

## Review Article

# Additive Manufacturing of Biopolymers for Tissue Engineering and Regenerative Medicine: An Overview, Potential Applications, Advancements, and Trends

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Received 17 July 2021; Accepted 28 August 2021; Published 9 September 2021

Academic Editor: Senthilkumar Rajagopal

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As a technique of producing fabric engineering scaffolds, three-dimensional (3D) printing has tremendous possibilities. 3D printing applications are restricted to a wide range of biomaterials in the field of regenerative medicine and tissue engineering. Due to their biocompatibility, bioactiveness, and biodegradability, biopolymers such as collagen, alginate, silk fibroin, chitosan, alginate, cellulose, and starch are used in a variety of fields, including the food, biomedical, regeneration, agriculture, packaging, and pharmaceutical industries. The benefits of producing 3D-printed scaffolds are many, including the capacity to produce complicated geometries, porosity, and multicell coculture and to take growth factors into account. In particular, the additional production of biopolymers offers new options to produce 3D structures and materials with specialised patterns and properties. In the realm of tissue engineering and regenerative medicine (TERM), important progress has been accomplished; now, several state-of-the-art techniques are used to produce porous scaffolds for organ or tissue regeneration to be suited for tissue technology. Natural biopolymeric materials are often better suited for designing and manufacturing healing equipment than temporary implants and tissue regeneration materials owing to its appropriate properties and biocompatibility. The review focuses on the additive manufacturing of biopolymers with significant changes, advancements, trends, and developments in regenerative medicine and tissue engineering with potential applications.

## 1. Introduction

The various aspects such as type of tissue and the hormones necessary for the discrepancy and physical size are restricted to this regeneration as the body can regenerate amazingly (critical defect). Any tissue damage beyond this crucial dimension requires external assistance approaches such as tissue engineering (TE) and regenerative medicine (RM), in

which the external hollows are termed yardsticks. These tissues offer a platform for cellular activity and new tissue creation [1]. In TE and RM, the scaffolds have a crucial role. These tissues are frequently supplied with growth agents in order to accelerate the differentiation between cells and selected lines to encourage the development of new tissue. For cell viability and cell prolife, the physical and chemical content plays a crucial part [2]. Biomaterial is classified

according to a wide variety of parameters, including chemical and physical composition, biodegradability, origin, and modification generations. Biomaterial is selected depending on the target tissue. Biomaterials are divided into ceramics, polymers, and composites based on their chemical composition. The biomaterial class of ceramics includes important components of inorganic metal or calcium salts [3]. The primary usage of these biomaterials has been orthodontal. Because of its resemblance with binding tissues, polymers are employed in soft tissue engineering. Mixes of ceramics and polymers comprise the composite class of biomaterials. The composites have orthopaedic and dental TE uses. Natural and manmade polymers of TE and RM are commonly employed [4]. The biodegradability and biocompatibility in natural biomaterials have plentiful availability such as collagen, chitosan, hyaluronic acid, and alginate that are commonly employed. One of the key aspects of natural polymers is the degradation of biomaterials [5].

Since these biomaterials are present in the extracellular matrix (ECM), cells are very compatible and respond to growth. Collagen is one of the most frequently used natural biomaterials in several applications of scaffolds. Biopolymers have recently gathered significant interest with a view to biocomposites with a multifunctional and high efficiency that have a low environmental effect, with exclusive accessibility, renewable, environmentally friendly, and lightweight qualities [6]. Biopolymeric composites should replace for the multifaceted application of synthetic materials in optics, biochemistry, and biomedical engineering [7]. The product data is divided into two dimensions. The data are sent through the machine from the basis of the product layer by layer, and the material is dropped layer by layer, which in an additive process infuses the newest layer of material into the old layer as shown in Figure 1. The researchers have received tremendous attention in recent years from biopolymers and biodegradable synthetic polymers. Biomedical applications require the production of sustainable, stronger, and lightweight biopolymeric materials [8]. The development or choice of ways to tackle the issues of architectural design however needs a compromise between visions and aims, which generally conflicts with new biomaterials [9].

## 2. Need of Bioprinted Scaffolds and Its Fabrication

Tissue engineering is an alternative method for tackling the increasing need for organ transplantation. TE and RM procedures can fill the gap between the number of transplants awaiting patients and donors available [11]. Organ failure and organ transplantation from another individual is the only effective way to treat organs including the kidney, liver, pancreas, and heart in degenerative illnesses. With the production of biomaterials and scaffolds, the TE process begins. These textiles are chemically and physically changed to fulfill particular parameters in the production process including biodegradability, porosity, size, form, and bioactivity [12]. Depending on the nature of biomaterial, production, and target tissue, these requirements may be different. Cells can seed the tissue and develop the desired tissue *in vitro* or in the body in order

to permit the host cells to enter and replace the tissue. Growth factors, hormones, and chemical indices are vital for these two methods since they define cell differentiation and tissue function [13]. Biomaterials not only permit physical cell attachment but also provide therapeutic agents such as medicines, proteins, factors for growth, and chemical indications. Most mammalian cells depend on anchor feasibility. The lack of a substratum for cellular attachment often causes the death of the cell [14]. Therefore, for surface chemical and structure of scrub materials, cell viability and function are of major importance. Three strategies—chemical alteration, change to physics, and surface coating—enhance the adhesion of cells on biomaterial and scaffold surfaces; some of the 3D porous scaffold strategies for tissue engineering purposes are represented in Table 1. The aim is to support scaffold and biomaterial cell growth and cell activity. This leads to the next stage when cells are inserted into the yards. The seeding grounds of the required cells conventionally include strategies for adding cells to scaffolds [15]. The primary cells perform the specialised function of the organ and the supporting cells, which secrete the supporting matrix, vasculature, and structural frame, during complex organ formation. Primary cells of diverse genotypes and phenotypes may be injected in order to distinguish these organisations or pluripotent cells among the required cell lines [16].

Several ways for manufacturing scaffolds exist. The manufacturing procedure is the next step to turn the biomaterials into fabrics. These manufacturing techniques are physical and chemical processes performed with the use of biomaterials for tissue engineering. Not all biomaterials are appropriate for a particular type of manufacture [17]. Biomaterials are therefore constantly updated to be used for every manufacturing procedure. Conventional production procedures include electrospinning, separating phases, drying freezes, autonomous assemblies, casting of solvents, textile technologies, injections of material, and additives. An ionic polymer solution is expelled via a fine aperture through a high voltage potential in the electrospinning process. Because of the potential difference, the solvent is sprayed in fine fibers as the solvent sprays and leaves a polymeric fragmentation [18]. Although this approach may use a wide variety of polymers, it still remains a constraint to produce scaffolds with complicated geometries and architectures. The use of a phase separation procedure can produce very porous and sophisticated three-dimensional scaffolds. A solution with distinct solvent systems is employed in this method of scaffold production [19]. One of the phases is separated with or without thermal solvents, leaving only the polymer solutions that you want. In the scaffold production method, it allows for the porosity of forged products but is restricted by the polymers and their incapacity to produce forged products with high resolution [20]. 3D printing comprises Fused Deposition Modeling (FDM), Laser Beam Melting (LBM), Selective Laser Sintering (SLS), Digital Laser Printing (DLP), PolyJet, Electron Beam Melting (EBM), and inkjet printing. Regardless of the 3D printing technique, all additives employ a common layer-by-layer design approach until the entire product is constructed. This means that a 3D structure is constructed by the continuous addition of 2D material layers. Additive production was first utilised to create

