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REVIEW ARTICLE

# Selective laser sintering in biomedical engineering

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**Abstract** Selective laser sintering (SLS) is a solid freeform fabrication technique, developed by Carl Deckard for his master's thesis at the University of Texas, patented in 1989. SLS manufacturing is a technique that produces physical models through a selective solidification of a variety of fine powders. SLS technology is getting a great amount of attention in the clinical field. In this paper the characteristics features of SLS and the materials that have been developed for are reviewed together with a discussion on the principles of the above-mentioned manufacturing technique. The applications of SLS in tissue engineering, and at-large in the biomedical field, are reviewed and discussed.

**Keywords** Solid freeform fabrication · Selective laser sintering · Tissue engineering

## 1 Introduction

Solid freeform fabrication (SFF) technologies, originally developed for industry, have been receiving a great amount of attention in the medical sector in the past few years. SFF-manufactured anatomical models find applications not only in oral, maxillofacial, and neurological surgery, but also in orthopedics and tissue engineering applications [54, 72, 86]. In medicine, they are mainly used for assisting diagnosis, planning treatment, and manufacturing implants [101]. The effectiveness of SFF models has been shown in various surgical procedures [9, 14, 49, 106]. Due to the additive nature of the processes incorporated in SFF technologies, they are also investigated for the fabrication of implants with special geometrical characteristics, like scaffolds for the restoration of tissues [64]. In the present paper the materials that have been developed for selective laser sintering (SLS), and their use in the biomedical field, are reviewed together with a discussion on the principles of the above-mentioned manufacturing technique.

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## 2 Solid freeform fabrication (SFF) techniques

Solid freeform fabrication refers to the physical modeling of a design using a special class of machine technology. Using an additive approach to building shapes, SFF systems join liquid, powder, or sheet materials to form physical object. Layer-by-layer, SFF machines fabricate plastic, ceramic, metal, and composite parts using thin, horizontal cross sections of the computer model. SFF is having a profound impact on the way companies produce models, prototype parts, and tooling. This impact is also being realized in production as some companies are now using it to produce final manufactured parts. This practice, termed solid freeform manufacturing (SFM), is developing into an attractive opportunity in order to speed-up the time-to-market of the final product. SFM may even become the most significant area of growth in this decade. In the biomedical field SFF systems quickly produce models and prototype parts from three-dimensional (3D) computer-aided design (CAD) model data, computerized tomography (CT), micro-CT, and magnetic resonance imaging (MRI) scan data as well as data created from 3D digitizing systems [65, 92].

Currently, the SFF techniques used for medical applications are electron beam melting (EBM), three-dimensional

printing (3D-P), stereolithography (SLA), SLS, direct metal laser sintering (DMLS), and fused deposition modeling (FDM) [13, 54–56, 69, 88]. Each of these different techniques builds up a model, layer-by-layer, using different processes and materials. EBM consists of a layer-based direct manufacturing process of complex parts by melting metal powder with an accelerated electron beam. 3D-P creates models by spraying liquid binder through ink-jet printer nozzles on to a layer of ceramic or metallic precursor powder: SLA by tracing a lower power ultraviolet laser across a vat filled with resin and SLS by a heat-fusible power by tracing a modulated laser beam across a bin covered with the powder. DMLS can be used as tools to directly produce a customized biomedical device in a biocompatible titanium alloy and FDM by heating thermoplastic material, extruded through a nozzle positioned over a computer controlled *x*–*y* table. As regards the materials EBM uses fine metallic powder, 3D-P a wide selection of powder materials, SLA UV-sensitive resins, SLS fine thermoplastic powder, DMLS a biocompatible titanium alloy powder and FDM thermoplastic pellets.

### 2.1 Selective laser sintering

Selective laser sintering, like most SFF techniques, is an additive fabrication process that quickly produces models and prototype parts from 3D CAD models, 3D digitizing system-acquired data, CT and MRI scan data. The physical object is manufactured layer-by-layer, transforming the three-dimensional problem in a bi-dimensional one. Objects are built layer-by-layer from CAD data files exported in the industry-standard exchange file format standard triangulation language (STL). STL format is a boundary representation that consists of a simple list of triangular facets (3D System Inc., 1988).

Fortuitously, SFF and anatomical scanning equipment (CT, MRI) are both layer-based methodologies. This has enabled relatively straightforward transfer of measurement data generated using these imaging methods as input data for a SFF system, making these manufacturing technologies particularly useful for many applications in biomedical engineering, as it enables to fabricate custom-made anatomical models or implants with a high level of accuracy [53].

Selective laser sintering was developed by Carl Deckard for his master's thesis at the University of Texas and patented in 1989. The schematic of the process is described in Fig. 1.

