POLYMERIC BIOMATERIALS AND 3D PRINTING

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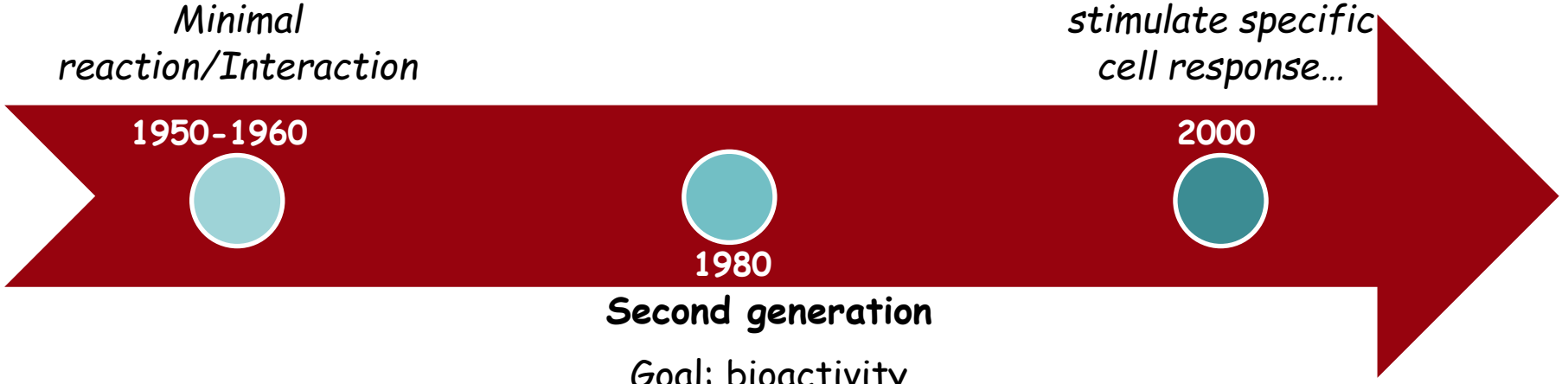
INTRODUCTION

A biomaterial is a nonviable material used in a medical device, intended to interact with biological systems.

