles that attract, capture, and sense toxins. This innovative system efficiently traps toxins using a liver-like microstructure. Their work shows that this device effectively neutralizes toxins, offering a promising path for advanced detoxification platforms. Leveraging the benefits of a 3D biomimetic structure for enrichment, separation, and detection, a bioinspired 3D detoxification device has been devised. This innovative device incorporates polydiacetylene (PDA) nanoparticles into a precisely designed 3D matrix resembling a modified liver lobule configuration, achieved through advanced 3D printing technology known as dynamic optical projection stereolithography (DOPsL). DOPsL employs a digital mirror array device (DMD) to create dynamic photomasks, allowing for the layer-by-layer photopolymerization of biomaterials into intricate 3D structures. Figure 7(a) visually illustrates the integration of PDA nanoparticles (green) within a PEGDA hydrogel matrix (grey) featuring a liver-mimicking 3D structure produced through 3D printing. This structure can attract, capture, and detect toxins (red), while the modified liver lobule-like matrix efficiently traps these harmful substances. This biomimetic 3D detoxifier holds promise for clinical applications, serving as an effective means of collecting and removing toxins. Furthermore, they have successfully immobilized toxins within 3D-printed hydrogel nanocomposites, each sporting distinct surface patterns in the form of flower-like shapes with varying diameters (large, medium, and small). When exposed to melittin solution, as depicted in figures 7(b), 7(c), and 7(d), the red fluorescence indicates interactions between PDA and melittin, offering insights into toxin localization.

Hydrogel 3D printing also offers precise control over the spatial distribution of drug-loaded hydrogel matrices. This technology enables the design of drug delivery systems that release therapeutic agents in a controlled and sustained manner, improving treatment efficacy and reducing side effects. Hydrogel-based implants can be 3D printed with encapsulated drugs or growth factors, allowing for site-specific and controlled release. This approach is used in cancer therapy, wound healing, and bone regeneration. Oral drug delivery systems can also be created using hydrogel 3D printing that releases drugs gradually, enhancing bioavailability and reducing the frequency of dosing. Patient-specific drug formulations can also be achieved through 3D printing, tailoring drug release profiles to individual patient needs, which is particularly relevant in cases of chronic diseases.

Hydrogel-based dressings with 3D printed structures provide an ideal environment for wound healing. These dressings can maintain a moist and protective environment, promote cell migration, and facilitate tissue regeneration. For example, 3D-printed hydrogel dressings can cover burn wounds, providing a barrier against infection, enhancing wound healing, and reducing pain and scarring. Hydrogel-based wound dressings can be infused with growth factors and antimicrobial agents, accelerating healing in chronic wounds like diabetic ulcers. Deptula et al. [77]., have reported various diverse applications of 3D printed hydrogels in the domains of wound healing and regenerative medicine. Notably, their research highlights the creation of skin wound bandages through 3D printed hydrogels and the integration of these hydrogels into tissue engineering strategies.

4.2. Hydrogel 3D printing across industries

While hydrogel 3D printing has gained significant traction in biomedical applications, its versatility extends to diverse industries beyond healthcare. Xiong et al [78]., have fabricated DLP based 3D printed wearable sensors possessing self-adhesion and self-healing