A laser beam is traced over the surface of a tightly compacted powder made of thermoplastic material. The powder is spread by a roller over the surface of a build cylinder. A piston moves down one object layer thickness to accommodate the layer of powder. Excess powder in

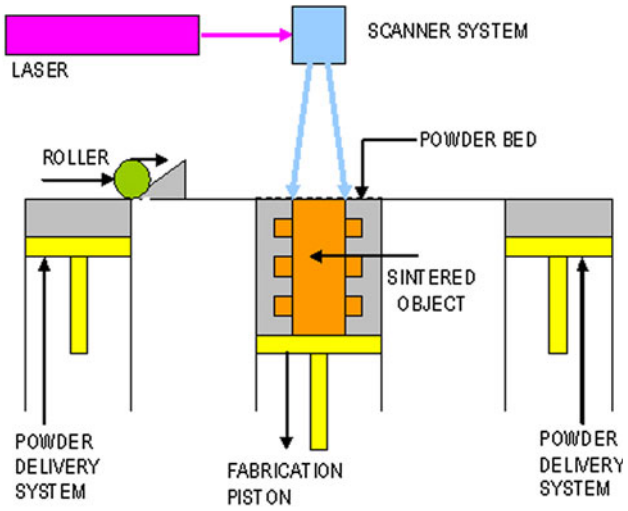


**Fig. 1** Schematic of SLS

each layer helps to support the part during the build. Heat from the laser selectively melts the powder where it strikes under guidance of the scanner system. The laser provides a concentrated infrared heating beam. The entire fabrication chamber is sealed and maintained at a temperature just below the melting point of the plastic powder. Thus, heat from the laser need only to elevate the temperature slightly to cause sintering, greatly speeding the process. Free poured (loose) or slightly compacted powders with particle size in the range of several microns to several-hundred microns are typically used for SLS [31]. The morphology and the granulometry of the powder are well known to be crucial parameters in laser sintering [20]. In fact these properties have an impact on the powder bed density and on the powder flowability. The flowability of the powder is a critical point because the powder has to be spread uniformly at a high temperature and with a thickness of about 100 μm. So to increase their density and flowability, the powders dedicated to SLS should have a specific granulometry and a good sphericity. Moreover, flowability agents are usually added, especially silica. Commercially available laser sintering powders with good flowabilities consist of general of spherulite particles with a narrow size distribution of $d = 60$ μm and a low share of fine particles below $d = 10$ μm [16].

The building process is carried out in a sort of two-phase mixing state. The laser merely introduces the energy that is necessary for the material to exceed the point of phase transition. For the subsequent creation of a coalesce film and thus fully dense parts the melting viscosity and surface tension are just as significant as the before shown powder density and flowability of laser sintering powders [76]. Temperature increase in the surrounding powder bed should be as small as possible, here. Another requirement

of this process, in terms of material properties is that the plastic material's crystallization temperature should be clearly below the crystalline melting point. In case the initial melting temperature is exceeded powders will start to melt, whereas if temperature is below initial crystallization temperature, the plastic melt produced up to then will start to crystallize, causing shrinkage, and curling. Dynamic differential scanning calorimetry (DSC), among others, can describe phase transitions and thus the differences in temperatures between crystalline melting and crystallization. On this basis, the possible range of processing temperatures during SLS production may be defined. Here it is desirable that the temperature between melting and crystallization along with the melting peak is high with a narrow temperature range for the melting process itself. When the heat supplied to a powder particle is insufficient to melt the whole particle, only a shell at the grain border is molten. The core of the grain stays unaffected. This way the molten material acts as a binder between the non-molten particle cores. This binding mechanism can arise as well with metals as with polymers, although the consolidation of polymer powders results also from other mechanisms (consolidation at the glass transition temperature, which is lower than the melting temperature, polymer chain rearrangement, and cross-linking). The partial melting phenomenon was modeled by Fisher et al. [29]. Using a simple thermal model, skin and core temperatures of the powder particles were calculated. This way the minimal pulse energy to fully melt the particle can be calculated. Below this value, the core temperature never exceeds the melting temperature and only partial melting is obtained. Parts made by partial melting are characterized by high porosity with initially only point contacts between particles. During laser heating, various sintering and rearrangement mechanisms induce the powder binding and densification [1]. Sintering gives rise to formation and growth of necks between the particles, which are in fact surface contacts. However, the laser-heating time in SLS, which is typically a fraction of a second up to about several seconds, is insufficient for complete material compacting by solid state sintering requiring usually several hours [40]. With partial melting sintering mechanism, complete elimination of the porosity is generally not possible because repulsion forces arise between particles at a high fraction of the binding liquid component [1]. As a result, the structure of discrete particles connected by relatively thin necks usually remains during and after SLS treatment. The various types of sintering mechanisms yielding powder binding depend strongly on temperature [40]. This indicates that calculation of temperature fields in the powder bed in SLS plays a key role in understanding the operating sintering mechanisms (depending on the powder type and process parameters) and in estimating the binding kinetics. However, the associated heat transfer phenomena taking place in SLS process are complex including incident laser radiation penetration into the powder bed, thermal radiation transfer, and thermal conduction through the gas filling the pores and through the contacts between the particles [4]. A nitrogen atmosphere is also maintained in the fabrication chamber to prevent the possibility of explosion in the handling of large quantities of powder. After the object is fully formed, the piston is raised to elevate the object. Excess powder is simply brushed away and final manual finishing carried out. In case of dealing with porous structures, grains entrapped in the bulk porosity can be removed using a compressed air jet. No supports are required with this method since overhangs and undercuts are supported by the solid powder bed. This saves some finishing time compared with SLA. However, surface finishes are not as good and this may increase the time. No final curing is required as in SLA, but since the objects are sintered they are porous. Depending on the application, it may be necessary to infiltrate the object with another material, such as for example bronze, to improve mechanical characteristics. Much progress has been made over the years in improving surface finish and porosity. The method has also been extended to provide direct fabrication of metal and ceramic objects and tools.