Williams, 1987



First generation

Goal: bioinertness

Minimal reaction/Interaction

Second generation

Goal: bioactivity

Resorbable biomaterials,

Controlled reaction with the physiological environment

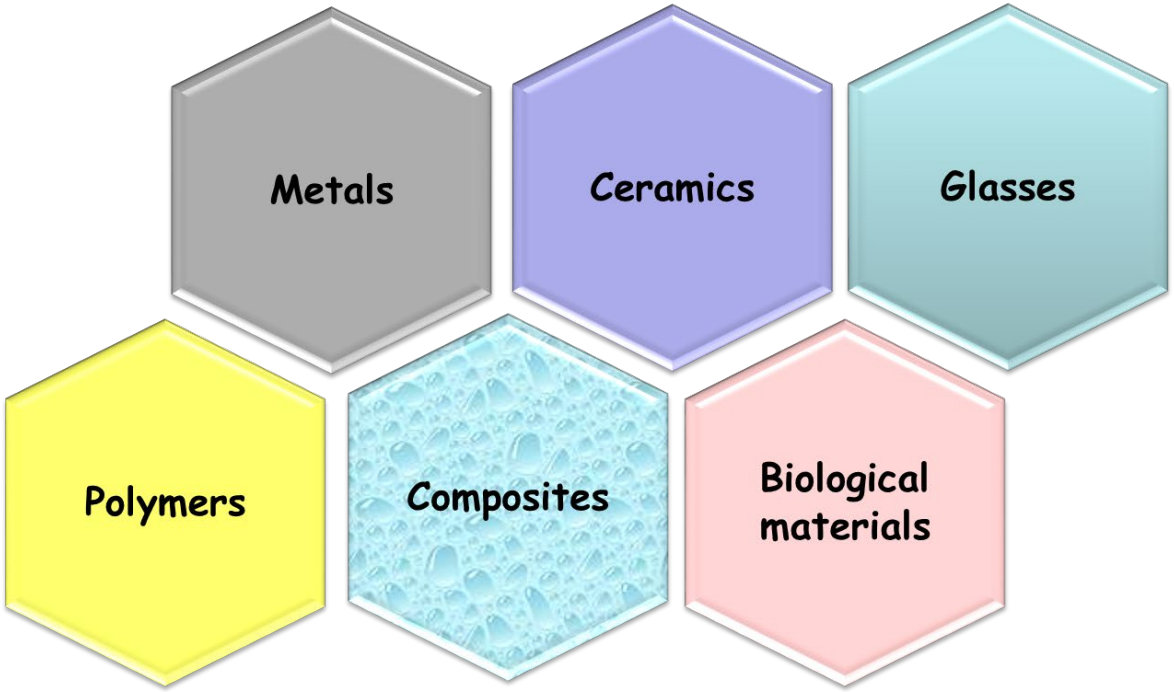
Third generation

Goal: regenerate functional tissue

Biointeractive, integrative, resorbable, stimulate specific cell response…

INTRODUCTION

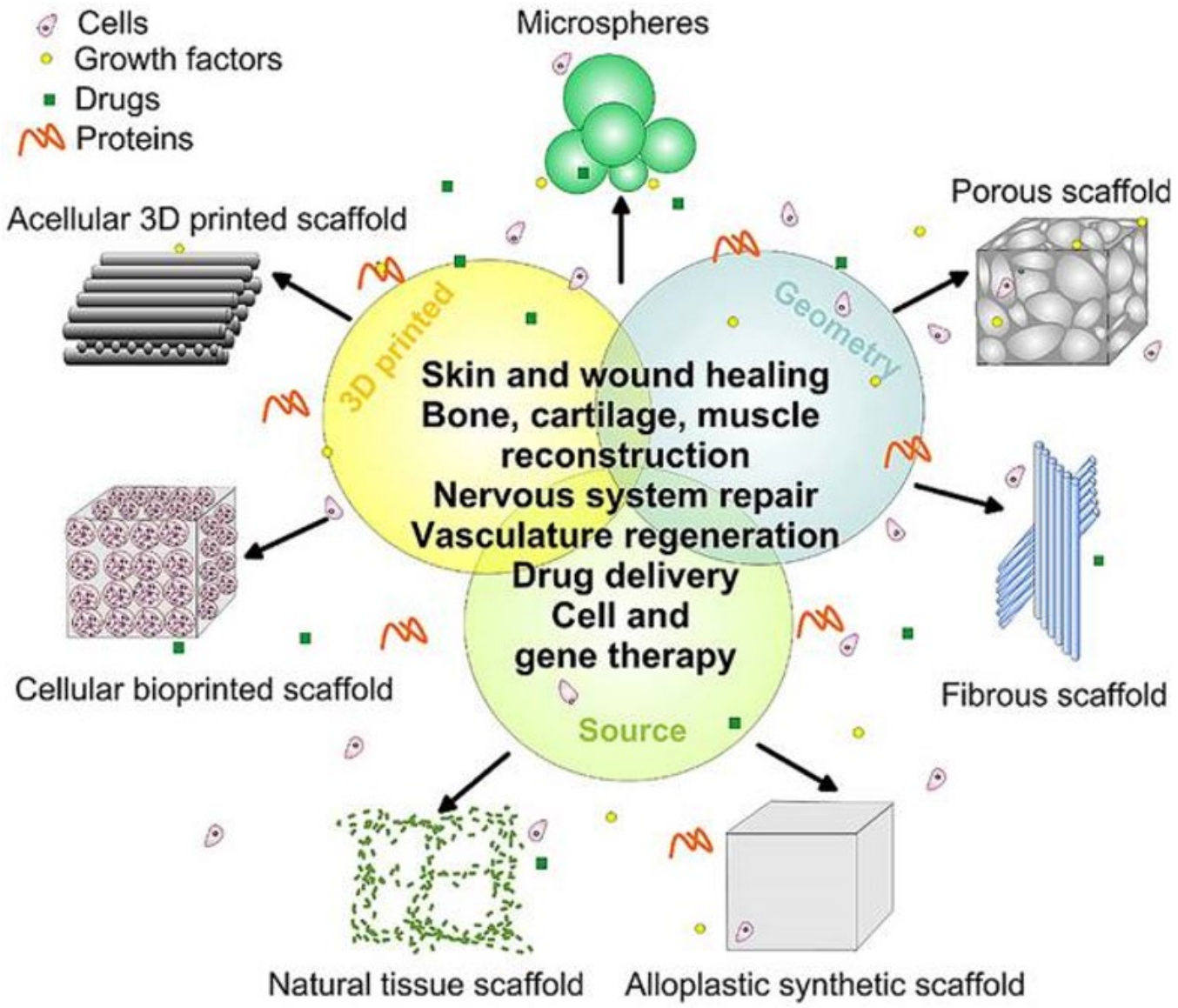
Biomaterials



Used as molded or machined parts, coatings, fibers, films, membranes, foams, fabrics and nano- or microparticles…