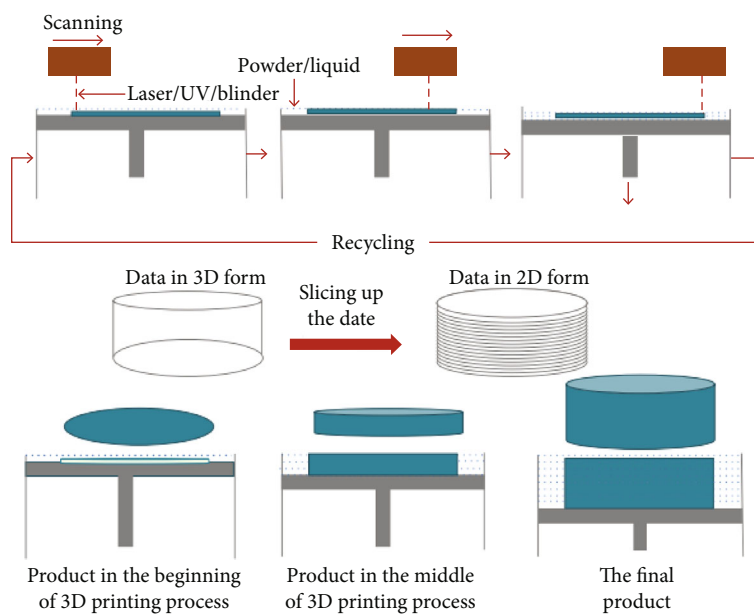


FIGURE 1: Schematic representation of 3D printing [10].

prototypes which were then adapted from many industries in mechanical and industrial applications [21]. This manufacturing approach has many advantages, including the capabilities to produce complex geometries, a large range of biomaterials, and various materials. Researchers have created new ideas and methods for the formation of tissues with multiple cell lines and organs using biodegradable polymers and cells [22].

### 3. Biopolymers and Types

Natural polymers are considered as polymers derived from living or biological resources, including plant, animal, or microorganisms and biological systems. Carbohydrate is also known as biopolymers (arabinoxylan, chitosan and starch, proteins such as gelatin and keratin, and polyhydroxyalkanoates (PHAs), poly(3-hydroxybutyrate) [P(3HB)]). In order to improve structural and functional qualities in the resulting composites, the synthesis of biopolymer composites is employed one by one or more biopolymers [30]. The composition of a biopolymer affects its functionality, while functional potential mostly depends on the behaviour of amorphous or crystalline components. Cellulose, for instance, is a structural polymer that has its crystalline shape. Chitosan is a famous component of the polysaccharide carbohydrate family. Biosustainability, biodegradability, and compatibility have been called for in the various industries [31]. It can readily be manufactured from marine sources (lobsters, crabs, and shrimps) and utilised for various biopolymer composites. Many concerns need to be considered before broad usage of biosustainable polymer are achievable, such as technical and production problems. Their functional features appear negative compared to established petroleum-based polymers and a fundamental hurdle to the wider application of biopolymer in numerous areas [32, 33]. For example, the performance of a component of biopolymers with single bonds is less than that of plastic

materials as it results in a poorer mechanical characteristic. These shortcomings can be addressed in numerous methods including greasing, mixing, combining, and strengthening with other suitable ceramics and polymers [34]. Polymers come from a variety of sources including commonly manufactured polystyrene and natural biopolymers such as cellulose, protein, and microbial polyesters that are vital for a biological system structure and function [35]. The three basic forms may be categorised as biopolymers or biobased polymer composites, which depend on their source.

- (1) Polymers such as starch, cellulose, arabinoxylan, and keratin are extracted or separated from biomass
- (2) Polymers created from ordinary chemical processing by means of renewable biopolymer are formed through fermentation of carbohydrate by monomers such as polylactic acid (PLA) and cellulose acetate (CA)
- (3) Polymers are obtained mostly from PHAs, although the creation of bacterial cellulose from digestion of microbial organisms. Biocomposite is used for the creation of materials formed from natural or biodegraded polymers, like chitosan, arabinoxylane, PHAs, or PLA [36, 37]

The green composites comprising biopolymer-natural components and degradable inorganic filler are known as efficient and sustainable biocomposites. They are the topic of attention because of environmental problems and laws [39]. Biopolymers are quite strong, natural resource-derived molecules. These products are biodegradable, easily recyclable, sustainable in trade and environment and are labelled as biosustainable products [40]. In multiple possible medical applications and in other applications, chemically altered biopolymers, e.g.,

TABLE 1: 3D porous scaffold approaches for tissue engineering applications [23–29].

S. No.	3D technology	Materials	Growth factors	Outcomes	Application
1	Robocasting	PCL and bioactive borate glass	Human adipose-derived stem cell- (hASC-) laden	Controlled release of bioactive glass	Bone tissue engineering
2	3D bioprinting	Polycaprolactone (PCL)	Saos-2 cells seeding	The nonorthogonal structures displayed advanced E moduli than the orthogonal one, with an optimistic stimulus on the biotic performance of the cells; complex standards for the mineralization, movement of osteogenic-related genes, and deposition of the mineralized matrix	Bone tissue engineering
3	Laser sintering technique	Alginate/alginate-sulfate	BMP-2	Alginate/alginate sulfate bioinks allowed good 3D cell printing. Enhancement of the release of BMP-2 was achieved using alginate sulfate. Propagation and discrepancy of the reproduced osteoblasts were better	Bone tissue engineering
4	Sol-gel method combined with 3D plotting	PCL and HAP	Not defined	Subchondral bone regeneration and articular cartilage development in a rabbit model	Osteochondral tissue
5	Electrospinning combined with 3D bioprinting	HAP/chitosan/silica	Mouse BMSC seeding	Compressive strength equivalent to the human trabecular bone	Bone regeneration
6	Phase separation process	PCL	Laden with L929 mouse fibroblasts	Multilayered structures—3D scaffolds—with loosely packed nanofibers, with improved exterior wettability (when compared to the 2D scaffolds)	Not defined
6	Phase separation process	Cartilage ECM-derived/PLGA- $\beta$ TCP-collagen type I	BMSC seeding	Improved OC regeneration. Chondro and osteogenic-induced bone marrow-derived mesenchymal stem cells (BMSC) with autonomous surroundings	Osteochondral tissue (OC)

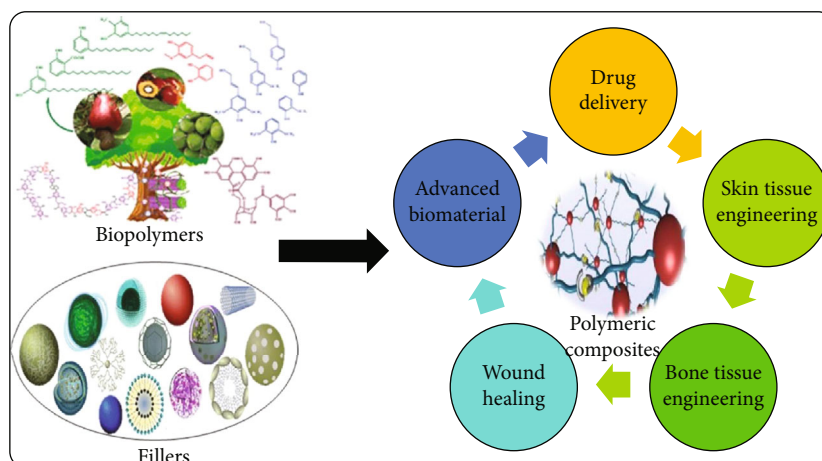


FIGURE 2: Potential applications of biopolymers in different aspects [38].