The advantages of SLS are the following: fast and economical process, durable, functional, large and complex parts, small series produced in one manufacturing process, no supports required since overhangs and undercuts are supported by the solid powder bed, all kinds of finishing degrees, as well as watertight, and autoclave sterilizable parts and moreover, high part accuracy and material versatility [53]. Disadvantages include that SLS-manufactured parts have little rough grainy and porous surface finish which is not as smooth as SLA but acceptable for most of applications, but parts can be easily primed and finished to smooth level. The larger shrink rates of SLS increase the tendency for the prototype to warp, bow, or curl subject to the part geometry. SLS feature detail is not as crispy and sharp as produced by SLA.

With the introduction of powerful high-quality lasers, the partial melting of SLS has been taken over by complete melting giving rise a new development of metal laser sintering (MLS) or selective laser melting (SLM). Needless to say, SLM is SLS done at high laser powers with an aim to achieve complete melting of powders [88, 91]. The working principle is based on fusing metal powder into a solid and melting it locally using a focused laser beam. The customized biomedical devices are built up layer-by-layer using a pre-alloyed biocompatible Ti6AlV4 alloy in fine powder form. SLS/SLM, unlike other rapid manufacturing processes, has got many commercial machine providers. 3D Systems and EOS are the major global players who are

continuously making and developing machines for both SLS and SLM (http://www.3dsystems.com, http://www.eos-gmbh.de). In general, $CO_2$ and fiber lasers (replacing Nd:YAG laser) are employed for processing polymers and metals/ceramics, respectively. EOS has introduced multiple focus diameter and online power control while 3D Systems employ thermal control systems to control accuracy and part properties. All machines are more or less same and do not differ significantly from each others. Besides, most of the machines come up with their own set of dedicated powders which limits the wider utilization of the machines themselves. Scan speed is the most significant factor in SLS/SLM on which build speed depends. Other significant factors are layer thickness, scan spacing, scanning strategy [8], complexity of the part, coating time, powder handling time, pre- and post-processing time [44]. The accuracy of the final parts depends mainly on types of materials, layer thickness, spot size, and scanning capability of the machine [53, 79]. Crystalline polymers shrink while amorphous polymer [i.e. polycarbonate (PC)] does not give shrinkage problem and is suitable for making patterns and molds [42]. It is relatively easy to control SLS in comparison with SLM as complete melting in the latter case gives rise to surface tension-driven difficulty. Decrease in layer thickness up to 20 μm causes a decrease in stair-step effect and increases the process accuracy. However, further decrease gives rise to an increase in porosity.

## 3 Materials used in selective laser sintering

The basic material developed for SLS technology is a polymeric powder with a 50-μm mean particle size diameter. Even though polymer is the most processed type of material in SLS, the consolidation phenomena invoked for polymers are probably still amongst the least understood or at least the least described in literature [39]. This explains why commercial applications of SLS today are limited to a small number of polymers: mainly polyamide (PA 12 and PA 11, e.g. Duraform, 3D Systems), polystyrene (PS, e.g. Primecast 101, EOS GmbH), thermoplastic elastomers (TPE, e.g. Duraform Flex, 3D Systems), polypropylene (PP, e.g. Duraform XR300, 3D Systems), some PC [3], and variants of these [78]. This leads to restrictions for many applications, e.g. in the industrial or medical field. Thus, research on further polymers with enhanced chemical or higher thermal stability plays a major role for applying additive manufacturing to serial production of individual components. Currently, great efforts are made to process new technical thermoplastics like polyetherketones (PEEK) by SLS [77].