properties using polymerizable rotaxane hydrogels. In their study, acrylated β-cyclodextrin combined with bile acid is self-organized into a polymerizable pseudorotaxane through precise host-guest recognition. This pseudorotaxane is subsequently photopolymerized alongside acrylamide to create conductive polymerizable rotaxane hydrogels (PR-Gel). PR-Gel exhibited robust self-adhesion to the skin, as depicted in Figure 8(a), and notably, it left no residue or caused any allergic reactions when adhered to the wrist. To assess its adhesion to various surfaces, including nitrile gloves, glass plates, silicone rubber, aluminum, and pigskin, lap-shear tests were conducted (Figure 8(b)). Although the adhesion strength between PR-Gel and these substrates fell within the range of 4.5 to 6.0 kPa, which is lower than that of some highly adhesive hydrogels, this moderate self-adhesion ensured a secure bond between PR-Gel and human skin, as demonstrated in Figure 4a. This feature guarantees stable signal transmission and consistent adhesion for wearable sensor applications. To showcase the self-healing capabilities, two cylindrical PR-Gel samples were cut and then reassembled at the incision point, serving as a qualitative demonstration. For better visual distinction, one of the samples was stained in a red-orange hue, as depicted in Figure 8(c). These mended gels exhibited resilience to tensile deformation without fracturing at room temperature. The self-healing prowess of PR-Gel underwent further scrutiny through structural damage and recovery assessments, involving continuous strain sweeps with alternating low (1%) and high (500%) oscillatory excitations. In Figure 8(d), the storage modulus (G') and loss modulus (G'') of PR-Gel during continuous strain sweeps illustrate its rapid self-healing properties post-damage. This process could be repeated multiple times, underscoring the reproducible restoration of the PR-Gel network.

