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4D Printed Shape Memory Polymers and Their Composites in the Field of Biology

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Abstract:
In the past two decades, stimulus-responsive shape memory polymers (SMPs) have made significant progress, demonstrating desirable characteristics such as shape memory properties, deformability, and biocompatibility in response to external stimuli. The development of SMP composites (SMPCs) has brought high resilience and new functions, including thermal actuation, electrical actuation, magnetic actuation and biocompatibility. The enhanced remote controllable features and functions further expand the application of SMPS in the biomedical field, such as surgical applications to replace hand-held surgical instruments and drug delivery systems. This article systematically introduces the preparation methods, thermal drive and magnetic drive mechanisms of SMPs and SMPCs in 4D printing, and focuses on reviewing their current application status and development potential in biomedicine. At the same time, the challenges and bottlenecks of current 4D printing technology are pointed out, such as material properties, printing accuracy and response controllability. In the future, the development of it still needs to rely on multidisciplinary cross-disciplinary cooperation and technological innovation, and make breakthroughs in new structural design, biocompatible material development and modeling tool optimization to achieve the next generation of high-performance smart medical solutions.

Keywords: Shape memory polymer composite; bone tissue scaffold; vascular scaffold; drug delivery device; 4D printing.

1. Introduction

Additive manufacturing, commonly referred to as 3D printing, constructs physical objects through the sequential layering of materials based on digital three-dimensional models. Emerging over the past three decades, it reflects the significant advancements in modern manufacturing technologies [1]; Shape memory polymer (SMP) is a kind of polymer material that can restore its original shape from the

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temporary shape under external excitation and realize the deformation function. It is an important branch of intelligent materials. It can be deformed into other temporary shapes under specific conditions and can be fixed under environmental conditions. When it is stimulated again, it can actively return to the original shape.

With features like low cost, easy processing, customizable performance, flexibility, and responsiveness to various stimuli, shape memory polymers (SMPs) have become central to the progress of 4D printing. Their seamless integration with 3D printing systems enhances their practical use and paves the way for smart, responsive devices. Also, they combine low density and large deformability. Their response to external stimuli can be tuned through chemical modification, enabling multifunctional behavior. These features make SMPs promising materials for applications in various high-tech fields [2]. In essence, 4D printing is a next-generation additive manufacturing technique that brings together smart materials and 3D printing to enable dynamic, functional structures [3]. The advent of this particular technology has brought new chances for the booming market of intelligent materials and biological fields such as minimally invasive medicine. This article first illustrates the rise and development of 4D printing technology, then reviews the research progress and potential applications of 4D printing SMPS and their composites in recent years from two aspects of thermal and magnetic drive. Moreover, case studies of SMP applications in the biomedical field are quoted to indicate views in Chapter 2. Finally, the urgent barriers and future expectations of 4D printing are pointed out.

2. Overview of SMPs in Biological Applications

Based on their intrinsic properties, SMPs can be categorized into two main types: thermoplastic and thermoset SMPs. Among them, thermoplastic SMPs are primarily processed using extrusion-based printing technologies, notably including fused deposition modeling (FDM) and direct ink writing (DIW). Both printing methods rely on a layer-by-layer and line-by-line deposition strategy to fabricate three-dimensional structures. However, they differ in the form of feedstock used: FDM employs thermoplastic solid filaments, whereas DIW utilizes viscous liquid inks. Some thermoplastic SMPs exhibit good biocompatibility, and when integrated with 3D printing technology, they enable personalized fabrication, offering immense potential for applications in the biomedical field. Due to the unique nature of the human environment, SMPs used in the field of biology are mainly divided into two types: thermally induced and magnetically induced.

2.1 4D Printing of Thermally Responsive SMPCs

Since the base SMP matrix in thermally responsive SMPCs is inherently heat-sensitive, the incorporation of fillers typically does not alter the thermal activation mechanism. As a result, a wide variety of functional fillers can be added. Based on the morphology of these fillers, thermally responsive SMPCs can be classified into particle-filled type, fiber-filled type (including both chopped fibers and continuous fibers), nano-paper-filled type, and hybrid-filled type, etc.