As regards the biomedical field several researchers investigated SLS of biocompatible semi-crystalline thermoplastics, both hydroxyapatite (HA)-reinforced and not, like polyvinyl alcohol (PVA) [10], PEEK [88], poly-ε-caprolactone (PCL) [97, 99, 105], poly(L-lactide) (PLLA) [107], poly(L-lactide-co-glycolide) (PLAGA) [80], polyethylene (PE) [32], and ultra high-molecular-weight polyethylene (UHMWPE) [71]. PVA, PCL, PLLA, and PLAGA are water-soluble polymers, while PEEK, PE and UHMWPE are not biodegradable. Polymer-based scaffolds containing bioactive bioceramics can be manufactured in which the bioceramics can serve two purposes: (a) making the scaffolds osteoconductive and (b) reinforcing the scaffolds. With this composite strategy, there are two approaches for making bioceramic–polymer composite scaffolds: (1) incorporating bioceramic particles in the scaffold through a variety of techniques and (2) coating a polymer scaffold with a thin layer of apatite through biomimetic processes. SLS was also investigated in the fabrication of porous structures manufactured of metals [33, 35], ceramics [2, 21, 30], and glasses [41]. As regards the DMLS, as previously described, the parts are built up layer-by-layer using a pre-alloyed Ti6AlV4 alloy in fine powder form [13].

## 4 Applications of selective laser sintering in biomedical engineering

Solid freeform fabrication processes have been recently introduced in biomedical applications when compared with their long-standing use in the manufacturing industries. In the past decades, SFF has been used in a variety of medical applications including the manufacturing of dimensionally accurate physical models of human anatomy derived from medical image data and the designing of implant and tissue using a variety of SFF technologies [13, 56, 69, 88]. As regards the possibilities for using SLS for biomedical applications they are numerous and are below listed.

### 4.1 Manufacturing of patient-specific anatomical models

Medical modeling, sometimes called biomodeling, refers to the creation of highly accurate physical models of human anatomy directly from medical scan data. The process involves capturing human anatomy data, processing the data to isolate individual tissues or organs, optimizing the data for the technology to be used and finally building the model using SFF techniques as described in Fig. 2.

Patient-specific anatomical models find applications particularly in oral [27, 48, 49, 75], maxillofacial [28, 52, 82, 96, 98, 102, 103], neurological surgery [59, 60, 85, 93]

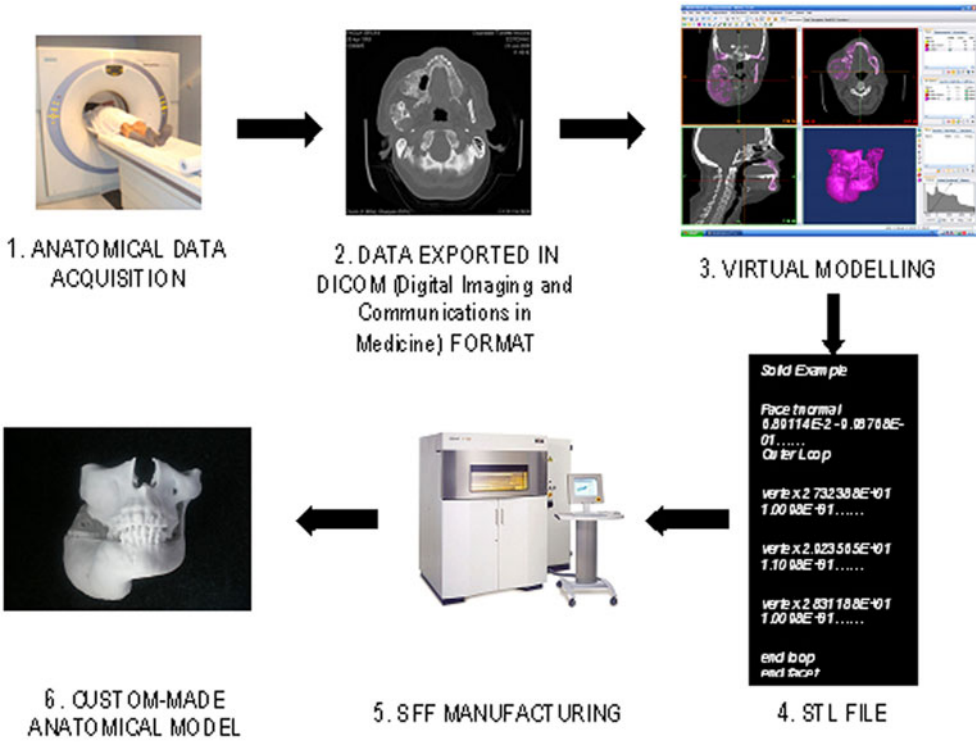


**Fig. 2** Custom-made anatomical models production chain

and orthopedics [36, 66, 73]. In medicine, they are mainly used for assisting diagnosis, planning treatment, and manufacturing implants [12, 15, 36, 90, 94, 95]. Custom-made anatomical models effectiveness has been shown in various surgical procedures [24, 25]. Patients find the medical models helpful for informed consent. Medical modeling is an intuitive, user-friendly technology that facilitates diagnosis and surgical planning, allowing surgeons to rehearse procedures readily and, moreover, improves communication between doctors and patients. Furthermore, SLS-manufactured models can be used in the reconstruction of post-traumatic defects, tumoral resections, and other complex craniofacial defects. SLS technologies, and SFF on the whole, can be of benefit in the pre-operating estimation of the quantitative surgical outcome, in the reduction of the operating time and in the production of more predictable results.