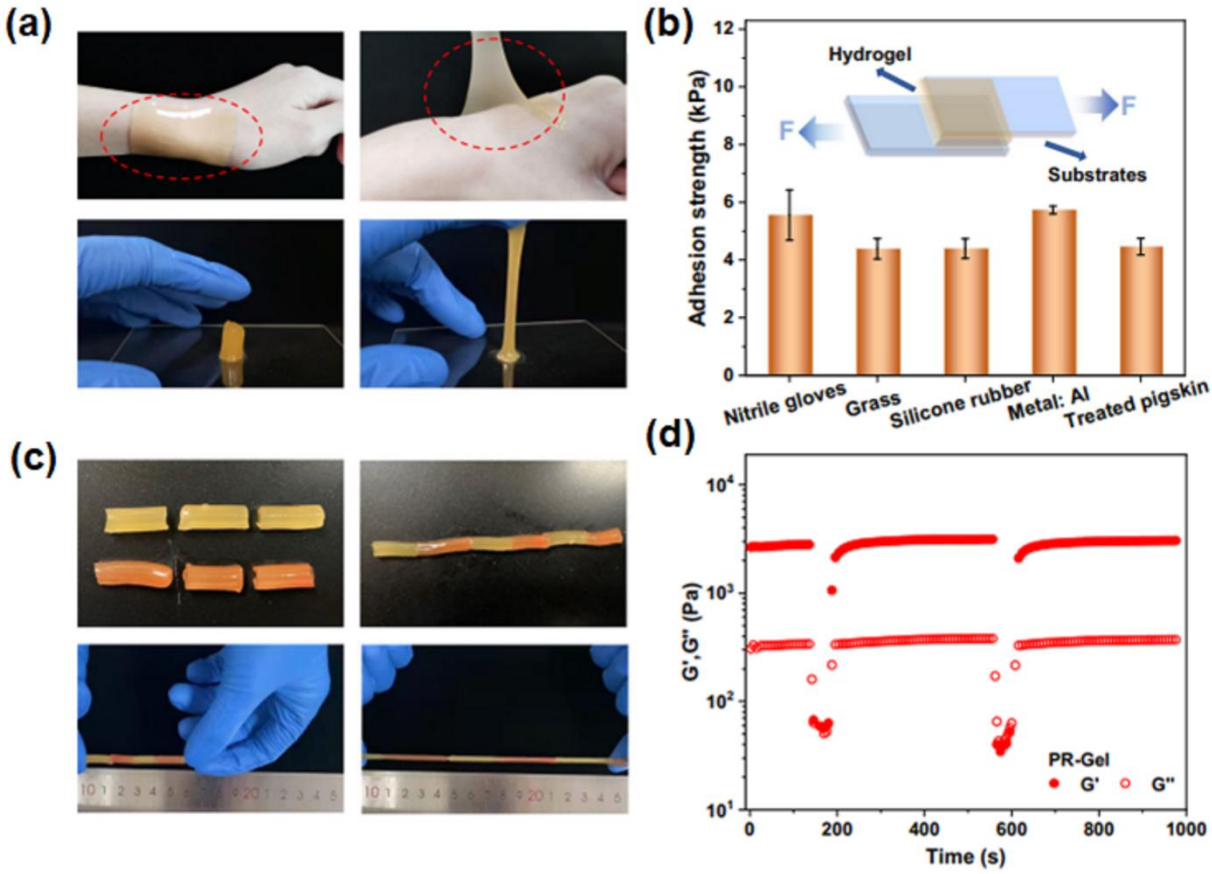

Figure 8. Shear Adhesive Strength and Self-Healing: (a) Photograph of PR-Gel (40 w/v%) stick onto wrist joints and a glass surface. (b) Represents the shear adhesive strength of PR-Gel (40 w/v%) on various substrates, including a nitrile glove, glass plate, silicone rubber, aluminum, and pigskin. The inset offers a schematic illustration of the lap-shear test conducted at 25 °C. (c) Self-healing

behavior of the PR-Gel (40 w/v%) at 25 °C, with the visualization aided by rhodamine B. (d) Storage modulus (G') and loss modulus (G") of the PR-Gel (40 w/v%) under alternating strains, oscillating between small (1%) and large strain (500%) at 25 °C. Reprinted from [78] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

The unique properties of hydrogels, such as high water content and tunable mechanical properties, make them intriguing candidates for various applications in industries like food, cosmetics, and electronics. In food industry, hydrogel 3D printing is being explored to create innovative food products with unique textures, shapes, and functionalities. This technology allows for precise control over ingredient placement, enabling the creation of complex food structures. Various food industries are researching the use of hydrogel 3D printing to fabricate personalized nutritional foods, tailoring the composition and texture to individual dietary needs. In the cosmetics industry, hydrogel 3D printing offers the potential to develop novel skincare products with enhanced absorption and release properties. Customizable shapes and designs enable the creation of cosmetics that adhere better to the skin. Several cosmetic industries are using hydrogel 3D printing to create intricate face masks that fit snugly on the face, enhancing the delivery of skincare ingredients and improving the overall application experience.

Hydrogel 3D printing is also being explored for applications in electronics due to its unique combination of properties, including high water content and the potential for conductive or responsive behavior. This technology can enable the creation of soft, flexible electronics. Hydrogel-based sensors with 3D-printed structures can be used in wearable devices to monitor physiological parameters, such as heart rate and hydration levels. Tetyczka et al. [79]., examine the integration of itraconazole nanocrystals on hydrogel contact lenses via inkjet printing, demonstrating the implications of this technique for ophthalmic drug delivery. Guo et al. [80]., introduce the 3D printing of electrically conductive and degradable hydrogel for epidermal strain sensors, which hold promise in wearable electronics.

