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4D printing innovations and the embracing of additive manufacturing transformations

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The transition from 3D to 4D printing has revolutionized additive manufacturing by introducing dynamic shape-changing capabilities. The limitations of 3D printing have led to the development of 4D printing, which uses ultraviolet light to deposit materials layer-by-layer, creating customizable soft fabric structures that can transform over time in response to external stimuli. The stimuli can be physical, chemical, or biological. Predetermined interaction mechanisms and mathematical modelling, facilitated by tools such as CAD and FEEA, play crucial roles in orchestrating these shape-shifting behaviours. 4D printing has applications in the medical, manufacturing, and educational sectors, with applications extending to adaptive medical implants and devices. Research on 4D printing focuses on various shape alterations, with promising transformative effects on manufacturing processes, medical interventions, and educational tools. As 4D printing progresses, it has the potential to revolutionize industries and provide innovative solutions to complex challenges. The interplay between stimuli and responsive materials, guided by advanced modelling techniques, opens new avenues for unprecedented development. The shift from 3D to 4D printing signifies a paradigm change in additive manufacturing, offering a glimpse into the future, where products dynamically adapt to their environment and user needs.

1. Introduction

For more than 30 years, three-dimensional (3D) printing technology has made countless contributions to the additive manufacturing industry and many other arenas, such as product design, biotechnology, and medicine.[1] Researchers are still discovering new models, methods, materials, unique designs, and the applications of 3D printing. This revolution has led to four-dimensional (4D) printing.

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In 3D printing, a two-dimensional (2D) object is printed layer-by-layer in the printer to create a 3D structure from bottom to top until a 3D volume[2] is created. However, conventional 3D printing cannot fulfil the demands of dynamic applications like self-folding packing, adaptive wind turbines, and soft grippers for surgery.[3]

4D printing depends on stereolithography, where materials are laid down layer-by-layer with the help of ultraviolet light during the printing process. This is an accurate and rapid process for customizing soft-fabric structures. 4D printing is a technology in which a 3D-printed structure is transformed to have a targeted shape or property by an external stimulus. Stimuli fall into one of these three categories: physical stimuli (*e.g.*, temperature, moisture, light, UV light, magnetic energy, and electricity), chemical Stimuli (*e.g.*, oxidants, reductants, ionic strength, and pH level), and biological energy (*e.g.*, presence of glucose and enzymes).[4] Different types of 4D printing bases are listed in Fig. 1.[5]

Not all structures undergo the desired change during exposure to a stimulus. A predetermined interaction mechanism is required to schedule the sequence of shape-shifting behaviours that occur when the stimulus is active for a sufficient period. Mathematical modelling is required to plan out the appropriate time and sequence of stimuli to affect the stimulus-responsive component with the help of geometric programming, such as computer-aided design (CAD) and finite-element-analysis (FEA).[6] Additive manufacturing methods, such as three-dimensional (3D) and four-dimensional (4D) printing, are used to create novel products. Time, an additional dimension in the case of 4D printing, is the only difference.[7] Recent research on 4D printing focuses on different types of shape-changing properties of 4D structures, like bending, twisting, stretching, and folding.[8]

4D printing technology impacts different sectors, such as medicine, manufacturing, and education. In healthcare, 4D printing technology fulfils the necessity of developing medical implants and devices. With the help of smart materials, 4D medical implants introduced into the human body can change their shape according to certain requirements over time. These smart materials have the capability to self-deform.[9]

2. History of 4D printing

Research into 4D printing has been extensive because of its enormous potential.[10] Modern commercial printed materials are primarily designed to be durable, elastic, transparent, colorful, or recyclable, among other properties, to fulfill various end uses.[11] However, more can be done to increase the utility of printed components, particularly given the rapid advancement of intelligent and active materials research. Several studies have focused on various aspects of the 4D printing process, from the materials used in the printing procedures to the development of the technology itself. This research focuses on the development of 4D printing and the various strategies used by the pioneers of this field[12] (Fig. 2).

The concept of 4D printing, in which time is the fourth dimension, was introduced. The innovative approach of 4D printing over 3D printing has attracted much interest from scientists and engineers throughout the field. The printed items are no longer static, which is crucial for 4D printing. It can change over time in a pre-programmed manner and is sometimes accompanied by functional evolution. Skylar Tibbits was the first to introduce 4D printing. Tibbits used one

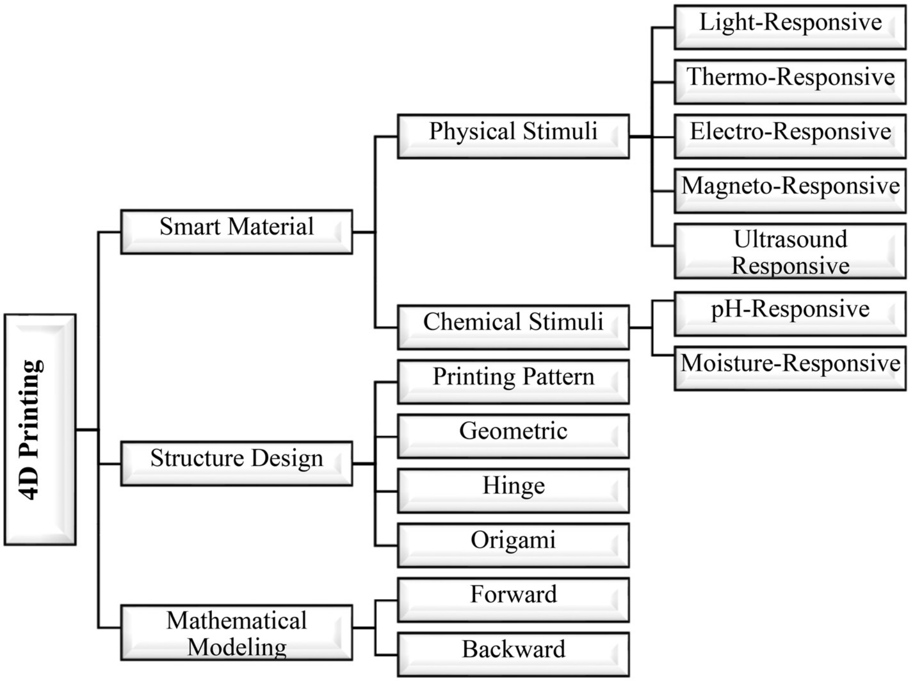

Fig. 1 Different categories of 4D printing bases.

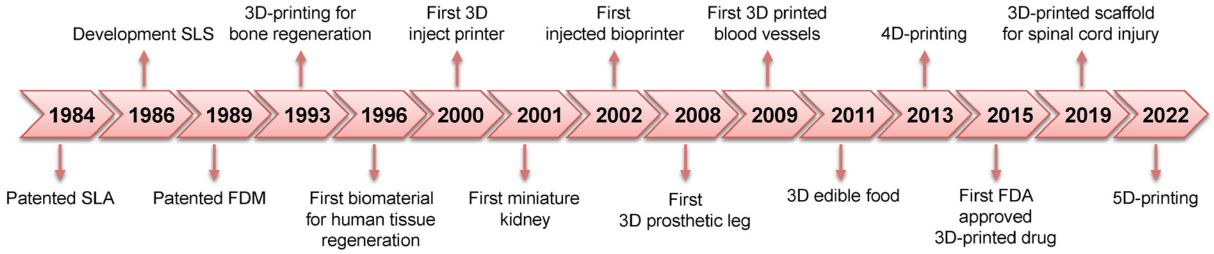

Fig. 2 History and milestones of AM in the biomedical field; adapted without modification from ref. 15, copyright MDPI.

such technique, materials composed of sections that expanded at various rates.[13] Tibbits showed how an initially static printed item can change over time. Shape-programming of non-electric materials was accomplished with this technique, where water was used as an activating agent. Jerri Qi's study on shape programming was a turning point for thermally sensitive materials. These materials can be shaped into the desired three-dimensional form by virtue of their shape memory effect, which manifests at the optimal temperature (Fig. 3).[14]

3. The key differences between 4D printing & 3D printing

The rapid development of 3D printing has paved the way for the emergence of 4D printing (Table 1). 4D printing involves the creation of objects using multi-material components that can change in response to external stimuli. Both 3D and 4D printing processes utilize additive manufacturing to create new products.[16]

The only difference in 4D printing is the time factor. Time is the extra dimension that makes 4D printing possible. 3D printing requires time for the final structure formation, healing, and cooling. In contrast, 4D-printed parts begin to act only after exposure to external energy.

The most common materials used by 3D printers are nylon, ABS plastic, resin, wax, and polycarbonate. Meanwhile, 4D printing technology uses smart materials, which are multimaterials with properties that can be transformed by external energy. Smart materials include piezoelectric, electrostrictive, magnetostrictive, thermoelectric, and shape memory alloys, like Cu–Al–Ni, Ni–Ti, and Cu–Au–Zn.

After material selection, hardware plays a crucial role in 3D printing. Various 3D printing machines are available for home and production use, each using different technologies.[17] For instance, Stratasys' Connex multi-material 3D printer allows the integration of multiple material properties into a single structure using water as an external activation factor. In addition, the RoVa4D Full-colour Blender 3D printer from ORD Solutions allows reasonably priced desktop printing of full colours using many materials.

Advancements in the printing industry have led to the development of new software tools that go beyond traditional modelling software. There is a demand for software capable of incorporating bioprinting, multi-material printing, 4D printing, and electronic printing processes. Some notable software includes Project Cyborg from Autodesk, ANVAS software from Mosaic Manufacturing, Foundry from MIT's Computer Science and Artificial Intelligence Lab, and Monolith multi-material voxel software. Advanced modelling software is required for 4D printing compared to that used for 3D printing.

