A Brief Description of Tissue Engineering and Biofabrication Techniques

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3rd Annual 3D Printing and Biofabrication Workshop

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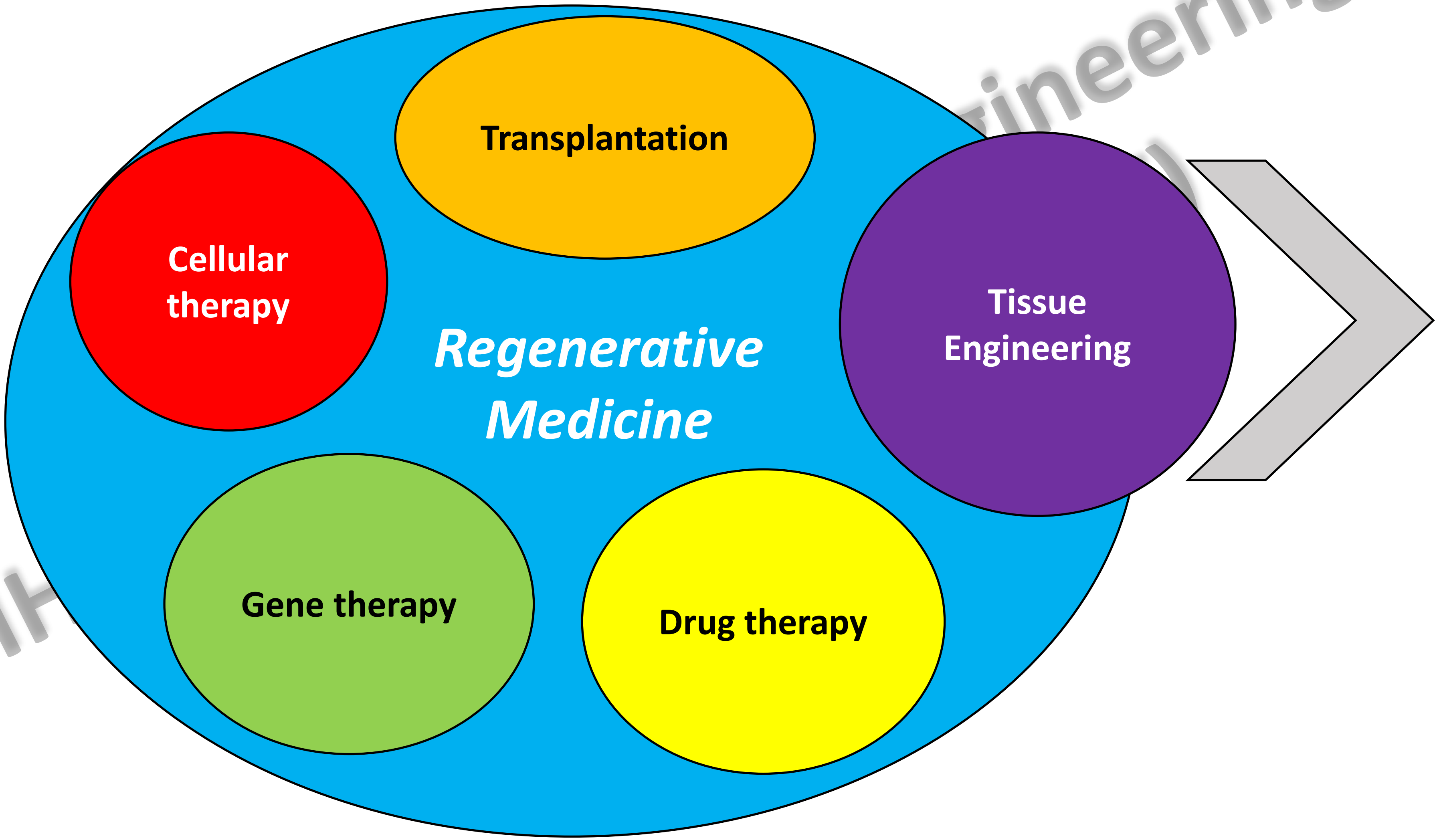
Goals

- Understanding the basic concepts of 3D Printing and Bioprinting
- The printing process: concept to product
- Opportunities and Limitations
- Applications in research
- Broad range of attendance

Tissue Engineering and Regenerative Medicine (TE/RM)



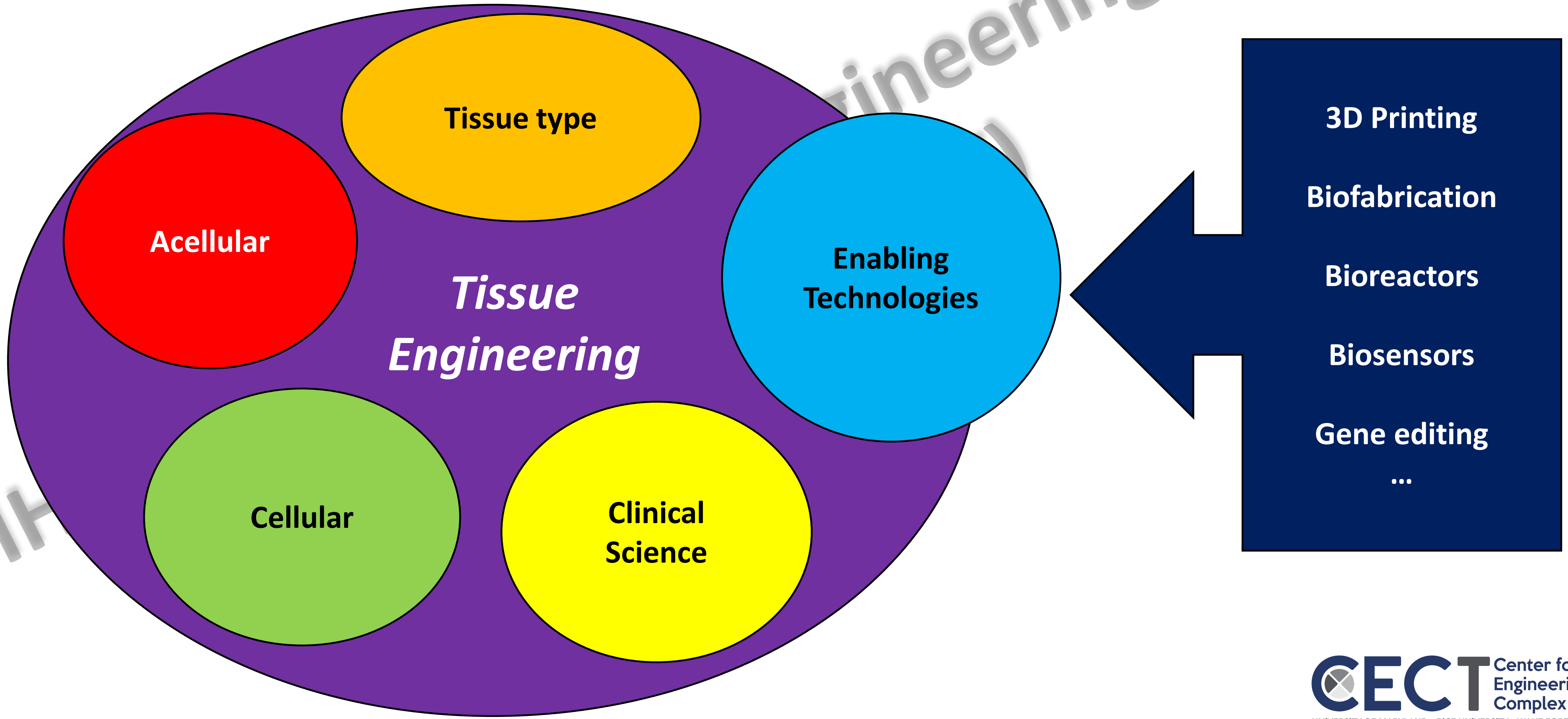
Applications in:

Investigative biology

Clinical implantation

Therapeutics

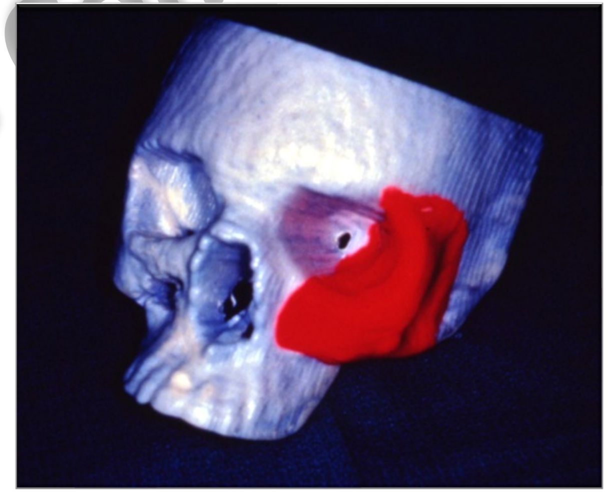
Tissue Engineering and Regenerative Medicine (TE/RM)



Addressing a biomedical need

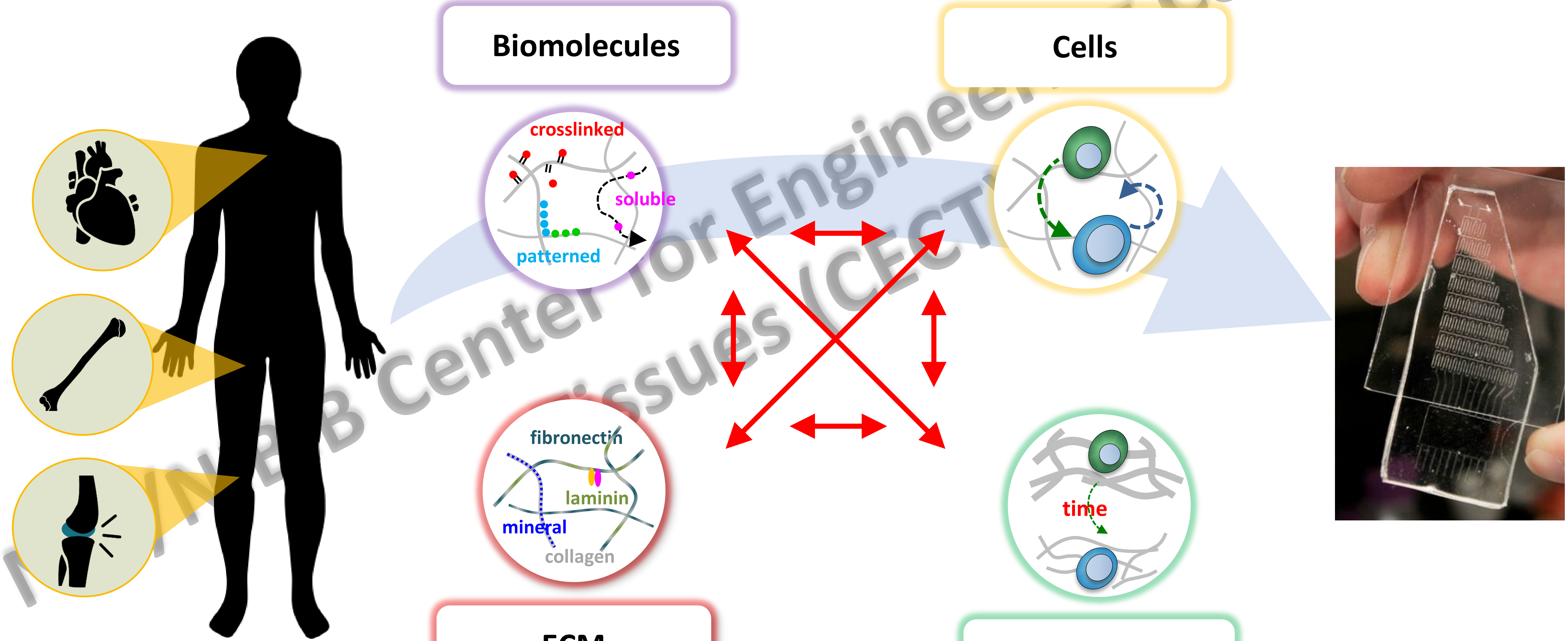
- Limited innate healing capacity
- Large tissue defects
- Scar tissue formation
- Other pathologies that limit desired regeneration

Source: Usatine RP, Smith MA, Mayeaux EJ, Chumley HS: *The Color Atlas of Family Medicine, Second Edition:* www.accessmedicine.com



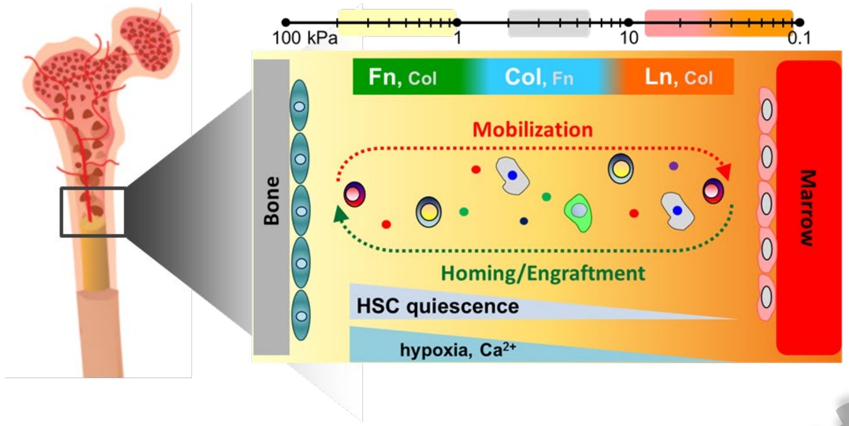
(Photo: Ann Surg Treat Res. 2014 Nov; 87(5):253-259)

