4D printing: Pragmatic progression in biofabrication

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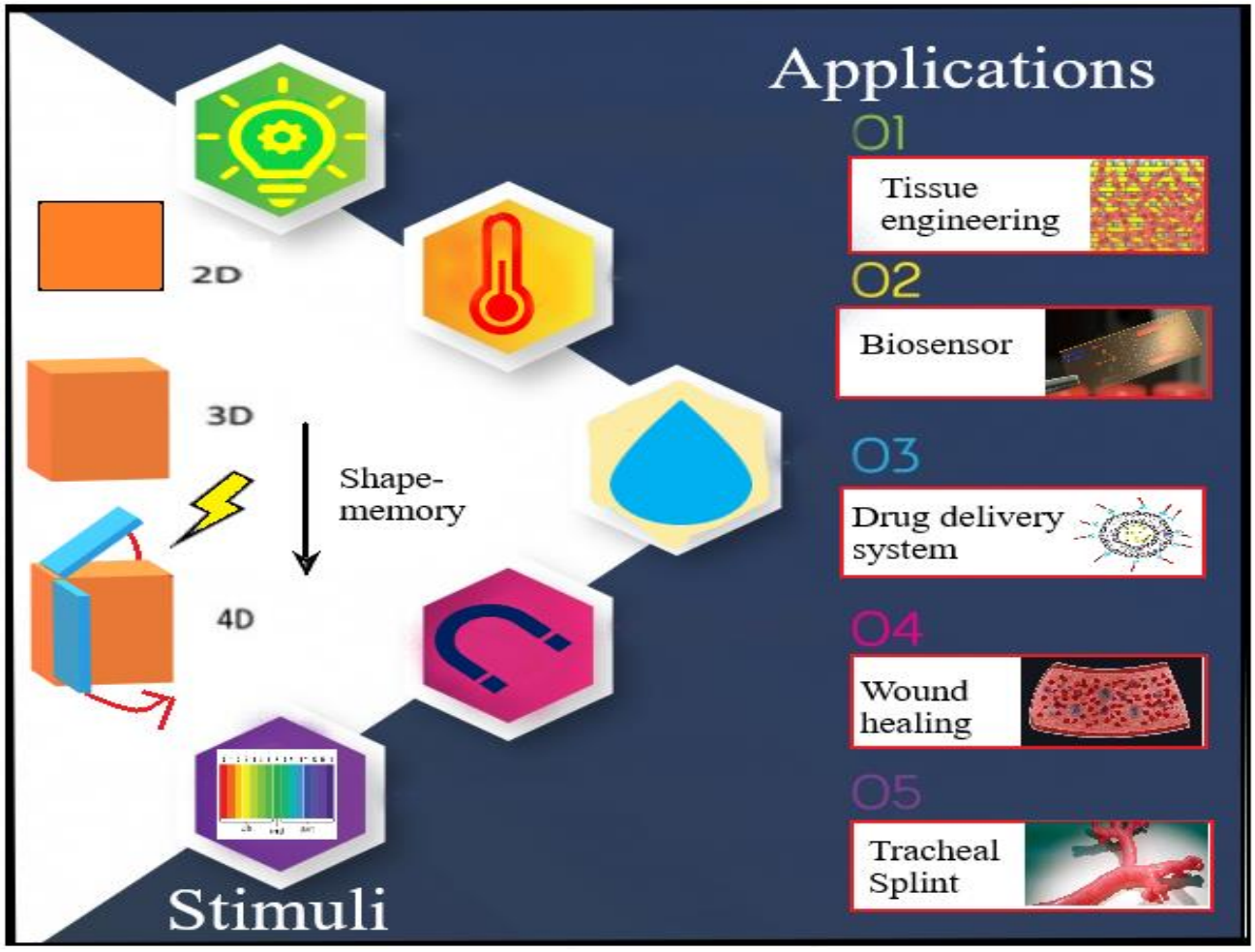
Graphical abstract



Abstract

Progress in three-dimensional (3D) printing of shape memory polymers (SMPs) has produced dynamic and 3D-printed assemblies that can be shaped fast and modified for specific and multifaceted designs. This potential has made 3D printing a popular fabrication method for future SMP parts and devices. Technology, biochemistry, medicine, computer science and biomaterials are among the areas of specialization, where 3D and four-dimensional (4D) printing techniques have penetrated to herald the next generation of manufacturing processes. Through layer-by-layer addition of diverse materials, 3D printing allows intricate assemblies with high precision. Two-dimensional (2D) cell philosophical function for drug transmission and biomedical procedure studies have many defects. In today's additive manufacturing (AM), 4D printing encapsulates additional magnitude, which is time. Intelligent materials that deform or change color emit an electrical current that becomes bioactive or performs a specific function in response to an external stimulus overlay to manufacture dynamic 3D structures, through a technique known as 4D printing. With this new dimension, 3D-printed substances can alter their form by themselves, conclude the impact of peripheral stimuli, such as light, heat, electricity and magnetic field, among others. For instance, the cartilage healing and physiological maturation techniques promote bone marrow to differentiate into osteoblasts. Furthermore, 3D and 4D printing procedures have much potential for biomedical applications. SMPs have also been developed as tools and stages for biomedical study. Summarily, this study focuses on a systematic compendious review of 3D and 4D printing techniques and their implications in biomedical techniques. Specific technologies intend to focus on such intelligent materials, and therefore it is essential to modernize the current voxel-based analysis, design methodology and explore effective printable technologies for fabricating organic components. It appears to be efficient in several fields, as it relies on

biomaterials rather than electricity and completely transforms the way smart products are manufacture.

Keywords: 3D/4D printing; shape memory polymers (SMPs); biomedical; stimuli; intelligent material; additive manufacturing (AM); biomaterial.

1. Introduction

Several transcription factors, an extracellular matrix (ECM) and diversity of signaling components compensate for interconnected cells, which are strenuous edifices. Hull [1] initially identified three printing dimensions in early 1986, and it gained attention in the regenerative medicine and medicinal sectors [2-4]. For example, three-dimensional (3D) printing, often identified as additive manufacturing (AM), is used in tissue regeneration to generate scaffolds that can restore or substitute injured interconnected cells and body parts. This procedure is accepted, because it offers personalized health services by printing precise organic products based on individual information [5-7]. Nevertheless, 3D bioprinting has a fundamental disadvantage in that it only considers the starting state of imprinted object, which beliefs to be unresponsive and static.

Subsequently, organic angiogenesis entails 3D structures, microarchitectures and ECM and interconnected cells with distinct functionalities produced by variable cell modifications. By diminish the limitation, bio-materials should respond to the new biological conditions throughout the duration. As a result, four-dimensional (4D) printing has been developed, as a workable solution.

The Tibbits group at the Massachusetts Institute of Technology (MIT) introduced and described four dimensions of printing in 2013 [8]. The related polymers, 3D printers, stimulation technique,

rules for inventive creation and implementations are extensively studied and explored. 4D bioprinting compounds, also designated as active origami or shape-morphing systems, use similar method of 3D printing to create structures by layering biopolymer. In particular, 4D bioprinting introduces new dimensions of change in response to external stimuli. It introduces the fourth dimension to the 3D component, enabling the structure, characteristic or performance to evolve across time [9]. The 3D-printed inert component can be changed further into a deterministic configuration by applying stimuli, such as light, moisture levels, pH, dissolvable, magnetic, electrical conductivity and strength. As a result, 4D printing is progressively premeditated to address challenges of research and used in various biological disciplines [10]. Additionally, by regulating the cross-linking or refabrication of stimuli-responsive compounds, the machine-driven characteristics of 4D-printed structures can be altered.