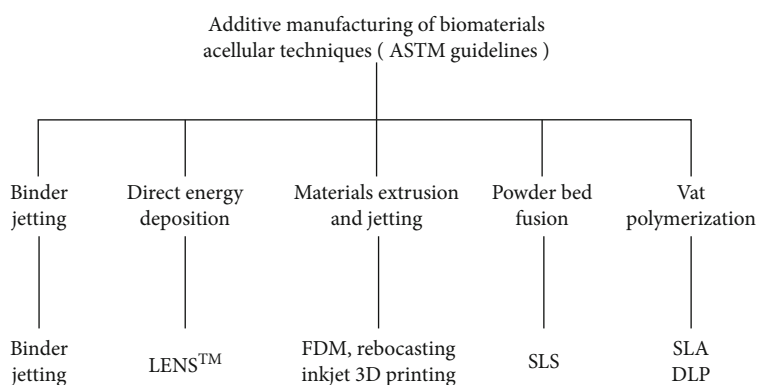


FIGURE 3: Acellular techniques for biomaterial additive manufacturing [46].

thiolated arabinosyl and cellulose acetate, have been used as shown in Figure 2. Environmental factors and microbial breakdown contribute to a conducive setting for their degradation. Biodegradable biopolymer composites are known as “green organic composites.” A number of in-organic fillers, including titanium, silica, and alumina, are characteristic for many green bio compounds. A number of viable and environmentally beneficial articles have already been offered with synthetic oil on the market by bioplastic advances [41].

#### 4. Properties of Biomaterials Appropriate for 3D Printing

The principle of bioprinting consists in impressing the biomaterial using a liquid layer procedure till it is entirely produced, immediately following the biomaterial exit of the cranium in a fluid condition; the biomaterial becomes shaped. This transformation process from sol to gel or phase is the key to the bioprinting of biomaterials [42]. The most commonly used biomaterials are polymers and composites, since they may be polymerized with different ways to make them “3D-printable.” Rheological characteristics and the cross-linking procedure are crucial factors which make biomaterials acceptable for 3D printing methods. Again, the criteria of bio inkjet printing are

distinct from those of extrusion-based bioprinting, depending on the method of bioprinting, whose qualities differ [43]. Furthermore, appropriate printing qualities are dependent on the type of the elements of the polymer biomaterial concerned. The creation of innovative polymers or hydrogel bioprinting systems should include rheological features such as viscosity, non-Newtonian, Barus effect, and cross-linkage. Non-Newtonian systems have a low fluid dilution viscosity and are time-dependent on shear pressure [44]. Polymers are shown to have higher viscosity and tend to clog the press nozzle during 3D printing and shear-thickening fluids. Polymers are thrown by dust out of the printed head during the printing process and expanded following expulsion [45]. This phenomenon is known as the effect of Barus. Ideal bioinks should have slight or no Barus effect to reserve 3D-printed object purpose. Figure 3 displays various additive manufacturing (AM) acellular approaches for biomaterials categorised in accordance with American Society for Testing and Materials (ASTM) recommendations.

#### 5. Polymers Fabricated by 3D Printing Technology

*5.1. Natural Biomaterial.* Promising options have been investigated using tissue engineering procedures while searching for

alternatives to traditional therapeutic strategies for repairing or replacing lost or dysfunctional human tissue and organ. Biomaterial-based scaffolds were beneficial for this search [47]. Gelatine, the principal hydrolyzed collagen ingredient, has spontaneously come into being in the extracellular matrix (ECM) and has the ability to suspend gel cells at low temperatures. Research studying the use of natural starch polymers with water-based binders in 3D direct printing has shown positive results, and the essential biodegradables can be mixed with the necessary mechanical qualities by synthetic polymers [48]. Polymers based on starches provide for extended time of breakdown and subsequently higher porosity with increased cellular integration which is ideal for the engineering of bone tissues [49]. For the Three-Dimensional Printing (3DP) method, a unique blend of polymer-based starch granules was produced (cornstarch, dextran, and gelatin). Scanned Electron Microscopy (SEM), Differential Scan Calorimetry (DSC), porosity evaluation, and compression testing tested the quality of the scaffolds [50, 51]. Analysis and testing have shown that new 3DP material combinations can build 3D pore scaffolding. In polymers for medication supply management, composites of starch and cellulose have demonstrated biocompatibility [52]. The density measures and mechanical tests demonstrate that, due to the small sintered level and the limit of joints, the mechanical qualities of the specimens built of bigger particles were less and that the enclosed pores were higher and more covered with small sizes of particles [53]. The results showed that biopolymer scaffolds could be produced by a process optimisation using starch and cellulose acetate to modulate laser power and scanning speed. The results are demonstrated. Specimens made of small particle size have adequate mechanical characteristics and porosities in the design and manufacture of tissue and drug delivery scaffolds with potential utility [54]. The application of 3D printing in tissue technique has permitted the production of tissue-analogous structures using innovative technologies for the printing of cells and matrix materials. The use of 3D printing to manufacture cell charging constructions has been shown to locate cells as intended and to have a high cell viability of the constructions manufactured [55, 56].

*5.2. Ceramic Scaffolds.* Ceramics are a sort of biomaterial, comprising calcium and phosphate, which comprises inorganic salts. Because of their osteoconductive and osteoinductivity, these biomaterials have significant potential for bone and dental TE. The inorganic composition of the bone tissue imitates calcium and phosphate salt [57]. These biomaterials stimulate the creation of new bones and are hence known as osteoconductants. Few compounds can cause a cell difference to the osteoblast lineage without applying growth factors that are hence known as osteoinductive [58]. Ceramic and polymer-based biomaterials are classified as composites. Chitosan, Poly-Lactide-Glycolic Acid (PLGA), and Polyethylene-Glycol Diacrylate (PEGDA) are the common polymers added. Materials such as zirconium oxide, graphene, silica, and bioglass were added to the composition of the skin in order to build composites with mechanical properties that are bone-like [59]. Many researchers created porous materials in 3D in order to enhance vascularization in the scaffolds. Many 3D-printed ceramics will eventually be exposed to sintering and freezing

techniques in order to improve mechanical characteristics and cytocompatibility [60]. The compressive strength was proven to consist of 3D-printed scaffolds employing strontium, hardystonite, gahnite, hydroxypropyl methylcellulose (HPMC), and sodium polyacrylate equal to 110 MPa bone, with 34% porous scaffolds. Because of the high mechanical qualities and the capacity to stimulate vascularization, the bone tissue engineering has a very great potential [61, 62]. 3D printing enables you to produce patient-specific grafts that fit the patient's needs with regard to histocompatibility, graft size, and bone development rates.

*5.3. Synthetic Biopolymers.* Bone is one of the most thoroughly studied of various tissues being actively investigated, because of its vital activities in daily living. The defective portion often must be removed by the surgery if the bone has disease or injuries. But regeneration is limited to a few millimetres away from the healthy bone [63]. The regeneration is only possible. Afterwards, the excised part of the bone is replaced by a graft, to restore its functionality. The most commonly used polymer for 3D porous scaffolds is Polycaprolactone (PCL), which is hydrophobically caused to limit cell-skin interactions, despite its strong biocompatibility and processability [64]. PCL is also semicrystalline, resulting in very lengthy degradation kinetic conditions, which is considered as soft and hard tissue compatible bioresorbable material, coupled with its hydrophobicity and its poor water absorption capacity. In the ranges 40%–85%–2,74%–55, 95 MPa and 1,17–5,03 MPa, the porosity, compressive steepness, and yield strength of the scaffolds varied. This range of rigidity closely fits the ringing bone in the maxillary region. In addition, as is apparent from the results of cytotoxicity testing, the selected manufacturing method for PCL scaffolds has proved practicable [65, 66]. In addition to PCL, some additional polymers are employed for tissue engineering in 3D printing. Poly(3-hydroxybutyrate) (PHB) is a natural, in-balanced growth-related, thermoplastic polyester that has garnered attention in biomedical fields, such as tissue engineering scaffold fabrication because of its biocompatibility and biodegradability [67]. Unlike conventional procedures, PHB may be processed by 3D printing without the need of chemicals such as plasticizers. A functional polyester with PCL-based aliphatic Phenylmagnesium Chloride (PhMgCl) has considerably greater hydrophilicity due to their backbone hydroxymethylglycolide-co- $\epsilon$ -caprolactone groups, which has recently been developed, leading to a significant increase in the adhesion, proliferation, and differentiation between human mesenchymal stem cells and PCL [68]. The PCL-based polyester was also developed. In order to test in vivo biodegradation and biocompatibility of 3-dimensional PhMgCl scaffoldings, 3D plasters utilising this polymer have been created via fiber filtering, increasing hydrophilicity, higher rates of degradation, and an enhanced interface between the cell material and the PCL (melt plotting). A normal external body response was seen in PhMgCl scaffolds to both types of scaffolds characterised by the presence of macrophages, lymphocytes, and fibrosis [69, 70]. The degree of interactions of tissue scaffolds and of vascularization in PhMgCl scaffolds was demonstrated to be higher

than that of PCL. Therefore, a potential biomass for bone and cartilage tissue engineering is the rapid and degradable PhMgCl that has shown good biocompatibility [71].