Polymeric biomaterials processed by 3D-printing

INTRODUCTION



Nicolova et Chavali, Bioactive Materials, 2019

3D PRINTING OF POLYMERIC BIOMATERIALS

3D printing: additive technology

Layer by layer deposition using computer-aided design (CAD) models

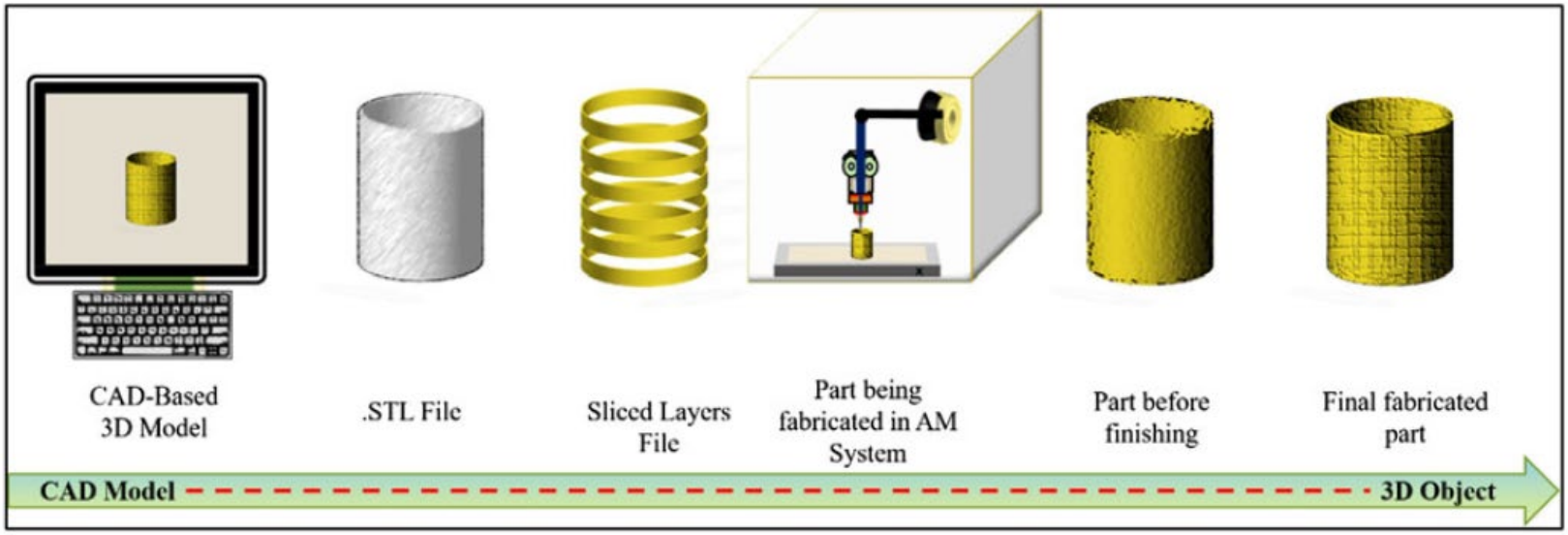
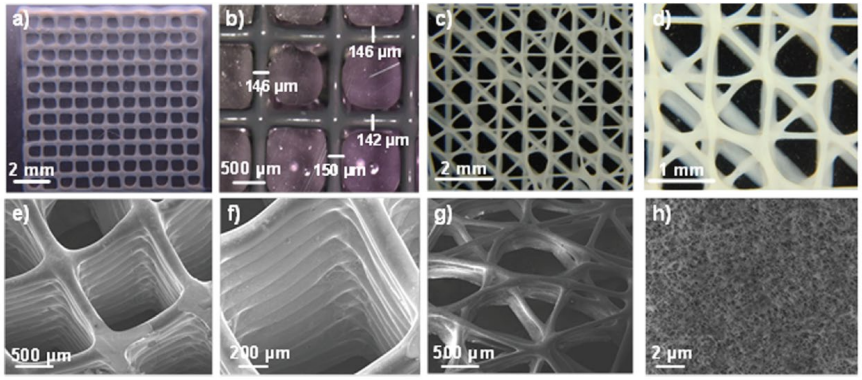


Figure 2. Overview and basic principle of additive manufacturing and processes involved in the design and fabrication of 3D objects.