Programmable 4D printing is already changing lives. The functions and characteristics of components, responses to environmental stimulation, and their biochemistry of receptor binding are systematically reviewed and reported in this study. The 3D-printed tissues and organs of the nearest future should be able to work in the body following transplantation, as must other printed structures without cells, such as prosthetics or biomedical implants. This solution has been initiated through application of 4D printing technique.

Furthermore, the biological implications of 4D printing technique, including the ability of 4D-printed structures to self-transform and self-maturate, would open up new possibilities for producing particular transplants with time-dependent advance performance. That would have significant benefits in the action of patients with inherited malformations and could be summarized based on the resources, printing type, stimulations and distortion form. 4D printing has provided

alternative to many conventional techniques. 4D printing needs technical advancements in various disciplines in the long term, involving software, modeling, kinematics and biochemistry.

Therefore, this compendious review considers functions, polymer properties, the need to respond to external stimuli and polymer reactivity. Printability and spontaneous shape-memory in retort to an exterior stimulus are the two vital standards of a 4D printing of smart materials. Biocompatibility is an additional significant feature for biomedical applications, and further significant criteria can take superiority reliant on the printing procedure used and the envisioned conclusive usage. In addition, the biological applications of 4D printing, including wound healing, biosensors, drug delivery system and tissue regeneration. They are studied and summarized within this report based on the materials, printing type, stimuli response and type of deformation type. Importantly, the present limits are specified to provide a base for this significant study.

Table 1 Application and estimates of 4D printing of shape memory polymers (SMPs) in biomedical field (Permission from (ref.no.20) copyright (2020) Springer link).

Biomedical application prospects	Material	Printing method	T_g
Cell scaffold	SOEA	SLA	~20°C
	Shape memory TPU	FDM	~32°C
	Castor oil/polycaprolactone triol/hexamethylene diisocyanate thermosetting SMP system	FDM	–8°C–35°C
	PU	DIW	25°C–37°C
	Nano-fibrillated cellulose reinforced SOEA	SLA	20°C
Vascular stent	α,ω-polytetrahydrofuranether-diacrylate	SLA	38°C
	SMP system after PLA/BP/Fe_3O_4 cross-linking	DW	66°C
	Polyurethane diacrylate and semi-crystalline polymer	DW	1.5°C
	PLA	FDM	65°C
	pNIPAM and pAAM	DIW	35°C
	PLMC	DIW	37.8°C–50°C
Bone scaffold	Thermoplastic HA/PLA shape memory composite	FDM	57.1°C
	PLA filaments and PLA/Fe_3O_4 filaments	FDM	~40°C
Tracheal stent	PCL	SLA	–
	Methacrylated polycaprolactone	SLA	37°C
Occlusion devices	PLA/Fe_3O_4	FDM	65°C–67°C
Medical equipment	Polyurethane diacrylate and semi-crystalline polymer	DW	1.5°C
	TAIC/PLA radiation cross-linking SMP	FDM	60°C–65°C
	Photocuring methacrylate	–	~82°C

2 4D Fabrication

2.1. From 3D to 4D Fabrication. In the early 1990s, the advent of AM was technologically advanced to enhance researchers to investigate and produce several forms of SMPs. Stereolithography (SLA), inkjet head 3D, powder bed and fused deposition modeling (FDM) printing are well known four primary printing procedures recognized in the studies. Based on the technique of 4D printing, the printed component exhibits a self-assembly process prior to 3D printing stage. The self-assembly implies formation of a pre-existing product with response dynamism vicissitudes to another configuration as a sign of peripheral stimulation. Thus, the 4D-printed structures can adapt to the natural morphologies of regions, alter through periods and under diverse stimuli, enabling novel techniques for articular cartilage creation.

Moving forward, with the idea of 4D printing, water-sensitive 4D designs are created, imprinted using two different polymers with varying moisture absorption capabilities [8]. A moisture layer is imprinted on one side, while a strong water resistance is on the other. The amount of the liquid substance rises slightly approximately 160%, once the produced component is submerged. Nevertheless, the hydrophobic compound persists. The superstructure crumples towards the rigid portion, due to the volumetric discrepancy generated by the liquid. When adjoining elements defies other elements well before structures, its bending ground to a standstill until the design is finalized. Hinges are constructed, using two different structural parameters so that when immersed in water, the creations regulated by significant changes might stretch into pre-designed 3D structures. When the sustainable support, comprising either the inflexible and reactive components are absorbed in liquid, it turns into the initials MIT, exhibiting a one-dimensional (1D) to two-dimensional (2D) form transformation, as illustrated in Fig. 1(a) [8]. The surface area on the left of Fig. 1(b) exhibits the expanded edges of a six-sided cube; for each hinge, a continuous stripe of reactive and rigid components is jagged. A sliding primordial architectural system, designated in Fig. 1(c), where the appropriate stacking orientation is proficient changing the spacing between the tiny hard discs that serve as stoppers [9]. Apart from deformation, very specialized hinge configurations can also produce different transitions, such as curving, meandering and longitudinal extension. Three modeled algorithms: a folding primitive, a ring and a linear stretching primitive are used.

From Fig. 1(c), the folding primitive is as follows: the longitudinal extending primordial (Fig. 1d); the width and proportion of extending controlled by altering the substantial extending ratio (indicated in red in Fig. 1d) and a circular formation is enlarged into a rigid strip figure, using the ring stretching primitive (Fig. 1e). The proximal and distal rounds triumph over various constituents. When the configuration is fully submerged, the extending middle ring forces it to

deform into a crossbar. Complicated formations might be planned and constructed by using different loop diameters in varied shapes.

