Introduction to 3D Printing

NIH Center for Engineering Complex Tissues (CECT)
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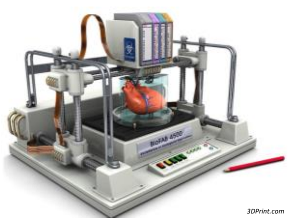
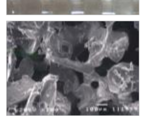
3D Printing and Biofabrication



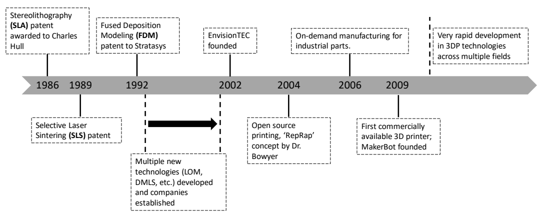
3DPrint.com

Fabrication approaches

- Bulk geometry (Macrostructure)
  - Shaping
  - Molding
  - Fiber bonding
  - Layered fabrication
- Interior geometry (Microstructure)
- Control over porosity, pore size, fiber size, interconnectivity etc.
  - Porogen leaching
  - Phase separation
  - Freeze drying
  - Gas foaming
  - Electrospinning



A Brief History of 3D Printing

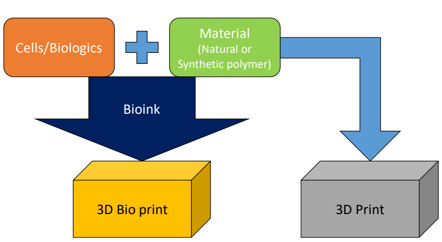


Emergence of 3D Printing in Healthcare and Medicine

- Dentistry (restorations, dental models)
- Tissue models (implantation, drug testing)
- Surgery (maxillofacial, cranial, cardiovascular)
- Medical devices (surgical instruments, prostheses, hearing aids)
- Drug formulations (drug delivery, personalized medicine)

Biofabrication 9:024102 (2017)

Bioprinting



3D Printing techniques

Light-based
- Stereolithography (SLA)
- Digital Light Projection (DLP)
- Laser-Induced Forward Transfer (LIFT)
- Selective Laser Sintering (SLS)

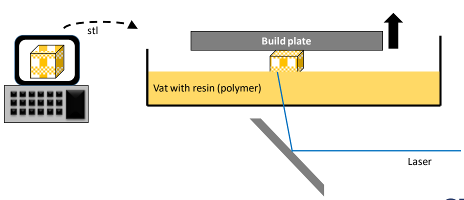
Extrusion-based
- Fused Deposition Modeling (FDM)
- Microextrusion printing

Inkjet
- Drop-on-demand
    - Piezo electric
    - Thermal
- Continuous

Others
- Electrospinning
- Scaffold-free

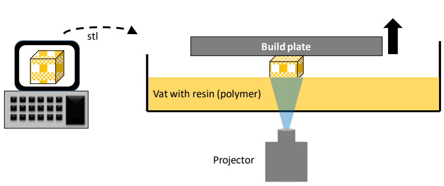
Vat Photopolymerization

Stereolithography (SLA)



Vat Photopolymerization

Stereolithography (SLA)



Vat Photopolymerization

Advantages

- High resolution (~20 μm)
- Controllable crosslinking to tailor mechanical properties
- Compatible with photopolymerizable materials

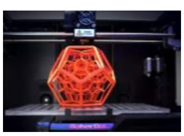
Disadvantages

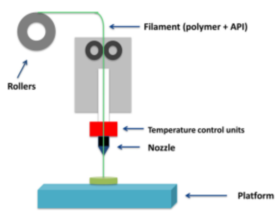
- Slow fabrication (hours) and requires support structures
- Photoinitiators/inhibitors are detrimental to cell viability
- Not always cell compatible
- Typically single-material
- Requires post-fabrication processing

Extrusion-based printing

Fused Deposition Modeling

- Thermoplastics (T_m ~ 200 °C)
- Layer-by-layer print





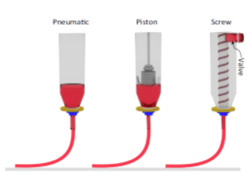
Konta et al., Bioengineering 2017, 4, 79

Extrusion-based printing

Microextrusion Printing

- Varying needle diameters
- Wide range of materials
  - High viscosity but ideally shear thinning