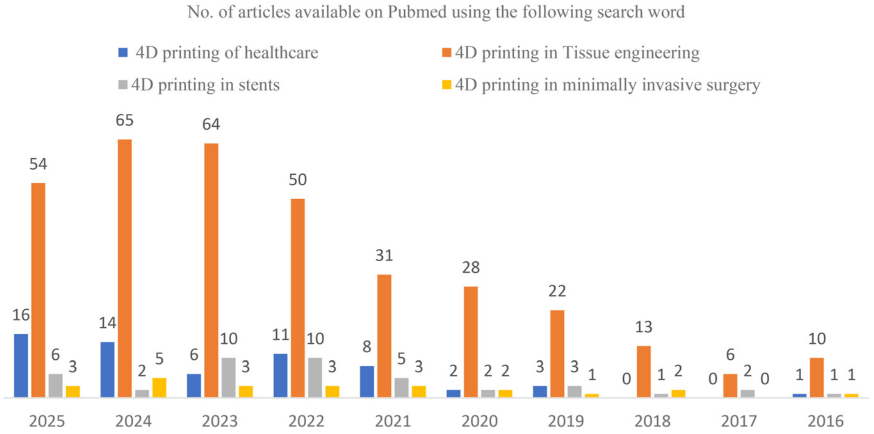

Fig. 3 Total number of published papers on 4D printing in different areas of application from 2016 to 2025, compiled from the PubMed database (as of 27 August 2025).

Table 1 Comparative analysis of 4D printing and 3D printing

Sl. no.	Characteristics	3D printing	4D printing
1	Build process	Layer-by-layer, from bottom to top, 3D printing replicates a 2D structure.	The evolution of 3D printing is 4D printing.
2	Material used	Nanomaterials, biomaterials, ceramics, metals, or thermoplastics.	Intelligent, multi-material, and self-assembling materials to create an object that alters its shape after being manufactured.
3	Design	3D digital information (scanning, drawing).	3D digital information for change (deformation).
4	Key features	Static elements, tailored design, decreased time and expenses.	Active elements, responsive to stimuli, self-repairing, and adaptable to the patient's circumstances.
5	Printer	3D printer (ex. stereolithography apparatus, material extrusion, and selective laser sintering).	Smart 3D printer (ex. modified nozzle, binder, and laser multi-material 3D printer).
6	Shape flexibility	No flexibility, characterized by rigidity. The object shapes are altered during this procedure.	With time and temperature changes, the object's form changes.
7	Programming of material	Do not use any programmable or advanced material.	Use programmable and advanced materials that provide a variety of functions.
8	Application	Medicine, engineering, dentistry, automotive, robotics, fashion, aerospace, defense, jewellery, toys, bio/medical devices, *etc*.	Dynamically changing configuration for all applications by 3D printing.
9	Future potential	Improved accuracy in medical production.	Innovative, customized healthcare options, tissue repairing.
10	Examples	Personalized implants, surgical models.	Drug-delivery systems that adapt to patient needs, prosthetics that can repair themselves and bio-implants that work with body tissues.

While an object is being printed, the process often remains unmonitored, allowing objects to be built overnight without human interference. 4D printing processes are becoming even simpler than 3D printing technology, and simple structures can be transformed into complex, large functional structures with the help of an external activating agent. Self-assembly structures sense and physically react to the surrounding environment without human involvement. The potential of 4D printing technology could lead to a massive shift in the design and manufacturing of objects and structures in the future.

4. Laws of 4D printing

F. Momeni and J. Ni established three fundamental laws that govern the shape-changing behavior of all 4D printed structures.[18] These laws enhance our understanding of the physics underlying the shape-changing capabilities of these structures. These are outlined below.

4.1. First law

This law states that all shape-changing behaviours, such as coiling, curling, twisting, and bending, of multi-material 4D structures result from the relative expansion between active and passive materials.

4.2. Second law

This law identifies four physical factors that contribute to the shape-changing ability of all multimaterial 4D structures: mass diffusion, thermal expansion, molecular transformation, and organic growth.

These elements result in relative growth between active and passive materials, leading to shape changes in response to a stimulus. Changes in mass owing to the absorption or adsorption of stimuli (such as water or ions) can result in shape deformation. Mass changes can also occur in response to electrical, thermal, chemical, or light stimuli. Thermal expansion can deform structures through temperature changes that affect atomic and molecular distances. Similar deformations can occur in response to electrical, light, and UV stimuli, as these can alter the temperature.

4.3. Third law

The third law of 4D printing states that the time-dependent shape-morphing behaviour of nearly all multi-material 4D printed structures is governed by two types of time constants. These constants can vary based on the stimulus and materials used. A mathematical bi-exponential equation for representing the fourth dimension was established for potential use in 4D structures.

5. 4D printers

Researchers have initially focused on examining traditional commercial 3D printers. However, it has been discovered that when using smart materials to print particular objects, the printing material can clump together in standard machines. To address this issue, some research teams have designed specialised 4D printers. For example, Choi *et al.* developed a printer featuring a coated extrusion nozzle designed explicitly for printing smart materials, such as thermal polyurethane (TPU), using material extrusion 3D printing.[19] The longer nozzle was coated with polytetrafluoroethylene to reduce friction, and the printer included a heating bed to prevent nozzle clogging by maintaining proper heat circulation. Another example is a 4D printer created by Ge *et al.*, which is an adaptation of micro-SLA printers capable of producing structures with a resolution of up to 1 micron.[20] This printer is not compatible with regular SLA printers because it employs photocurable smart materials, which are significantly more energy-intensive than regular acrylate-based polymers.

6. 4D printing methods

Additive manufacturing (AM) can be categorized into three main types based on the base material used: solid-based, powder-based, and liquid-based AM (Fig. 4). Solid-based AM encompasses various methods, including laminated object manufacturing (LOM), fused deposition modeling (FDM), wire and arc additive manufacturing (WAAM), and electron beam freeform fabrication (EBF3). Powder-based additive manufacturing includes techniques such as selective laser sintering (SLS), electron beam melting (EBM), selective laser melting (SLM), and laser metal deposition (LMD). Liquid-based methods primarily consist of material jetting (MJ) and vat-based printing techniques, which include stereolithography (SLA) and digital light processing (DLP).[21] Three significant 4D printing methods are discussed here: SLA, FDM and SLS (Table 2).

6.1. Stereolithography (SLA)

Ge *et al.* introduced a novel printing method that utilizes high-resolution projection.[23] This method allows for modifications of material properties, benefiting from its high-resolution projection. Stereolithography is applicable in producing electronic devices, jewelry, fashion items, and biomedical applications. The process involves creating a layer-by-layer structure through the solidification of a photocurable hydrogel. A UV laser is used to scan the hydrogel, which results in the formation of covalent bonds between polymer chains[22] (Fig. 5). The optimization of the 4D printing process can be achieved by controlling factors such as the power of the UV laser, scan speed, exposure time, wavelength, and spot size.

6.2. Fusion deposition method (FDM)

The core objective of the fused deposition modeling is to enable shape memory or shape shifting *via* a heating mechanism.[25] During the fusion deposition process, the material undergoes thermal and mechanical training. Key printing parameters that influence the process include speed, temperature, and deposition path (Fig. 6). Additionally, layer orientation and thickness are critical design parameters that allow for self-folding and self-twisting features.[26] The difference in thermal expansion coefficients is responsible for the shape-shifting action. During fabrication, internal stress develops within the printed material due to rapid heating and cooling cycles. Advanced 4D bio-printing is achieved using bio-composites, aiming to enhance strength and self-shaping, making 4D bio-printing beneficial for engineering and biomedical applications.[27]

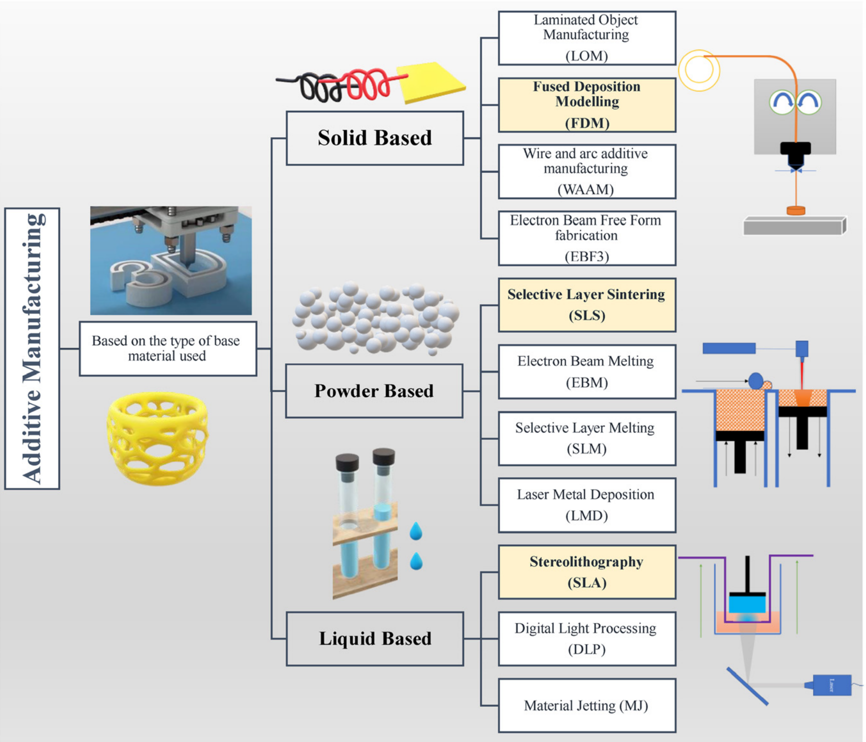

Fig. 4 Classification of AM methods based on the base material used, including solid-based, powder-based, and liquid-based materials; adapted from ref. 22, copyright MDPI.