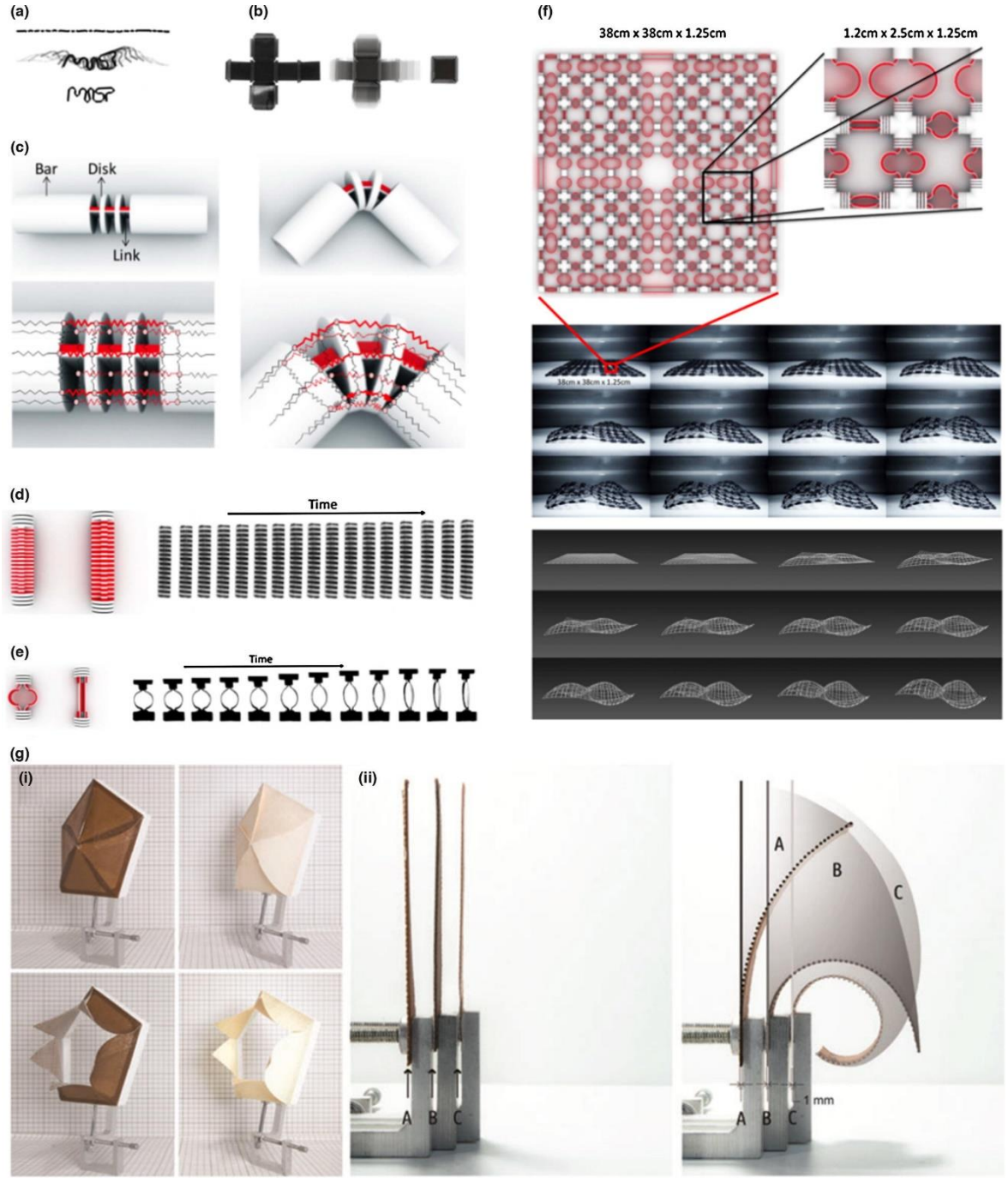


Fig. 1 (a) A solo constituent distorts into the letters, (b) a flat pleats mechanically into a bolted exterior block, (c) the construction strategy of the foldaway primeval and red

fragment is a liquid intensifying substantial, (d) a rectilinear elongating primeval, (e) a circle is extending primeval, (f) an instance is entrenching dynamic primitives of elongating and collapsible on a network, putting up a self-evolving distortion into a multi-layered binary curvature exterior, (g, i) the recital of the receptive 3D-printed opening (left), as associated with the veneer-composite structure aperture (right), acclimatizing to comparative moisture vicissitudes: exposes at truncated comparative moisture (low) and closes at high comparative moisture (up); (ii) three 1-mm-thick examination illustrations (left), automates to retort with diverse curvature varieties, due to variation in relative humidity level (right) [9]. (Reprinted with permission from (ref.no.9) copyright (2017) Elsevier).

In addition, when immersed in freshwater, a planned matrix is distorted into a layer with two fold circumference, as illustrated in Fig. 1(f) [9]. Organic wood material is utilized to 4D print hygroscopically active buildings, using comparable stacked system design components. This is particularly fascinating, since timber is one of the most prevalent sustainable resources [10]. Micro-wood fibers have been combined with appropriate 3D printing biopolymers to create printable timber fibers, using FDM [9]. Corrugated wood fibers recollect their hygroscopic action, bulging and contracting in reaction to moisture vicissitudes, also asymmetric characteristics, due to shear pressures generated on the substrate during the printing procedure. These properties enable 3D-printed wood constructions to react to humidity and show 4D effects. Different curling or folding distortions are mechanized by defining each structure of layer and alignment, sheet elevation and stack interconnections [11,12]. The printed aperture can sense comparative moisture, as illustrated in Fig. 1(g), and opens at low comparative moisture and completions at high relative moisture [9]. The morphological alteration is driven by the compressive tension between the two

materials. During implementation of nylon in the creation of complex-shaped mixtures, remarkably monofilament is retained inside the curvature during the structural transition, whereas the timber remains outside. When acrylonitrile butadiene styrene (ABS) is utilized, the opposite is observed [14].

Besides, with multilayer architectural engineering, utilization of micro inks to print 4D biomimetic modeling of intricate, texture natural counterparts, such as florae and verdures that change shape when uncover with water has been investigated [15-18]. Smart materials can alter their forms in response to a stimulus, and their detection gives rise and defines the innovative technique of 4D printing [19,20]. Thermo responsiveness, chemo-responsiveness or combining the two can achieve a morphological remodeling among a quick and lasting form. SMP components can therefore be developed into a primed 4D-printed product, using 3D printing processes [21-23], as depicted in Fig. 2.

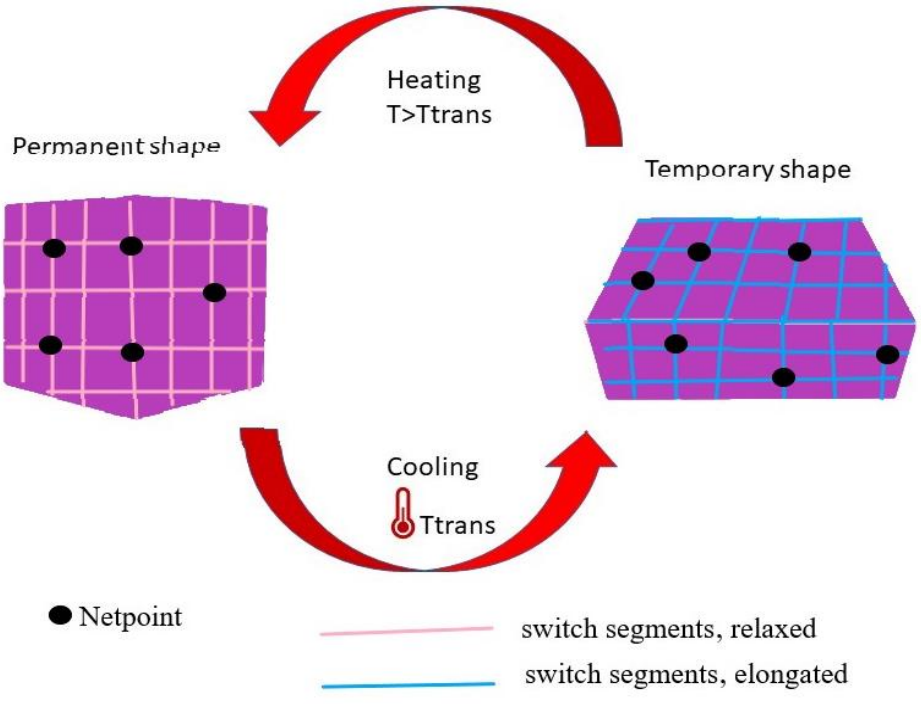


Fig. 2 Procedure for production of computerized SMPs.

