

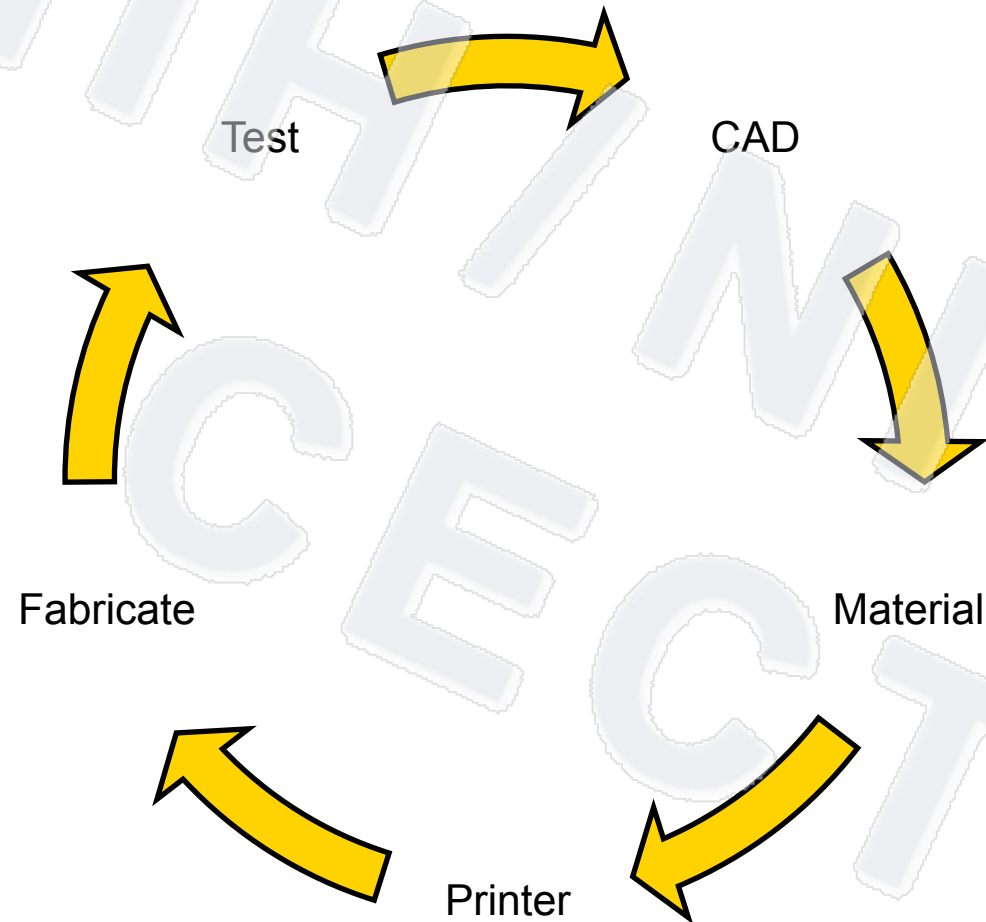
The 3D Printing Process: Concept to Reality

NIH Center for Engineering Complex Tissues (CECT)
June 7, 2019

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Assistant Director, CECT
University of Maryland