Table 2 Overview of FDM, SLS and SLA printing methods[22]

Category	Fusion deposition method (FDM)	Selective laser sintering (SLS)	Stereolithography (SLA)
Operational principal	Material extrusion	Laser sintering	UV curing
Resolution (layer thickness)	50–400 microns	50–150 microns	25–100 microns
Printing (speed)	Fast (simple designs)	Slow (due to cooling/powder handling)	Medium (depends on resin curing)
Heat source	Heated nozzle	High-power laser	UV laser
Accuracy	Moderate	High	Very high
Surface finish	Rough texture	Powdery texture	Smooth, glossy finish
Design complexity	Simpler geometries	Excellent (supports not required)	High (supports needed)
Advantages	Rapid printing method, low cost for producing parts, a broad range of materials is necessary	Functional components, greater design flexibility, no need for support structures	Capable of producing fine-detailed parts, precision-engineered results, suitable for diverse applications
Disadvantages	Lower surface quality, requires support structures	Uneven surface texture, long process time	Cost maintenance, restricted material options
Polymer	Polylactic acid, polypropylene, polyvinyl alcohol, acrylonitrile butadiene styrene	Polymethyl methacrylate, polyethylene terephthalate	Polycaprolactone, polyethylene glycol, trimethylolpropane carbonate, poly tetrahydrofuran ether

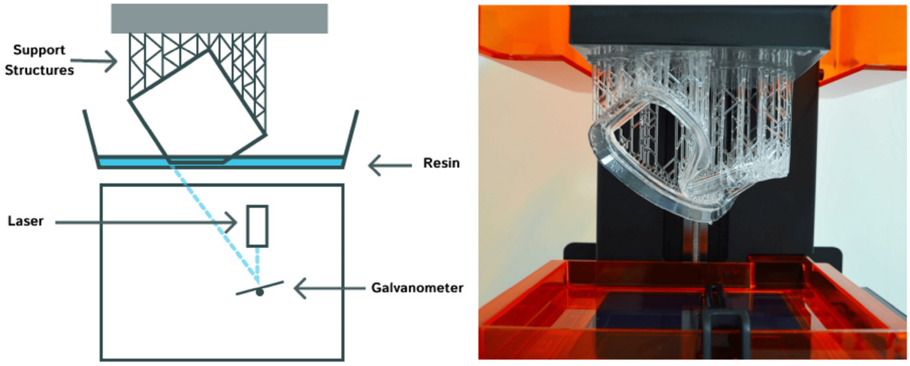

Fig. 5 Diagram illustrating the SLA 3D printing process, along with a sample print; adapted from ref. 24, copyright MDPI.

6.3. Selective laser sintering (SLS)

Support materials are not required for the manufacture of these components.[28] SLS is a 3D printing technique that uses laser energy to selectively heat and fuse powder particles into a solid object. An SLS system includes a spreading platform, powder bed, and laser system (which includes the laser and scanner)[29] (Fig. 7). The powder is evenly spread onto the building platform and processed in layers, with each layer created by predetermined laser scanning elements called vectors. The laser fuses the material at temperatures below its melting point. After each layer is fused, the powder bed lowers, and a new layer is added. This process repeats until the object is fully constructed. Once completed, the object cools in the printer and is extracted from the loose powder.

7. The choice of materials for 4D printing

More accurate and flexible material placement has been made possible by the recent advancements in multi-material 3D printing, which are essential for 4D printing.[30] Plastic, metal, and ceramic materials are frequently used in 3D printing to create 3D objects. Unfortunately, these materials are unsuitable for 4D printing due to their lack of responsiveness to external stimuli. As a result, selecting the right materials is crucial for 4D printing. In 4D printing, two major types of smart materials are used: hydrogels that expand when in contact with water or other solvents and shape memory polymers (SMPs) that respond to external stimuli, like temperature, pH, magnetic field or UV radiation (Table 3).[31]

7.1. Shape memory materials (SMMs)

Shape memory materials can revert to their original shape when stimuli are applied, a phenomenon known as the shape memory effect (SME). Smart materials with the SME can return to their original shape. Researchers have become interested in the transformable features of materials that show SME because these properties allow the building of a structure that can be activated after printing.[32] Shape memory materials are a class of materials that display the smart memory effect, which are divided into shape memory alloys (SMA), shape

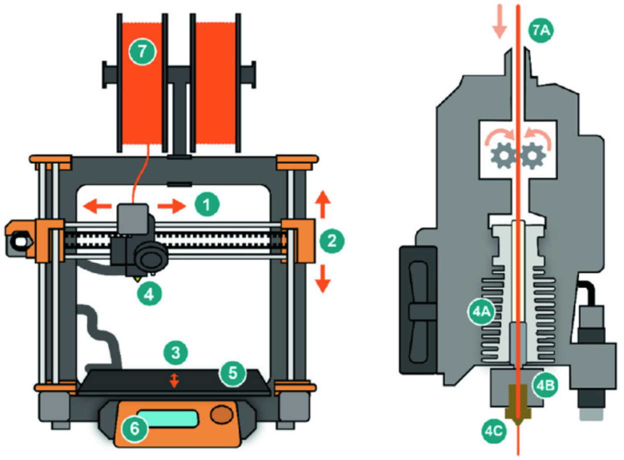

Fig. 6 Schematic of the fused deposition modeling (FDM) 3D printing technology illustrated in two parts. The left image displays the overall structure of a typical FDM printer, with the following parts labeled: (1) *x*-axis motor, (2) *y*-axis motor, (3) *z*-axis motor, (4) hot nozzle, (5) printing bed, (6) controller display board, and (7) filaments. The right image provides a closer view of the printing nozzle, where the components are labeled as follows: (7A) feed filament, (4A) heating wires, (4B) hot end, and (4C) extruded materials; adapted without modification from ref. 24, copyright MDPI.

memory polymers (SMP), shape memory hybrids (SMH), shape memory ceramics (SMC), and shape memory gels (SMG).[3]

Shape-changing materials respond to stimuli, morphing temporarily and returning to their original shape when the stimuli are removed. According to Zhou, the transition is often restricted to simple changes, such as stretching or shrinking, but inhomogeneous expansion can lead to surface topography changes, like buckling, folding, and bending. Shape memory polymers (SMPs) are popular for 4D printing (Table 4). They have a wide range of glass transition temperatures, allowing their stiffness to be tailored. In contrast to SMAs, which can achieve only about 7%–8% of plastic strain, SMPs can exhibit a form recovery property up to 400% of strain. SMPs are advantageous due to their simple manufacturing methods, low costs, and great recovery. When exposed to stimuli, they can revert to their preprogrammed shape from a deformed configuration. SMPs exhibit high elastic deformation, low density, biodegradability and biocompatibility for medical applications.

7.2. Shape memory effect (SME)

The main characteristic of shape memory materials (SMMs) is the ability to recover their programmed shape from a temporary shape. Applying the stimulus causes what is referred to as the shape memory effect. SMMs require a programming process to deform the material into a temporary shape, followed by a shape recovery process triggered by the right stimulus.[34] The rate of shape change from a temporary shape depends on the material's responsiveness and the physical design of the geometrical part.

The shape memory material's network elasticity determines the "memory" of one or more shapes. The majority of SMMs have a one-way shape memory effect, while some have a two-way shape memory effect. Eujin *et al.* explain the one-way shape memory effect as the process where the SMP returns from its temporary shape to the original permanent shape under an applied stimulus.[35] SMP, with a two-way shape memory effect, can remember two different shapes when exposed to stimuli. The material can change from a temporary shape back to its permanent shape, and this change is reversible.

The two-way SME can be found in liquid crystalline elastomers and photo-actuated deformation polymers. Chen *et al.* successfully demonstrated the two-way shape memory behavior using a polymer laminate prepared from a 1.0 mm-thick active layer of PHAG5000 polyurethane-based shape memory with a 1.0 mm-thick substrate of PBAG600-based poly-

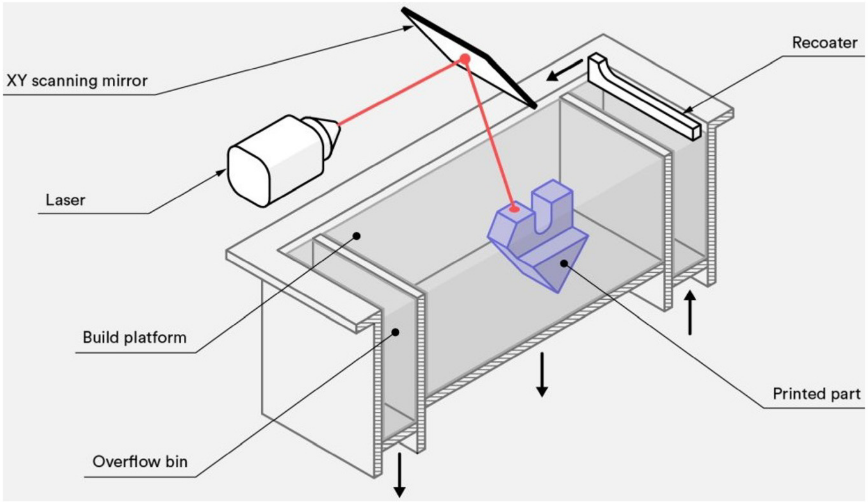

Fig. 7 Diagram of selective laser sintering (SLS) 3D printers; adapted without modification from ref. 24, copyright MDPI.