Elements of Tissue Engineering

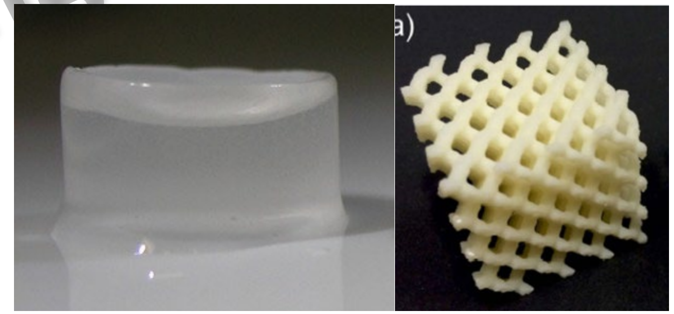


Main Challenges in Tissue Engineering

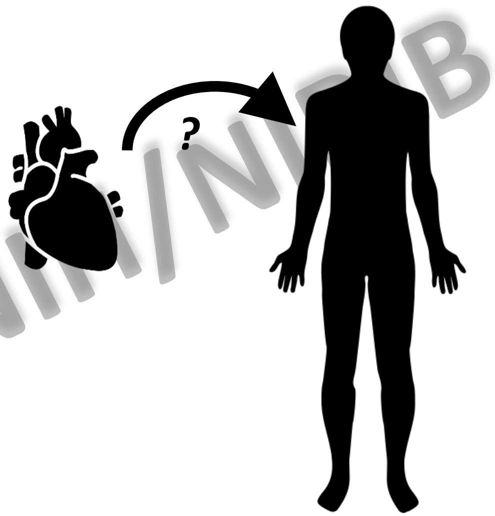
Tissue heterogeneity



Biomaterial choices impact cell function

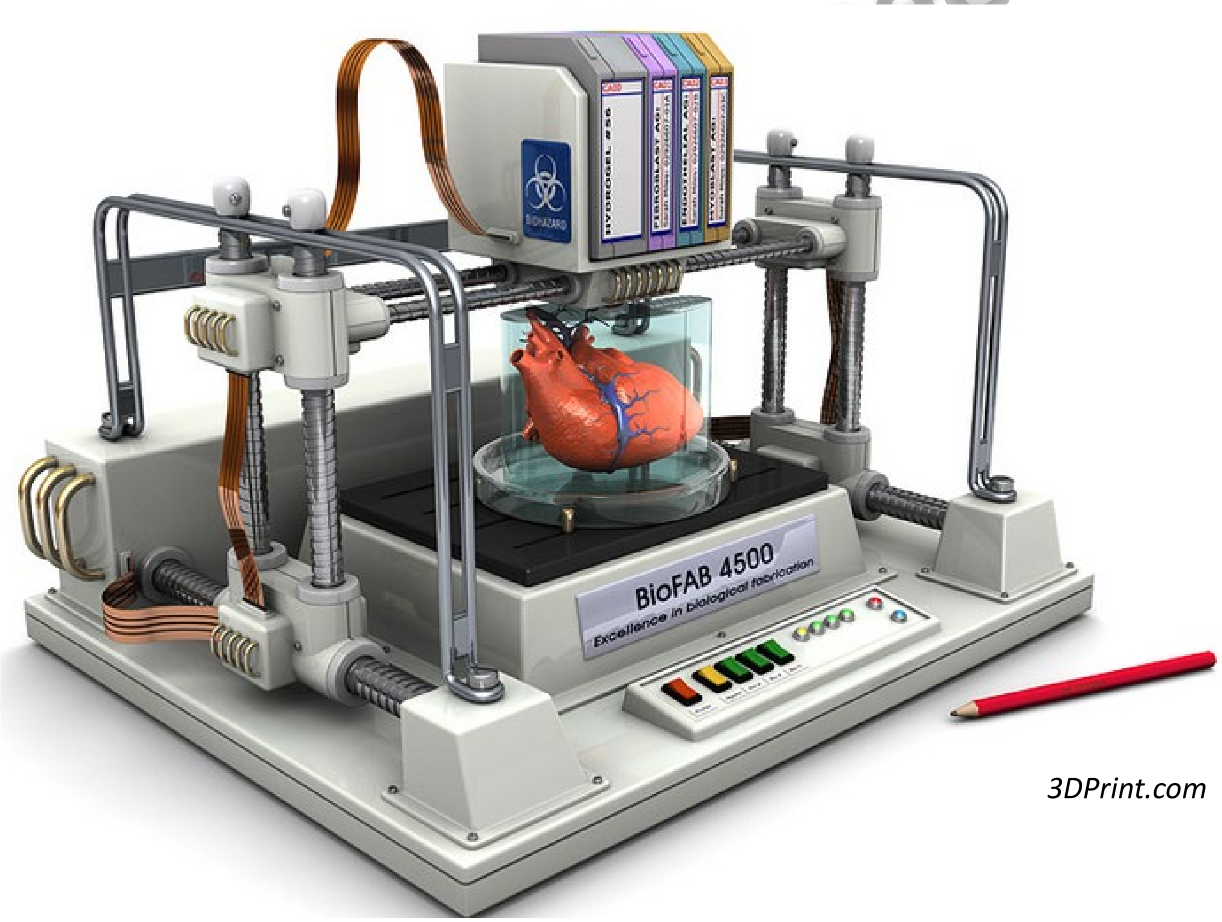


Physiological translation



Size and Vasculature - keeping everything alive!