Fig. 3 shows digitized illumination, irradiating a printed solution placed among two slides distanced by a separator from an industrial printer. The light is detected to diminish along the incline or the variation in width using these configurations, enabling alternative healing circumstances. Ensuring the elimination of the unreacted biological reagent, a biopolymer film with various structural forms and in-built tension in the films, due to a variation in width is created. The planar layer, raise into a 3D configurational by releasing tension from the layer [10]. 2D illumination configurations make it simple to create complicated continuous structures converted into provisional ones and retrieved after heating. Moreover, when a particular SMP hydrogels responses to a specific stimuli, they could endure configurational changes based on the gradation of inflation [37].

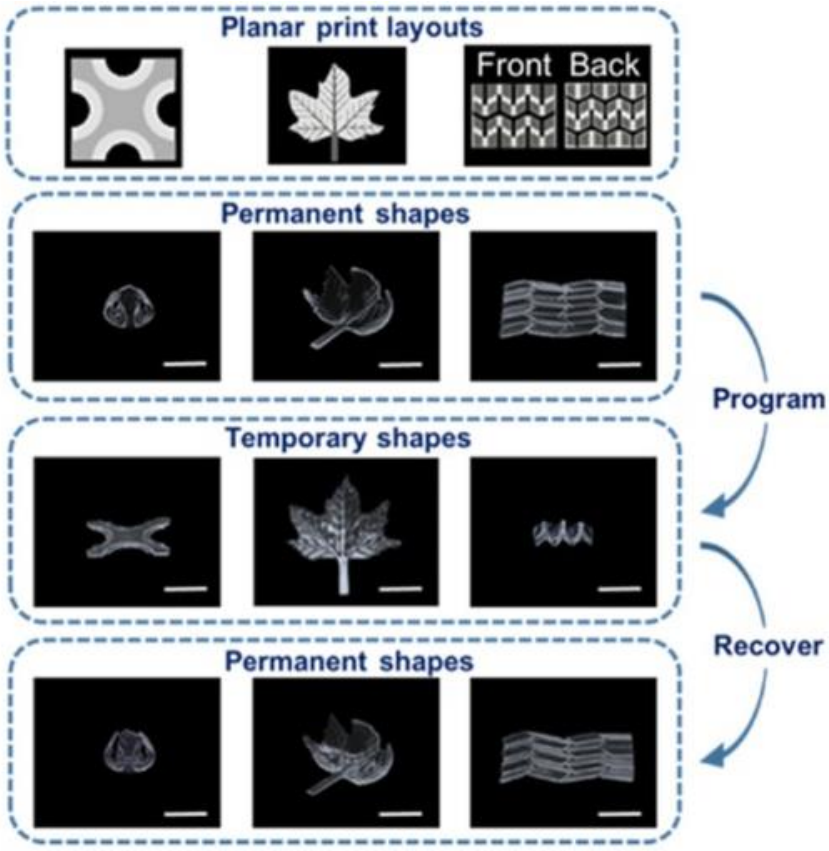


Fig. 3 Computerized production of multifaceted perpetual forms and verified their shape-memory performance. The gloomy context signifies no light acquaintance in the two-dimensional motif arrangements, and the bright and dark regions indicate the light contact of 14 and 30 s, correspondingly [73]. (Reprinted with permission from (ref.no.73) Copyright (2019) MDPI)

2.2 Shape Memory Polymers. Smart or stimuli-responsive materials (SRMs) are efficient protuberant type of resources, as a result of their capacity to remember the form automated to them, termed as shape memory effect (SME) with the assistance of stimuli [24]. When 3D printing technique is used, these materials are manipulated through 4D printing, making the design to meet some specific application. Thus, this technique instigates extensive research-oriented final engineering applications. The union of 3D printing techniques and smart materials enables researchers to manufacture 4D stimulated substances, below exterior stimuli over a period [25]. Smart materials can alter the form of response to stimuli, and research on them leads directly to the definition of the concept of 4D printing. Thermo-responsiveness, chemo-responsiveness or a mix of the two can be utilized to achieve a geometric rearrangement among a transient and persistent form. SMP substances, therefore, can be developed into a primed 4D-printed product, using AM processes. SMP is gaining popularity, due to sensory stimulation and complex interactions that resemble time-dependent configuration modifications in 4D-printed materials [26-28]. Thermally, SMPs are most commonly used variants, with various adjustable power-driven, thermodynamic and optical characteristics [29]. In thermodynamically originated SMPs, biochemical or physical covalent bonds usually determine the permanent form. At the same time, a thermal conductivity (T_{trans}), often a melting temperature (T_m) or a crystallinity temperature (T_g) controls the structural

transitioning sequences that secure the alternate solution. When the degree of SMPs is high beyond the T_{trans}, the molecular shifting segmentation becomes tender, allowing distortion to create the deformity. But, whenever the temperature drops below the T_{trans}, the molecule changing sections compress, immobilizing the pre-intended temporary form. When the SMPs are subjected to a temperature greater than the T_{trans}, the molecular shifting segmentation becomes flexible again, enabling the intermix connections to restore the composition to its previous shape. Various resources with different form of fixing and shape retrieval procedures are distinct in addition to high-temperature SMPs, as shown in Fig. 4. Oblique heat treatment is one of the actuating modalities. Direct heat activation of SMPs is the most common type of SMP used in 3D-printed inks.