Table 3 Smart materials and their applications

Function	AM method	Description	Material	Application
Cell shapes	Advanced structured materials	Honeycomb, tetra chiral and hexachiral cells, *etc.*	Polymers, resins, metallic powders, *etc.*	Automotive, aerospace, biomedical, art, *etc.*
Auxetic shapes		Cells that shrink or expand along two directions	Polymers, resins, Ti_6Al_4V powder	Stents, implants
Specific patterns		Reproduce the principal directions of the stress	ABS, PLA	Biomedical
Topological optimization		Distribution of material(s) according to the objective functions	Polymers, resins, metallic powders, *etc.*	New lighter structure
Shape memory	Responsive materials	Multi-materials change shape with external stimuli	NiTi, UV-responsive materials, ceramics, monomers	Aerospace, defence, biomedical, textiles
Self-assembly		Automated folding or molecule aggregations	PCL, TPU, PLA copolymers and nanoparticles	Biomedical
Self-actuating		Automated actuation by external stimuli	Piezoelectric materials, carbon nanostructures	Actuators, sensors, touch screen
Self-evolving		Activation when exposed to water	Viscoelastic ink, acrylamide monomer, nanoclay, glucose, NFC	Robotic behavior
Self-sensing		Automated detection of external stimuli	PLA and graphene, piezoelectric materials, carbon nanostructures	Biomedical, robotics

Table 4 Comparison between SMPs and SMAs[33]

Property	SMP	SMA
Density (g cm^{-3})	0.9–1.2	6–8
Extent of deformation	Up to 800%	<8%
Required stress for deformation (MPa)	1–3	50–200
Stress generated upon recovery (MPa)	1–3	150–300
Transition temperature (°C)	−10 to 100	−10 to 100
Recovery time	>1 s	<1 s
Processing condition	<200 °C; low pressure	>1000 °C; high pressure

urethane.[36] The effect was observed by bending upon heating from 25 to 60 °C and reverse bending upon cooling from 60 to 25 °C.

Erkeçoğlu explained that the main difference between one-way and three-way shape memory effects is that the three-way shape memory effect has one intermediate shape between its original and temporary shapes.[37] A "multiple shape memory effect" occurs when there is more than one intermediate shape. This effect can be achieved either by heating a programmed shape memory polymer to temperatures above its glass transition and then its melting transition or by combining multiple two-way shape memory polymers with different glass transition temperatures.[38] Fig. 8 illustrates the three-way shape memory effect with two distinct thermal transition temperatures: T_{low},1 (70 °C) and T_{low},2 (0 °C). These temperatures are attributed to the presence of two separate crystalline domains in the original shape. Li offered various methods for managing triple-shape memory effects, including blending, grafting, and blocking of copolymers, SMP hybrids, or other polymer laminates.[39]

7.3. Shape memory polymer types

SMPs are gaining interest because of their dynamic behavior stimulated by external stimuli, which helps them change their shape over time in 4D printing. Different types of stimuli, including temperature, moisture, electricity, light, and magnetic fields, are reviewed (Table 5).

7.3.1. Thermo-responsive SMPs. SMPs are the most popular among researchers because of their printing simplicity. Ge *et al.* created an SMP flower that bloomed when heated.[40] This technique is also used to create intelligent grippers that do not require assembly or electromechanical components. The glass transition temperatures (T_g) of SMPs are often higher than their operating temperatures. They are programmed above their glass transition temperatures under specific heat and mechanical treatments, followed by cooling to set them in a temporary form without an external load. When the temperature rises above its T_g, the specimen then reverts to its original, fixed shape.[41]

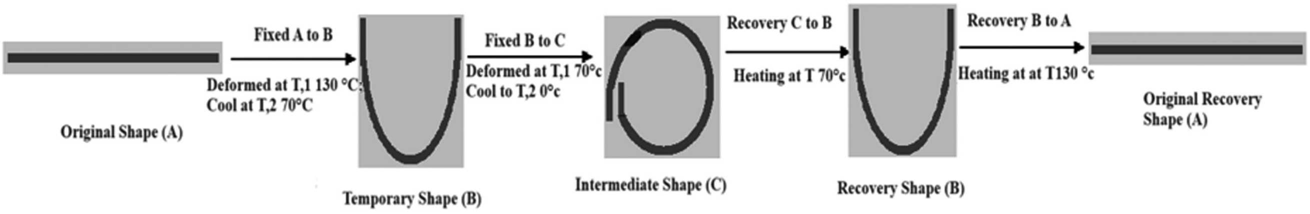

Fig. 8 Three-way shape memory effect.

Table 5 Stimulation methods for 4D printing

Stimulation method	Material type	Theory	Key properties	Advantages	Disadvantages	Applications	Ref.
Water/ humidity/pH	Hydrogel	Swelling/ shrinkage	Swell or shrink in response to water or pH changes	Clean/ convenient	Slow response	Tissue engineering, drug delivery	60 and 61
Temperature	Shape Memory Polymers (SMPs), Liquid Crystal Elastomers (LCEs)	Internal stress inequality	Can "remember" and return to original shape after deformation/ exhibit large reversible shape changes due to molecular alignment (LCE)	Controlled adjustable	Slow response, complicated	Biomedical devices, aerospace components, soft robotics, sensors	62–64
Light	Photo-responsive polymers	Photo-thermal effect	Undergo structural changes when exposed to specific wavelengths	High-resolution/ remote control	Complicated	Optical switches, smart textiles	65–68
Electric field	Electro-responsive materials	Electro-thermal effect		Fast	Operating inconvenience	Adaptive structures, deployable systems	69 and 70
Magnetic field	Magneto-responsive materials	Magnetic drive	Change shape or orientation under magnetic influence	Remote control	Operating inconvenience	Actuators, remote-controlled devices	71–73
Cell traction force (CTF)		Actin binding and interaction		Biological compatibility	Cell traction force is small and hard to control, high design requirement		74 and 75

Wang *et al.* developed a phenomenological model and introduced the theory of phase evolution to characterize the glass transition behavior of SMPs.[42] In a typical shape memory cycle, the SMP sample first changes from its initial shape at a temperature above its transition temperature and then cools to a lower temperature while adhering to external limitations. The stress–strain relationship iterative formats are presented for phase generation and vanishing processes, providing closed-form analytical solutions for shape memory behaviour and effective assistance in 4D printing design using shape memory materials. The model shows promise for expansion into other soft materials with similar phase-evolution characteristics.

7.3.2. **Moisture-responsive.** Hydrogels made of hydrophilic polymeric materials are used in 4D printing because of their ability to swell to volumes up to 200% more than their initial density in response to external stimuli. In addition, the hydrogel group of polymer materials has a high degree of printability. The benefit of using hydrogels is that they are biocompatible and simple to print with direct ink writing.[43] Gladman *et al.* mixed hydrogel ink with cellulose fibrils, which can be aligned by shear pressures brought on by the interface of the ink and print bed.[44] The programming of the 4D-printed structure is made possible by this alignment, which increases the transverse swelling strain to four times that of the longitudinal strain. A film was made using the material, and when the film was exposed to a water gradient, bending deformation occurred as a result of the unequal absorption of water. The broad use of 4D printing technology depends on finding sustainable and affordable solutions to these challenges.

Mulakkal *et al.* created and tested a cellulose-hydrogel composite to demonstrate its suitability for printing responsive structures using four-dimensional printing techniques. The primary emphasis was on a cellulose-hydrogel composite ink for additive manufacturing.[45] When cellulose pulp fibres were combined with a carboxymethyl cellulose hydrocolloid, an ink with a high total cellulose content and good fibre dispersion inside the hydrogel matrix was produced. Villar *et al.* used two picoliters of water droplets combined with a lipid interface at two different osmotic pressures. When the osmotic pressure was high, the droplets expanded, and when it was low, they contracted until the osmotic pressure balanced.[46] However, hydrogels have a significant structural drawback, making them weak and extremely brittle.

In some cases, researchers wait for hydrogels to dry and shrink over an extended period. One solution to this problem is the use of a secondary polymeric network called an interpenetrating polymer network (IPN) hydrogel, which is formed by crosslinking hydrogel polymers.[47] Highly flexible and biodegradable hydrogels with cellular structures are developed by crosslinking sodium alginate with PEG (Fig. 9).[48]

7.3.3. **Photo-responsive.** The exposed surface area of a photo-responsive material absorbs light as heat, making light an indirect stimulus, unlike moisture and heat. Liu *et al.*[37]

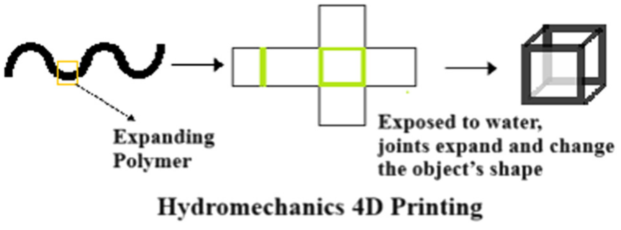

Fig. 9 Hydromechanical 4D printing.[49]

showed a self-folding structure that can be controlled successively.[50] The rate at which the light power is absorbed as heat by the joints is influenced by the colour of the joint and the light source. Owing to its abundant energy source and wireless and controllable features, it is considered a successful activated 4D printing technique.

Kuksenok *et al.* employed light differently as a catalyst for deformation.[51] Light is a typical stimulus that controls polymers through remote induction. A trigger made of various wavelengths of light may alter the polymer form. Since light does not harm cells by raising the material's temperature or causing other physiological changes, this stimulation is appropriate for use in biomedicine and *in vivo* drug administration.