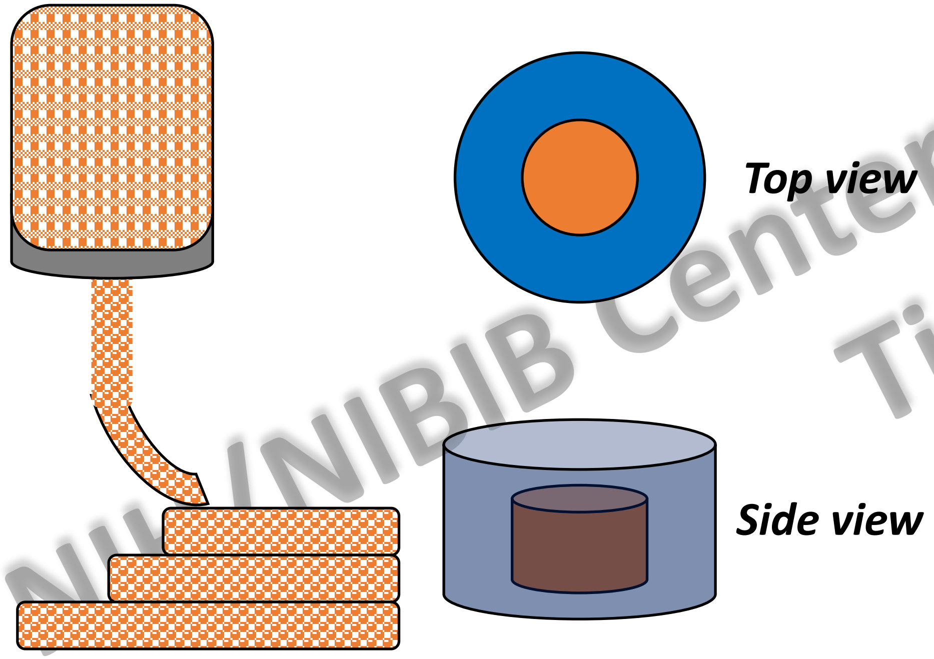
3D Printing and Biofabrication



3DPrint.com

3D Printing in Healthcare and Medicine

Layer-by-layer deposition of materials to create complex 3D structures

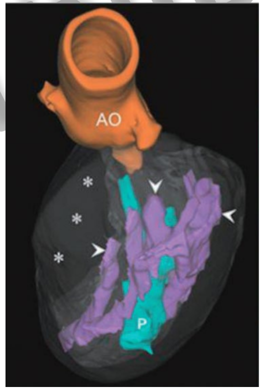


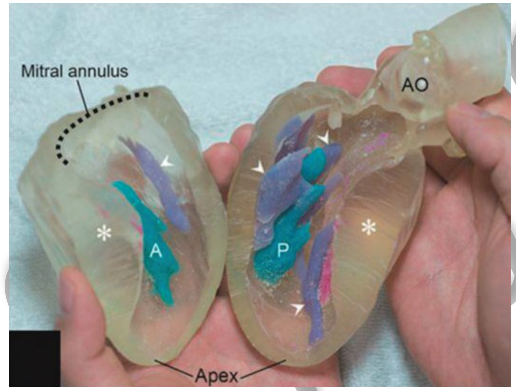
- **Dentistry** (restorations, dental models)
- **Tissue models** (implantation, drug testing)
- **Surgery** (maxillofacial, cranial, cardiovascular)
- **Medical devices** (surgical instruments, prostheses, hearing aids)
- **Drug formulations** (drug delivery, personalized medicine)

3D Printing in Healthcare and Medicine

Personalized treatments for patient-specific anatomies

CT image (cardiac)





Images adapted from Korean J Radiol 2016;17(2):182-197

Address pressing **TE challenges**

Tissue Heterogeneity

Complex Architecture

Vascularization

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

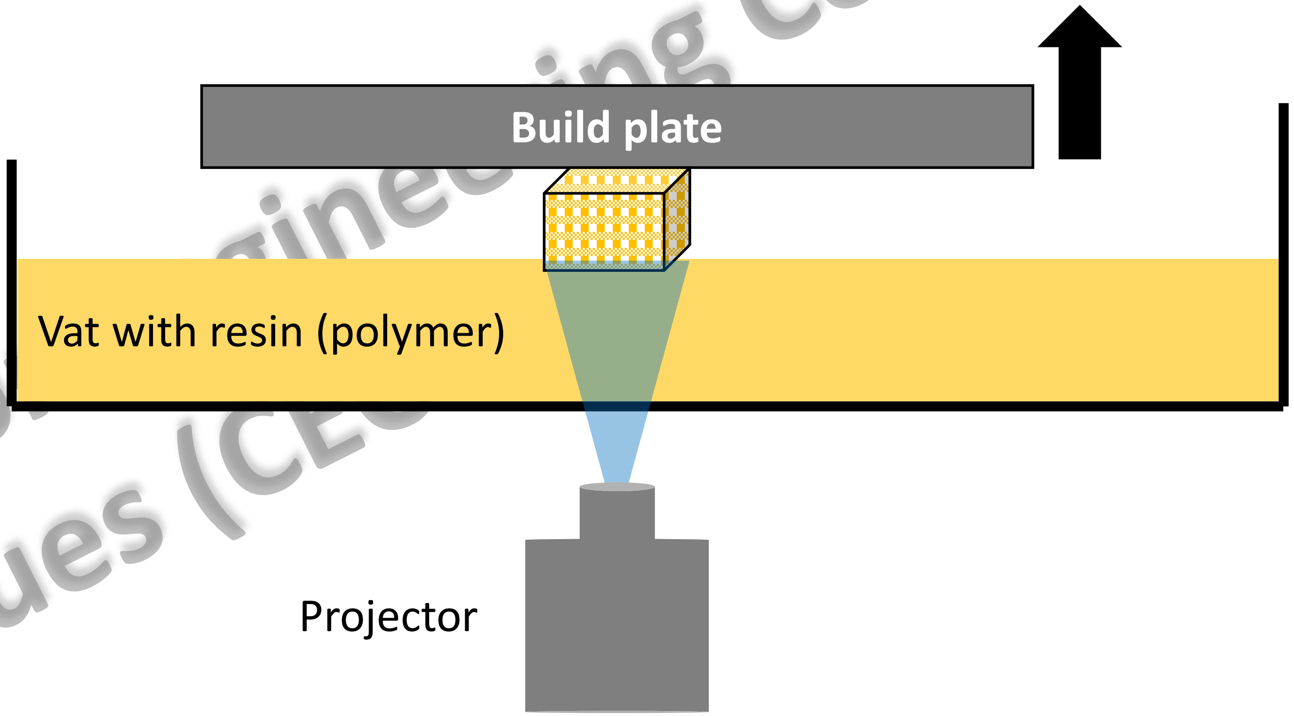
Others

- Electrospinning
- Scaffold-free

Stereolithography

- Vat photopolymerization

- Light-sensitive materials



Stereolithography

- High resolution (~20 µm)
- Controllable crosslinking to tailor mechanical properties
- Compatible with photocrosslinkbale polymers
  - PEGDA
  - ECM / Proteins