Fiber-reinforced SMPCs offer distinct advantages such as low density, high strength, and high modulus, but the controllable deformation of SMPCs is a major challenge. Cellulose fibers in plants have the characteristics of hydrophilicity, high strength, and high modulus, making them a natural fiber filler that can be used as a filler for medical materials.

Mulakkal et al. developed a cellulose-reinforced hydrogel composite ink and investigated its physical properties, including stability, swelling properties and rheological properties [4]. The mixed use of carboxymethyl cellulose hydrocolloid and cellulose pulp fibers results in a high total cellulose content in the ink and good dispersion of the fibers in the hydrogel matrix. When the printed structure undergoes dehydration or hydration processes, it can deform according to pre-designed rules.

2.2 4D Printing of Magnetically Responsive SMPCs

To date, most 4D-printed structures rely on environmental stimuli such as temperature and humidity to induce shape transformation. While these elements cause the deformation process of complex structures, they usually require a relatively long time to respond. Although electroactive SMPCs allow remote control, they generally require contact-based actuation. Magnetic field actuation, by contrast, offers the dual benefits of contactless operation and rapid response.

To enable magnetic responsiveness in SMPs, magnetic fillers—such as magnetic particles or short magnetic fibers—are added into the polymer matrix. Under the action of an alternating magnetic field, magnetic fillers will generate hysteresis losses, which are released in the form of heat, causing deformation of polymer materials [5].

Soft intelligent structures responsive to magnetic fields have broad potential in areas like supple robotics and biomedical devices. Roh et al. developed a magnetically driven structure capable of complicated shape transformations [6]. They prepared printable ink by blending PDMS with magnetic particles and used 4D printing to fabricate a floating mesh structure.

The ultra-soft actuator is prone to deformation under the magnetic force of carbonyl iron particles and the lateral capillary force. The deformation can be designed through the magnetic field gradient and programmable modules. This reticular structure, which is reconstructed in a magnetic field and responds to external stimuli, can serve as an active tissue scaffold for cell culture or as a soft robot that mimics surface organisms.

Zhu et al. formulated printable composite inks by blending iron nanoparticles with PDMS. When exposed to alternating magnetic fields, these printed structures exhibit rapid shape recovery [7]. The soft magnetic particles within the ink possess low coercivity and high magnetic susceptibility, enabling instantaneous magnetization & demagnetization switching upon magnetic field activation & deactivation. As demonstrated by a 3D-printed butterfly in Figure 1, PDMS/Fe structures achieve magnetically actuated deformation—exhibiting wing flapping from minimum to maximum amplitude within 0.7 seconds.

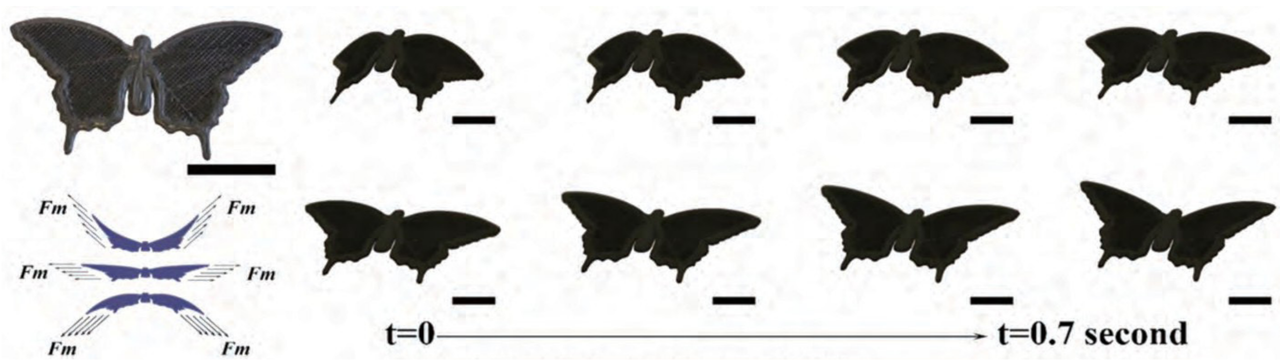

Fig.1 The printed butterfly flaps its wings in the magnetic field [7].