### 4.2 Implantable devices

The implantation of devices directly prepared by SLS has been reported in just one case. EOS, one of the world manufacturers of laser sintering systems, has shown the first PEEK craniofacial test implant at the co-located Pacific Design & Manufacturing West shows [22]. The test implants were fabricated in Germany using the EOSINT P 800 system using biocompatible PEEK material that is increasingly being used as an alternative to titanium for craniofacial implants for patients with head injuries or congenital deformities. As regards sintering processes in the direct fabrication of customized implants, the literature reports about DMLS, a useful technique for preparing three-dimensional porous bodies with complicated internal structures directly from titanium powders without any intermediate processing steps, with the products being expected to be useful as a bone substitute or customized implant as showed in Fig. 3 [13, 54, 63, 74]. SLM uses a high-powered ytterbium fiber laser to fuse fine metallic

**Fig. 3** Custom-made skull plate manufactured in medical-grade titanium using SLM technology

powders together to form functional three-dimensional parts.

Other papers analyzed the feasibility of utilizing SLS to fabricate polymeric drug delivery devices (DDDs) that are difficult to make using conventional production methods. Cheah et al. [7] investigated two features, namely porous microstructure and dense wall formation, inherent in SLS fabricated parts for their potential roles in drug storage and controlling the release of drugs through the diffusion process. Leong et al. explored the feasibility of using biodegradable polymers as the matrix to build DDDs using SLS. The biopolymers studied include PCL and PLLA. The relationship of the various SLS parameters such as laser power, scan speed, and part bed temperature with the porosity of the DDD matrix was studied. Methods of fabricating a DDD matrix with varying porosity and density to optimize drug loading and diffusion rate were investigated. The relationship of the SLS parameters and the microfeatures of the DDD matrix such as dense wall layers and internal pores were also investigated. Porosity of more than 50 % was attained and this indicates that feasible quantity of drug can be loaded into these devices [50]. As regards the field of oral implantology, some papers report on the investigations to produce dental prosthetic framework bases and restorations by means of SLS. Kruth et al. [43], for example, presented the fabrication of dental prosthetic implant framework bases by means of SLS using polymer-coated 420 stainless steel powder (LaserForm ST-100) on a SLS Sinterstation 2000 machine followed by an infiltration with bronze during a 24-h furnace cycle to produce a fully dense part. Strub et al. [83] described the use of SLS to fabricate either ceramic or metal dental restorations (Hint-ELs, Griesheim, Germany). Other applications of SLS for the indirect manufacturing of implantable devices include the fabrication of wax patterns by SLS from wax powder or polystyrene powder for application in maxillofacial surgery [102, 103]. In such applications the SLS machine fabricated the polystyrene resin prototypes of the anatomical defect. The above-cited papers demonstrate that the SLS resin prototype was an acceptable substitute for the conventional plaster/stone moulage cast/mold for laboratory processing.

### 4.3 Tissue engineering

The term “tissue engineering” was up to the mid 1980s loosely applied in the literature in cases of surgical manipulation of tissues and organs or in a broader sense when prosthetic devices or biomaterials were used. The term “tissue engineering” as used nowadays was introduced in medicine in 1987 [81]. A key point in tissue engineering was given by the close cooperation between Langer and Vacanti [45] and may be referred as the beginning of this biomedical discipline. The field relies on the use of porous 3D scaffolds to provide the appropriate environment for the regeneration of tissues. In order to promote tissue growth, the scaffold must have a large surface area to allow cell attachment. This is usually done manufacturing highly porous scaffolds. In these scaffolds, the pore size should be large enough so that cells penetrate the pores, and the pores must be interconnected to facilitate nutrient and waste exchange by cells deep within the construct [37]. 3D models and relative SLS manufactured scaffolds are showed in Fig. 4.

These characteristics (porosity and pore size) are often dependent on the method of scaffold fabrication [51]. Several methods have been developed to create highly porous scaffolds, including fiber bonding [57], solvent casting/particulate leaching [58], gas foaming [62] phase separation [61], soft lithography and electrospinning [68].