A. Sandeep Kranthi Kiran et al. Nanocomposites, 2019

⇒ Production of complex 3D objects with controlled structure, microarchitecture, and porosity

Scaffolds

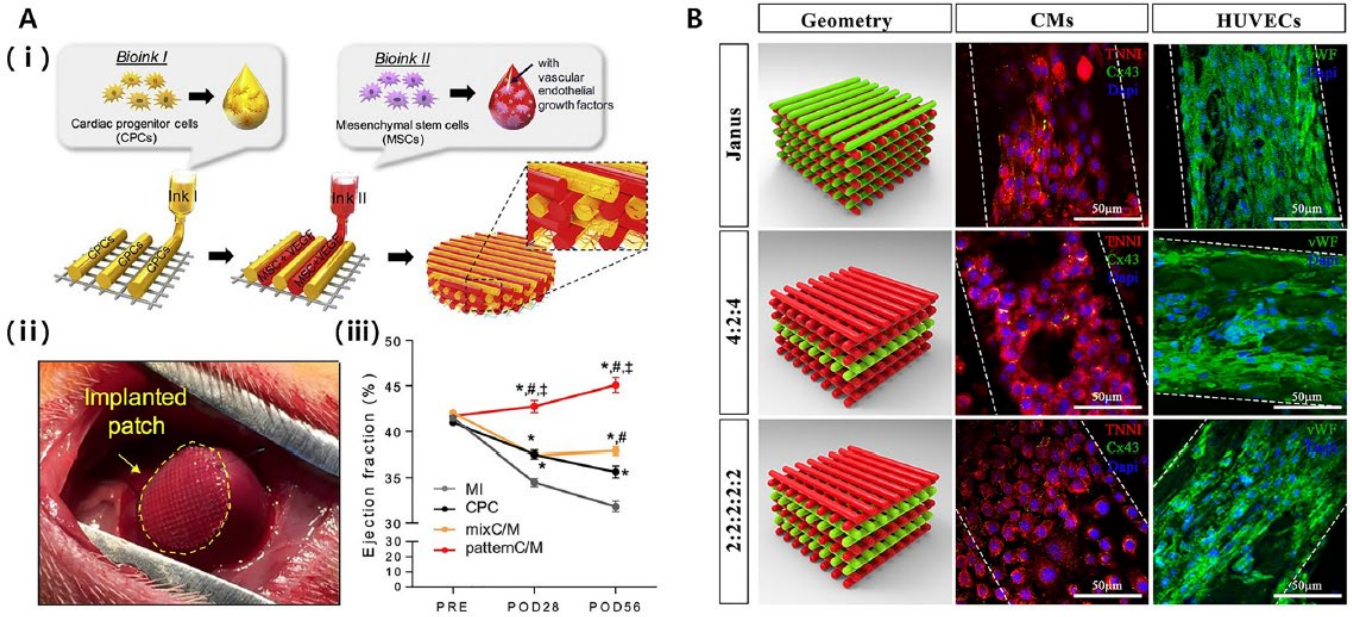


Mora-Boza et al, Biomaterials Science, 2019

Barios-Murel et al, Materials, 2020

Orthoses and prosthetic devices

Tissue engineering and regenerative medicine



ALL3DP

FIG. 4. (a) (i) Schematic representation of fabricating the multicellular and multilayered pre-vascularized cardiac patch by using an hdECM bioink and the supporting PCL framework. (ii) Macroscopic view of the implanted patch. (iii) Ejection fraction values at baseline and after 4 and 8 weeks. Error bars represent ($^*p<0.05$ comparison with MI; $\#p<0.05$ comparison with CPC; $\ddagger p<0.05$ comparison with mixed group C/M containing both CPC and MSCs), POD: post-operative day. [Reproduced with permission from Jang *et al.*, Biomaterials **112**, 264–274 (2017). Copyright 2017 Elsevier.[98]] (b) Janus-based 3D bioprinted cardiac tissue constructs consisting of HUVEC and hiPSC-CMs. Representative images showing the expression of cardiac troponin I (TNNI, red) and Cx43 (green) in cardiomyocytes and the von Willebrand factor (vWF, green) in HUVECs at seven days. Scale bar, 50 μm. [Reproduced with permission from Maiullari *et al.*, Sci. Rep. 8(1), 13532 (2018). Copyright 2018 Authors, licensed under a Creative Commons Attribution (CC BY) license.[100]]