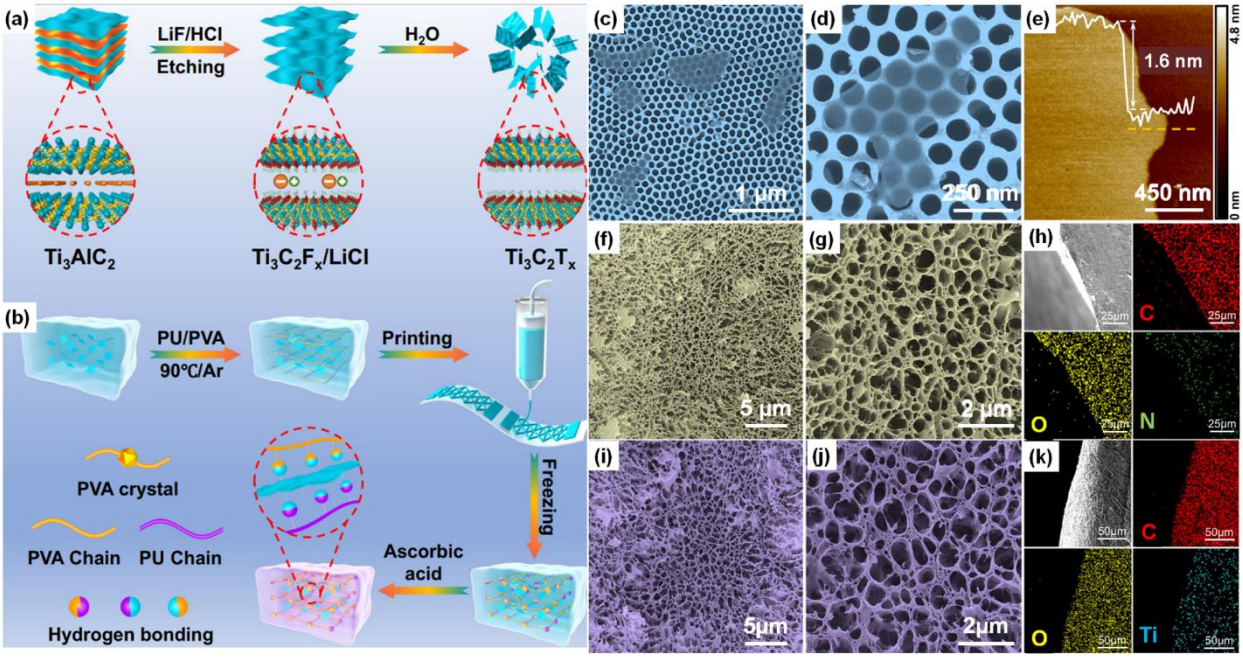

Figure 9. Synthesis of MXenes and Hydrogel: (a) Pictorial representation of the synthesis process of Ti3C2Tx flakes. (b) Demonstration of DIW printing of MXenes attached polyurethane/polyvinyl alcohol (PU/PVA) hydrogel. Morphology and Structure of Materials: (c, d) SEM morphology, (e) AFM image of Ti3C2Tx flakes. (f, g) Microstructure of pristine lyophilized gel, (h) Corresponding elements distribution. (i,j) Microstructure of Ti3C2Tx loaded lyophilized gel, (k) depicts elements

distribution within this structure. Reprinted from [81] under a Creative Commons Attribution License 4.0 (CC BY) https://creativecommons.org/licenses/by/4.0/.

