

# Research Progress of Shape Memory Polymers in Biomedical Fields

Xinwang Lin \*

College of Chemistry, Fuzhou University, Fuzhou, China

\* Corresponding Author Email: williamlin337@gmail.com

**Abstract.** When external stimulation is applied, Shape Memory Polymer (SMP) can maintain its shape and spontaneously revert to its initial form when the stimulation is removed. With the increasing demand for smart materials in biomedical engineering, shape memory polymers have attracted extensive attention due to their unique stimulus-responsive properties. Because of their superior qualities, SMPs are progressively being utilized in the biomedical industry. SMPs are currently employed in biological domains, including tissue repair, drug delivery, and surgery. This thesis summarizes the high stretchability, biodegradability, and biocompatibility of SMPs. It also details their fundamental operating mechanisms and four common actuation types (thermal-responsive, light-responsive, electric-responsive and chemical-responsive). The thesis also highlights the current clinical applications of SMPs in drug delivery, dentistry, and tissue regeneration. Systematic research on the multi-response mechanism of SMP and its applications in biomedicine is conducive to promoting the innovative development of intelligent medical devices in the field of precision medicine.

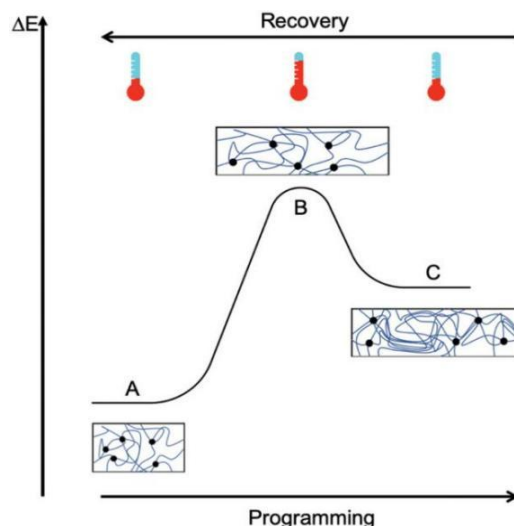
**Keywords:** Shape Memory Polymer; Reversibly Cross-linked Network Structure; Thermo-responsive; Light-responsive; Chemical-responsive; Drug Delivery; Dentistry.

## 1. Introduction

A novel kind of smart material called shape memory polymer (SMP) may alter its size, shape, hardness, and other characteristics in response to various environmental stimuli (e.g. light, electricity, water, heat, pH, etc.). SMP can be categorized as light-responsive, electric-responsive, thermal-responsive, or chemical-responsive based on the various kinds of external stimuli. The SMP has gradually become a new type of material used in the biomedical field due to its high stretchability, biodegradability, biocompatibility and other properties. Therefore, SMP can be used in specific biomedical fields such as drug delivery, dentistry, tissue regeneration therapy, etc. [1]. This article aims to focus on the basic principles and application directions of SMP's shape memory effect (SME). This thesis first introduces the mechanism of SMP's shape memory effect, then introduces the classification of SMP, and focuses on the specific application fields of thermal-responsive SMP in biomedicine and finally proposes prospects.

## 2. The Mechanism of Action of SMP

One possible mechanism of action for thermal-responsive SMPs is called a reversible cross-link network structure. It is known that the lower the chemical potential energy ( $E$ ), the greater the entropy ( $S$ ). Chain entanglements of polymers with a high enough molar mass operate as a physical crosslink by preventing the complete polymer chain from moving. SMP molecules contain numerous crosslinking nodes (as indicated in black dots in the figure). These nodes become easily movable when heated to a certain temperature,  $T_0$ , as shown in Figure 1, shape B. Applying external force to the SMP at this point can cause it to change shape. When the temperature drops below  $T_0$ , these nodes reform, resulting in the SMP's temporary shape, C. The transient shape, C, reverts to its initial shape, A, if the temperature is increased above  $T_0$  and the external force is eliminated [1].



**Fig 1.** Potential energy diagram of thermoresponsive SMPs [1].

As shown in Fig. 1, a permanent shape with a greater entropy value, A, can be programmed to a temporary state C with a lower entropy value by heating and deforming. The temporary shape C can be heated to return to the permanent shape A. The polymer goes through a transition state B, where the polymer chains are mobile and can rearrange, when it transitions between the temporary and permanent shapes.