VARIOUS 3D PRINTING TECHNOLOGIES

- **Stereolithography**

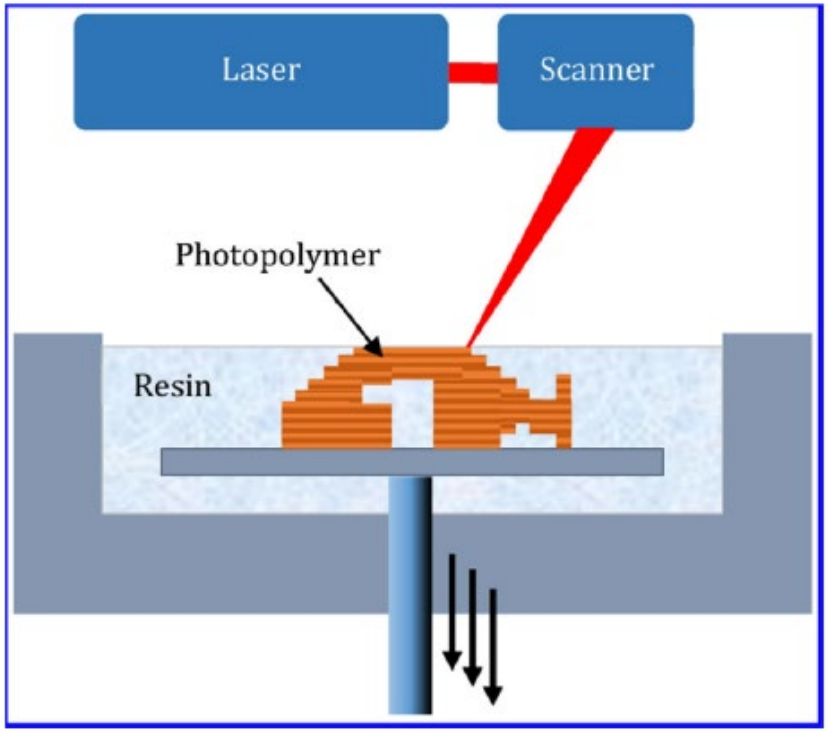
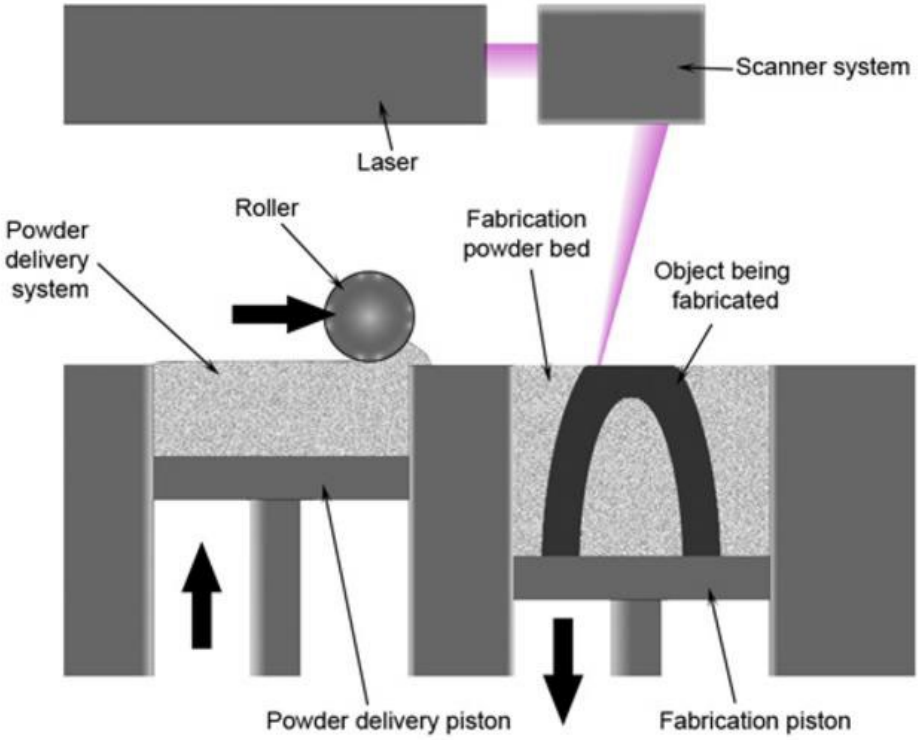