3. Case Studies of SMP Applications in the Biomedical Field

With the development of minimally invasive techniques, the demand for miniaturized medical devices is increasing. SMPs can be implanted into tissues through small incisions. The invention of intelligent micro-devices has paved a new way for the development of clinical applications. In biomedical applications, particularly minimally invasive surgery, reducing implant dimensions and surgical trauma remains a key clinical challenge. 4D-printed SMP devices address this through volumetric miniaturization for compact storage. Upon implantation at target sites, stimulus-triggered shape recovery activates therapeutic functionality.

3.1 Biomedical Scaffold

Figure 2 illustrates a tracheal stent structure and its unfolding process in an external magnetic field [8]. Tracheal stents fabricated from bio-based SMPs exhibit outstanding performance and can be actuated remotely without physical contact, showing strong potential as alternatives to conventional stents.

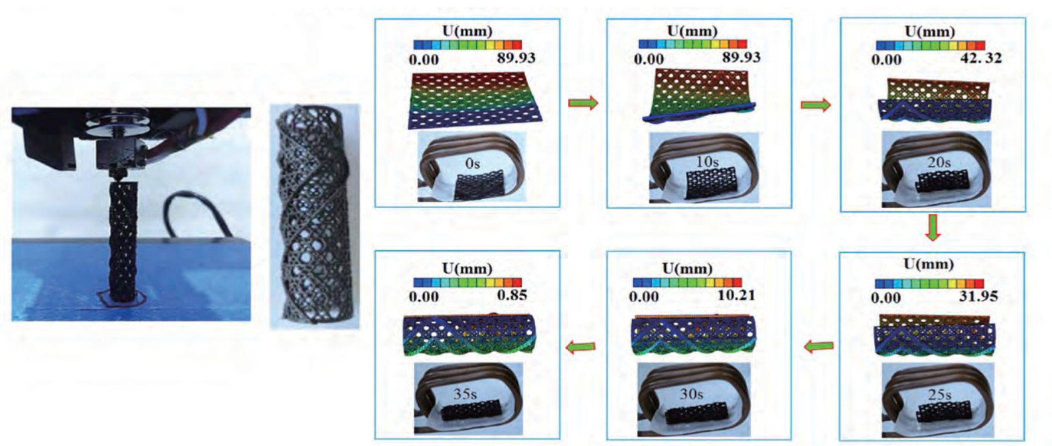

Fig. 2 The unfolding process of printed tracheal stent [8].

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With the advancement of 3D printing technology, it has become possible not only to rapidly fabricate structurally complex scaffolds but also to customize stents tailored to individual patients, ensuring that the structure and dimensions precisely match specific anatomical requirements. From the perspective of material selection, the materials used to make these memory-based supports should be safe for the human body, strong enough to maintain structure, and able to change or return to their original shape when exposed to the right temperature. The traditional responsive deformable support designed through a double-layer structure usually only causes isotropic shape offset, and due to the lack of fine-tuning for the contraction mismatch of the interlayer interface, it is impossible to precisely control the shape.

Therefore, in the biomedical field, how to achieve minimally invasive delivery through 4D printing to break through the spatial limitations during the surgical process and trigger secondary, functional shape deformation under physiologically relevant conditions is of great significance for biomedical applications.

At present, there are mainly three treatments for cardiovascular diseases: drug therapy, bypass surgery and vascular stent interventional therapy [9]. Compared to slow-acting medication and the higher risks of bypass surgery, vascular stent intervention offers clear advantages. It is minimally invasive, effective, and currently widely used to treat vascular narrowing [10]. By supporting the vessel walls, stents help restore normal blood flow, making this approach a promising option for managing cardiovascular diseases.