F.P.W. Melchels et al. / Progress in Polymer Science 37 (2012) 1079–1104

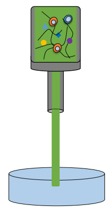


Knowlton et al., Trends in Biotechnology, 2015, Vol. 33, No. 9

Extrusion-based printing

Microextrusion Printing

- A method of crosslinking is essential if the individual polymer strands will not fuse
- Photo-induced
  - GelMA – photoinitaitor
- Chemical
  - Alginate – CaCl2
  - Gelatin – Transglutaminase
- Thermal
  - Collagen



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Extrusion-based printing

Advantages

- Ability to deposit large cell populations in a spatially controlled manner
- Very fast fabrication (minutes) and broad range of possible materials
- Capable of different crosslinking techniques: access to larger library of materials
- Multi-nozzle printing enables multi-material printing with varying properties

Disadvantages

- Modest resolution (~100 µm)
- Limited viscosity range of materials
- The high shear stresses within the printing nozzle can be deleterious for cells
- Customization required for each material type

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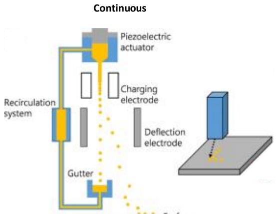
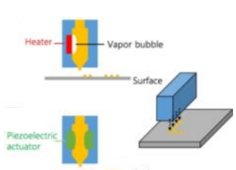
Inkjet Printing

Continuous



Drop on demand



Cho at el., Inkjet-based 3D printing, IOP Science, 2015

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Inkjet Printing

Advantages
- Typically low cost
  - Commercial inkjets modified
- Bioinks with low viscosity or cells w/media can be printed with reliable accuracy
- Cell-friendly

Disadvantages
- Cell membrane damage
- Bioinks require low viscosity
- Requires rapid gelling or support substrate

Summary

	Biomaterials	Cell viability / resolution	Speed	Cost	Advantages	Disadvantages
Inkjet	Low-viscosity suspension of biologics	~90% 20 – 100 um	Fast	Low	• High resolution, speed • Concentration gradients	• Poor vertical structure incorporation • Limited bioinks
Pressure-driven	Hydrogels, select thermoplastics	40 – 80% >100 um	Slow	Medium	• Many bioinks available • Broad operating ranges	• Gelation limitations • Shear stress
Laser-assisted	Hydrogel, media, cells, proteins	>95% >20 um	Medium	High	• Nozzle-free, non-contact • High precision	• Slow • Requires metal film • Limited materials
Stereolithography	Light-sensitive polymers, curable acrylics	>90% ~12 – 200 um	Medium	Low	• High accuracy • Many available resins	• Photopolymerizable-only • Issues with cell viability • Post-processing

Li et al. J Transl Med (2016) 14:271

Other methods

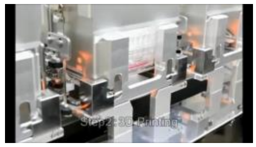
LIFT (Laser Induced Forward Transfer)

Laminate Object Manufacturing (LMO)

Micro and Nano-scale printing (**Nanoscribe**)

Scaffold-free fabrication

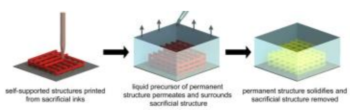
- No biomaterial/ECM for cell support
- Kenzan method for spheroid-based 3D Printing
  - Fusion of cell spheroids on a needle array Cell-secreted EXM and biomolecules
- High cell density applications



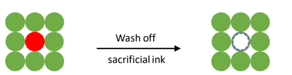
Sacrificial templating

A material that is 3D printed (either for support or as a feature), along with the bioink of interest, only to be removed upon completion of the print

- Pluronic F-127, Glass carbohydrate



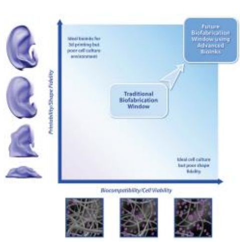
O'Bryan et al., MRS Bulletin, 42(08):571-577



Print desired bioink/sacrificial ink

'Cavity', infused with cells

Tradeoffs while printing



Kyle et al., Adv. Healthcare Mats. 2017, 6, 1700264

Takeaways

- Various 3D printing techniques
- Advantages and disadvantages of each
- Application specificity for each printing technique