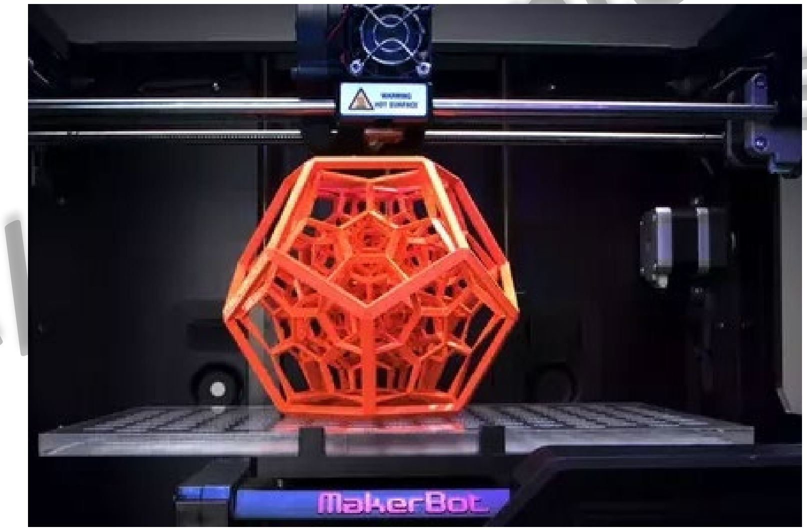
- Slow fabrication (hours) and requires support structures
- Typically one-material print
- Not always cell compatible
- Few photoinitiators and photoinhibitors suitable for biological applications
- Print orientation influences architecture