These days, materials commonly used for blood vessel supports mainly include certain types of stainless steel, alloy materials and polymer materials. Among alloy supports, nickel-titanium alloy and lead alloy are the most widely used materials. Among them, nickel-titanium alloy stents have more advantages in clinical applications because they are more convenient to operate and cause less damage to tissues [11,12]. As illustrated in Figure 3a, a schematic diagram shows the use of a compressed metal stent for the treatment of arterial stenosis [13]. A corrugated metallic stent integrated with a collapsible balloon is delivered intravascularly via catheter to occluded sites. Balloon inflation subsequently expands the device, displacing atherosclerotic deposits laterally. Nevertheless, such balloon-expandable metallic stents exhibit limited biodegradability in physiological environments and pose risks of iatrogenic vascular trauma.

Polymeric scaffolds predominantly utilize shape-memory polymers (SMPs) or their composites (SMPCs), exhibiting stimuli-responsive deformation. Their inherent biodegradability and favorable biocompatibility confer significant biomedical potential. Figure 3b shows a schematic diagram of SMP vascular stents used in minimally invasive surgery [13]. Before implantation, the SMP stent is pre-programmed as a compact temporary structure; After implantation, through appropriate heating, the stent can automatically expand and dilate the blood vessel.

Jia et al. prepared biodegradable self-dilating vascular stents using shape memory polylactic acid (PLA), which can be compressed into a temporary fine-diameter shape for implantation [14]. The compressed shape memory PLA scaffold has excellent shape fixation ability and can return to its original shape under thermal stimulation. Lin et al. prepared personalized vascular stents with a negative Poisson's ratio structure, using shape memory PLA as the raw material to achieve the memory function of the vascular stents [15]. In vitro feasibility tests have shown that this stent can rapidly expand simulated narrowed blood vessels, demonstrating a promising application prospect in the treatment of vascular stenosis.

Shi et al. developed a bidirectional shape memory cellulose vascular stent using a single-layer cellulose membrane through an environmentally friendly method [16]. By adjusting the thickness of different layers and the cutting direction, it is easy to prepare bidirectional shape memory cellulose scaffolds with different structures (such as annular, helical and helical ring) (as shown in Figure 3c). In vitro studies have shown that this helical bidirectional shape memory cellulose scaffold can adjust its shape and effectively maintain the dilated state of blood vessels.