### 3. Types and Preparation Methods of SMP

#### 3.1. Thermo-responsive SMP

Thermal-responsive SMPs can be programmed to activate in response to external thermal stimulation. Thermal activation was the first reported method for externally actuated SMPs and remains the most widely used method for shape deformation. Typically, thermal-responsive SMPs are prepared by modifying thermal-responsive polymer networks. Hao Zheng et al. used polyurethane (PU)-based polymers to prepare thermal-responsive SMPs. These polymers can be processed at a certain temperature to change from a straight permanent shape to a hooked temporary shape. These fibers undergo shape deformation when thermally activated and can be used for neural stimulation in nerve regeneration therapy [2]. Dora C. S. Costa et al. proposed a method for preparing polyurethane-based polymers: by embedding a thermosensitive polyurethane network between a non-thermosensitive biopolymer hydrogel network (such as methacrylated chitosan (CHTMA), gelatin (GELMA), laminarin (LAMMA) or hyaluronic acid (HAMA)), the material can exhibit a rapid shape recovery rate ( $\approx 100\%$ ) at body temperature ( $37^\circ\text{C}$ ). This material can achieve shape deformation at physiological temperature ( $37^\circ\text{C}$ ) [3].

#### 3.2. Light-responsive SMP

Based on the LSMPC classification, we divide light-responsive SMPs into three categories according to the wavelength of the driving light: ultraviolet (UV), visible light (VIS), and infrared (IR) [4]. This section only introduces the SMPs driven by UV and IR in detail.

##### 3.2.1. UV-driven SMP

UV radiation has wavelengths ranging from 10 to 400 nm and is classified as UVA (315~400 nm), UVB (280~315 nm), UVC (200~280 nm), and UVD (10~200 nm).

As shown in Fig. 1a, azobenzene and its derivatives can undergo reversible cis-trans (E-Z) isomerization when exposed to UV and visible light. When the azobenzene group is combined with other macromolecules, the material undergoes a reversible macrostate transition or reversible shape memory effect [5].

Despite being extensively researched as a photosensitive chemical group, azobenzene still has many drawbacks, the most prominent of which is the thermally unstable *cis* isomer. Consequently, graded responsive SMP (SR-SMP) was developed.

Under UV irradiation, the azobenzene group generates the *cis* isomer, decreasing the distance between polymer chains, enhancing the hydrogen bonding contact, and keeping the distorted form even in visible light. Because VIS cannot disrupt strong hydrogen bonds, the distorted shape may be persistent over an extended period of time. However, high temperatures diminish the hydrogen bonding contact, causing thermally induced shape recovery. Figures 1e~1h show similar step-by-step reactions.

### 3.2.2. IR-driven SMP

Infrared (IR) has a wavelength ranging from 760 nm to 1 mm, falling between microwave and visible light. The infrared spectrum is classified into three wavelength ranges: near infrared (NIR, 760 nm~3  $\mu$ m), mid-infrared (MIR, 3  $\mu$ m~30  $\mu$ m), and far infrared (FIR, 30  $\mu$ m~500  $\mu$ m). When IR is given to photoresponsive form memory materials, the shape memory effect is caused by indirect heating using photothermal converters and thermally responsive shape memory materials. At the same time, research on near-infrared (NIR)-induced SMP has also been reported in recent years. NIR not only has extremely low phototoxicity, but also has better tissue penetration, which makes NIR-based SMH more attractive in biomedical applications. Yang Zou et al. proposed that the introduction of Fe<sup>3+</sup> ions can prepare near-infrared light-responsive SMP. Near-infrared hydrogels were prepared using PVA and tannic acid (TA)-Fe<sup>3+</sup> complexes as raw materials by Zou Y. et al. [6]. In addition to the above-mentioned hydrogels, Fe microparticles and Fe<sub>3</sub>O<sub>4</sub> nanoparticles have high saturation magnetization and efficient photothermal effects. As a result, they can be mixed with shape memory materials to create composite materials that are responsive to magnetic fields and NIR. For example, adding Fe microparticles to thermoplastic polyurethane can form artificial magnetic cilia that can be driven by magnetic fields and light (780 nm); Fe<sub>3</sub>O<sub>4</sub> nanoparticles are doped into shape memory polymers (e.g. PLA/ENR, PCL/DA4, and gP(TMA-co-LA-co-VI)), which exhibit significant magnetic-/light-induced shape memory effects under alternating magnetic fields and NIR irradiation[4].