For instance, Luo *et al.* verified that near-infrared rays (NIR) caused shape deformation in an alginate/polydopamine (PDA)-based scaffold. The photothermal agent and room-temperature folding rate of the FDA-approved alginic acid scaffold are both compromised by dehydration.[52] It has the potential to convert the absorbed light into heat, thereby accelerating the dehydration and deformation of the alginic acid scaffold. The intensity and duration of light exposure can be used to modulate the bending of the alginic acid/PDA bilayer. Light is helpful because it can enable high-resolution control in terms of location and time as an external stimulus meant to alter the colour of printed items.

Jeong *et al.* showed how to create SMPs in many colors using a 4D printer.[53] They accomplished a remote drive using light based on colour-dependent selective light absorption and multicolour SMP composite heating. Under red lighting, the thermomechanical programming structure curves into an n-shape.

7.3.4. **Electro-responsive.** Similar to light, an electric field can be used as a stimulus in 4D printing. An electric-field-induced resistive drive introduces a conductive filler into an SMP. Miriyev *et al.* created a soft, printed artificial muscle consisting of silicone elastomer and ethanol.[54] When an electric field is generated, heat is created through resistance, forcing ethanol to evaporate. The volume of ethanol increases significantly when it transitions from liquid to gas, thereby enlarging the entire matrix. A current is applied to polypyrrole membranes to regulate the water absorption or desorption.

Okuzaki *et al.* created a tiny origami robot utilizing the polypyrrole membrane.[55] The feet of this robot have a unique design that makes it less resistant to forward motion. In an electric field, the voltage moves the head forward by absorbing moisture, and the tail rises when the voltage is reduced owing to desorption.

7.3.5. **Magneto-responsive.** Magnetoresponsive materials are used to create 4D-printed objects that react to magnetic fields. When exposed to alternating magnetic fields, shape memory nanocomposites with magnetic nanoparticles, such as iron oxide (Fe_3O_4), exhibit shape-changing effects. Fe_3O_4-based poly (lactic acid)-based SMPs were printed to create scaffolds whose properties change under an alternating magnetic field. These scaffolds can be used as stents in the biomedical field because they expand under alternating magnetic fields. Breger *et al.* integrated magnetic nanoparticles into a micro-clamp that was hydrogel-printed and used a magnetic field to enable remote control.[56]

In Mohr *et al.*'s study, Fe_2O_3 nanoparticle-filled thermoplastic SMP composites were magnetically induced. Heating in an alternating magnetic field can induce the form recovery of SMP composites.[57] Using ferromagnetic nanoparticles combined with AAM-carbomer ink in a Petri dish, Cheng *et al.* created a magnetic hydrogel octopus that could be remotely controlled using a magnetic field and could move freely.[58] The limitation on the print size results from the requirement that it be light enough to be affected by the magnetic field. Bodaghi *et al.* introduced a novel concept for creating bi-stable magnetorheological elastomer (MRE)-based electroactive composite actuators using 4D printing technology. The researchers combined MRE composites with 4D-printed conductive shape memory polymers to develop a functional, lightweight, and bistable composite actuator with programmable magnetic patterns. The actuator is composed of silicone resins loaded with strontium ferrite magnetic particles and a thin conductive carbon black polylactic acid (CPLA) core, which is 4D printed and embedded in the composite.[59] Table 5 and Fig. 10 describe some of the stimuli and their application for 4D printing.

8. Smart design

Apart from utilizing smart materials, one way to create 4D-printed structures is by manipulating the product's design. By adjusting the design and orientation of smart materials, it is feasible to induce specific physical changes in the final product under certain conditions. This was demonstrated by Ge *et al.*, who designed a structure with SMP fibers oriented in a specific manner.[20] When exposed to heat, the printed structure underwent complex shape transformations with curvatures that varied based on the initial orientation of the fibres. Therefore, the combination of smart materials and smart design in 4D printing enables the creation of structures with intricate physical changes.[76] By employing both smart materials and thoughtful design, 4D printing can produce structures that are too complex to be achieved using only 3D printing. Additionally, beginning with a simple morphology in the initial design stage enhances the speed and cost efficiency of the process, while also improving the logistics of storage of such objects. In addition, many of the problems that might arise with 3D printing, such as feedstock blockage and structural collapse before solidification, can be circumvented if 2D structures are printed first. When necessary, the structure can take on the required 3D form to achieve its intended function.

9. Mathematical modeling of 4D printing

Mathematical modelling plays a crucial role in the advancement of 4D printing technology. This allows researchers to

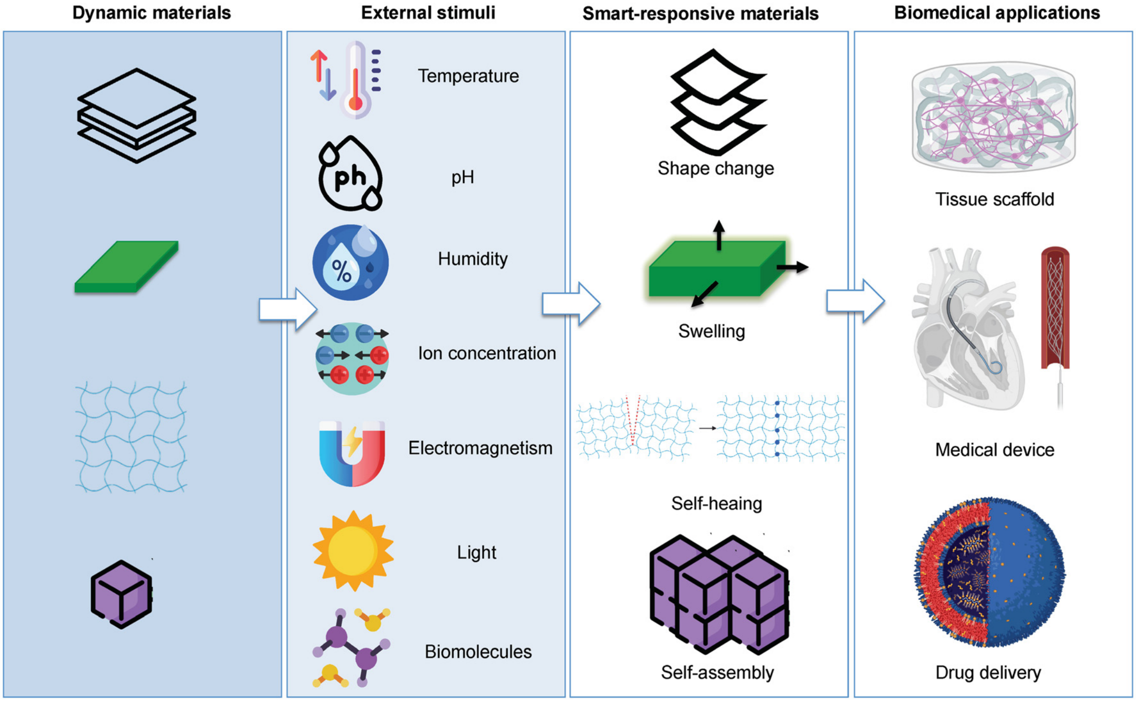

Fig. 10 Schematic depicting the various types of stimuli and the corresponding responses in smart materials, including shape alteration, swelling, self-assembly, and self-repair, highlighting their potential applications in the biomedical sector; adapted without modification from ref. 15, copyright MDPI.

design and optimise complex self-assembling structures. By integrating traditional constitutive models with emerging machine learning techniques, we can enhance our understanding of the behaviour of 4D-printed materials. The 4D printing process relies on mathematical models to achieve various objectives. These include predicting how the shape will change over time, developing theoretical models to avoid collisions during the self-assembly process, and reducing the need for repeated experiments.

By using mathematics and theoretical models, researchers can predict the final shape more accurately, significantly reducing the number of test experiments required. The key components of the theoretical model for 4D printing include the final desired shape, material structure, material properties, and stimulus properties. By using Gladman *et al.*'s categorization, 4D printing mathematics can be divided into the forward problem and the inverse problem.[77] The forward problem involves determining the final desired shape given the material structures, material properties, and stimulus properties. In contrast, the inverse problem entails determining the material structure, print paths, and nozzle sizes given the final desired shape, material properties, and stimulus properties.

Mathematical modelling is crucial for predicting the behavior of 4D-printed structures. There is increasing interest in utilising machine learning-based modelling approaches. These innovative techniques aim to establish structure–property relationships and design-shape transformations of 4D bioprinted constructs.[78]

Additionally, Wang *et al.* studied the mathematics of the single-loop foldable 8R (revolute joint) with multiple modes, which is related to folding.[79] Their work provides valuable mathematical tools for addressing forward and inverse problems in 4D printing processes.

Research was conducted by Purushottam Suryavanshi *et al.* 2025 [80] on novel shape memory-responsive cellulosic composites (RCC) designed for 4D printing, offering self-initiated, reversible shape transformation. By combining experimental, theoretical, and computational approaches, the study refines the material performance for sophisticated biomedical and pharmaceutical uses. This investigation presents RCC composites uniquely blending starch and AffnisolTM. RCC-based filaments were used to print single-layer strips using fused deposition modeling 3D printing technology, demonstrating reversible, contactless shape changes in response to swelling and heat. The programming phase involves swelling and heating the composite strip, followed by shape recovery through heating. Shape deformation during self-activated programming was estimated using experimental, theoretical, and computational methods. The study tested varying thicknesses (1.5, 2.0, and 2.5 mm) and temperatures (25 °C and 37 °C) to confirm the model's effectiveness in predicting the bending curvature. The model showed less than 13.96% discrepancy between the theoretical and experimental modeling, with lower thicknesses achieving less than 2.0% difference. These RCC materials demonstrated potential for reversible 4D printing and aligned with the adopted methodologies for predicting the bending curvature. This study introduces new composite materials for 4D applications, with models for predicting the bending curvature.[80]

10. Application of 4D printing in healthcare

The integration of 4D printing in healthcare has transformed the design and functionality of medical devices. This technology enables materials to maintain a fixed shape, transform and adapt in response to specific biological stimuli over time. As a result, it creates new possibilities for medical applications where adaptability, self-repair, and real-time environmental responses significantly enhance patient care.[16]

These advancements utilise smart materials that react to changes in temperature, humidity, pH, or mechanical stress. This enables the development of patient-specific solutions that can improve the efficiency and longevity of medical devices. With these innovations, 4D printing has the potential to revolutionise healthcare, offering solutions that are more adaptive, efficient, and personalised than ever before.