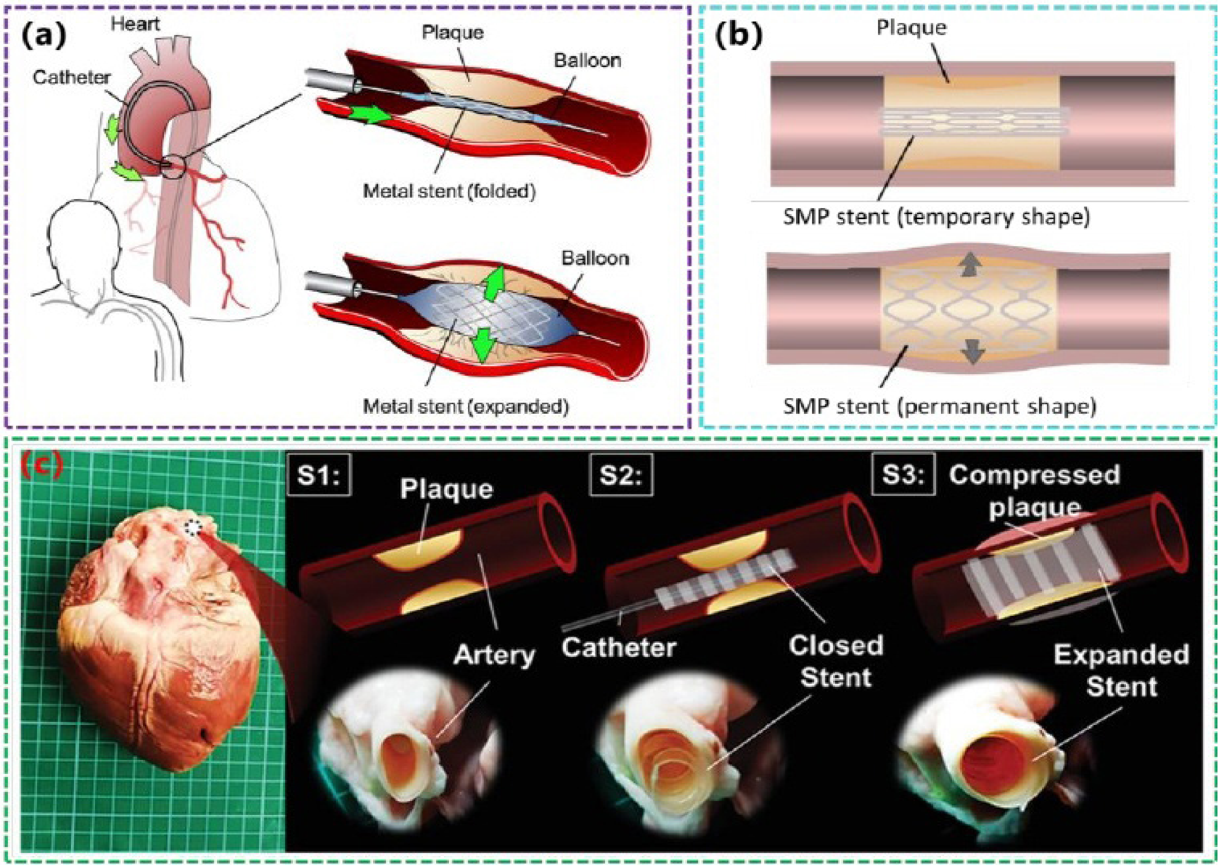

Fig. 3 (a) Schematic diagram of implantation of balloon-dilated metal stents for the treatment of arterial stenosis [13]; (b) Schematic diagram of the release process of the SMP stent [13]; (c) Vascular stents based on bidirectional shape memory films [16].

Wang Huanan's team developed an innovative strategy to design a stimulation-response scaffold based on the natural phenomenon that many withered leaves or flowers spontaneously curl up and transform from flat structures to tubular structures after dehydration [17]. This scaffold can be programmatically transformed from a flat 2D structure into various curled 3D tissue simulation structures. This bionic strategy is used to develop shape-deforming scaffolds that can be programmed in multiple steps to transform into various tissue simulation structures. Based on in-depth research on the mechanism of leaf transformation and the bionic 4D printing manufacturing strategy, the team combined the bionic design strategy of the „mesophyll" layer and the „vein" layer to design the hydrogel pattern and fine-tuning the stiffness of the polycaprolactone film, which can precisely control the curling direction and curvature of the scaffold, thereby manufacturing 3D structured tissue simulation structures with various curling directions and bends. This strategy of coordinated regulation of curling curvature and curling direction provides a new idea for designing more complex structures of deformable hydrogels. In addition, Wang Huanan's team achieved a secondary response of the primary transformation structure under physiological conditions by designing a spatiotemporal cross-linking strategy for the active layer double-network hydrogel, providing better adaptability to deliver and adapt to the local tissue shape for application in vascular reconstruction.

3.2 Bone Tissue Engineering

The dynamic process generated by the interaction of cells within bone tissue is called bone remodeling, which is a necessary condition for bone regeneration and the maintenance of structural integrity. Although bones have an inherent regenerative ability, severe bone defects require the implantation of bone substitutes to promote stability and tissue reconstruction.

SMPs and SMPCs have become promising reconfigurable scaffold materials for the treatment of irregular bone defects because they can be extruded and formed above the transition temperature to adapt to irregular bone defects. Polymer materials such as polycaprolactone (PCL), shape memory polyurethane (SMPU), and PLA possess thermally activated shape memory properties, and their unique

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functions can simplify the complex clinical bone graft surgical procedures. In addition, these materials exhibit excellent chemical stability, good biocompatibility and degradability, and thus have been widely applied in the field of bone tissue engineering. Tissue engineering is currently the most effective method for treating craniofacial bone defects of critical dimensions [18]. The PCL porous scaffold features irregular boundary matching, interconnected porous network structure and excellent biological activity for bone defects, meeting the ideal requirements for promoting bone tissue regeneration.