Fig. 1. Illustrative scheme to introduce the configuration of stereolithography. Reproduced with permission [43]. Copyright 2015, Academy of Dental Materials.

Li et al, Material Science & Engineering R, 2020

- **Selective laser sintering (SLS)**



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➢ Extrusion-based 3D printing

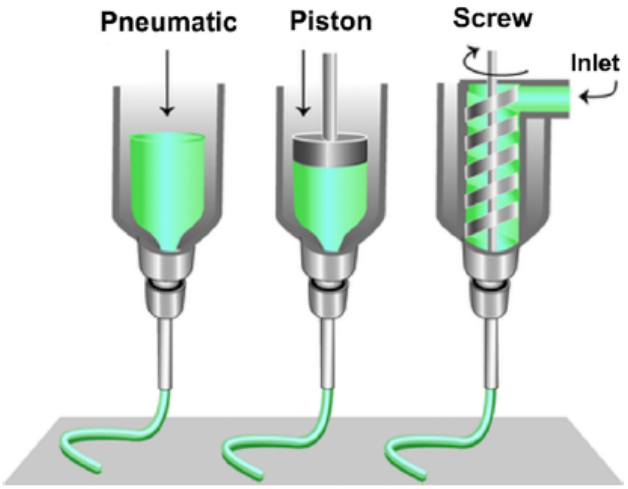

Fig. 4. Schematic diagram to illustrate the working principles of extrusion-based 3D printing technique.
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Li et al, Material Science & Engineering R, 2020

Fused deposition modeling (FDM)

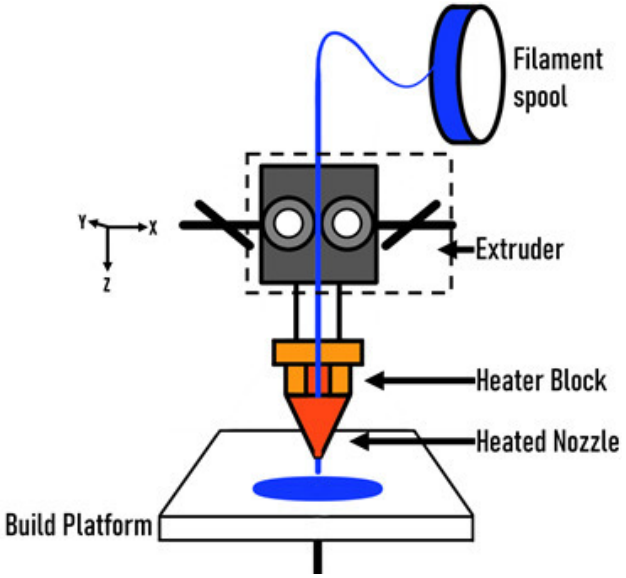

Image credit: Christian Cavallo Consulting

➢ Inkjet 3D printing

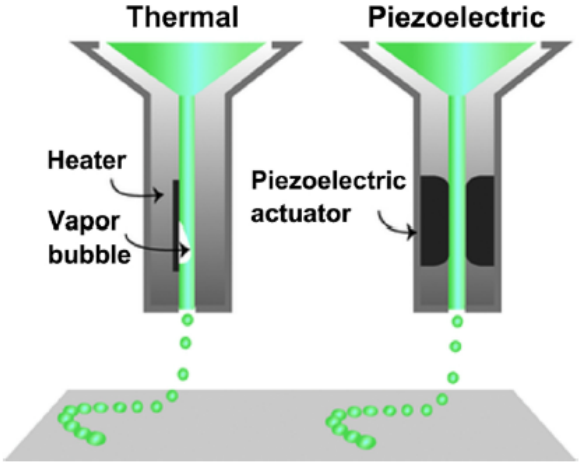

Fig. 5. Schematic diagram to show the working principles of inkjet printing technique.
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Li et al, Material Science & Engineering R, 2020