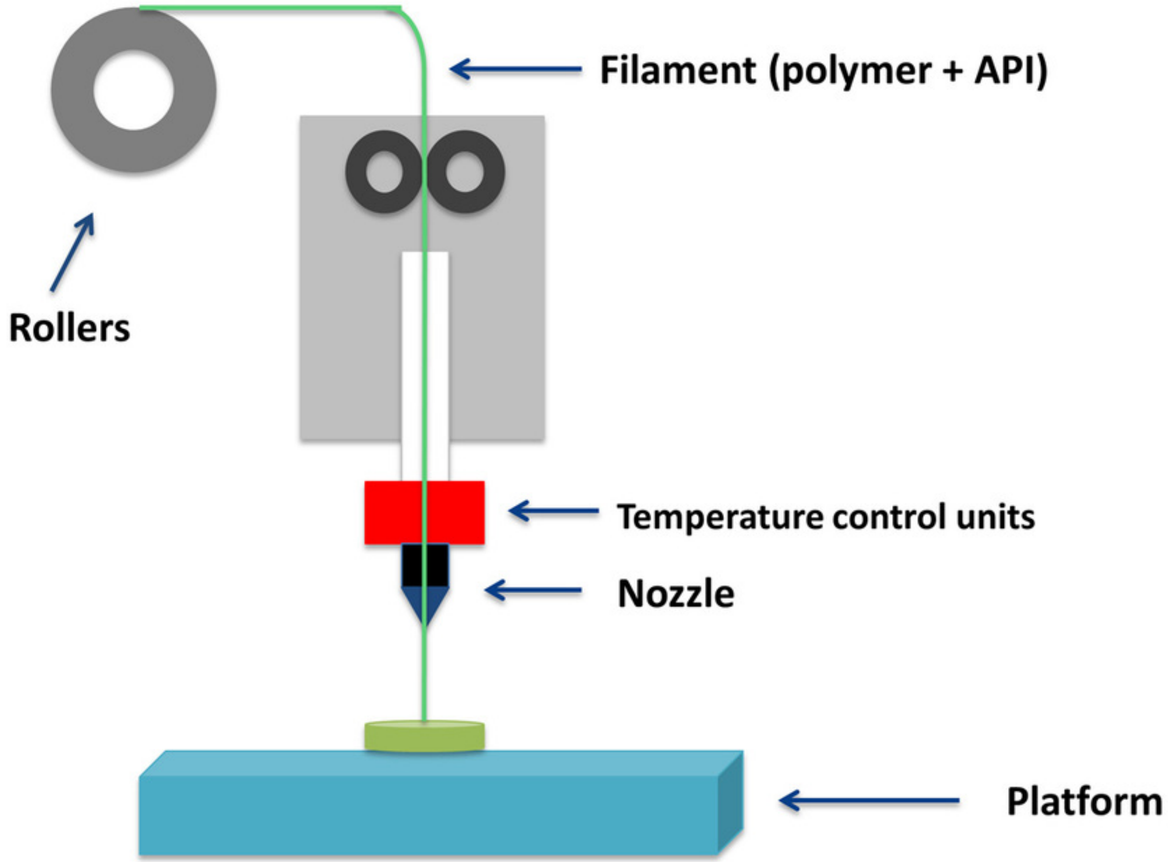
Can’t play media

Extrusion-based Printing

Fused Deposition Modeling

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



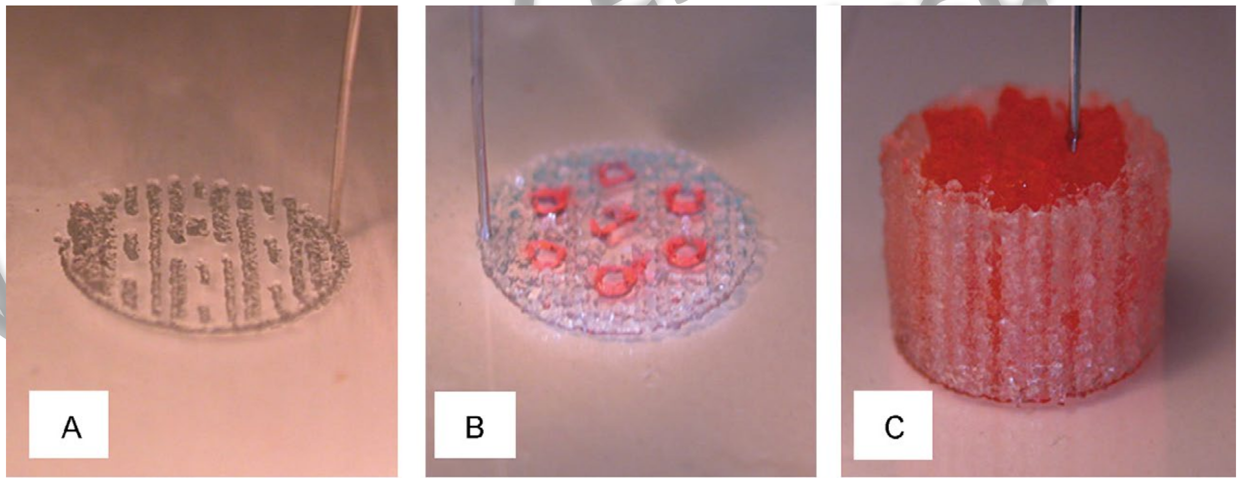


Konta et al., Bioengineering 2017, 4, 79

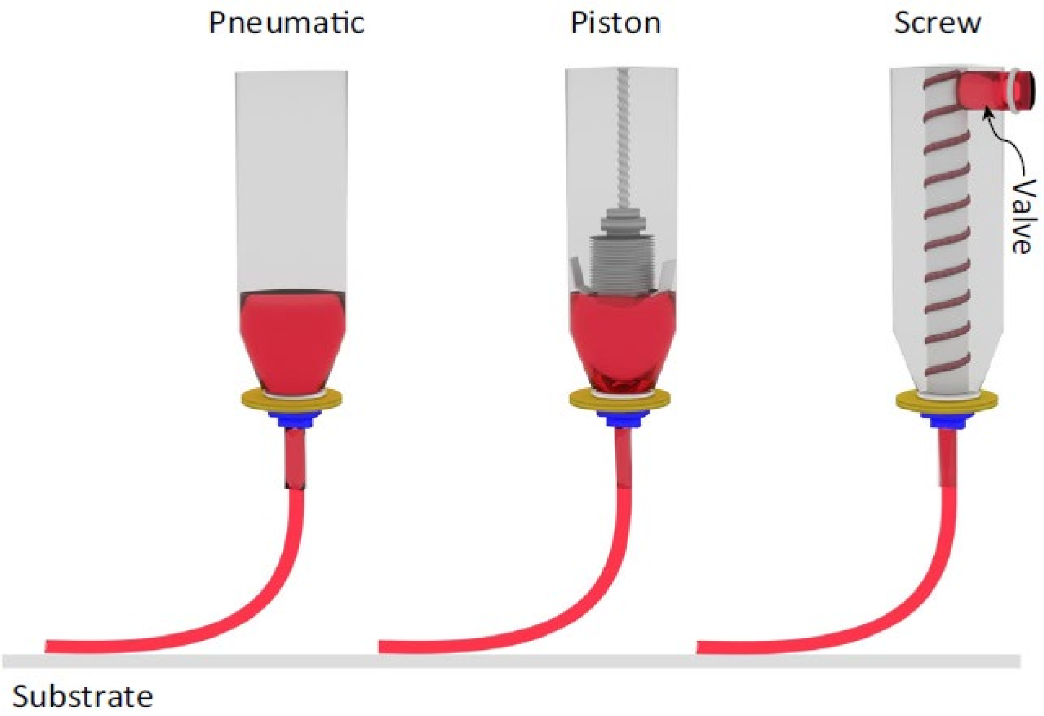
Extrusion-based Printing

Microextrusion Printing

- Extrusion of materials through a needle and a syringe



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



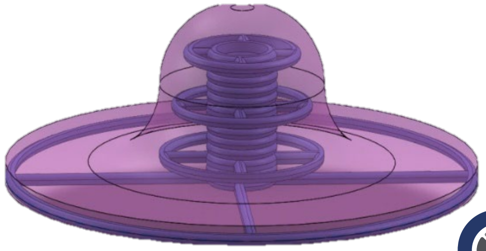
Knowlton et al., Trends in Biotechnology, 2015, Vol. 33, No. 9

Extrusion-based Printing

- Deposit large cell populations
- Fast fabrication (minutes)
- Broad range of printable materials
  - Hydrogels, ceramic, polymers
- Multi-material printing
- A lot of printing customization

- Modest resolution (100 µm onwards)
  - Needle and material dependent
- Material properties dictate printing success
- High shear stress in nozzle can kill cells
- Chances of mid-print failures

Can't play media



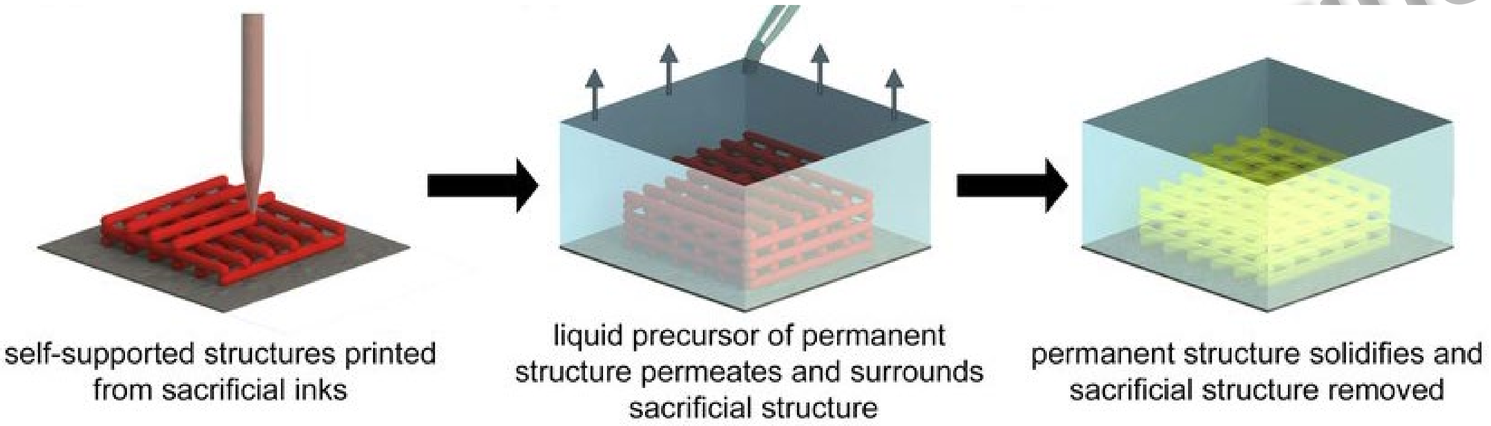

Other methods

- Inkjet Printing
  - Patterning of cells in low viscosity materials
- LIFT (Laser Induced Forward Transfer)
  - Precise deposition of materials on micro scale
- Scaffold-free fabrication
  - Leverage assembly and natural ECM deposition of cells
- Laminated Object Manufacturing (LMO)
- Micro and Nano-scale printing (Nanoscribe)