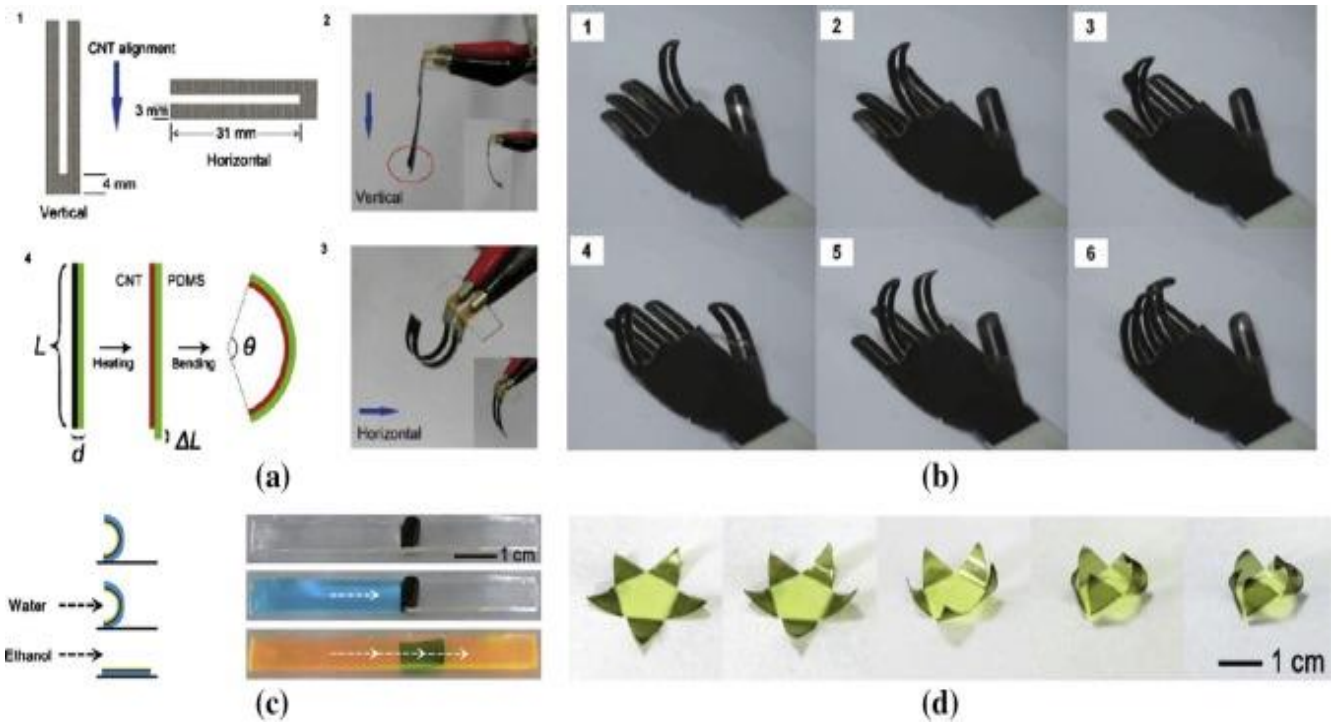


Fig. 4 SMPs binary assembly covering (a) nano paper and stimulated underneath electric current and (b) sequence of solvent involvement rounds [75]. (Adapted with permission from (ref no 75) (copyright (2016) Elsevier).

3. 4D Printing Technique for Biomedical Applications

Across many industries, 4D printing technique of additively manufacturing products is an enabling new engineering and manufacturing advances in the biomedical field. For example, 4D printing emerges recently as a next-generation tissue regeneration application. The main distinction between techniques of 3D and 4D printing is that 4D operates to fabricate dynamic 3D-manufactured biostructures that alter configuration in response to the stimulation of post-printing process (Fig. 5).

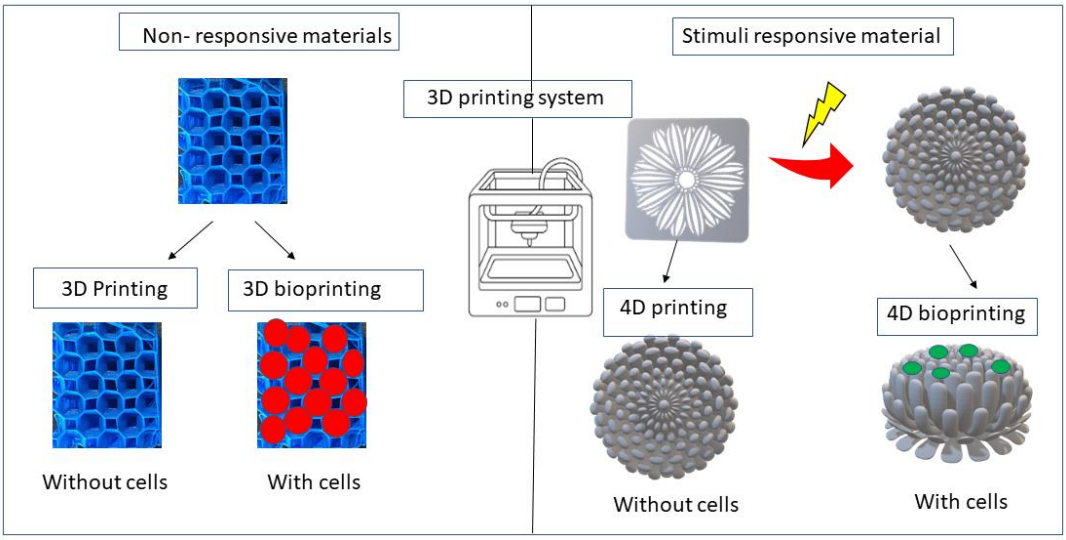


Fig. 5 Representation of core differences between 3D and 4D printing techniques.

4.1 Biosensors. Experts are concentrating on creating sophisticated gadgets that analyze hyperglycemia and deliver hormone, as the global rate of diabetes rises. Temperature, electromagnetic waves as well as changes in the moisture levels, pH and electrolyte intensity of the external environment are all examples of external stimuli that cause dynamic reaction of composites [30-32]. Identification of variations in the external factors by studying modifications or performance of active substances is attributed to these characteristics. Based on poly (ethylene

glycol) diacrylate, for example, a liquid-responsive hydrogel sheet with unidirectional mobility has been created [33]. The film shows the varied temperature of pink hue, impulsive distortion and mobility, when exposed to various elevated temperatures. Furthermore, biopolymeric dynamical substances have a range of properties that allow each of these activities to generate by a distinct impulse response [34]. Several kinds of sensors for detecting bioavailability are also formed [35,36]. As a result, the amount of structures that respond to glucose has risen. Inkjet printers create a novel glucose sensor by integrating glucose oxidase and nanoparticles into carbon and polymer nanotubes [37]. This sensor accomplishes a statistical approach of insulin levels through a multiple catalyzed reaction: in the primary stage, oxidase catalyzes glucose deterioration to generate hydrogen peroxide and in the next stage, platinum nanocrystals catalyze hydrogen peroxide depletion to generate hydroxide ions, which stimulate the local pH change. Afterwards, the pH-responsive conduction of polyaniline is employed as a biochemical resistant biosensor to measure glucose levels (Fig. 6).

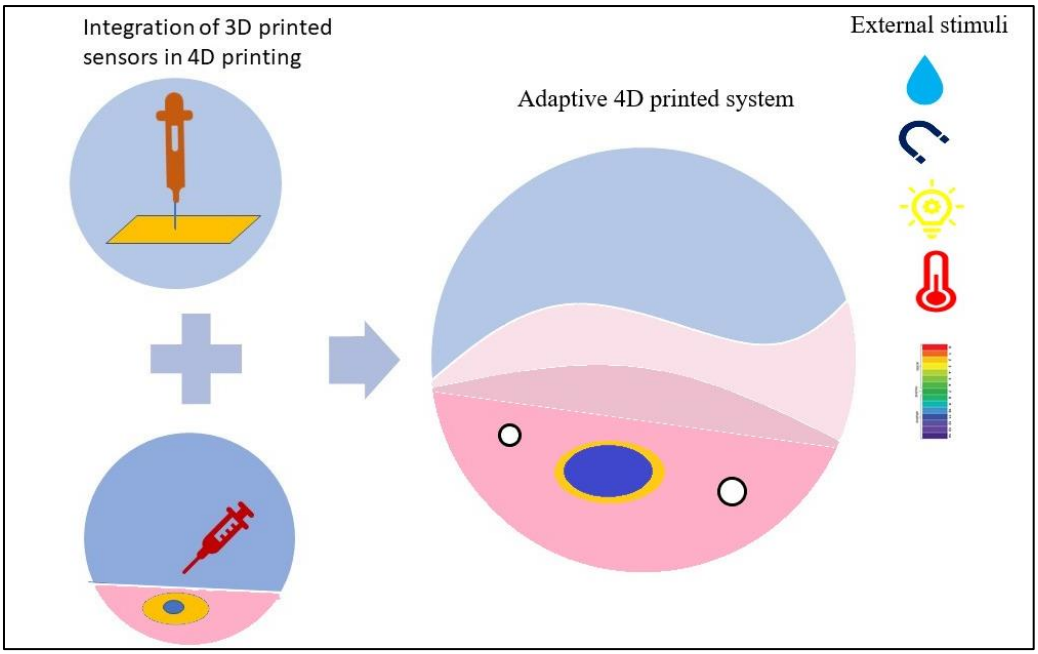


Fig. 6 Configuration of adaptive 4D-printed structures.