10.1. Tissue engineering

4D printing is an emerging technology. 4D bioprinting combines the 3D bioprinting process with the time factor, allowing printed medical models to change their shape and functionality. 4D bioprinting requires the realisation of dynamic operations to produce complex and dynamic tissues *in vitro*. The possibility of creating biomimetic blood vessels *in vitro* has undergone a substantial shift due to recent techniques (*e.g.*, 4D printing) to understand blood vessel structure.[81] For example, self-folding polymers can be used to create artificial blood vessels; when exposed to water, these polymers encapsulate various cells and form multilayered tube-like structures. By taking advantage of the self-organization ability of cells, 4D printing may be used to produce vasculature.[82] Vascularization is a crucial problem in tissue engineering that must be solved since there is an immediate need for functioning tissues.[83,84] A promising solution to this problem is 4D bioprinting. The cells mixed with the hydrogels can be bioprinted layer-by-layer to form cylinder-shaped structures imitating the vasculature.[85] Vascular cells can then quickly achieve maturity after stimulation by maturation factors, leading to vascularisation. Biocompatibility and biodegradability are essential to prevent the body from rejecting the materials, and mechanical strength is also necessary to support cell growth.[86] Although this method has been used with both synthetic and natural polymers, with several reported results, the complexity involved, such as growing organs in a lab, requires the use of different fabrication processes.

An alternative approach is the cell traction force, which generates vasculature through residual stress and elastic modulus. A different technique allows for self-folding by a tangential tension produced by the cells on the extracellular matrix components (EMC) or underlying layer.[87] Through the cell traction force, the 2D patterned microplates roll up in the diagonal direction. By adjusting the angle of the diagonal lines, the diameter of the tubes can be adjusted. Bovine carotid artery endothelial cells (EC) and regular HUVECs have been employed to create cylindrical tubes resembling vascular structures.[88]

Recent studies have demonstrated the shape memory scaffolds' potential for use in the minimally invasive delivery of functioning tissues.[89] Shape-memory scaffolds can regulate the transmission process remotely and accurately using bioelectronics and biodegradation machines.[90] Different studies have shown that bioscaffolds can fully recover to their initial state at the normal human body temperature and have a high capacity for cell adhesion and development. Miao *et al.* employed this technique to fix a novel renewable soybean oil epoxy acrylate on a biomaterial to stimulate the development of bone marrow mesenchymal stem cells.[91] To potentially repair peripheral nerve injury, a programmable nerve-guiding conduit was created using stereolithographic 4D bioprinting. Some stimuli, such as high temperatures and extreme pH, should be avoided during tissue engineering when living cells are involved.[92] The use of 4D printing for tissue engineering is currently in the proof-of-concept study stage, and there is still a long way to go before this method is widely used in clinical practice.

10.2 Stent

The medical process known as angiography involves inserting the proper materials into the arteries to identify any blocked spots.[93] Using the body heat of the patient as a stimulus, 4D printing can create stents that can expand and assume the desired shape. During angioplasty, guidewires are used to open blocked arteries. Guidewires direct this medium, which is fed through a catheter, to its intended location. Initially, stainless-steel guidewires were used in this procedure. However, directing these guidewires inside the human body is challenging because of their propensity for distortion and bending. These days, many nitinol guidewires are employed for this purpose because of their great flexibility and good kink resistance.[94] The exceptional flexibility and elasticity of nitinol enable it to move without deformation through various intricate pathways in blood arteries. Nitinol is biocompatible because it forms a passive titanium oxide coating that shields it from corrosion and reduces its susceptibility to chemical breakdown.[95]

The primary function of a stent is to sustain a hollow structure. For instance, stents unblock or widen arteries affected by coronary artery disease. In the past, stents had to be surgically implanted into patients' bodies after being manufactured, considerably increasing the safety risk. Scaffolds are now being produced using smaller stimuli-responsive materials thanks to the development of 4D bioprinting.[96] The danger of surgery is significantly reduced after transplantation because the stent will naturally conform to the right size and shape with the right stimulation. Ionov *et al.* created a self-folding stent with a hollow structure using 4D printing and a hydrogel, which has a minimum diameter of 20 μm. The polymer may experience a reversible shape change when the Ca^{2+} ion concentration changes.[97] The cell survival rate of stents manufactured from these biocompatible hydrogels is comparatively high.

There are various steps in the fabrication of stents due to their complex and patient-specific geometries.[98] Using 4D printing, customised stents can be fabricated quickly. To further reduce the surgical invasion of the implantation site, the stent can be "shape memory" printed at the final diameter and then "programmed" to a lower diameter for easier and more precise insertion. The stent will shrink to its original diameter at body temperature after being implanted.[99] For use in minimally invasive surgeries, Ge *et al.* created a shape memory stent that was printed in a high resolution.[40] First, the temporary shape of the stent can be sustained at a small diameter. The diameter of the blood vessel can be increased by implanting the stent, and the stent can transform back into its original form when heated. Liao *et al.* used 4D bioprinting to create an adaptable structure.[100] When the temperature changes, the structure can expand and shrink. Vascular stenosis is typically treated using stents. The trachea is a more common intraluminal feature. The presence of the illness causes the trachea to narrow or collapse. Cohn *et al.* used shape memory thermosetting polymers to create the heat-driven lumen device.[101] The device can be transformed into a tracheal stent as the temperature increases. The outline of the SMP structure can be minimised by custom design, thereby reducing the harm to the human body.

The advancement of 4D-printed smart stents holds significant promise, especially in the realm of vascular structures, where their ability to adapt can greatly enhance therapeutic outcomes. By employing shape memory alloys or hydrogel-based composites that react to temperature changes, these stents can be engineered to fit the vessel's dimensions more accurately once they are in place. This level of adaptability allows for improved patient-specific customization during stent placement and the optimization of mechanical force exerted on the vessel wall, thereby minimizing the risk of further injury or excessive tissue damage. Additionally, smart stents that can adjust to other biological factors, such as variations in pH levels due to localized inflammation or tissue healing, could reduce the necessity for additional procedures or interventions. 4D-printed smart stents can improve patient outcomes through personalized medicine customized to individual conditions. This approach is expected to reduce stent failures and enhance treatment effectiveness for cardiovascular and vascular conditions.

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4D bioprinting has enabled the creation of smart stents in a novel manner. The need for 4D bioprinted stents in the medical field will increase in the future. Improvements in biocompatibility and adjustments to human biological characteristics remain challenging in this area.

10.3. Microfluidics

Microfluidics has numerous uses in biomolecular, biodefence, cell analysis, high-throughput screening, DNA chip technology, diagnosis, and treatment.[102,103] Low power consumption, low cost, and unrestricted miniaturisation are required for the operation and management of microfluidic devices. Some micro and smart components can fulfil these requirements. As a result, the use of soft and stimulus-responsive hydrogels in microfluidic devices represents a promising future development.[104] It can precisely control the fluid by changing its shape in response to external stimuli. For instance, D'eramo *et al.* developed 2 μm horizontally resolved microfluidic actuators using poly(*N*-isopropyl acrylamide) hydrogel columns.[105] Elevating the hydrogel system temperature above the lower critical solution temperature can create up to 7800 microcages in 0.6 s. To regulate microfluidics, Beebe *et al.* created a pH-responsive smart hydrogel actuator.[106] They created several pH-responsive hydrogel forms using photolithography, and the reaction time required was less than 10 s. According to their chemical components, each hydrogel gate reacts to a certain pH value and then automatically identifies the fluid. By *in situ* γ-irradiation, Zhu *et al.* created poly(*N*-isopropyl acrylamide)/graphene oxide (PNIPAM/GO) nanocomposite hydrogels that are photothermally sensitive and exhibit excellent photothermal characteristics.[107] Using a near-infrared (NIR) laser, the phase transitions can be remotely managed, and through laser exposure or non-exposure, they can be fully reversed.