**5.4. Synthetic Biopolymer-Based Composites.** As the main scaffolding materials in the preparation of multimaterials, two photocross-linkable hydrogel biopolymers Poly-(Ethylene Glycol) (PEG-DMA, MW 1000) and poly-(PEG-DA, MW 3400) have been employed. In distinct zones of the scaffold, multimaterial scaffolds were created using a tilt of regulating concentrations, including fluorescent, bioactive PEG marking, or bioactive PEG [72]. Fluorescence microscopy was used for the presence of the fluorescent component in particular parts of the skull, and selective bioactivity microscopy was used to illustrate cell localization with the help of the PEG bioactive pattern in the sections. Successfully demonstrated multimaterial spatial control. Moreover, after SLS manufacture, the balance swelling behaviour of these two biopolymers was established and used to build constructions in a swollen state with the given dimensions [73]. Multimaterial SL is used, and different bioactive ligands or growth factors are relatively easy to conjugate to PEG to manufacture custom three-dimensional constructions with a specific bioactivity that can be controlled by a space [74]. Most of the present procedures use water-insoluble images incompatible with live cell manufacturing and ultraviolet (UV) radiation that harms cellular DNA. Several researches show the use of water-soluble dimethacrylate poly(ethyleneglycol) (PEG-DMA) to produce stereolithographic structured, cell-containing hydrogels. The cell viability and activity of the scaffolds with their porous internal architecture was greater than that of solid scaffolds, perhaps because of the increased exchange of oxygen and nutrients inside the scaffolds [75, 76]. A well-defined pore network, a limited pore dispersion, and significant pore interconnection characterised the porous hydrogel structures. Cell compatibility of the resin with the building structures. Human mesenchymal stem cells are attached to the surfaces of the hydrogel structures, and after seeding, they exhibited their propagating form. After five days of cultivation, cell growth was found [77]. In tissue engineering, medications, cell transplants, and other biomedical applications, these hydrogel structures can therefore be used [78].

Compared to materials such as PCL and PLA that offer a better native biocompatibility, Acrylonitrile Butadiene Styrene (ABS) is not extensively employed in medical devices. Biological applications demand protein and other biomolecular adhesion components during flow reduction [79]. The chemical modification of the ABS surface to the engineering hydrophilicity and biocompatibility is therefore very important. Surface changes have proven to be an excellent technique for increasing material biocompatibility for many years now, in particular through the grafting of PEG [80]. A method for producing watertight microfluidic equipment with chemical dissolution via acetone has proved to impair water movement between layers of a porous FDM ABS device, while keeping the structural fidelity of printed microstructures to 250  $\mu\text{m}$ . The photographic grafting of PEG groups will next present a way to building a stable, biocompatible ABS surface that will improve the biocompatibility of ABS by reducing the biocom-

patibility of biofluidity [81, 82]. Surface and protein-adhesive studies have shown that this modified ABS is a versatile material to be used to model fusion deposition for the forming of micro-fluid-resistant biofuel channels that expand the range of potential applications in ABS-based FDM microscopic and laboratory on a chip application [83]. Compounds of polymers and inorganic bioactive materials are currently being developed to increase mechanical stabilisation of scaffolds and enhance the interaction of the tissue [84]. Combination of biodegradable polymers and ceramics such as hydroxyapatite (HA) and tricalcium phosphate (TCP) created third-party composition scaffoldings. The development of biomaterials in the nanosized osteoconductive Calcium Phosphates (Ca Ps) including HA, tricalcium phosphate, and substituted HA and TCP was recognised as being small in size, high surface-to-volume relationship, and biomechanical similarities with natural bone structure combined with bone structures such as collagen, poly(L-lactide) (PLLA), and chitosan [85, 86].

Hydroxyapatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ), the chemical resemblance with calcium phosphate mineral present in biological hard tissues, has received a lot of interest. HA is used for a range of biological applications such as a controlled medication release matrix and a bone tissue transporter material [87]. Recently, the advantage of nanosized hydroxyapatite (nHA) compared with typical microsized has been emphasised. nHA can operate as a carrier of therapeutic agents to enable the extracellular or intracellular regulated release of drugs, and, at the same time, it is highly absorbent into the body for hard tissue regeneration [88]. The bone tissue engineering application has been of major interest to PCL/HA composites. The use of PCL and HA biocomposite materials to manufacture tissue scaffolds via SLS technology. Experiments with cell culture have shown that Saos-2 cells can live on the manufactured fabric and proliferate. The results reveal that PCL/HA biocomposites have the advantage of being tissue engineering bodies produced by SLS. In addition to pure PCL, the mechanical features of the PCL-HA composites were improving. They also show that the mechanical properties of these boots can be anticipated with great precision before production [89, 90]. The ability to adjust the material properties and the anatomical form of fabric-engineered constructions for patient and site recovery strategies is an extension of mechanical features of composite materials at any loading of fillers combined with a direct production method and a complicated anatomical component production process [91, 92]. In combination with the natural manufacturing process to fabricate the sophisticated anti-anatomical protein techniques of the composite materials at all loads of fillers. It can adapt material properties and building designs for both patients and site rehabilitation plans [93].

The cell interactions of polymer engineering tissue scaffolds are known to benefit from bioactive glass. The best response will probably be obtained if the glass has no cover on the surface of the scaffold [94]. The recent creation of a 3D fiber draws technology to produce perfusable glass grills, which are similar to patterned vascular systems and are covered with a thin layer of poly-(d-lactideco-glycolide). The very porous and surface scaffolds were used to distribute bioactive glass homogeneously. The presence on the surface of composite

scaffolds of calcium phosphate deposits in vitro bioactivity [95]. The metabolism of fibroblast was boosted by bioactive glass. Investigations have shown that SLS technology allows for the production of well-defined composites, where bioactive glass is equally scattered on the surface and readily available for quick cell and ion release. An undesirable polymer layer covering BG particles can be prevented by Stereolithography (SLA) on the surface of the skin [96]. The study revealed that the bioactive and biodegradable cell support of regenerative medicine photocross-linked composite and PCL scaffolds produced by SLA technology has a high potential [97].