Liu et al. developed a shape memory nanocomposite scaffold loaded with BMP-2, which was composed of chemically cross-linked poly(ε-caprolactone) (c-PCL) and hydroxyapatite (HAP) nanoparticles [19]. The incorporation of HAP nanoparticles not only enhanced the mechanical stability and osteoconductivity of the scaffold but also improved the quality of in vivo micro-CT imaging. In vitro shape memory tests show that the stent can fully recover from a temporary shape to its original shape at 37 °C. During the in vivo implantation process, a 42 °C temperature-controlled pump was used to maintain the body temperature of the anesthetized animals, and the shape memory recovery process carrying the BMP nano-SMP composite material (nano-SMPC) scaffold was observed (see Figure 4a). 3D micro-CT imaging and quantitative analysis showed that bone formation in the SMPC scaffold group increased significantly compared with the control group. SMPC scaffolds show promise in addressing large-volume scaffold implantation in complex and dynamic in vivo environments. This study provides a simple engineering method for the implantation of multi-functional stents, aiming to treat or repair diseased organs and tissues in the human body.

Wang et al. engineered a porous osseous scaffold comprising hydrophilic polyethylene glycol, biodegradable polycaprolactone (PCL), and citrate-phosphate hybrid particulates [20]. The construct demonstrates tunable mechanics, modifiable porosity, and significant thermal-induced shape recovery. Figure 4b shows the morphological comparison after compression and recovery of the bone scaffold. Scanning electron microscopy (SEM) images show that the pores of the compressed sample are squeezed, the pore walls are closely packed, and the porosity is reduced. However, after heating, the scaffold returned to its original form, and the shape and structure of the pores were also restored, which was confirmed by the micro-CT reconstruction images of the pore structure. This scaffold can adopt a less invasive temporary shape at higher temperatures and restore its permanent form when reheated. This feature has significant advantages. It not only supports minimally invasive implantation, reducing the risk of surgical infection, but also can rapidly complete morphological transformation in a humoral environ.