Liu et al [81]., have introduced a cost-effective, specialized 3D printing technology, Direct ink writing (DIW), for creating hydrogel sensors enhanced with two-dimensional transition metal carbides (MXenes). These sensors exhibit exceptional strain and temperature sensing capabilities for shape memory solar array hinges. In their approach, Figure 9(a) illustrates the MXenes preparation process, which involves a fluoride-based salt etching system to minimize the risks associated with concentrated hydrogen fluoride (HF) dilution. Notably, this process uses LiF crystals dissolved in a hydrochloric acid (HCl) aqueous solution to gradually form HF with lower concentration under low-temperature conditions. This mixture is then blended with Ti_3AlC_2 powders to create a black suspension, ensuring sufficient etching without excessive oxidation. Subsequent steps involve washing, intercalation, sonication, and argon protection to obtain delaminated $Ti_3C_2T_x$ flakes. Subsequently, extended centrifugation was employed to separate the delaminated $Ti_3C_2T_x$ flakes from the multi-layered aggregates. Given the presence of electronegative groups on $Ti_3C_2T_x$, polymer hydrogel networks were established as depicted in Figure 9(b). The typical procedure involved the even dispersion of lyophilized $Ti_3C_2T_x$ flakes, followed by the addition of glycerol and polymers. The resulting black mixture was heated to facilitate the dissolution of PVA under an argon (Ar) atmosphere, preventing unnecessary oxidation of $Ti_3C_2T_x$ due to high temperatures. The resulting liquid precursor was then injected into a syringe and utilized in the DIW printing process. The SEM images provided in Figure 9(c, d) depict the Ti3C2Tx flakes displaying a sleek 2D nanosheet morphology, with lateral sizes ranging from 0.4 to 1 μm. As shown in the atomic force microscope (AFM) image 9(e), these $Ti_3C_2T_x$ flakes exhibit a smooth surface with an average thickness of 1.6 nm, consistent with the thickness of a $Ti_3C_2T_x$ bilayer structure. To examine the intricate internal microstructure of the hydrogel networks, the printed hydrogel underwent a process of lyophilization following solvent replacement. As illustrated in Figure 9(f) and 9(g), the unaltered printed hydrogel showcases a porous network structure characterized by random orientation and a hierarchical distribution of pore sizes. The cross-sectional morphology of the printed hydrogel, along with its corresponding energy dispersive X-ray spectroscopy (EDS) elemental mapping, is displayed in Figure 9(h), confirming the uniform distribution of elements C, O, and N. Analyzing the EDS element distribution, it becomes evident that the relative content of N elements is lower than that of C and O. This indicates that the hard domains, comprised of nitrogen-containing groups within the polyurethane (PU) network, are less abundant than the soft domains, which in turn impacts the mechanical strength of the hydrogel. Similarly, when 0.25 wt% $Ti_3C_2T_x$ flakes are introduced into the precursor, the resulting printed hydrogel exhibits an unoriented porous framework with random pore size distribution, resembling that of the pristine hydrogel, as depicted in Figure 9(i) and 9(j). Furthermore, EDS analysis of elements C, O, and Ti (Figure 9(k)) confirms the homogeneous distribution of Ti_3C_2Tx flakes within the hydrogel.

Yang et al. [82]., summarize recent advances in 3D printing of electrically conductive hydrogels for flexible electronics, demonstrating their significance in the development of next-generation electronic devices. Zhang and collaborators [83]., also provide a review on 3D printing hydrogels for actuators, offering insights into the development of responsive materials for various applications. Chen et al. [84]., explored the utilization of 3D printed hydrogels in the development of soft thermo-responsive smart windows, showcasing their adaptability in architectural and environmental applications. Guo and colleagues [85]., investigate the use of biomass-derived hybrid hydrogel evaporators for cost-effective solar water purification, providing sustainable solutions for clean water access. **Table 3** summarizes the various 3D printed hydrogels employed for several applications.

Table 3. Summary of various 3D printed hydrogels employed for several applications. 874

Hydrogel Used	3D Printing Technology	Applications/Remarks	Reference
Laponite® incorporated oxidized alginate–gelatin composite hydrogels	Extrusion-based 3D printing	Integration of natural hydrogels into advanced manufacturing processes	Cai et al. (2021) [22]
Cellulose derivative	Extrusion-based 3D printing	Biodegradable support material	Cheng, Y. et al. (2020) [43]
Gelatin-oxidized nanocellulose hydrogels	Extrusion-based 3D bioprinting	Bioprinting applications for tissue engineering	Zhou, S. et al. (2022) [44]
Gelatine methacrylate/Laponite nanocomposite hydrogel	Facile extrusion 3D printing	High concentration nanoclay for bone tissue regeneration	Dong, L. et al. (2021) [45]
Pre-crosslinked alginate	Semi-solid extrusion 3D printing	Advanced printable hydrogels	Falcone, G. et al. (2022) [46]
Photoresponsive polypeptide hydrogels	3D-extrusion printing	Stable constructs composed of photoresponsive polypeptide hydrogels	Murphy, R. D. et al. (2019) [47]
Chitosan hydrogels	Extrusion 3D printing	Simulations of extrusion 3D printing of chitosan hydrogels	Ramezani, H. et al. (2022) [50]