Although the above-cited conventionally produced scaffolds hold great promise and have been applied to engineer a variety of tissues with varying success, most are limited by some forms of flaws, which restrict their scope of applications. Among the main limitations are manual intervention required, use of inconsistent and inflexible processing procedures, use of toxic organic solvents, use of porogens, and shape limitations. For this reason, SFF techniques play an important role in the manufacturing of advanced tissue engineering scaffolds. Diverse papers explored the viability of using the powder-based SLS technique for fabricating polymeric and composite TE scaffolds with desirable macro- and micro-structural characteristics. Lee et al. [46, 47] looked into the development of bioceramic scaffolds that can aid the regeneration of hard tissues for recovery of bone defects and injuries via laser sintering of HA powders that were coated with a secondary polymeric binder, poly (methylmethacrylate) (PMMA). A slurry comprising of predetermined mixing ratios of ceramic particles and PMMA was sprayed dried to obtain the PMMA-coated HA powders. In addition, diluted methanol was used in the fabrication process. Since the use of organic solvents is highly undesirable for the processing of TE scaffolds as mentioned, other researchers circumvent the use of solvents utilizing pure biopolymer powders and physically blended mixtures of polymers and HA powders. Tan et al. [87–89] proposed the use of polyetheretherketone (PEEK) powders and physically blended mixtures of PEEK and HA powders. They studied the feasibility of sintering such powder blends and the influence of SLS process parameters on the sintering quality and resulting microstructure of the sintered specimens. The results observed from the micrographs indicate the viability of them being used for building TE scaffolds and ascertain the capabilities of the SLS process for creating highly porous scaffolds for TE applications. Other researchers proposed the use of

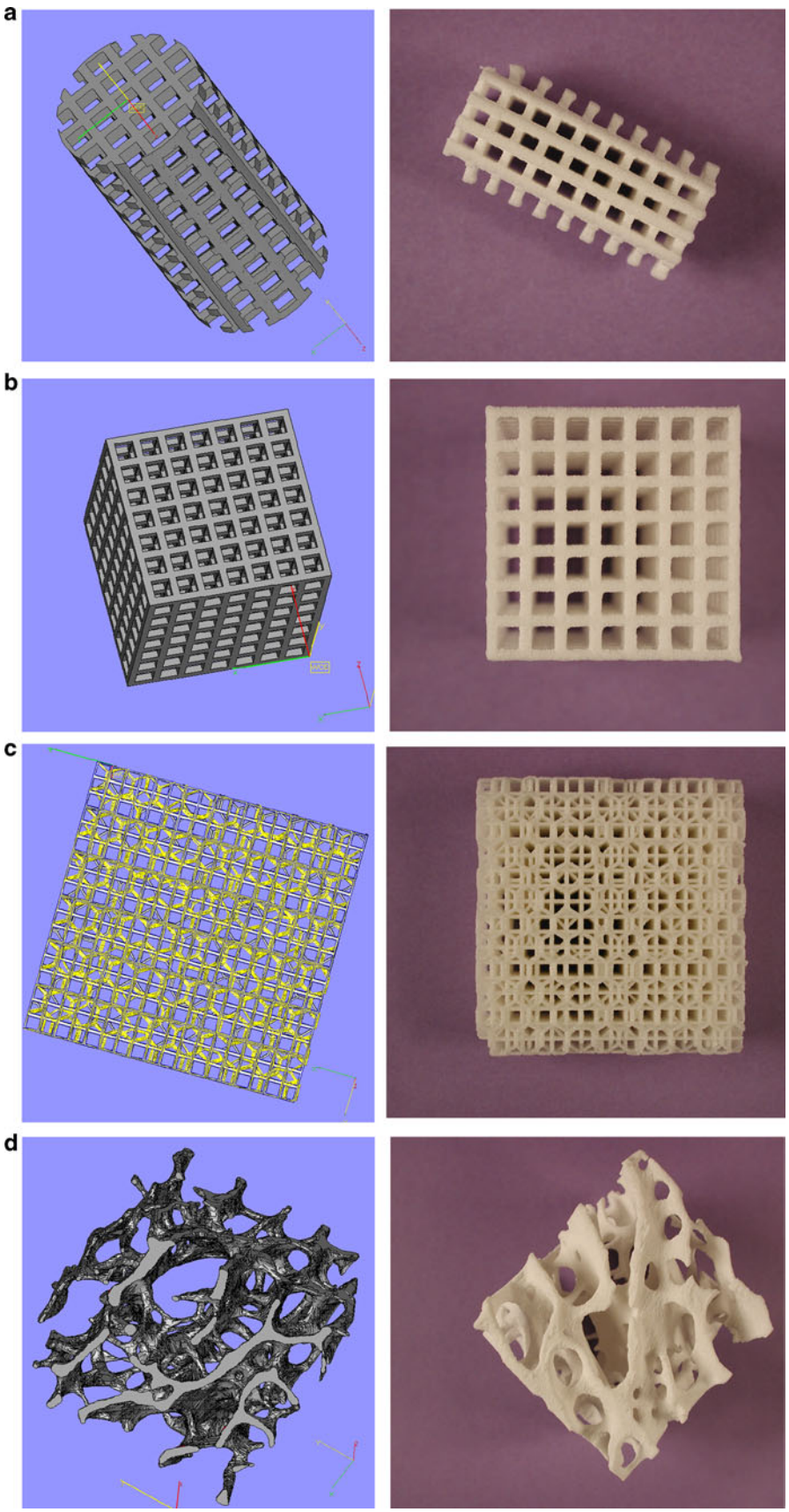


**Fig. 4** 3D models (*left*) and relative SLS manufactured scaffold (*right*). **a** Cylindrical with interconnected porosity (500 μm *x*/*y*/*z*). **b** Square with interconnected porosity (500 μm *x*/*y*/*z*). **c** Three-layers superposition. Hexagonal, square and octagonal periodical structures with 500 μm side each. **d** Human trabecular bone tissue acquired from micro-CT