**5.5. Peptide-Based Biopolymers.** A new class of biomaterials known by the outstanding chemical, physical, and biological properties of the peptide-based biopolymers is produced; protein engineering and macromolecular assembly converged to enable peptide-based biomaterial to expand [98, 99]. Prototype examples include poly-amino acids, leucine zip-based peptides, peptide amphiphiles, ionic oligopeptides in beta-sheet and peptides in beta-hairpin, and prototype peptide-based biomaterials; poly-amino acids, polypeptides, silk proteins; and coiled-coil domains. Biopolymers can also readily be functioned to strengthen cell connections and create an appropriate platform for cellular activities and functional tissues [100, 101]. This section examines two major classes of technical biopolymers based on peptides: the auto-assembly of polypeptides; the formation of gels by means of environmental stimuli and polypeptides. The application of in situ gelation chemically cross-linking elastin-like protein (ELP) hydrogels was impaired by low water soluble, toxicity problems, absence of biocompatible cross-linking reactant and product reactants, and delayed gelation kinetics [102]. While peptide biomaterials have become ever more essential materials in regenerative treatments, their use is restricted by the short lifetime and thermal instability. Many of these constraints can be overcome using new technology, and the usage of peptide-based biomaterials can therefore be further extended to applications for which it is presently impossible [103, 104].

**5.6. Polymer Scaffolds.** Polymers are often used in 3D printing biomaterials. The use of polymers in the manufacture of additives is extended to various tissues, including the most transplanted organs liver, kidney, and heart tissue. Biodegradable and nondegradable polymers can be used for 3D printing; however, the advantages of biodegradable polymers are greater and are therefore extensively used [105]. Biodegradable polymers are usually categorised as natural or synthetic based on their origin. In recent times, numerous synthetic polymers have been produced with programmable degradation rates. The degradation rate is vital because it needs to match the pace of the new tissue synthesis [106]. The scaffold design also incorporates natural and synthetic polymers in combination. In one or two physical stages, whether solid or fluid polymers often occur in bioprinting. Solid polymers are mainly utilised in FDM printers, while liquid polymers are used in extrusion and inkjet printers [107]. Liquid polymers are solutions of solvent systems which can be polymerized or interconnected with monomers or oligomers. Hydrogels are

a polymer type that holds water and hence imitates the natural tissue environment. They are used to cell encapsulation, medication delivery systems and packs in a number of applications [108]. Vascularized tissues with tremendous promise in organ manufacturing were imprinted 3D using hydrogen and cell combinations. In efforts to build scaffolds for specific tissues, a variety of 3D printing methods were utilised. Modeling deposition fused provides an economical way of building up scaffolds that use widely available biodegradable polymer filaments with regulated porosity and architecture [109, 110]. However, thermal deterioration and spatial resolution are the limitations of FDM printers. For extrusion-based printing, the suspension, solution, or emulsion is supplied with a pneumatic, piston, or screw-driven system to produce pressure [111], given the varying viscosity of many hydrogels; pressure-oriented extrusion methods are effective.

## 6. Applications of Biopolymer Materials in Biomedical Fields

**6.1. Drug Delivery.** The revolutionary potential as carriers for the provision of genes, biomolecules, or biological agents has been displayed by polysaccharide-based composites, including arabinoxylan, xanthan gum, and chitosan [112]. These are employed as medicine carriers with excellent bioactivity, low cytotoxicity, nonantigens, processability, reversible loading, and release mechanisms for cartilage repairs and vascular grafts. They are used for treating cancer. Other assets that improve your medication delivery application are emulsification, gel formation, foaming, and moisture absorption [113]. These polymeric materials have also been acknowledged as excellent controlled drug delivery systems because of their unique mechanical and cross-link features, suitable biodegradation in various environments and at specific areas [114]. Such biomaterials can be directly synthesised or included into engineering particular and specific places of resultant nanocarriers with multifunctional features. Some biomaterial kinds have been employed efficiently as hydrogels, movies, tubes, microspheres, and microneedles and based on chitosan, guar gum, and arabinoxylan.

Controlled drug delivery tries to steadily give treatments at the desired spot, usually in the blood, and to maintain an efficient therapeutic window [115, 116]. The results are cost-effective and desirable, reducing or eliminating unpleasant side effects, complications in the dose, and increasing patient recovery and comfort. It is claimed that regulated breakdown and sustainable release following accumulating at the target site are the most wanted pharmacological properties of biomaterial systems [117]. This controlled release of implanted medicines or other therapeutic substances can be primarily controlled using triggers like temperature, pH, and ion concentration. In order to manage the release of therapeutic usage, the aimed system of drug supply must typically activate the cellular areas [118]. Therefore, to optimise the synthesis or functioning of precursors, composition conditions of manufacture, and drug encapsulation technique, a tailored drug delivery approach must fit into the required release kinetics [119]. The medicine or other nutrient should be delivered at a controlled rate and dosage by ensuring that all factors such as size, shape, surface



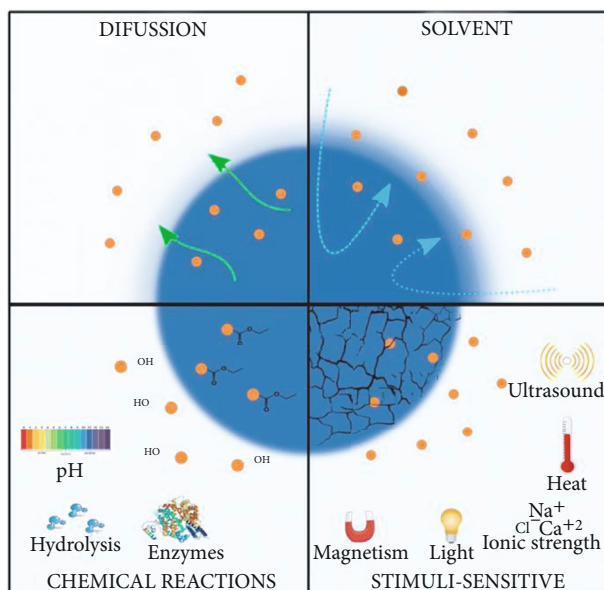


FIGURE 4: Mechanisms for controlled drug release using diverse types of carriers [121].

morphology, bioavailability, and biodegradability are suitable and particular to the intended spot. The biomimetic polymer nanoparticles were made in various sizes, and the therapeutic ingredients were loaded effectively. Such accurate nanodrug carriers assisted to imagine inflammatory regions in molecular form and resolved possible inflammations and immune responses [120]. Figure 4 shows various types of carriers to control drug release mechanisms.

**6.2. Tissue Engineering (TE).** Tissue engineering involves the treatment or regeneration of faulty tissue through biomaterial scaffolds. It requires polymer composites with the requisite composition, desired technical qualities, and adequate physicochemical behaviour in order to promote the formation of biological tissue. It has expanded in depth and importance as an advanced discipline of its own, having been classified as a biomaterial subsection [122]. As tissue technology deals with different applications, the result is usually related to applications which substitute, repair, or rebuild part or complete tissues (bone, cartilage, blood vessels, bladder, skin, and muscle). The tissues implicated are typically responsible for the appropriate functioning of particular architecture, morphology, and mechanics [123]. Tissue engineering phrase also is employed in the artificially produced protection and support system to combine complex biochemical pathways via cells (skin, hip replacement). Capable technology for 3D bone scaffolding is bone tissue engineering (BTE) that contains living cells and bioactive chemicals. BTE focuses on the perception of the skeletal structure as the bone dynamics increase the clinical ability to address unsettling skeletal and segmental anomalies [124, 125]. In other circumstances, contemporary technology and advancement of bone biochemistry are important to efficiently grow or rebuild bone tissue. Bone can be used for a wide range of multifunction, leading to physiological and endocrine stimulation [126].