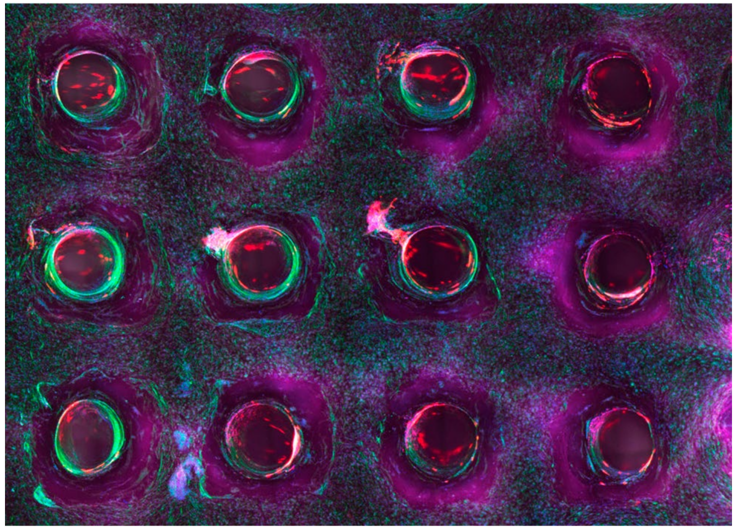
Sacrificial templating

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

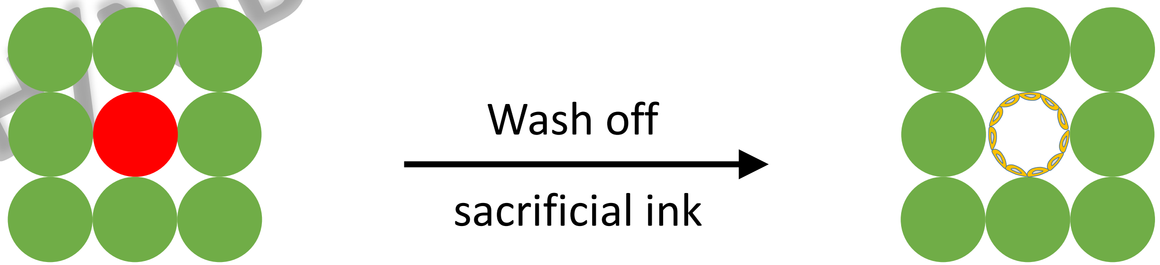
- Pluronic F-127, Glass carbohydrate



O'Bryan et al., MRS Bulletin, 42(08):571-57



Kolesky et al., PNAS 113 (12); 3179-3184 (2016)

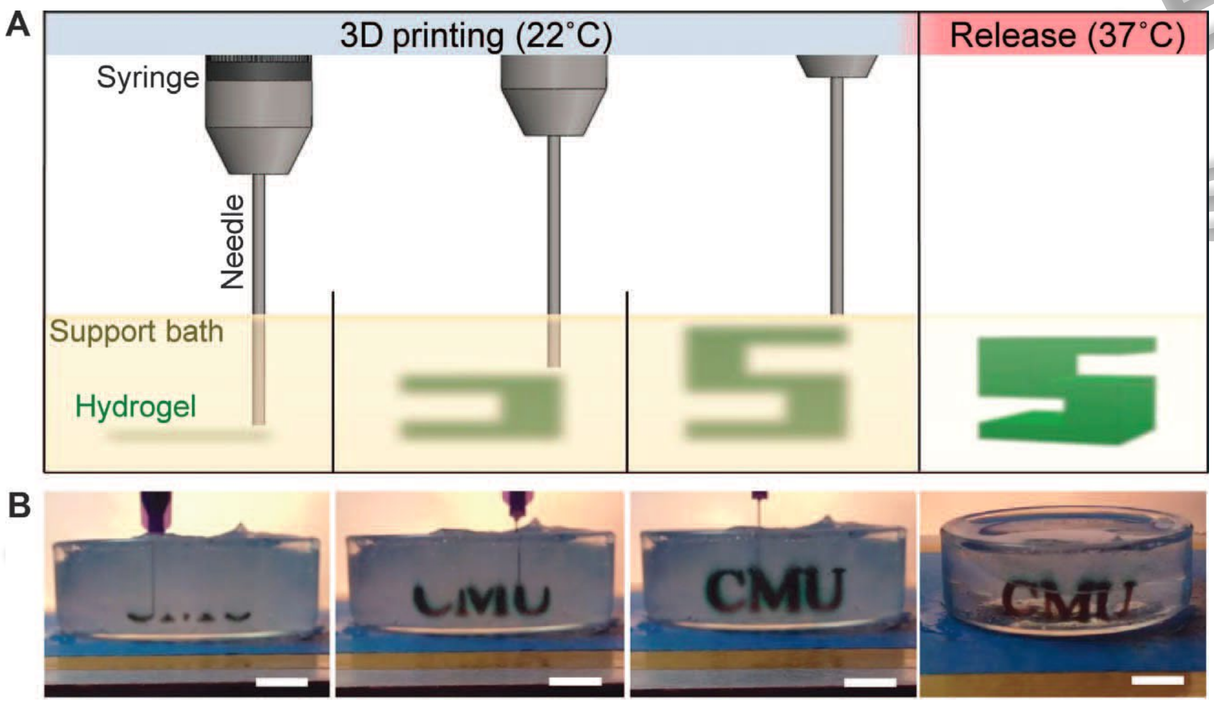


Print desired bioink/sacrificial ink

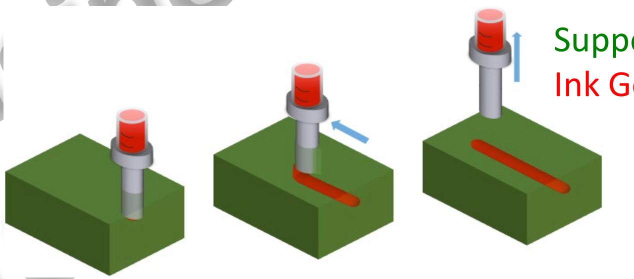
'Cavity', infused with cells

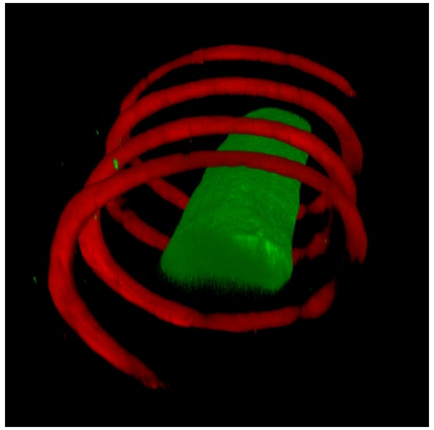
Gel-in-gel printing

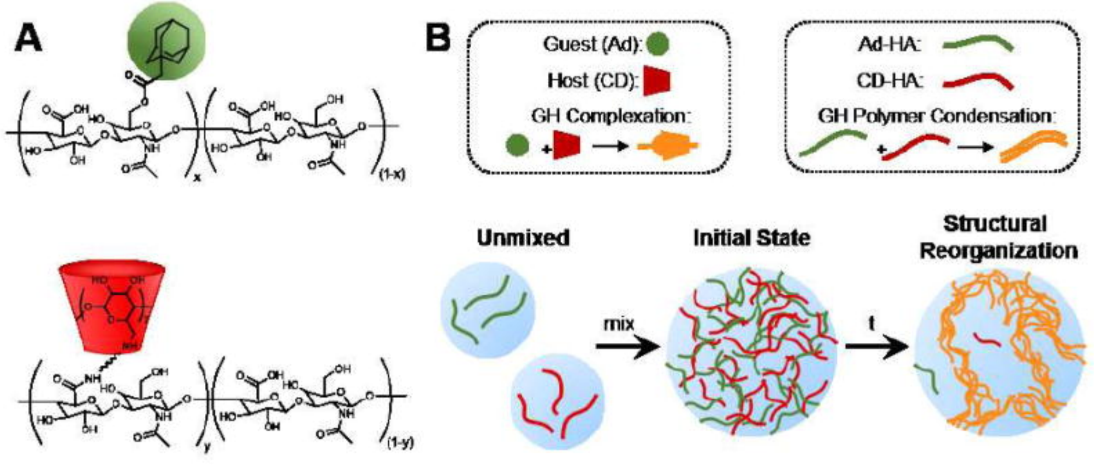
- Extruding a bioink into another support bioink/bath for structural stability
  - Gelatin microparticles
  - Guest-host complexes