a biocomposite blend comprising of PVA and HA in SLS to study the feasibility of the blend to develop scaffolds [10, 89, 100]. The biocomposite blends obtained via spray-drying technique and physical blending were subjected to laser-sintering to produce test specimens. The SLS-fabricated test specimens were characterized using scanning electron microscopy and X-ray diffraction. The test specimens were also tested for bioactivity by immersing the samples in simulated body fluid environment. The results obtained ascertained that SLS-fabricated scaffolds have good potential for TE applications. Williams et al. [97] employed SLS to create scaffolds in polycaprolactone (PCL). With respect to SLS, PCL has certain advantages relative to other polymers such as poly lactic acid (PLA). PCL is more stable in ambient conditions; it is significantly less expensive and is readily available in large quantities. The main features of PCL are the low glass transition temperature and the low melting temperature that facilitate the prototyping process. The main drawbacks are represented by its hydrophobicity and, then, by its long degradation period in clinical conditions. Blends between PCL and a polysaccharide (starch, gellan, or dextran) were selected as materials for the fabrication of laser-sintered scaffolds by a new custom-made prototype machine by Ciardelli et al. [11]. Blending PCL with a suitable hydrophilic natural polymer was found to be a promising and easy method to improve PCL biocompatibility. In fact fibroblasts adhered to the manufactured scaffolds at higher rate and extent than to pure PCL. Huang et al. [34] studied the possibility to engineer implantable liver tissues. For the fabrication of such a scaffold, biodegradable PCL and 80 % (w/w) NaCl salt particles, serving as porogen, were thoroughly mixed and applied in a SLS apparatus. The integration of a scaffold design to provide a 3D flow-channel network, precise 3D microfabrication techniques, optimized seeding methods, and the adopted perfusion culture show good results for the development of large implantable liver tissues in vitro. Smith et al. [82] investigated the manufacture of a computer-designed scaffold for temporomandibular joint replacement. Using a Yucatan minipig animal model, they have created a condylar ramus unit (CRU) scaffold by SLS using PCL powder. Diverse researchers investigate the use of biocomposite material, consisting of PCL and HA, to fabricate TE scaffolds using SLS [23, 99, 104]. In the above-cited papers the seeded cells were able to live and replicate on the fabricated scaffolds showing the favorable potential of PCL/HA biocomposites. PCL scaffolds have been investigated also in terms of mechanical properties with respect to the natural bone tissue showing that mathematical relations correlating scaffold porosity and compressive stiffness readings can be formulated and compiled [6, 26, 84]. Thus, the construction of bone tissue engineering scaffolds endowed with oriented porous architectures and with predictable mechanical properties through SLS could be demonstrated.

Duan et al. [17–19] proposed the use of calcium phosphate (Ca–P)/poly(hydroxybutyrate-co-hydroxyvalerate) (PHBV) nanocomposite microspheres for the manufacturing of three-dimensional Ca–P/PHBV scaffolds via SLS for bone tissue engineering applications. PHBV belongs to the class of polyhydroxyalkanoates (PHAs). PHAs are natural aliphatic polyesters, produced by many Gram-positive and Gram-negative bacterial cells as intracellular carbon and energy storage compounds, under unbalanced growth conditions. PHAs are attractive as biomaterials for applications in TE due to their biocompatibility and easy processability, as well as to the broad range of mechanical and biodegradation properties related to the large variety of PHAs homopolymers and copolymers [67]. Another class of biodegradable synthetic polymers is often utilized for the preparation of 3D scaffolds in bone and cartilage TE. Such polymers are saturated poly-α-hydroxy esters, including poly(lactic acid) (PLA) and poly(glycolic acid) (PGA), as well as poly(lactic-co-glycolide) (PLGA) copolymers [70]. PLA exists in three forms: L-PLA (PLLA), D-PLA (PDLA), and racemic mixture of D,L-PLA (PDLLA). The chemical properties of these polymers allow hydrolytic degradation through de-esterification. Once degraded, the monomeric components of each polymer are removed by natural pathways. Poly-α-hydroxy esters have been extensively studied for the fabrication of scaffolds via SLS for applications in TE. Tan et al. [89] proposed the use of a biocomposite blend comprising of PLLA and HA in SLS. Results observed from the scanning electron microscope (SEM) micrographs indicate the viability of the blend used for building TE scaffolds and ascertain the capabilities of the SLS process for creating highly porous scaffolds for TE applications. Simpson et al. [80] investigated 95/5 PLLGA for the role of a porous scaffold, using the SLS fabrication process, with powder sizes of 50–125 and 125–250 μm. SLS parameters of laser power, laser scan speed, and part bed temperature were altered and the degree of sintering was assessed by SEM analysis. Composites of the 125–250 μm polymer with either hydroxylapatite or hydroxylapatite/beta-tricalcium phosphate (CAMCERAM II) were sintered, and SLS settings using 40 wt % CAMCERAM II were optimized. The results have shown that such a composite and fabrication method has potential in the fabrication of porous scaffolds for bone tissue engineering. Zhou et al. [107] focused on the use of bio-nanocomposite microspheres, consisting of carbonated hydroxyapatite (CHAp) nanospheres PLLA matrix, to produce TE scaffolds using a modified SLS machine. Porous scaffolds were successfully fabricated from the PLLA microspheres and PLLA/CHAp