REQUIREMENTS FOR PRINTABLE MATERIALS

Have the capacity to form 3D structures
Self-supporting devices
(essential for good shape fidelity)

Can be mechanically reinforced (UV, chemical, physical crosslinking…)

Have tunable mechanical properties

Be biocompatible

Have adequate rheological properties to be printable
Appropriate viscosity
Shear-thinning and thixotropic behavior

Polymers
Hydrogels
Bioinks

Be biomimetic and display bioactivity

Have adequate degradation kinetics

Form non toxic degradation byproducts

Be able to control the release of active substances

POLYMERS USED FOR 3D PRINTING OF BIOMATERIALS

Solid polymers-based inks
for FDM (filaments) and SLS (powder beads)
-polylactic acid (PLA)
-polycaprolactone (PCL)
Important properties: melting temperature, elastic modulus, elongation at break

Table 1
Common polymers used in 3D printing and their properties.

Name	Melting point	Stiffness	Limitation	Advantages
ABS	105 °C	30 MPa	Not biodegradable and shrinks in contact with air.	Good strength and flexibility.
PLA	175 °C	230 MPa	Long-term biocompatibility.	Good mechanical properties; Low cost.
PCL	60 °C	216 MPa	Long degradation time (3 years).	Excellent rheological and viscoelastic properties upon heating; Low cost.
PC	110 °C	2250 MPa	Absorb moisture from the air affecting performance and printing resistance.	Tunable mechanics and porosity.
PEEK	350 °C	3.6 GPa	High melting point.	High mechanical and thermal resistance; Very strong and at the same time much lighter than some metals.
PP	165 °C	1.6 GPa	Low temperature resistance; Sensitivity to UV rays.	Lightweight.
Polyamides	250 °C	10 MPa	Most used for SLS technology.	Good stability, flexibility, and shock resistance.
TPU	235 °C	100 MPa	Cannot withstand high temperatures.	Tunable stiffness.

Pugliese *et al.*, Annals of 3D printed medicine, 2021

POLYMERS USED FOR 3D PRINTING OF BIOMATERIALS

Polymeric hydrogels based inks
Proteins
Polysaccharides
Important properties: gelation mecanism and kinetics, rheological properties, mimicking native extracellular matrix microenvironment and ability to incorporate cells

Table 2
Common Hydrogel inks used in bioprinting and their biological and physical-chemical properties.

Name	Molecule Type	Shear-Thinning	Biological Interactions	Gelation Process
Collagen	Protein	No	High cell adhesion	Thermal/Enzymatic
Fibrin	Protein	No	High cell adhesion	Thermal/Chemical/Enzymatic
Gelatin	Protein	Yes	Medium cell adhesion	Thermal/Chemical/Enzymatic
Spider Silk	Protein	Yes	Low cell adhesion	Self-assembly
Matrigel	Protein	Yes	High cell adhesion	Thermal
Gelatin Methacrylamide	Protein	Yes	Medium cell adhesion	Chemical/Enzymatic
Self-assembling peptides	Peptide	Yes	High cell adhesion	Self-assembly
Alginate	Polysaccharide	Yes	Low cell adhesion	Ionic/Chemical
Chitosan	Polysaccharide	No	Low cell adhesion	Ionic
Gellan Gum	Polysaccharide	Yes	Low cell adhesion	Ionic
Agarose	Polysaccharide	Yes	Low cell adhesion	Thermal
κ-Carrageenan	Polysaccharide	Yes	Low cell adhesion	Ionic/Thermal
Methylcellulose	Polysaccharide	No	Low cell adhesion	Thermal

Pugliese *et al.*, Annals of 3D printed medicine, 2021

CONCLUSION

3D printing of polymer-based biomaterials provides:
-patient specific designs
-high structural complexicity
-rapid on demand fabrication with low cost

Bottlenecks: lack of biomaterials, hydrogels and bioinks that are biocompatible with appropriate biomechanical properties to meet the different needs
Necessity to develop appropiate quality controls and regulations

Towards 4D printing…

-Dynamic and stimuli-responsive bioinks (change of function with T, magnetic field, light, pH…)

-Scaffolds with shape memory
(can recover quickly from changes once implanted in the body)