4.2 Wound Healing and Repairing. For constructing 3D bio-mimetic fibers, such as dermis, self-healing, synthetic conductive polymers are created. Hydrogel substances, for instance, have 3D connectivity stability and high moisture capacities, resembling the ECM in terms of circumstances [38]. Therefore, soft hydrogels are appropriate resources for use as substrates in regenerative medicine [39-41]. Several marketed goods, such as bandages, cochlear implants and health supplements, include hydrogels [42]. Hydrogels filled with bioactive chemicals, including medicines and antigens, are a prominent topic for investigation, and they have much potential for synthetic transplant innovation [43-45].

Moreover, self-healing hydrogels can inherently and autonomously mend injured cells and reinstate normality, demonstrating a novel mechanism comparable to 4D printing and endorsing the use of self-healing hydrogels in multiple organs transplantation (Fig. 8). The composition of hydrogel, combined with attractive force factors, drives direct link creation via restorative chemical angling hydrocarbon chains or quasi ionic bonds, resulting in self-healing. Even though, 4D printing of self-healing hydrogel materials has yet to be standardized, various hydrogel materials with 4D printing prospects are anticipated and evaluated.

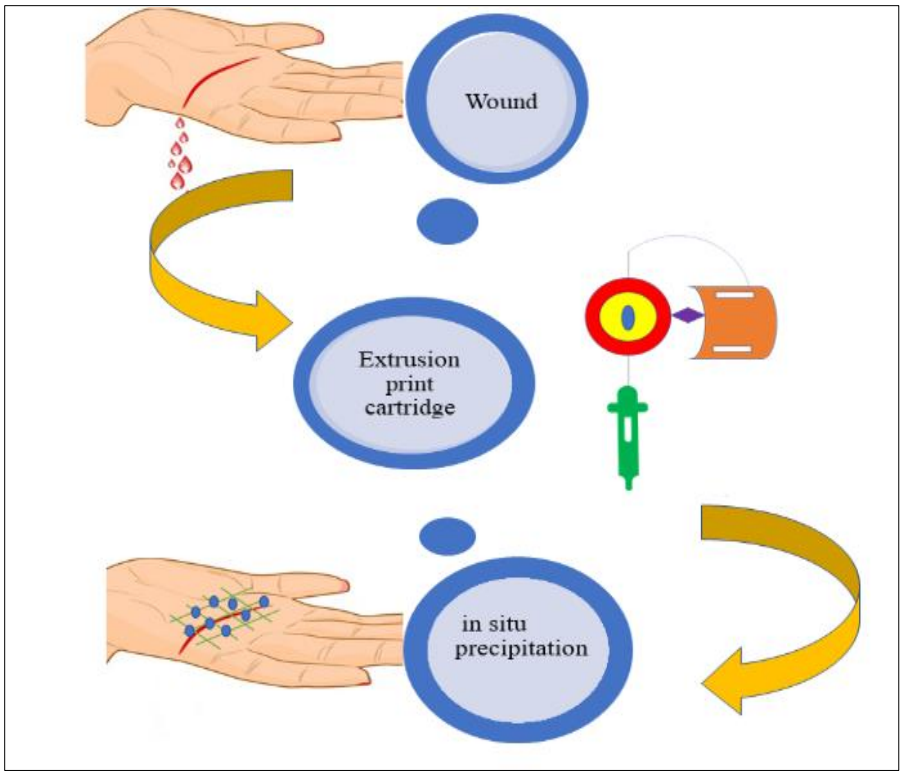
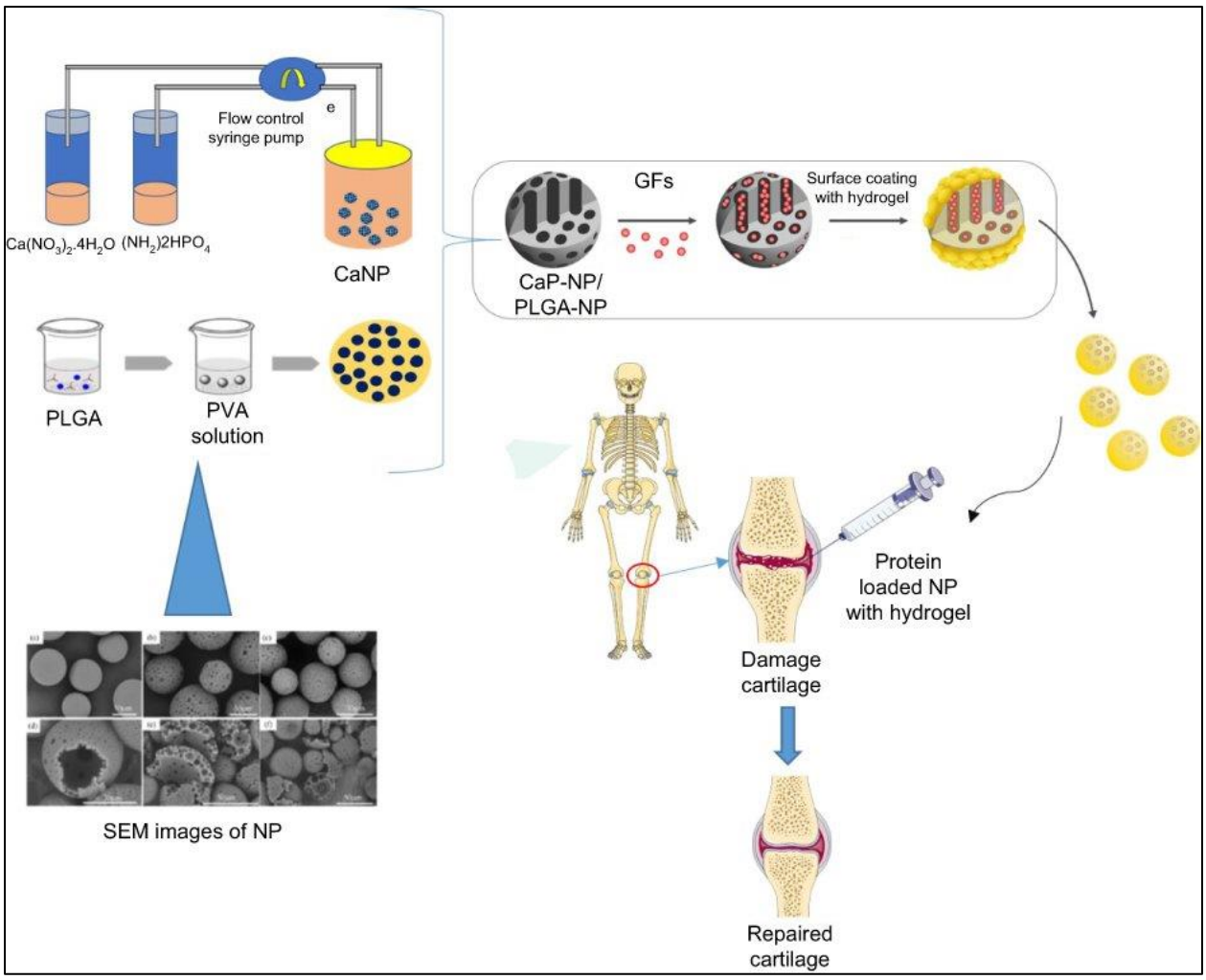


Fig. 8 Process of wound healing in 4D printing.