nanocomposite microspheres. In particular, the PLLA/CHAp nanocomposite microspheres appeared to be promising for porous bone TE scaffold production using the SLS technique. Kanczler et al. [38] successfully cultured fetal femur-derived cells on selective laser-sintered poly(D,L)-lactic acid (SLS-PLA) scaffolds. In fact alkaline phosphatase activity was noted after 7 days. Moreover, SSLS-PLA scaffolds and SSLS-PLA scaffolds seeded with fetal femur-derived cells implanted into a murine critical-sized femur segmental defect model aided the regeneration of the bone defect providing a template for cell osteogenesis both in vitro and in vivo. Duan et al. [18] study investigated three-dimensional nanocomposite scaffolds based on CHAp/PLLA nanocomposite microspheres manufactured via SLS. CHAp/PLLA nanocomposite scaffolds exhibited a similar level of cell response compared with PLLA polymer scaffolds. The nanocomposite scaffold provided a biomimetic environment for osteoblastic cell attachment, proliferation, and differentiation showing great potential for bone tissue engineering applications. Bukharova et al. [5] studied the biocompatibility of porous PLA carrier matrices obtained by means of surface SLS. Carrier matrices had no cytotoxic activity, but maintained adhesion and proliferation of cells. Subcutaneous transplantation of tissue engineering constructions from these carriers and bone marrow-derived multipotent stromal cells did not cause the inflammatory response and pathological changes in rats.

SLS has been investigated for the production of bioactive implants and tissue scaffolds also using composites of high-density polyethylene (HDPE) reinforced with HA by Hao et al. [32].

As previously said although many conventional fabrication techniques exist for TE scaffold production, these techniques are manual-based processes with characteristics that may not be suitable for achieving customized production. Further to this, imperfections in the fabricated scaffolds, due to the poor flexibility and control offered by such techniques, limit the application of the scaffolds themselves. Computer-controlled fabrication via SLS technology may hold the key for a generic solution in automating scaffold production that can cater for variations in the shapes and requirements of different tissues and organs and also size variations between different individuals.

Moreover, diverse articles investigate the cellular response to some of the above-cited biomaterials used for scaffolding by SLS. Duan et al. [18], for example, found that in vitro biological evaluation showed high cell viability and normal morphology and phenotype after 3 and 7 days culture on all the proposed scaffolds. Moreover, the incorporation of Ca–P nanoparticles significantly improved cell proliferation and alkaline phosphatase activity for Ca–P/PHBV scaffolds, whereas CHAp/PLLA nanocomposite scaffolds exhibited a similar level of cell response compared with PLLA polymer scaffolds.

Bukharova et al. [5] showed that the proposed polylactide carrier matrices had no cytotoxic activity, but maintained adhesion and proliferation of cells. Subcutaneous transplantation of tissue engineering constructions from these carriers and bone marrow-derived multipotent stromal cells did not cause the inflammatory response and pathological changes in rats. The proposed nanocomposite scaffolds provide a biomimetic environment for osteoblastic cell attachment, proliferation, and differentiation and have great potential for bone tissue engineering applications.

## 5 Conclusions

Selective laser sintering is an additive manufacturing technology where parts are constructed by the sequential and controlled deposition of powder in a layer-by-layer fashion. In each layer the powder surface is selectively scanned according to the cross-sectional data of a previously created 3D CAD model. In the scanned regions particle coalescence is associated with a significant reduction in surface energy, which is the main driving force of sintering. SLS has the potential to fabricate complex geometries with intricate and controllable internal architectures. SLS enables the processing of numerous biocompatible polymers available in the form of powders. It has a strong prospective for biomedical applications, especially in combination with medical imaging techniques such as MRI and CT. It has proven to facilitate, speed up, and improve the quality of surgical procedures such as preoperative planning, implant design, and placement and complex surgeries. The use of biocompatible polymers has enabled the direct manufacturing of DDDs and biodegradable tissue engineering scaffolds. Moreover, the introduction of Ca–P based composites has turned SLS into a widely applicable technique for biomedical engineering purposes.

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