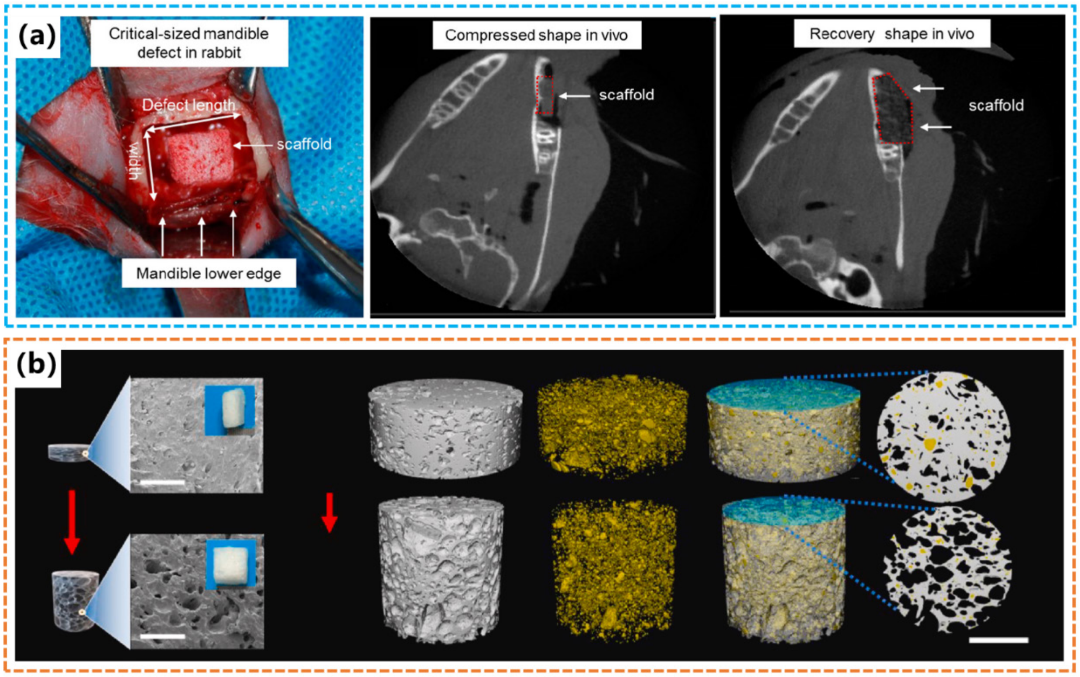

Fig. 4 (a) In vivo shape memory recovery process of BMP-2 loaded SMPC scaffolds observed by cone beam computed tomography [19]. (b) Macroscopic and microscopic images of porous bone scaffolds before and after shape recovery [20].

3.3 Application in Drug Delivery Carriers

The combination of drug delivery systems with SMP or SMPC has attracted much attention because it can utilize the shape memory effect to achieve the stable fixation of drug carriers at the target site without external operation. In addition, the controllable shape memory effect enables the drug to achieve prolonged release at the target site, eliminating the need for multiple injections or surgeries. In the field of drug delivery, water-triggered drive is currently regarded as a more suitable method in SMP/SMPC applications.

To overcome the application limitations of flavonoids such as luteolin in the treatment of gastric cancer due to poor water solubility, a shape memory PLA gastric retention drug delivery system (GRDDS) has been developed in recent years (see Figure 5a) [21]. This system can enhance the relative bioavailability of luteolin, prolong its release and in vivo circulation time, and provide a potential practical strategy for oral administration. King et al. fabricated porous drug-loaded scaffolds using digital light processing 4D printing technology (see Figure 5b) [22]. The drug release curve shows that this stent can achieve adjustable and controllable drug release. During the two-week in vitro culture of mouse fibroblasts, the scaffold demonstrated good cytocompatibility

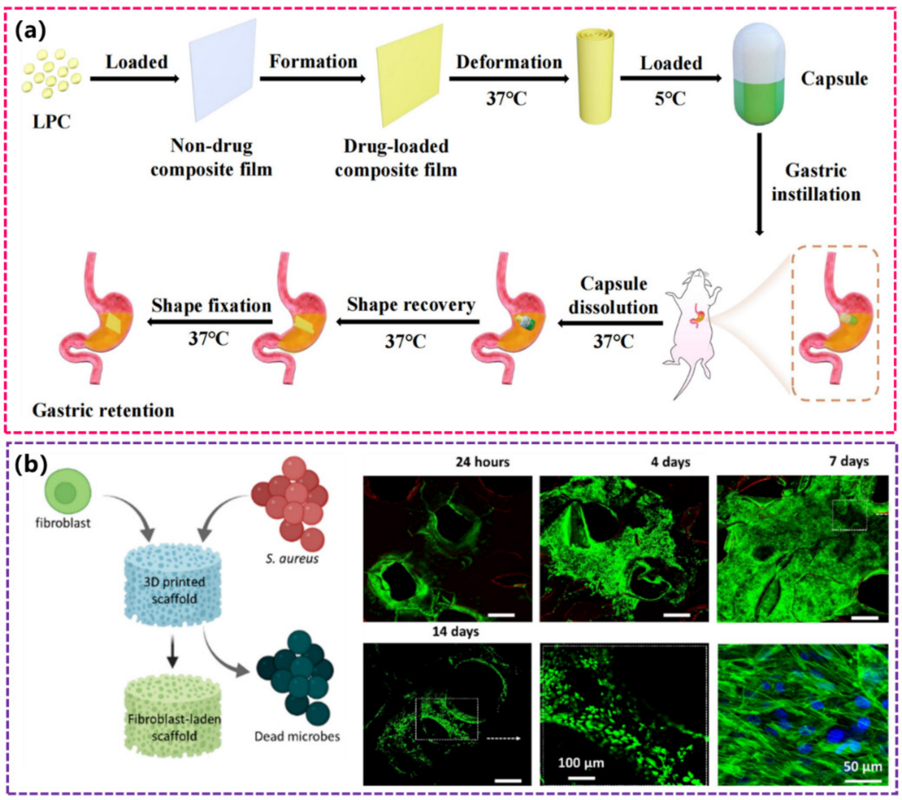

Fig. 5 (a) Schematic illustration of the PLA-based GRDDS [21]. (b) Schematic of cytocompatibility of 4D printed prodrug scaffolds and results of cell culture experiments [22].