The bone endures a continual resorption and repair process which takes place due to internal intermediates and external mechanical standards, exchanges of chemicals, and structural remodeling [127]. Bone had been named the greatest intelligent material historically and most precisely due to its limited regenerative flexibility. The freshly cured bone with adjacent host bone and, most importantly, the native bone functions include bone fusion [128, 129]. Functional bone tissue engineering adds to functional and architectural diversity; the bone is an exceedingly complex tissue. Particularly, the Extracellular Bone Matrix is made from a nonmineralized organic matrix as well as an inorganic mineralized component [130]. For nanocomposite construction, the compressive strength and resistance of the thigh-bone fractures and the load-bearing applications are important [131]. Suitable compounds for extracellular matrixes or sticky ligands which enable stem cells and regenerate bone tissue might be applied so quickly in different procedures of engineering [132, 133]. Bone tissue engineering should focus on producing scaffolds of angiogenesis, combining growth stimuli and the porosity structure necessary for vascular growth [134, 135]. The processing of these scaffolds with micro- and nanometre-surface geomorphology is indispensable to cell bond, propagation, and discrepancy as shown in Figure 5.

However, bone tissue engineering is regarded as an alternative in situations when donor availability is restricted, or where there is a risk of disease transmission, donor site difficulties, or even limitations of external materials to reshape and respond to physiological conditions. This is true whether the scaffold is acellular or seeded with stem cells, which can directly develop into bone cells, to replace a broken portion of bone. The scaffold's composition and structure are critical. Bone tissue engineering's primary goal is to create scaffolds that not only act as a scaffolding for the implantation of cells but also send regenerative signals to cells to accelerate bone healing and repair. Structural bone scaffolds are 3D architectures and environments that are designed to (1) promote cell adhesion and survival, (2) accelerate bone remodeling and remodeling, (3) provide osteoconductive structural guidance, and (4) in some cases, act as carriers for growth factors, antibiotics, or gene therapy. The epidermis which works as an anti-illness shield is the most waterproof layer and plays a significant role in bodily temperature and humidity regulation. More than 90 percent of epidermal cells are keratinocytes [137]. Langerhans, melanocytes, and Merkel cells dominate the bulk of epidermal cell populations. The dermis and skin base are around 90 percent of the skin's weight. It is an extracellular matrix of soft tissues consisting of a variety of cells, lenses, and hair follicles. The dermis has a strong vascularization, and the nerve ends with a blood vessel [138]. Fibroblast is the largest dermal cell containing collagen and elastin and giving mechanical strength to the skin. A more deeply elastic, mucous tissue-cell skin that store fat, blood vessels, and nerve is present in the pulmonary hypoderm. Traumas such as physical penetration, venom, fire, illness, and operation are the major reason and contribute to the chance that important organs are infected, injured, or dehydrated by this disease [139]. Skin replacement technology offers a potential foundation for better care for combating chronic

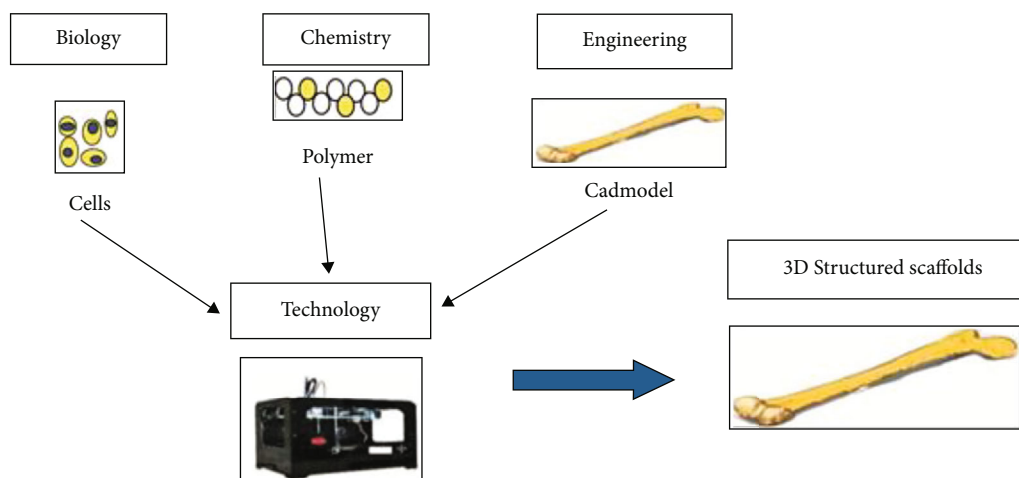


FIGURE 5: Representation of multidisciplinary fields used in the 3D printing technique for TE applications [136].

TABLE 2: Biopolymeric materials in tissue engineering and wound healing [146–155].

Biomedical field	S. No.	Polymeric material	Prominent characteristics
Tissue engineering	1	Chitosan	Recyclable, biocompatible, uncontaminated
	2	Gelatin	Bioactive, biocompatible, hemocompatible, cell adherence
	3	Arabinosylan	Biocompatible, uncontaminated, cell observance, bioactive, cell explosion
	4	Collagen	Biodegradable, fibrous, biodegradable, cell proliferation
	5	Xyloglucan	Cell explosion, environmental, cell discrepancy, biocompatible
	6	Fibrinogen	Biocompatible, hemocompatibility, cell propagation, decomposable
	7	Arabinosylan/guar gum/gelatin/collagen	Antiseptic, biocompatible, decomposable, bioactive, continuous drug release, cell propagation
Wound healing	8	Chitosan	Biocompatible, antibacterial, cell proliferation, bioactive
	9	Alginate/fibrinogen/hyaluronic acid/xyloglucan	Fiber protein, biocompatible, recyclable, rubbery, sterile, cell obedience
	10	Bacterial cellulose/pectin	Antibacterial, cell adherence, cell differentiation, biocompatible, bioactive, cytocompatible

and acute skin damage. However, given the mechanical and physiological aspects of active skin, cellular basis technology and simulated extracellular matrix are required for skin tissue engineering to connect with the surrounding tissue [140, 141]. No substantial skin prototype is currently available to accurately replicate the natural skin structure, composition, organic consistency, or visual environment. Alternatives of the skin might have crucial, easy-to-use, and wound-specific characteristics [142].

These biomaterials are sufficiently water-sensitive and have specific affinity to host places. Their biochemical and mechanical qualities are sufficient, their privation is controlled, their disinfection is nontoxic and nonantigenic, and their inflammation is minor [143]. They can also join the congregation at low operational cost with minimum injury and suffering of angiogenesis. The ultimate objective of tissue technology is to achieve the maximum of these needs to prepare intelligent skin substitutes [144]. In addition, the new skin electronic properties or aesthetic structure do not restore poly-

meric composite materials. In order to extend skin growth to provide the typical usefulness and beauty of healthy skin, the changes in stem cell biology and skin morphogenesis are necessary [145]. Some of the biopolymeric materials and their features are represented in Table 2.

**6.3. Wound Healing.** Wounds are a form of uneven skin punching, breakdown, or skin deformation owing to a chronic or thermal trauma. Injuries can be classed as chronic or acute injuries depending on the healing procedure. Chronic injury is predominantly tissue lesions, usually within 8 to 12 weeks, which appear to have totally resolved [156]. Acute injuries continue to occur and are still more than 12 weeks of recuperation. Various neurological factors can lead to wound-healing impairments or the failure to correctly heal. Chronic injury examples are bedsores and leg ulcers. As the basis for the wound gradation, skin layers and polluted areas are used and only the epidermal skin surface is involved with surface wounds [157, 158]. The word partial thickness injury is