Cellulose hydrogel	Extrusion 3D printing of solution	Cellulose hydrogel skeleton by extrusion 3D printing of solution	Hu, X. et al. (2020) [48]
Multicomponent hydrogel-based bioinks	Extrusion 3D bioprinting	Bioprinting for various applications using multicomponent hydrogel-based bioinks	Cui, X. et al. (2020) [49]
Itraconazole nanocrystals on hydrogel	Inkjet Printing	Ophthalmic drug delivery	Tetyczka, C. et al. (2022) [79]
Hydrogel-based bio-inks	Thermal inkjet bioprinting	Printability improvement via saponification and heat treatment processes	Suntornnond, R. et al. (2022) [51]
Hyaluronic acid hydrogel	Photolithography and light-cured inkjet printing methods	Comparing different methods for creating hyaluronic acid hydrogel micropatterns	Chen, F. et al. (2022) [53]
Nanocomposite hydrogels	Stereolithography	Creating hydrogel structures with vascular networks	Kalossaka, L. M. et al. (2021) [54]
Ascorbic acid-loaded hydrogels	Stereolithography	Controlled drug release from 3D printed hydrogels	Karakurt, I. et al. (2020) [55]

PEGDMA hydrogels	Stereolithography	Investigating the impact of 3D printing on hydrogel properties	Burke, G. et al. (2020) [56]
Hydrogel structures	Stereolithography	Low-cost 3D printing of hydrogel structures	Magalhães, L. S. S. et al. (2020) [57]
PEGDA hydrogels	Micro-stereolithography	Studying the impact of photopolymerization in micro-stereolithography	Alketbi, A. S. et al. (2021) [58]
Hydrogels with tunability	Stereolithographic 3D printing	Developing hydrogels with mechanical tunability and self-welding properties	Sun, Z. et al. (2022) [59]
Nanocellulose/PEGDA	Stereolithography	3D cell culture, tissue engineering	Tang, A. et al. (2019) [28]
Hydrogels	DLP 3D Printing	Creating hydrogels with hierarchical structures	Sun, Z. et al. (2023) [62]
Supramolecular hydrogels	DLP 3D Printing	Tough supramolecular hydrogels with sophisticated architectures as impact-absorption elements	Dong, M. et al. (2022) [63]

Cellulose hydrogel	DLP 3D Printing	Cellulose hydrogel for strain sensing	Guo, Z. et al. (2023) [64]
Cellulose-based hydrogels	DLP 3D Printing	3D printing of fully cellulose-based hydrogels by DLP	Cafiso, D. et al. (2022) [65]
Antimicrobial hydrogel	DLP 3D Printing	Developing an antimicrobial hydrogel using sustainable resin and hybrid nanospheres	Wang, L. et al. (2022) [66]
Antheraea pernyi silk fibroin	DLP 3D Printing	Using silk fibroin bioinks for DLP 3D printing	Zhang, X. et al. (2023) [68]
Double network hydrogels	DLP 3D Printing	3D printing of high-toughness double network hydrogels	Xiang, Z. et al. (2022) [69]
PEDOT-based photopolymerizable inks	DLP 3D Printing	DLP 3D printing of PEDOT-based photopolymerizable inks for biosensing	Lopez-Larrea, N. et al. (2022) [70]

5. Current Challenges and future trends in Hydrogel 3D Printing

5.1. Current challenges

Inspite of various versatile properties and applications of hydrogel 3D printing, there persist several challenges associated with it such as resolution limitations, post-printing processing, scalability, etc. Achieving high-resolution printing remains a challenge due to the complex rheological properties of hydrogels. Precise deposition of fine features is hindered by factors like nozzle clogging and the tendency of hydrogels to spread upon deposition. Also, many hydrogel 3D printing methods require post-processing steps, such as curing or crosslinking, to enhance mechanical stability and can be time-consuming and may introduce variability in the final product. Scaling up hydrogel 3D printing to produce

large quantities of intricate structures is also challenging. Maintaining consistent print quality, gelation kinetics, and resolution across a larger volume is a significant hurdle.