4.3 Tissue Regeneration. As the assembly or role of progressive resources equipped via 4D printing can vary over a period, which delivers the cells with the needed strain, it displays function as a scaffold [9,46]. While fostering excellent adhesion and dissemination of human mesenchymal stem cells (hMSCs), the scaffold is bonded to a preceptor at -19 ^{o}C and entirely restores to its original shape at 38 ^{o}C. Furthermore, studies have involved regenerative medicine to regulate fibroblasts via nerve compression and enhance the efficiency of ultimate interconnected cell [47-51]. Hendrikson et al. [52] printed 4D SMPs with controlled time-dependent configuration alterations that trigger genomic growth and maturation, using polyurethane. The fibroblasts planted on the scaffold and its nuclei, overstresses by nerve compression throughout scaffolds distortion. At 40 ^{o}C, the form of the scaffolds is reverted from temporal to primary, enabling them

to put into individuals via minimally invasive surgery. It is utilized to regenerate interconnected cells that undergo biomechanical alterations, as a result of physical exercise.

Consequently, there is need for biopolymers that respond to a stimulus in order to manufacture for various implementations (Fig. 9). Therefore, it is critical to examine the stimulation circumstances of a particular species to design conceptions that are appropriate for that setting. For example, one of the most researched parameters for 4D printing in regenerative medicine is temperature. Recently, there is a reported recent study on the reactivity of cells to physiological reactions, such as temperature, photo-responsiveness, magneto-responsiveness and biochemical signals, including pH and moisture [53].



Note: GF= growth factor; NP = nanoparticles; PLGA = poly (L-lactic-co-glycolic acid); PVA = poly (vinyl alcohol) and SEM = scanning electron microscope.

Fig. 9 Production of cross scaffold for tendon tissue engineering by Ca nanocrystals or PLGA microparticles laden with GFs and assorted with hydrogel for tendon rejuvenation [72]. (Reprinted with permission from (ref.no.72) copyright (2019) American chemical society).

4.4 Larynx Damage. The bronchial tract is a respiratory tube that humidifies and purifies airflow, yet it is susceptible to stress. Consequently, a variety of SMPs and nanoparticle pulmonary prostheses are formed. Stents are important medical features that enable to enlarge blood flow. 4D printing plays a vital role in the creation of a variety of stents. SLA was used to produce a highly responsive bronchial tube out of methacrylate polycaprolactone [54]. The stent swells and fits nicely with the trachea structure at core temperature, eliminating necessity of surgical stimulation. Morrison et al. [48] enhance the response to treatment of three children with tracheobronchomalacia by transplanting an absorbable trachea prosthesis made of polycaprolactone that can change form over the period and disintegrate over the period, as depicted in Fig. 10. Its decomposition variables are high for humans [55].

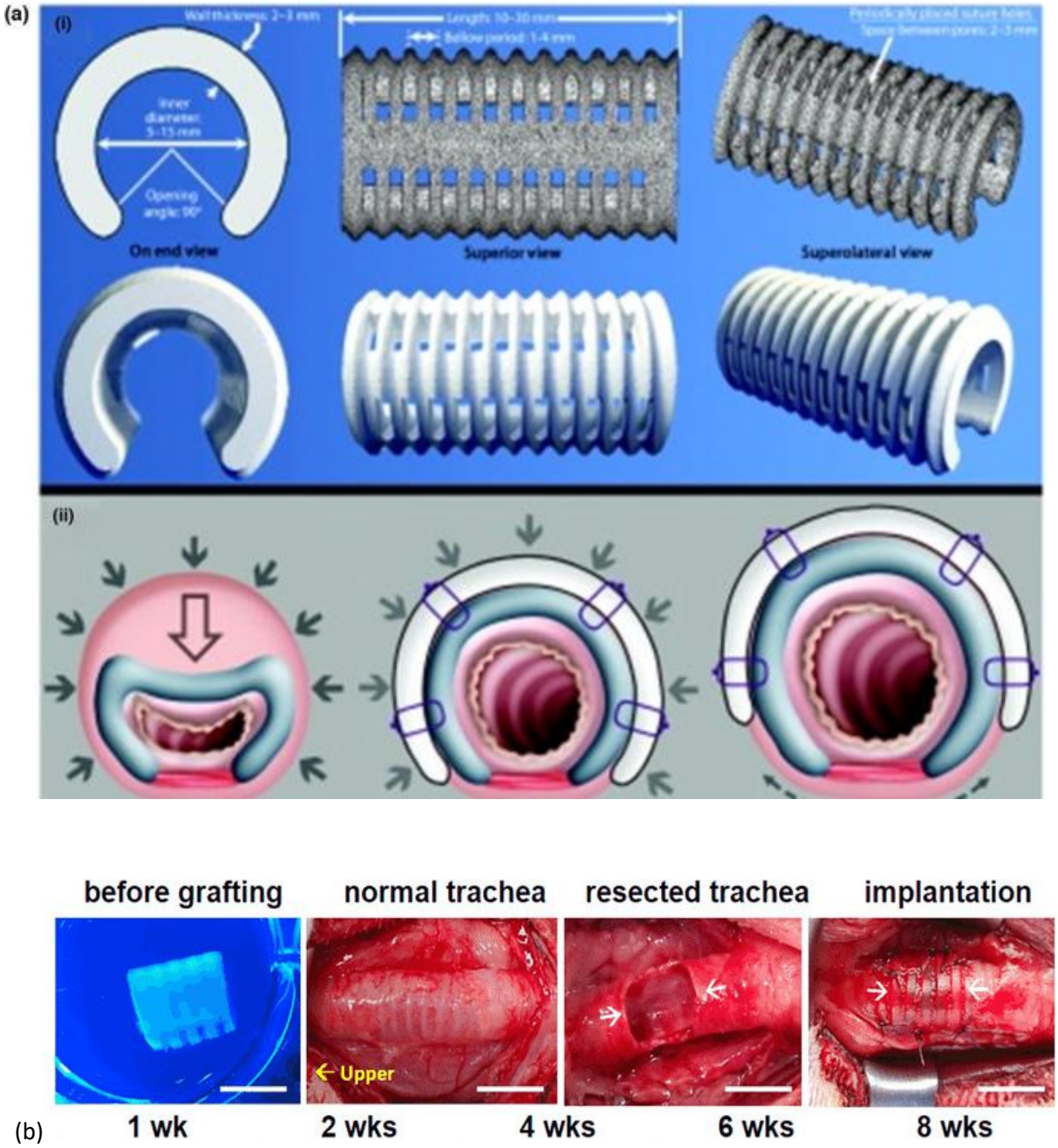


Fig. 10 Replacement of 4D bio-printed windpipe, showing (a) digital image-based design of the 3D-printed tracheobronchial splints and (b) grafting of the engineered trachea [48,71].