Hinton et al. Sci. Adv. 2015;1:e1500758

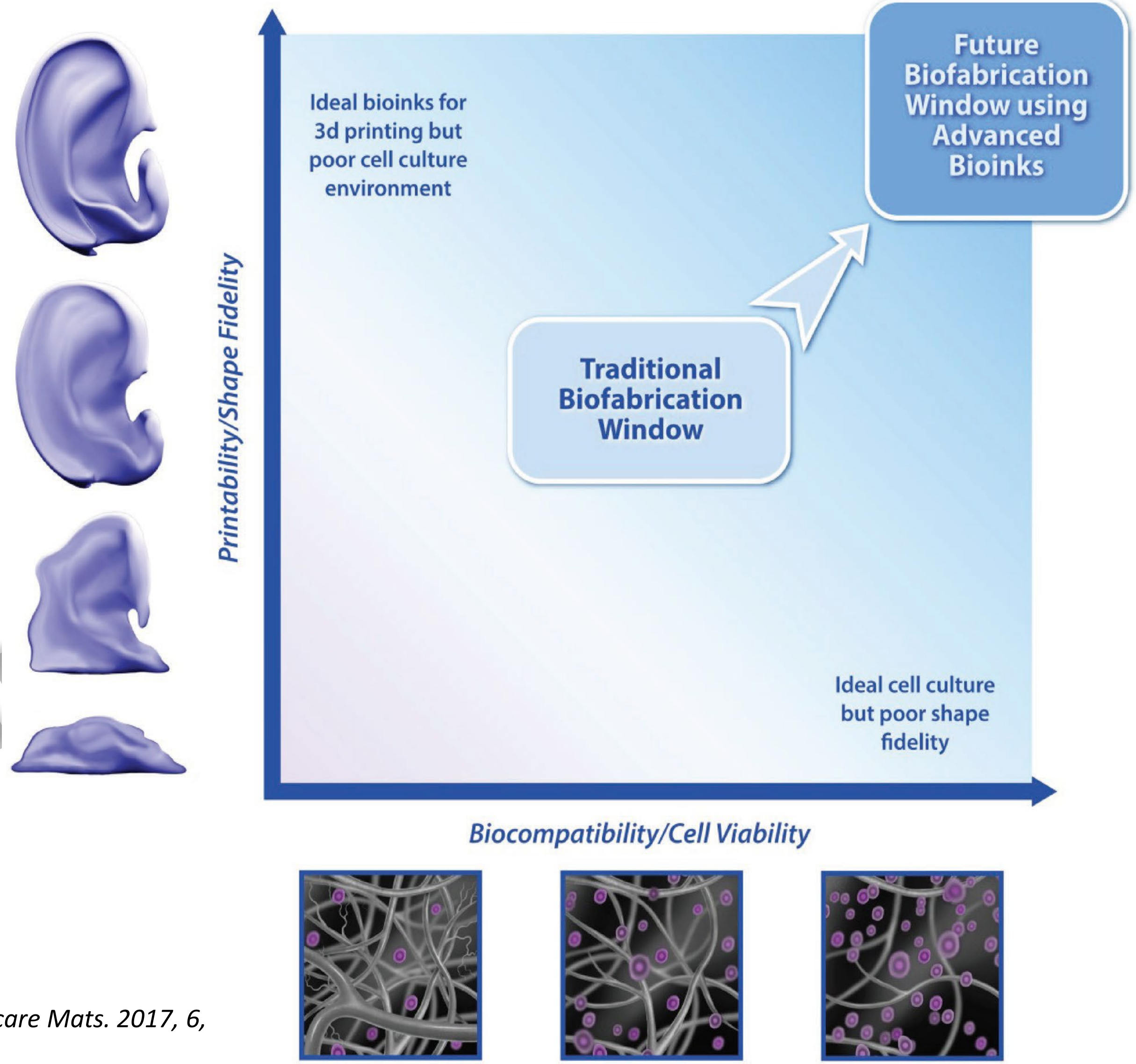




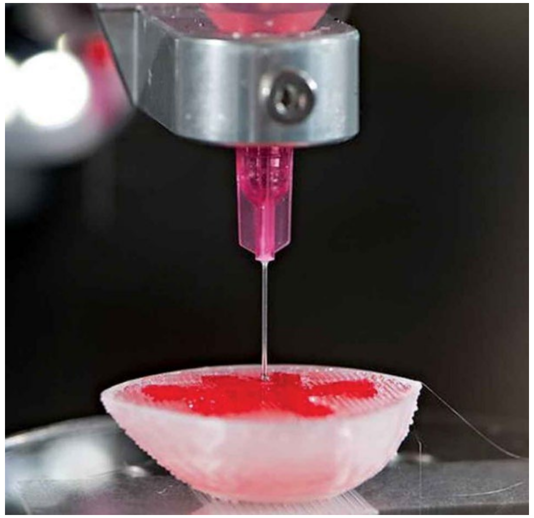


Soft Matter, 2016, 12, 7839

Tradeoffs while printing



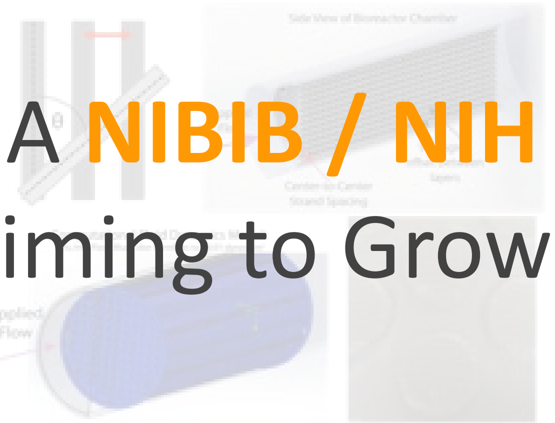
Balancing complexity with utility



Courtesy WFIRM

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

CECT Center for Engineering Complex Tissues



A NIBIB / NIH Biomedical Technology Resource Center
Aiming to Grow the **3D Printing & Bioprinting Community**

John Fisher (University of Maryland): **3D Printed Bioreactors for Dynamic Cell Culture**
Antonios Mikos (Rice University): **Bioprinting for Complex Scaffold Fabrication**
Anthony Atala & James Yoo (Wake Forest University): **Bioprinting for Cell-Laden Constructs**

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