### 3.3. Chemical-responsive SMP

Chemical-responsive SMPs change shape in response to external chemical stimuli such as solvents, ions, and pH. Liyuan Qiao et al. suggested a method for creating chemically responsive SMPs using an IPN constituted of a stable network of Pluronic F127 diacrylate macromer (F127DA) and a reversible network of sodium alginate, which can be converted into an SMP that uses Ca<sup>2+</sup> as a chemical stimulus for drug delivery [7]. Bo Liu et al. suggested an AA-AN copolymer that generated shape memory hydrogels under pH, with non-covalent hydrogen bond interactions modulated by pH. In addition, the authors generated pH-responsive shape memory hydrogels based on AN by copolymerizing it with N-acryloyl-2-glycine (ACG). Under acidic conditions, the rigid copolymer network is made up of the protonated carboxyl groups of ACG and the cyano groups of AN, which form dipole-dipole interactions; under neutral pH conditions, the P(AN-co-ACG) hydrogel strips shape deform to form microcoils, which can be used to make microcatheters [8]. Yande Cui et al. polymerized a terpolymer of AAm, AA, and acrylamide adamantane (Ad-Am) monomers in the presence of a hydrogel based on  $\beta$ -cyclodextrin-modified encapsulated cellulose nanocrystals ( $\beta$ -CD-TCNCs), in addition to adjusting pH. These gels were coordinated by Fe<sup>3+</sup>/-COO<sup>-</sup> ions and programmed into different forms (stretching, twisting, and curling) via host-guest interactions to improve hydrogel and shape recovery in the presence of a solvent (ethanol), which induces network contraction. These hydrogels were then employed to create tendril-inspired hydrogel artificial muscles [9].

### 3.4. Electric-responsive SMP

An electric-responsive hydrogel can be reversibly driven under the stimulation of external pressure imbalance or Maxwell stress. Xinyu Wang et al. proposed a method for preparing low-voltage electroactive hydrogels. They added liquid metal (LM) (gallium and zinc) to poly( $\epsilon$ -caprolactone) (PCL), and the resulting LM-SMP film can be formed into a permanent shape after thermal programming. The LM-SMP exhibited excellent shape memory properties (shape fixation rate of 95% and shape recovery rate of 99%). Due to the high conductivity of the liquid metal, the LM-SMP can be electrically driven at a low voltage (about 2 V), thereby realizing the electrically driven recovery of the LM-SMP, as shown in Figure 2. This shows that the combination of SMP and LM is expected to become a promising technology for application in electrically driven systems such as soft robots and advanced electronic devices [10].

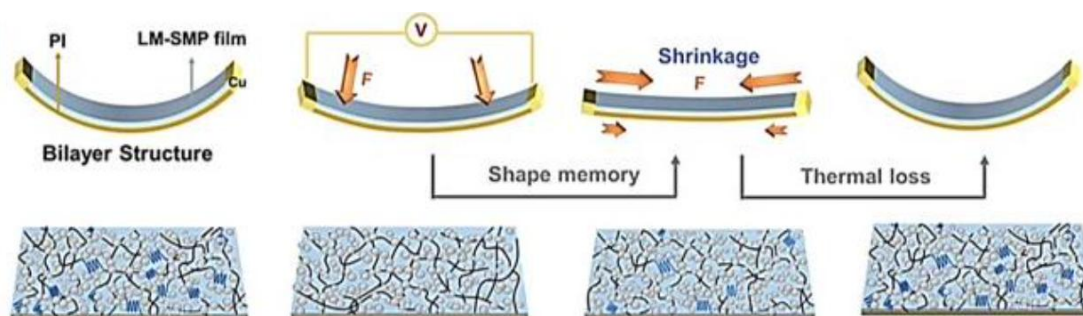


Fig 2. Shape memory effect mechanism of LM-SMP film [11].

## 4. The Application Fields of SMP

### 4.1. Drug Delivery

A frequent application for SMP is medication delivery. Because of the shape memory effect, SMP can be utilized to fix medication delivery devices at the target spot without requiring external manipulation. Drug loading in copolyester polyurethane SMP has been demonstrated to have no significant effect on the material's shape memory ability, indicating that shape memory materials can be efficiently employed for drug release in aquatic environments [1]. Researchers created a drug-releasing shape memory polymer based on poly (methyl methacrylate-butyl acrylate) that can be prompted to recover using ultrasound while releasing a copper sulfate model compound, as illustrated in Figure 3. This release mechanism enables medication release to be halted at any time while the SMP form is partially recovered. This enables multi-step recovery, in which multiple intermediate forms are used, and medication release is time controlled.