10.4. Drug delivery

With characteristics like excellent biocompatibility and flexibility, hydrogels are often employed in biomedical applications.[108] It is still quite difficult to accurately release medicine at lesion sites. The release of medications at the site of action based on changes in the environment and under controlled circumstances is referred to as the "ideal drug-delivery system". Researchers are currently aiming to achieve this. Structures that can regulate the rate and localisation of drug release can be produced *via* 4D printing. Hongyan *et al.* developed a self-folding polymeric bilayer hydrogel for drug encapsulation and therapeutic release. One layer is the pH-sensitive swelling layer, which is made of crosslinked poly(methacrylic acid) (PMAA), and the other is the mucoadhesive layer (non-swelling layer), which is made of poly(hydroxyethyl methacrylate) (PHEMA). The hydrogel can self-fold into mucus due to the swelling of PMAA, and it also facilitates mucoadhesion due to the presence of PHEMA.[109] The PHEMA layer helps minimise drug leakage in the intestine, which acts as a diffusion wall. Using a bilayer structure, acid orange 8 and bovine serum albumin were encapsulated in a hydrogel for unidirectional drug release in the mucosal epithelium. A novel technique was put out by Dai *et al.*, which employed thermally sensitive double network hydrogel (pluronic F127 diacrylic macromolecule and poly(lactide-*co*-glycolide))-based shape memory when exposed to near-infrared light.[110]

By integrating graphene oxide (GO) into the hydrogels, the shape memory characteristics were improved, and the mechanical properties were improved by the inclusion of PLGA, which acted as a second network. The folded hydrogel must be exposed to NIR light for 300 s to completely transform back into its original shape. The key element affecting the drug release rate is the surface area created by the change in the shape of the structure. Consequently, the surface area decreases, and the drug release rate decreases when the temporary form is altered. Larush *et al.* developed a drug-release device using Digital Light Processing (DLP) technology, which releases medications in response to pH and shape-dependent swelling.[111] 3D printing technology improves conventional solid dosage forms by enabling control over drug release through adjustments in pH and surface area. The responsiveness of the printed object plays a significant role in drug release and can potentially change the systemic pH to facilitate drug release at a particular site in the gastrointestinal tract. Based on 4D bioprinting, Akbari *et al.* created a directly activated drug-delivery system. They began by printing various porous sensors, primarily composed of alginate fibres and pH-responsive substances. Alginate fibers that had been loaded with gentamicin were used to print the drug-eluting stent concurrently.[112] The procedure for working is as follows: if the sensor detects a shift in pH, the drug-eluting stent may deliver the medication to the site of the shift, eliminating any microbes. Researchers must have a particular knowledge base in medicinal chemistry, pathology, and bioengineering technology to create an effective drug-delivery system.

The transition points of SME in thermoresponsive materials can be adjusted to match physiological temperatures for targeted drug release. Porous polymers, with their lightweight and extensive surface area, serve as effective drug carriers. Moisture-responsive polymers activated by bodily fluids offer another research direction. Hydrogels can encapsulate drugs, antibodies, and biological elements for drug delivery.[113] Vehse *et al.* developed PEGDA scaffolds using microstereolithography, incorporating acetylsalicylic acid before printing.[114] The drug remained stable under UV light, but the polymer chain network was disrupted, reducing the structure's compressive strength. Gioumouxouzis *et al.*[12] identified PLA, PVA, and polyacrylics as suitable biocompatible shape-memory polymers for drug-delivery systems.[115]

10.5. Splints

For biomedical devices, splints are a crucial component because the device's fit on the subject is necessary for the device's proper functioning. Traditional biomedical devices, especially when large, are often unable to adapt to a subject's growth over time. 4D printing can accommodate shape changes based on the subject's growth. In several infant patients with tracheobronchomegaly (TBM), Morrison *et al.* successfully implanted 4D-printed external airway splints during surgery.[116] TBM is a life-threatening disorder that causes excessive collapse of the patient's airway during breathing. The splint is designed to fit the expansion of the airway, preventing uncontrolled compression. Miao *et al.* 4D-printed (using stereolithography) a nerve guidance conduit (NGC) that performed a variety of responsibilities for the regeneration of nerve tissue, utilising a natural photocrosslinking monomer (soybean oil epoxidised acrylate, SOEA). Due to the NGC's shape memory property, it is easy to readjust (through thermal stimulation) it during implantation.[91]

10.6. Minimal invasive surgeries

4D printed structures are desirable for personalised medical devices because of their shape-memory characteristics. Printed surgical implants would enable minimally invasive procedures and speed up patient recovery because they can be deformed into a small temporary shape before being implanted into the body to function in an unreachable area.[117] 4D printed structures can be locally activated by a patient's body fluid, pH, or temperature or triggered by external stimuli (*e.g.* magnetic power or electric charge). Kashyap *et al.* printed radio-opaque and porous semi-crystalline thermoplastic shape memory polyurethane (SMPU) for use in endovascular embolization (EE).[118] EE is an invasive surgical procedure for treating abnormal blood vessels in the brain and other body parts by blocking blood flow.[119]

To realize the full potential of the technique, more research into the biomedical uses of porous SMP-printed scaffolds is necessary.[11] Porous SMP foams have better advantages in this industry due to their larger volumetric extension, lightweight, and higher surface area compared to conventional solid SMPs. According to Miao *et al.*, indirect doping materials can be used to design thermo-responsive SMPs that react to the physiological temperature (≈37 °C).[91] Yang *et al.* invented a surgical procedure for improved conduit implantation that involves momentarily opening and closing the initially closed conduit.[97]

Implementing 4D printing may reduce the risk of difficult surgeries because minimally invasive implantable devices have smaller incisions and faster recovery times. The overall improvement in operation and surgical complications would enhance the patient experience in general.

10.7. AI-based 4D printing

AI-driven 4D printing presents an innovative solution to the complex challenges associated with modeling and controlling 4D-printed robots. As these robots become increasingly sophisticated and capable, the demand for advanced tools to manage their complexity grows. AI techniques have emerged as promising strategies to tackle these challenges.[120]

AI technologies are employed to train models using labeled data to predict robot performance and enable these robots to develop optimal control strategies through interaction with their environments (Fig. 11). The challenges inherent in 4D printing include highly nonlinear and time-variant dynamics, morphing hysteresis, and the multi-domain nature of 4D-printed robots.

Supervised learning, a branch of AI, is utilized to model the intricate dynamics of 4D printing, thereby reducing the need for extensive physics analyses.[15] Reinforcement learning is particularly well-suited for closed-loop control tasks, facilitating autonomous policy training and online learning to accommodate time-variant properties. Additionally, some research focuses on leveraging AI to fine-tune parameters in controller development.

11. Challenges of 4D printing

The future of 4D printing is promising, but there are challenges related to materials, design, and technology. One significant challenge is the limited availability of suitable AM printing technologies for 4D printing. The current technologies have drawbacks, such as high equipment costs and limited material choices. Additional research is needed to address these challenges and improve the performance of 4D printing (Fig. 12).[121]

Innovative structures must have the ability to dynamically adjust to the environment and the ability to sense and respond to environmental variations.[122] For example, soft robots require membranes that can deform before the actuator operates, but current design and 3D-printing technologies do not directly support this. More research on smart structure design is needed to address these challenges and advance 4D printing, which has the potential to revolutionize production rates in many industries.

Some of the problems with 4D printing include a lack of material for certain uses, delayed actuation, and inaccurate control during the intermediate deformation stages. To further enhance the adaptability and practicality of 4D printing, future research should investigate dependable supplementary approaches for applying stimuli and comprehending the effects of structural patterns and restorations.[123,124]

4D printing has many problems, such as its inability to handle complicated things, the lack of printers that can print with several materials, high cost, long printing time, and limited dependability. Stimuli-responsive materials are restricted to specific environmental conditions, leading to varied response times and limited size and accuracy in the spatial manipulation of 4D-printed structures. Therefore, new, easily tunable materials must be developed for better adaptability to complex microenvironments.

The challenges of advanced simulation and topological transformation in manufacturing, as well as material constraints, are addressed using 4D-printing software. Chung *et al.* examined various 4D-printing software. They analysed the limitations of six software programs designed to fully accommodate the key stages of the 4D printing process.[125] These software solutions are designed to perform specific functions at each stage of the 4D printing process, collectively providing all the necessary operations for 4D printing. Commercial software and mathematical models are currently used, but further development is needed to cater to all responsive materials for 4D-printing applications. Additionally, hardware and software development must consider ease of operation and multitasking features.

To advance 4D printing innovation, rational computer design of stimuli-responsive processes is essential for fabricating complex objects in self-transformation, robotics, and bioengineering applications.[126] Minimal activation of mechanical deformation occurs in stimuli-responsive materials through heat and swelling. Cui *et al.* emphasized the integration of nanomaterials into stimuli-responsive polymers to achieve dynamic and remote-controlled shape transformations.[127]

It is also crucial to evaluate and address the ethical dimensions of 4D printing in healthcare, particularly with regard to personalized medicine. Dynamic, adaptive technologies

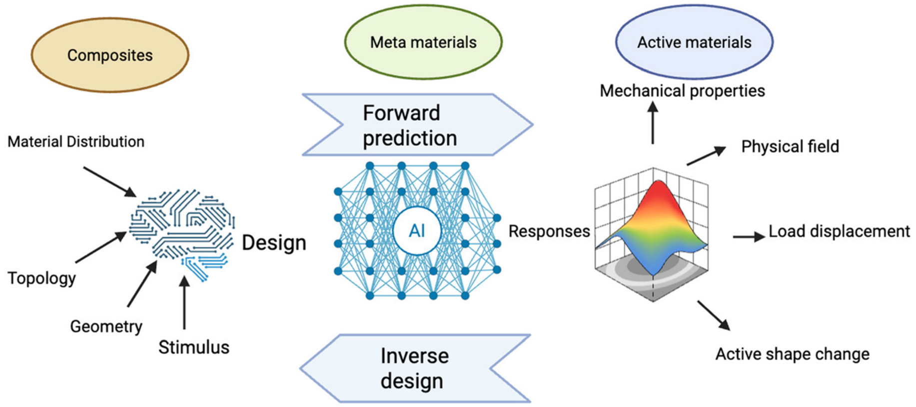

Fig. 11 Analysis of forward and inverse challenges in 3D/4D printing with machine learning and artificial intelligence.