defined as injury involving the epidermis, deep epidermis, muscles, soft tissue, and follicular tissues. The wounds are combined with subcutaneous fat or deep tissues besides the epidermis and the skin surface [159]. The physiological wound repair is part of coordinated teamwork among various biological systems. The wound is entirely treated in a cascade with controlled operations. Hysteresis and coagulation of your blood start with lesions, mainly in order to avoid first sight exsanguinations, taking place in every area of the body [160]. The lesion is also a long-term secondary target and a matrix for cell adherence. A carefully managed balance of endothelial cells and thrombocytes relies on the homeostasis and fibrin produced at a site of the injury [161]. The neurological system of response in damaged veins causes vascularization, which blocks blood flow over several minutes. The waterfall of coagulation is caused by homeostatic behaviours and proliferation and differentiation [162]. Platelets bond when blood spills, causing a release of the coagulation factor: fibronectin, fibrin, vitronectin, and thrombospondin. Coagulation retains homosexuality and a cell migration matrix in homosexual and inflammatory treatments [163, 164]. Many biopolymers are routinely used in wound care and treatment, including fibrous proteins and different polysaccharides. These biocompatible, biodegradable polymer matrices preserve an atmosphere similar to the extracellular environment. The process of sluggish wound treatment is accelerated [165]. For cell adhesion, proliferation, migration, and differentiation, the biopolymeric matrix provides an ideal microenvironment. Using biopolymer-based wound care materials, three-dimensional cross-linked polymeric networks can keep the wound wet and oxygenated. As a result of the use of wound healing dressings, the wound is regenerated, prevented, and protected from disease-causing bacteria. Dermal and epidermal tissue healing and regeneration rely on it. This wound healing material is identified as hydrogels that can be packed for localised therapeutic delivery with spatially and temporally controlled cells, medications, and peptides. Hydrogels have been utilised for biomedical and therapeutic applications, such as tissue engineering, regenerative medicine, cancer treatment and infectious diseases, controlled drug delivery, and peptide delivery [166]. Hydrogels adhere to the application site shape to provide for considerably more therapeutically practical formulation of loaded hydrogels in biomedical applications. While hydrogels are believed to be exceptionally biocompatible with poly(ethylene-glycol) (PEG), hydrogels based on PEG, hydrogels used on are considered extremely biocompatible. High systemic biocompatibility of PEG and utilisation of biomaterials generated from ECM increase the distribution of cell growth [167]. As a result, the multifunctional wound-care material PEG-based cross-linking hydrogels with good loading components, such as cells, medicines, and peptides, are being developed [168].

**6.4. Bioprinting.** Bioprinting includes production of AMs in complex and functioning living tissues, utilising biocompatible cells, supported components and materials. In regenerative medicine, biopharmaceutical products are generally used to support tissue and organ transplant, especially the development of hydrogel [169]. Many forms of bioprinting are available, including inkjet printing and AM-based extrusion. One study generated 3D cell architectures through

neural cell sheets employing an alternative human pluripotent embryonal carcinoma (NT-2) cells and fibrin gel inkjet printing approach [170]. The Vascular Endothelial Growth Factor (VEGF) presence in 3D-bioprinted scaffolds that incorporates alginate into one of their matrix mixes promotes vascularization in gelatine microparticles.

The hydrogels developed containing hyaluronic acid and semi-interpenetrating systems with a dextran basis [171]. The use of neural stem cells to produce artificial neural tissue was organically printed with collagen and VEGF-releasing fibrin gel. Hyaluronic acid-based scaffolds were created through layer-by-layer deposition through bioprinting [7]. In order to print bespoke steaks with cell inclusion, many such techniques have integrated other conjoined natural polymers such as dextrin and gelatin. This has led to the development of sophisticated materials with biological activity by adding growth factors such as Bone Morphogenetic Proteins (BMP-2) by use of microfabrication technologies [172]. Many of the bioprinting approaches mentioned could be adjusted and optimised with or without cell utilisation for bone tissue engineering. The survivability of cells in situ following the printing method is part of many issues related to cell printing [173]. New methods used for obtaining 3D cell-charged structures with proper mechanical and biological properties have been applied with collagen-based bioinks [174]. The 3D printing techniques for polymers are shown in Figure 6.

**6.5. Advanced Functional Biomaterials.** In order to design and synthesise multifunctional polymer material, a better understanding of the sequence, structural, and functional features of natural polymers plays an essential role. These innovative artificial biomaterials are self-assembled and stimulated to encourage cell contact and growth under particular conditions [176, 177]. The complexity of posttranscriptional changes has limited sophisticated and multifunctional biomaterial protein synthesis that utilises bacterial resources and the conundrum of target genes [178]. Other changes have been intended to properly control spatial and temporal releases. The development of the structure and de novo design for protein-based biomaterials has been made easier by progression in gene therapy and manipulation approaches [179]. Due to the existence of multifunctional domains on the protein structure, the structure of produced biomaterials is linked to significant versatility, such as cell binding places and enzymatic domains. The design and production of new biomaterials based on artificial proteins have been promised recently in genetic engineering. Compared with its native counterparts, these biomaterials have a unique performance, such as improving self-assembly in fiber architectures [180, 181]. The significant necessities for choosing a bioink for 3D printing in biomaterial characteristics is shown in Figure 7.

**6.6. Materials and Manufacturing Advances and Trends.** The selection of optimum biomaterials will be a vital part of effective bioprinting of therapeutically relevant tissue. Based on the availability and knowledge of these materials, numerous polymers were examined during the bioprinting stage for traditional 3D printing and fabric production [183].

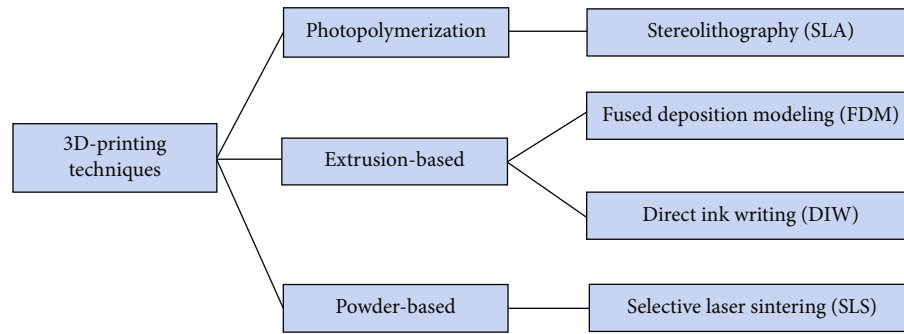


FIGURE 6: 3D printing techniques for polymers [175].

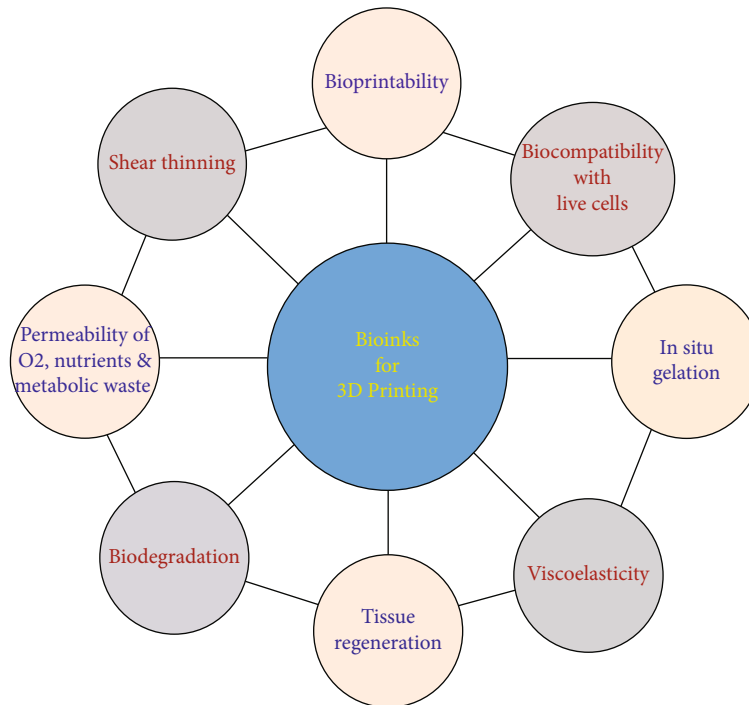


FIGURE 7: Bioink for 3D printing in biomaterial features [182].