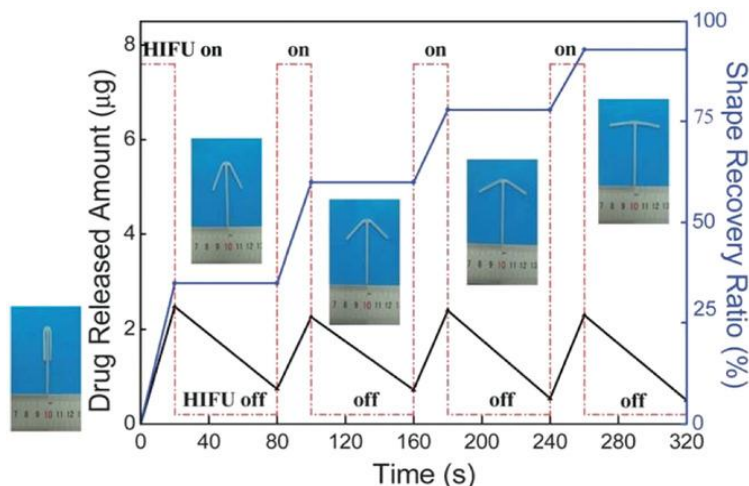
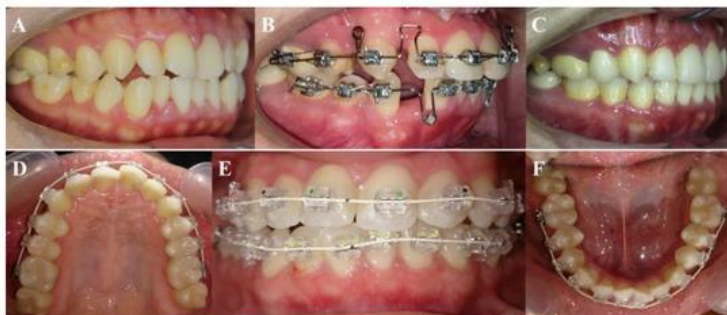


Fig 3. Release mechanism of drug-releasing shape memory polymer based on poly (methyl methacrylate-butyl acrylate) [1].

## 4.2. Dentistry

Since SMP has good biocompatibility and good durability in implants and restorations, it can be used in orthodontics. SMP can effectively prevent biological damage and durability problems in implants and restorations, and can prevent caries, root canal treatment, and the formation of biofilm in implants. Because it does not emit metal ions, SMP can be utilized as a good alternative for metal wire in orthodontic therapy. In addition, SMPC and SMPNC have a wide range of uses, including slow release, root canal filling agents and fillers, and biofilm prevention agents [12].



**Fig 4.** Shape memory and Teflon-coated nickel-titanium wires are used in orthodontic therapy [12](A) Before treatment; (B) During treatment; (C) After nickel titanium alloy treatment; (D) Prior to treatment; (E) During treatment; (F) Following Teflon-coated nickel titanium wire treatment.

Figure 4 depicts the usage of shape memory nickel-titanium wire and Teflon-coated nickel-titanium wire to repair misaligned teeth in orthodontics. Jung and Cho demonstrated the usage of SMPU as an arch wire in dental models. A melt-spun polyurethane (SMPU) is made from 4,4-methylenebis (phenyl isocyanate) and polycaprolactone (PCL) diol. The SMPU filament is stretched to the necessary length to straighten the teeth and then linked to stainless steel brackets. This correction procedure is more visually appealing than traditional nickel-titanium wire repair [13].

## 4.3. Tissue Regeneration Therapy

The biocompatibility, tunable mechanical properties, inhibition of nonspecific cell attachment, and selective biofunctionalization of shape memory hydrogels are key features for their use in tissue regeneration therapy. A shape memory hydrogel-based intervertebral disc (IVD) scaffold consisting of a physically cross-linked, highly compressible dual network of alginate and cellulose networks is used to treat IVD degeneration. Taking advantage of the shape deformation memory, shape memory hydrogels have been widely used in the development of reconfigurable scaffolds. For example, the gelatin-based shape memory hydrogel developed by Guoliang Ying et al. was prepared from an aqueous two-phase emulsion bioink containing a pregelled gelatin methacryloyl (GelMA)/cell and polyethylene oxide (PEO) blend. Injectable macro-micro-nanoporous cell-laden GelMA hydrogels based on gelatin methacryloyl (GelMA) were constructed by 3D extrusion bioprinting technology. Compared with standard GelMA, the microporous hydrogels exhibited better mechanical properties and recoverability [14].

## 5. Conclusion

SMP materials have clearly increased their biomedical applications, which now include general medicine, medication delivery, dentistry, neurology, orthopedics, and corrosion protection. Simultaneously, progress has been achieved in the structural and shape memory mechanisms of SMP. People have performed substantial research to better understand the material's design functions, biological response, and, ultimately, appropriateness for bioapplications. Because of their features like biocompatibility, multifunctionality, low cost, and ease of stretchability, they are projected to advance in practical applications such as personalized medicine and tailored devices. Current obstacles include gaining a thorough understanding of these SMPs through in vivo studies, as well as

conducting substantial preclinical research to convert them from laboratory scale to clinical application.

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