5.2. Future Trends and Advancements

Hydrogel 3D printing faces current challenges related to resolution, post-printing processing, and scalability, the future holds promising trends and advancements. As materials, techniques, and applications continue to evolve, hydrogel 3D printing is poised to reshape industries and contribute to breakthroughs in personalized medicine, tissue engineering, and various other fields. Future advancements will likely introduce innovative hydrogel formulations with improved printability, biocompatibility, and mechanical properties. Hybrid hydrogels combining natural and synthetic components might become more prevalent, allowing for tailored materials for specific applications. Researchers are likely to develop improved printing techniques that enhance resolution and speed. This might include advancements in nozzle design, improved droplet formation in inkjet-based systems, and refined light-based curing methods in SLA and DLP. Advances in multi-material 3D printing could enable the integration of hydrogels with other materials, such as polymers and ceramics, allowing for the creation of complex and functional hybrid structures.

Hydrogel 3D printing will likely explore incorporating bioactive agents directly into printed structures. This could lead to the creation of constructs with integrated therapeutic properties, reducing the need for post-printing functionalization. Research into intricate scaffold architectures will continue, with a focus on enhancing tissue integration, nutrient transport, and cellular responses. This could involve the exploration of gradient structures and hierarchical designs. The field might see an expansion into personalized medicine, with the capability to tailor hydrogel formulations and structures for individual patients. Point-of-care 3D printing could become feasible for producing patient-specific implants and drug delivery systems. As hydrogel 3D printing matures, more efforts will be directed toward regulatory approval and clinical translation of hydrogel-based medical devices and implants.

As technology continues to evolve, 4D printing technologies has also been developed for hydrogel printing. Very recently, Wang and Guo [86]., provide insights into recent advances in 4D printing hydrogels designed for biological interfaces and delves into the innovative use of hydrogels that exhibit dynamic shape changes over time, showcasing the potential for applications in biological systems. Seo et al. [87]., have also introduced a hydrogel production platform that utilizes photo-crosslinkable and temperature-reversible chitosan polymer in combination with stereolithography 4D printing technology. This platform enables the creation of hydrogels with dynamic movement, opening up new possibilities in tissue engineering and regenerative medicine.

6. Conclusion

In the realm of 3D printing, the union of hydrogels and technology has fostered a dynamic landscape ripe with innovation and promise. This review has traversed the rich tapestry of hydrogel 3D printing, elucidating its profound impact on diverse domains and hinting at the limitless possibilities on the horizon. From their humble beginnings as unique, water-rich materials, hydrogels have evolved into versatile substrates, capable of being sculpted into intricate structures with unparalleled precision. The convergence of hydrogels and 3D printing has unlocked doors to a myriad of applications spanning biomedical engineering, industrial production, and beyond. The biomedical sector, in particular, stands as a beacon of hope for hydrogel 3D printing's transformative power. The creation of tissue-engineered constructs, regenerative implants, and precise drug delivery systems has revolutionized healthcare and holds promise for further breakthroughs. The ability to replicate the intricacies of human biology, coupled with the advent of personalized medicine, offers a glimpse into a future where hydrogel 3D printing plays a pivotal role in

enhancing the quality of life. Yet, this review acknowledges that challenges persist. Resolution limitations, post-printing processing intricacies and the quest for scalable manufacturing methods are reminders that there is still much terrain to conquer.

Looking forward, the future appears promising. The trajectory of hydrogel 3D printing is set to be marked by advanced material development, enhanced printing techniques, and novel applications that defy current boundaries. As we journey further into this frontier, we anticipate the emergence of innovative solutions, new industries shaped by hydrogel capabilities, and a profound impact on scientific and technological advancement.

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