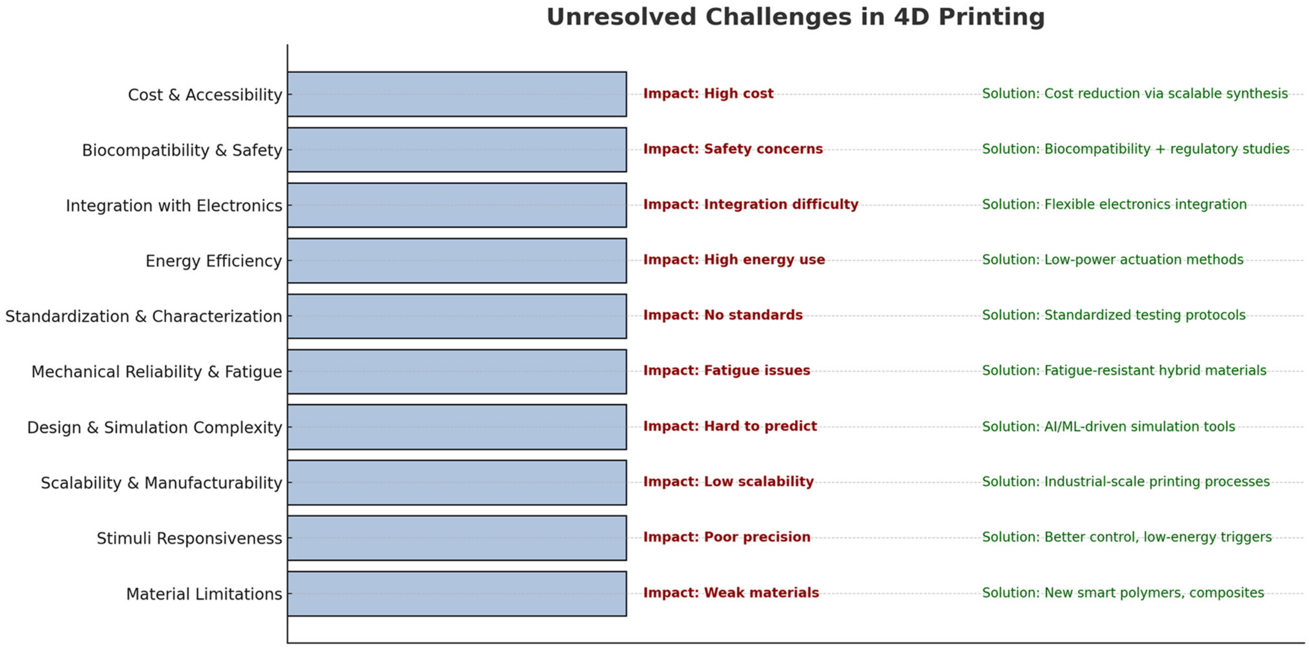

Fig. 12 Possible solutions to the problems that have so far plagued 4D printing.

require robust informed consent procedures, ensuring that patients fully understand potential risks and long-term effects. Furthermore, equitable access to these advanced medical solutions must be prioritized, with policies designed to promote both affordability and widespread availability.

By developing new standards, fostering cross-disciplinary collaboration, and implementing pilot programs, regulatory bodies and stakeholders can create practical pathways for the safe integration of 4D-printed medical devices in clinical practice, ultimately benefiting patients through increased innovation and customization.

12. Future prospective of 4D printing

Future work will focus on realising 4D-printed parts that eliminate the need for mechanical load. New 4D-printing software is required for different types of 4D-printing techniques. There is a need to develop highly customizable materials that undergo appropriate deformation in response to various external stimuli.[128,129] The form of printed components is one area where 4D printing trends may shift as the technology evolves. The use of SMPs raises the bar for what can be done to make current 3D printers compliant. The reversible shape-changing effect of a multi-material layered composite has been investigated recently. The materials used in this composite exhibit diverse responses to stimuli, enabling the composite to transition between stable and rigid forms without mechanical stress. The design includes a hydrogel, elastomers, and a layer of thermoresponsive SMP.

Bingcong Jian *et al.* discussed the future applications of two-photon polymerisation (TPP)-based 4D printing. TPP can be utilised in biomedical microrobots, and future applications may involve more advanced targeted drug-delivery systems capable of navigating complex biological environments to release medications with unprecedented precision. The ability to create intricate 3D structures at the micro-and nanoscale could lead to significant advancements in tissue engineering, potentially allowing for the development of complex, functional tissue structures at the cellular level. Additionally, the shape-changing capabilities of 4D-printed structures could be further developed to create self-repairing materials on the micro and nanoscale.[130]

Other novel works involve parts capable of self-assembly and disassembly, such as a multi-polymer 3D-printed trestle design with four equal, active composite strips connected to the centre. SMPs come in various types, each with distinct transformation temperatures, moduli, biocompatibility, and quality, making them suitable for diverse applications. The development of new materials can lead to innovations in printing technologies, deformation behaviours, and constitutive models.[131] The additive manufacturing industry is still growing, and the ongoing exploration of new materials and techniques has led to significant advancements in 4D printing.[132] This new technology provides feasible manufacturing processes for small-scale structures.

4D-printed products have potential applications in the human body, such as wearable sensors, artificial muscles, and implantable biomedical devices.[133–135] The 4D printing market has witnessed the development of new eco-friendly products and partnerships that promote efficient resource use and sustainable consumption. Future research should explore the generation, storage, and use of passive, abundant energy sources to activate shape memory or stimuli-responsive materials.

Regulatory challenges present substantial hurdles to the advancement and adoption of 4D-printed medical devices, largely because existing approval frameworks do not account for the unique qualities of these technologies. Unlike conventional devices, which are static and unchanging after placement, 4D-printed devices are engineered with materials that can actively transform in response to environmental cues. For example, material transformation properties refer to the ability of certain materials to change shape, structure, or function when stimulated by factors, such as temperature, pH levels, or moisture, within the body. These dynamic characteristics mean that a 4D-printed stent—such as one designed to expand in response to body heat—does not behave like a traditional stent. Its adaptive nature complicates standard safety assessments, which typically rely on predictable, fixed device performance.

Current regulatory systems, including the FDA and European Medicines Agency (EMA), are tailored to evaluate static devices and lack protocols for assessing devices whose form and function may shift after implantation. This gap introduces complexity in determining the long-term safety and efficacy of 4D-printed devices. Regulatory bodies must therefore develop new standards that specifically address the unique behaviors of materials used in 4D printing. This includes creating testing protocols that account for material transformation properties, ensuring that devices remain safe and effective as they adapt over time within the human body.

The approval process is further complicated by limited long-term data for these innovative materials and by the unpredictable ways they may interact with biological systems. For instance, the performance of a temperature-responsive stent may vary depending on individual patient physiology, making it challenging to establish universal safety benchmarks. The personalized nature of 4D-printed devices also raises issues for standardization and mass approval, as each device may be tailored to the needs of a specific patient.

To address these challenges, regulatory agencies should consider launching pilot programs that enable controlled clinical testing of adaptive devices. These programs would generate valuable data on device performance and inform future approval processes. Additionally, agencies could form interdisciplinary committees composed of engineers, clinicians, regulatory experts, and patient advocates. These groups would be tasked with drafting preliminary guidelines and standards for the safe approval and monitoring of 4D-printed medical devices.

13. Conclusion

With the progression of additive manufacturing technologies and the expansion of our understanding of smart materials, accessible stimuli, mathematical modelling, and geometric programming, researchers have begun to investigate the potential of 4D printing as a new technology. This article offers a general introduction to 4D printing, touching on topics such as technology, design, and materials that should be considered when creating 4D-printing components. The use of smart materials for 4D printing has opened up new potential applications for this technology. Additional research is necessary before 4D printing can be considered a commercially viable option. One example is the requirement for computer-aided design software to integrate multi-scale physics simulations with the ability to visualise smart material attributes. The repeatability and appropriateness of the spacing between the voxels that represent the materials depend on the reliability of the fabrication equipment. Finally, new metrology equipment or other forms of measurement may need to be developed to ensure part quality. Further research is needed to ascertain commercial viability, including on computer-aided design, fabrication systems, and metrology equipment.

Conflicts of interest

All authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors. Thus, no informed consent is applicable in this work.

Abbreviations

1D	1-Dimension
2D	2-Dimension
3D	3-Dimension
4D	4-Dimension
AM	Additive manufacturing
CAD	Computer-aided design
EA	Finite element analysis
ABS plastic	Acrylonitrile butadiene styrene
TPU	Thermal polyurethane
SLA	Stereolithography
LOM	Laminated object manufacturing
WAAM	Wire and arc additive manufacturing
FDM	Fused deposition modeling
SLS	Selective laser sintering
SLM	Selective laser melting
LMD	Laser metal deposition
PLA	Polylactic acid
Ti_6Al_4V powder	Titanium aluminum vanadium
NiTi	Nickel titanium
PCL	Poly(ε-caprolactone)
NFC	Nuclear fuel complex
SMA	Shape memory alloys
SMP	Shape memory polymers
SMH	Shape memory hybrids
SMC	Shape memory ceramics
SMG	Shape memory gels

SMMs	Shape memory materials
SME	Shape memory effect
IPN	Interpenetrating polymer network
PEG	Polyethylene glycol
NIR	Near infrared rays
PDA	Polydopamine
EMC	Extracellular matrix components
HUVEC	Human umbilical vein endothelial cells
PMAA	Poly(methacrylic acid)
PHEMA	Poly(hydroxyethyl methacrylate)
DLP	Digital light processing
TBM	Tracheobronchomegaly
SMPU	Shape memory polyurethane
EE	Endovascular embolization
NGC	Nerve guidance conduit
SOEA	Soybean oil epoxidized acrylate
MRE	Magnetorheological elastomer

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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