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4.5 Drug Delivery System. Implications for drug delivery as well as standards and restrictions on biomaterials used in medicinal applications are very challenging. Yet, by choosing the suitable component and methods, such desirable qualities can be achieved [56]. Upgraded polymeric materials with various functionalities, such as sustainable shape-memory impacts or a mixture of controlled drug release based on bio-degradability, have been created [57]. An instance of such a grouping is a triflingly hostile implantable expedient generally used for administered drug release, anti-inflammatory determinations or introducing rejuvenation procedures [58-60] SMP-based medications can have managed drug release and can also use as bio-functional implantation. It has been demonstrated that even slight changes in the microscopic architectures of polymers might result to significant alterations in subatomic characteristics, enabling us to personalize a product to meet specific demands of a patient [61]. For example, a thermally receptive theragripper (TG) composed of degradable poly (propylene fumarate) (PPF) and compatible poly (N-isopropylacrylamide-co-acrylic acid) (pNIPAM-AAc) has simplified the precise delivery of the drug. The TGs are bolted at temperatures more than 30 ^{o}C, which permits them to impulsively grip the material, as they arrive in humans from an unconscious state. This behavior supports the TGs to be necessarily powerless at a particular site and delays the delivery of the drug, resultantly better managing the drug concentration and decreasing the unwanted or unhealthy effects of the drug [62]. Patients with diseases, including gastrointestinal (GI) cancer and inflammatory bowel disease (IBD), among others can gain from this study, if the resources are pragmatic in the hospital, because aggressive drug delivery approaches and universal medicines for chemotherapy drugs can be evaded [63]. The 4D-printed polymers achieve precise control to transport and distribute medicines, bio-molecules and cells in a programmed method, as simply depicted in Fig. 11. By self-folding or self-unfolding as well as bulging and de-swelling, the 4D-printed substances

achieve a precise control to transport and distribute medicines, molecules and cells in a programmed technique. Due to their benefits in boosting medication absorption and stability, they alter biocompatibility, enhance pharmacokinetics and reduce negative impacts [64-68]. According to a few studies, pH value of a mortal tumor micro-environment ranges from 5.6 to 7.9 [69,70]. For instance, Griset et al. [70] create pH ionic strength interlinked nanocrystals.

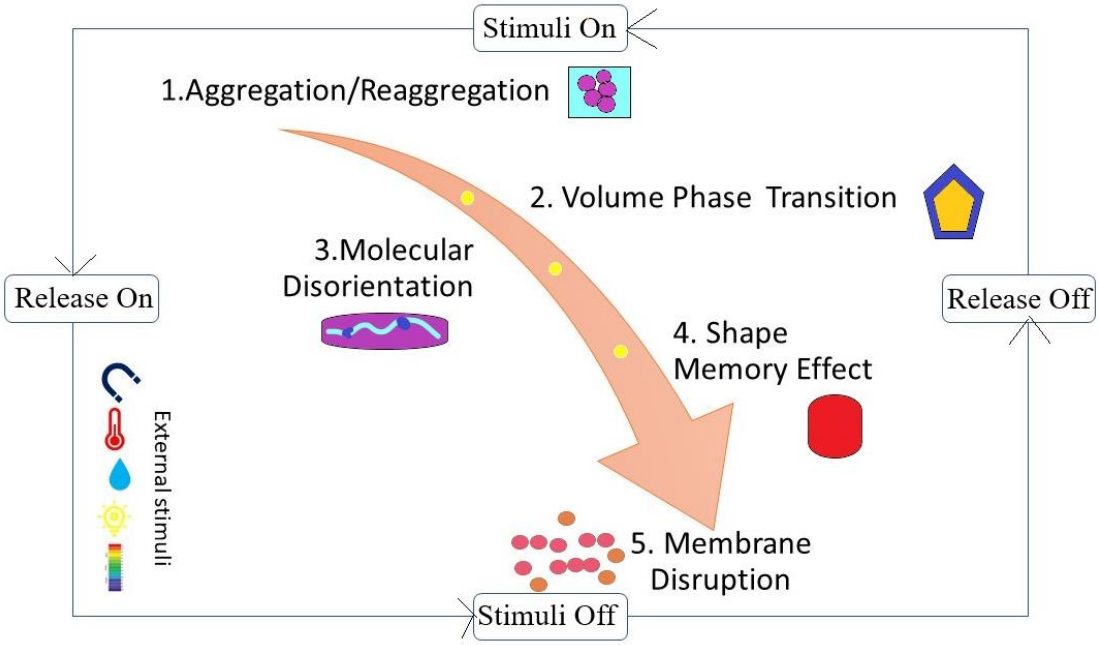

Fig. 11 Illustration of biochemical SRMs.

5. Future Challenges and Concluding Remarks

Through the rapid progression of 3D printing techniques and their biomedical applications over the last few years, SRMs have gained popularity. Hence, various studies have orchestrated a new age of 4D printing. Despite the fact that 4D printing is a new revolutionary innovation, it has already had a beneficial impact on the medical and industrial sectors.

4D/AM is still in its adolescence, and printing components are continuously studied. A printer built particularly for 4D printing is presently insufficient. For the production of high-precision surgical equipment, the associated technique must be known. The present bioprinting precision and substantial recital, on the other hand, are insufficient to fulfill this criterion. Additionally, biotic atmosphere is diverse, dynamic and inimitable. Microfluidic systems use a network of tubes and compartments with dozens of micrometers in diameter to regulate tiny quantities of liquids, ranging from 107 to 1016 mL. Biomimetic milieu of microfluidic devices offers an ideal plate for reaching cell biological potentials to create functional tissue.

Furthermore, while 4D printing has demonstrated significant implementation potential and began to inspire research, it is still in its initial phase of exploration. 4D printing needs technical advancements in various disciplines in the long term, involving programming, modeling, biomechanics and biochemistry. For millennia, self-assembling polymers are investigated extensively, but only a tiny percentage of these substances are studied for AM. Multi-responsive structures activated by a variety of stimuli demand a significant amount of work and knowledge.

Conclusively, the nanostructures must fulfil particular degradability and bioactivity parameters for multiple organs reformation implementations. Biomedical research of functioning artificial cells in the body can benefit from 4D bioprinting. The potential for 4D biomimetic to produce bones on a massive scale is exciting. The second frontier of 3D printers is five-dimensional (5D) printing, where the print head and printed component have fifth magnitude, known as flexibility in this technique. 5D print preserves 25% of the overall components used in the printing procedure concerning 3D printing. It creates curvy segments rather than a fixed-line. The print component moves throughout this procedure. Summarily, AM of different biomaterials continues as far as

quest to improve biomedical and other industrial sectors progresses, especially with requirement, necessity and hence advent of new efficient and sustainable products and processes.

Acknowledgement

The authors are grateful to Dr. C. P. Ramanarayanan, Vice-Chancellor of DIAT (DU), Pune, for his encouragement and support. We also appreciate Ms. Niranjana Jayprakash for her technical support. Lastly, we sincerely acknowledge the support of Prof. C.S. P Rao, Director of NIT, Andhra Pradesh.

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