4. Problems and Development directions of 4D printed SMPs

Since the concept of 4D printing was proposed, it has aroused great interest and extensive attention. Within a few years, many printing methods, printing materials and driving methods have been developed. It has broad application prospects in fields such as biomedicine, aerospace, smart devices, bionics, robotics, origami, smart clothing and smart home.

However, like many other emerging technologies, 4D printing still faces many challenges. Firstly, 3D printing technology is not yet mature, with disadvantages such as low printing accuracy, low efficiency, and low strength of printed structural components. Printing accuracy is influenced by multiple factors. On the one hand, it is the accuracy of the printing equipment itself; on the other hand, it is the setting of printing parameters, such as printing speed, extrusion speed, printing temperature, layer thickness, etc. At present, the printing accuracy can reach

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several micrometers. In the current immature printing technology, if one demands higher accuracy, it is highly likely that the printing speed will have to be sacrificed. It takes tens of minutes to several hours to print a test piece a few centimeters in size. If the printing time is too long, it will be at a disadvantage in large-scale production. 3D printing adopts a manufacturing process of „layer-by-layer manufacturing and layer-by-layer superposition". The bonding strength between the layers of printed parts is far inferior to that of parts cast as a whole in traditional molds. If the method of layer-and-layer superimposition manufacturing can be changed, it will not only solve the problem of the connection strength between the layers of the printed structure but also improve the printing efficiency. Therefore, the development of an integrated printing method is one of the future development directions of 4D printing technology. Secondly, SMPs materials have slow response and low functionality. It takes tens of seconds or even minutes for the material or printed structure to deform, with obvious insufficient driving force and slow response. In addition, some bionic research or tissue engineering can currently only imitate the shape and simple deformation movements such as bending and twisting and cannot replicate the cellular activity of animals and plants. Therefore, they cannot demonstrate the special functionality of tissue structures. In the field of biomedicine, for the expandable stents implanted in the body during minimally invasive surgery, thermal drive for stent deployment is clearly impractical. Currently, magnetic drive is the safest driving method, but magnetic drive requires relatively large equipment, has a wide magnetic field range, and cannot precisely act on the treatment site. Clearly, it cannot provide very convenient services. Therefore, it is extremely necessary to develop precise and convenient non-contact driving methods.

Finally, the printed structural components lack functional application verification. At present, the intelligent structural components printed by 4D are still in the laboratory research and development stage. Printing some simple structures to demonstrate their functions such as deformation and color change is still far from practical application and large-scale production.

5. Conclusion

This article focuses on introducing three aspects: the preparation, driving and application of SMPs and SMPCs based on 4D printing technology. Firstly, it expounds the existing problems of the current 4D printing technology and the exploration of new printing technologies; Secondly, from the perspective of fillers, analyze the research status and progress of different driving methods of 4D printed SMPCs; Finally, this article elaborates on the current application status and development potential of 4D printed SMPs and SMPCs from the perspective of biomedical application fields. The evolution of 4D printing demands interdisciplinary convergence across additive manufacturing, materials with stronger performance, innovative structural architectures, and computational modeling. In the field of biology, although traditional polymers have laid the foundation for biomedical devices, SMPs and SMPCs offer opportunities for the development of next-generation biomedical solutions. With the continuous deepening of research work, the shape memory effect and biological performance of SMPs is constantly improving and enhancing, and the breadth and depth of their application in various fields, especially in biomedical applications, will continue to expand.

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