However, in bioprint applications, materials are not the most physiologically suitable. Many of these are exceedingly physiologically active, leading to improper cell contact and premature or undesired differentiation of the stem cells [184]. The focus is currently on new biopolymers and hydrogels, which imitate better the nanostructural characteristics and reactivity of ECM and other constituents in the true tissue microenvironment. But those new hydrogels and biopolymers more biocompatible are not necessarily appropriate to conventional methods of bioprinting [185]. Many lack the structural stability to optimise bioprinting and can collapse if they are too soft. An interesting field of research is to optimise the microarchitecture for these biopolymers. Substances are combined with the proliferative and cytocompatible impact of a softer material to optimise the usefulness of all of them, the mechanical properties of one single substance [186, 187]. For example, an “integrated tissue organ printer” is utilised to put companies into the soft hydrogel cell scaffold. Tricalcium phosphates with gelatine and hyaluronic acid bioprinting can be successfully com-

bined [188]. In general, the effectiveness of the bioprinting process has to be enhanced. The existing bioprinting method is time consuming and currently cannot reliably supply the number of cells needed for varied tissue types.

As mentioned before, a change in cell shape, changed signalling pathways, and even cell death is often caused by imposed force through the printing process [189]. In order to make more efficient cell death and loss, the huge effort is involved in each bioprinting project. Improved methods for monitoring and assessing cell death are part of the solution. Vascular networks may be the main task in converting bioprinting into the lab for the production of functional tissues [190]. Tissues of even minimal complexity will not survive without proper channels for nutrition delivery and waste removal. In vivo, the diffusion of oxygen is limited by a vascular network for tissues that are beyond 100-200  $\mu\text{m}$ . Infected tissues will have nutritional restrictions without a vascular network which result in inadequate development of tissue or necrosis [191]. In order to properly

perfect bioprinted tissue, an early enough developmental network must be established for the prevention of death of tissue and for the endothelium to be attached and grown. As a result of the development process, all tasks in normal development must be played by the vascular structures, including the maintenance of selective waste and nutrient barriers, and inflammatory reactions, coagulation, and other homeostatic processes [192, 193]. Today, problems with bioprints are mostly related to restrictions on printing resolution and speed. Capillaries, for instance, can have a diameter of about 3 mm while a droplet of 20 mm is currently used by the highest-resolution laser-based bioprinters.

Conventional methods or additive manufacturing can be used to create bone scaffolds. Pore size, shape, distribution, and interconnectedness of pores are all difficult to manage using conventional approaches. To add living cells in conventional procedures would be very impossible because of manufacturing circumstances. If pores are distributed in an unintended manner, it could have a negative impact on cell distribution and, ultimately, the development of new tissue. Other organic solvents left behind in the scaffold microstructure can negatively affect cell survival or function. Due to low-cost items and simple instrumentation, these techniques are still employed today [194]. As a result of the absence of hazardous solvents in AM procedures, the biocompatibility of scaffolds is much improved as well. If necessary, scaffolds can be constructed with two or more materials. Despite the high resolution of SLA and SLS, their applicability in the manufacture of bone scaffolds is extremely limited. Photosensitive polymers required for SLA use in bone tissue have a low biocompatibility. As a result of the high-intensity laser beam, SLS is not generally used in bone tissue applications. In spite of its low resolution and limited material options, FDM solvent-free and ultraclean procedure is likely to be the greatest technology for incorporating live cells, which could explain why FDM-created PCL bone scaffolds have won FDA approval.

Even if printing resolution is increased to such an extent that a complex capillary network can be produced, time with the currently available technology is prohibitive [195]. The cell viability may be impacted if the printing cannot be finalised fast. In consideration of these issues, several solutions have been proposed. One of the most promising is attempts to vascularize in vivo with the addition of angiogenic substances to biomedical tissue implants, inducing the host vasculature growth. This method has to be refined, despite encouraging outcomes [196, 197]. Alternatively, vascular networks of synthetic origin have been attempted. While the bioprinting of vessels with bigger diameters has been successful, synthetically created small microvascular grafts with fewer than 5 mm show poor patentability and are now unrealistic [198]. Inappropriately, the basic problem of tissue death prevention and timely growth of mature, functional vasculature has still to be overcome [199].

*6.7. Challenges and Future Directions.* Two types of tissue engineering difficulties exist: novel bioink research and development for specific tissues or universal bioink for all tissues and the regulatory category. Ideally, a universal bioink must be a biomaterial mix that promotes survival in the angiogene-

sis and in nerve intercalation of natural tissues, chemical indicators, and growth factors. These challenges can be overcome by providing new technologies, such as additive fabrication, which allow the production of complicated fabrics. Vascularization is one of the most essential difficulties for developing sustainable angiogenesis solutions involving the addition of angiogenic growth factors, platelet additions, bone marrow clots, and bioreactors. Since numerous heads loaded with cell type can be used by bioprinters, a vasculature is placed into a 3D imprint. The use of sacrificial biomaterials within the skin is another technique to address vascularization. Sacrificial materials provide mechanical support throughout the construction of the 3D printing process. During the postprocessing, processing of the buildings from the channels or empty regions in the building can be quickly dissolved or removed as circulatory channels.

Graphene and their composites and metal nanoparticles have also taken on a crucial importance as fillers into biopolymers reinforced their mechanical characteristics, such as tensile, effect, bending, and other structural qualities in medical applications, to create the necessary biomaterials. The main issues of the usage of biopolymers for synthesising biocomposites are mechanical behaviours and inadequate dispersion. The fillers produce agglomerates with a matrix of biopolymers that leads to feeble interfacial connection with defective structural harmonics and imperfect mechanical characteristics. The outcome is a large number of additional unusual properties, such as susceptibility to high temperatures, humidity, low impact strength, shelf life, and more. Future guidelines lead to new biomaterial in order to meet the above concerns and to be economically viable, recycled, and eco-friendly.

## 7. Conclusion

The biopolymers are the greatest option for synthetic petroleum polymers with considerably renewable, biodegradable, and environmentally sound characteristics. Biopolymers are not supported by mechanical properties such as high strength of tensile, impact strength, bending force, and thermal stability. However, they are able to perform load-bearing applications using their ceramic composites using a mechanical strength. There is yet more attention to be paid, inventions and improvements by using reinforced elements to adapt biocomposite microstructural features, the standard mixing techniques.

- (i) These composites lead to many other unusual qualities such as sensitivity to high temperatures, susceptibility to moisture, low impact, and shelf life
- (ii) In order to address the specified factors and to fit economic viability, recyclability, and eco-friendly ways, future direction leads to new biomaterials. This combination of synthetic and natural macromolecular chemistry leads essentially to biomedical applications since polymer structure management can lead to functionality being manipulated
- (iii) Bioprinters can automate the assembly process and permit the preprogram and intricate manipulation

of biopolymers, from macromolecular to the live cell. This is done to achieve architectural and biochemical complexity which is never previously achievable especially in biomedical fields of tissue engineering and regenerative medicine

- (iv) Tissue engineering has generated both natural and synthetic polymers through the technique of 3D printing, and various other materials have been developed. In combination with polymers, fiber and particles are developed to produce materials with enhanced bioactivity, biocompatibility, and physical and chemical qualities

### Data Availability

The data used to support the findings of this study are included within the article. Should further data or information be required, these are available from the corresponding author upon request.

### Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

### Acknowledgments

The authors thank Chennai Institute of Technology, Chennai, and Saveetha School of Engineering, SIMATS, Chennai, for the technical assistance. The authors appreciate the supports from Wollo University, Kombolcha Institute of Technology, Ethiopia. This research was performed as a part of the employment of Wollo University, Kombolcha Institute of Technology, Ethiopia.

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