Slide information courtesy Dr. Max Lerman

Iterative process with optimization



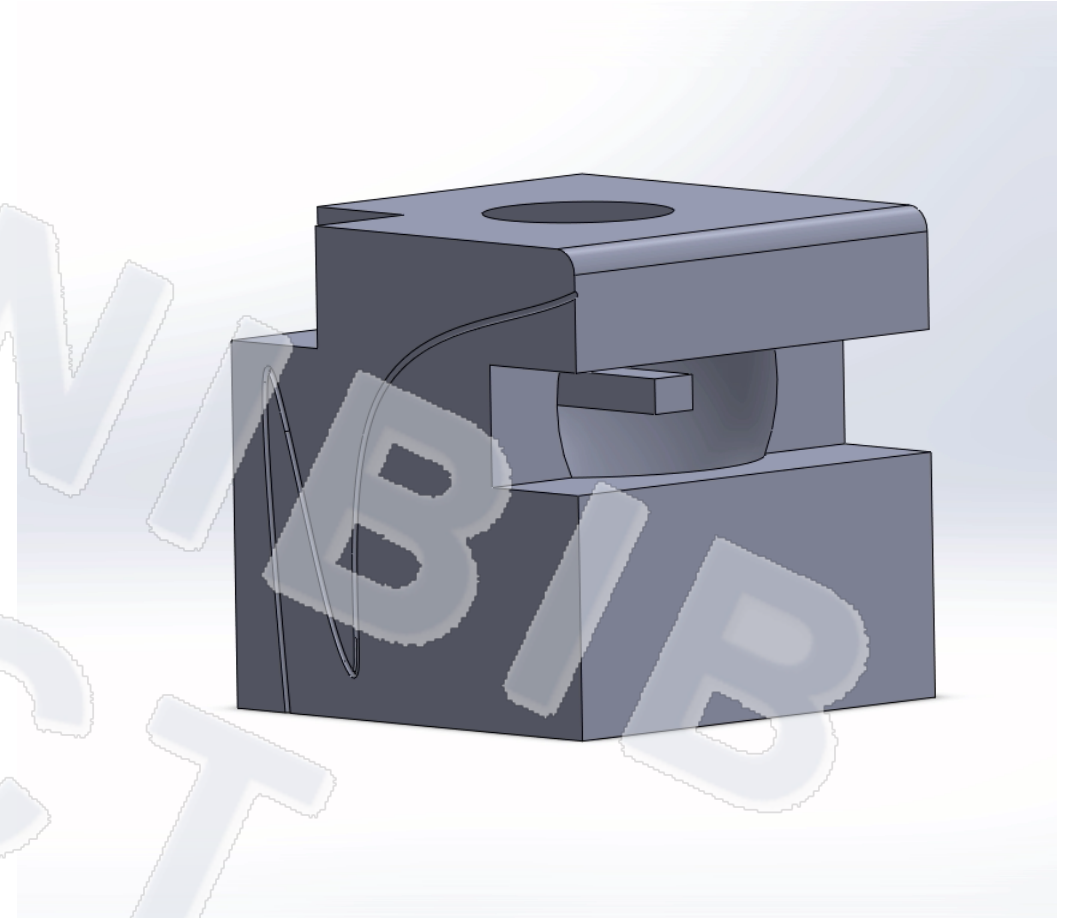
When to use 3D printing

- Rapid prototyping
 - Quick turn around time (hours)
 - Small volumes (dozens)
 - Highly customizable (Soft design)
- Biological relevance
 - Will a 3D printed construct give you a different answer?
- Enabling platform
 - Large tissues



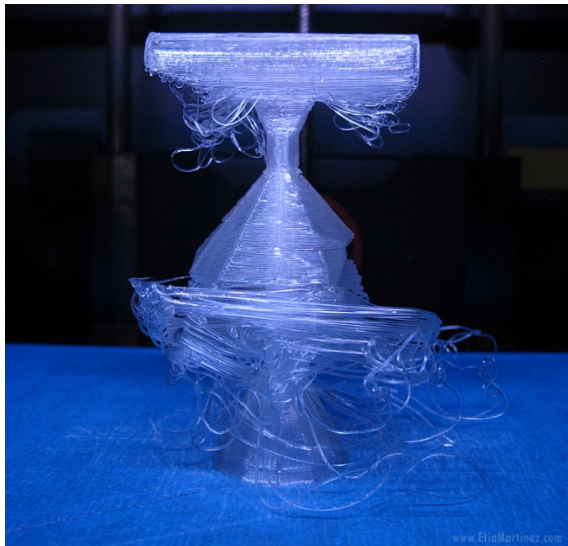
When to use 3D printing

- Early design decisions
 - Internal features
 - Overhangs
 - Indents
 - Texture
 - Orientation

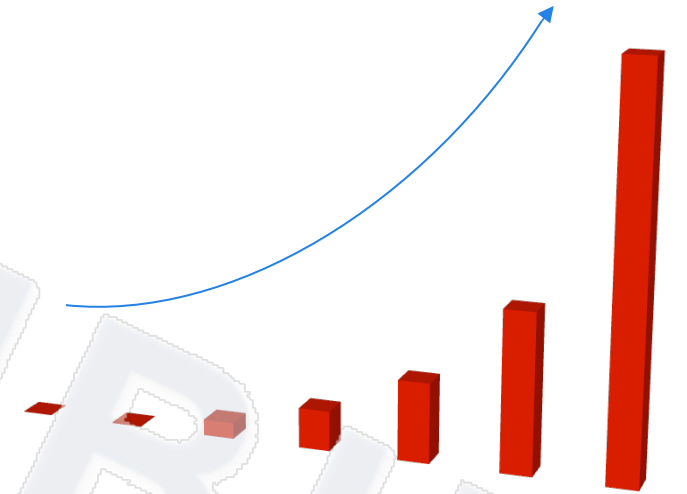


Planning, planning, planning

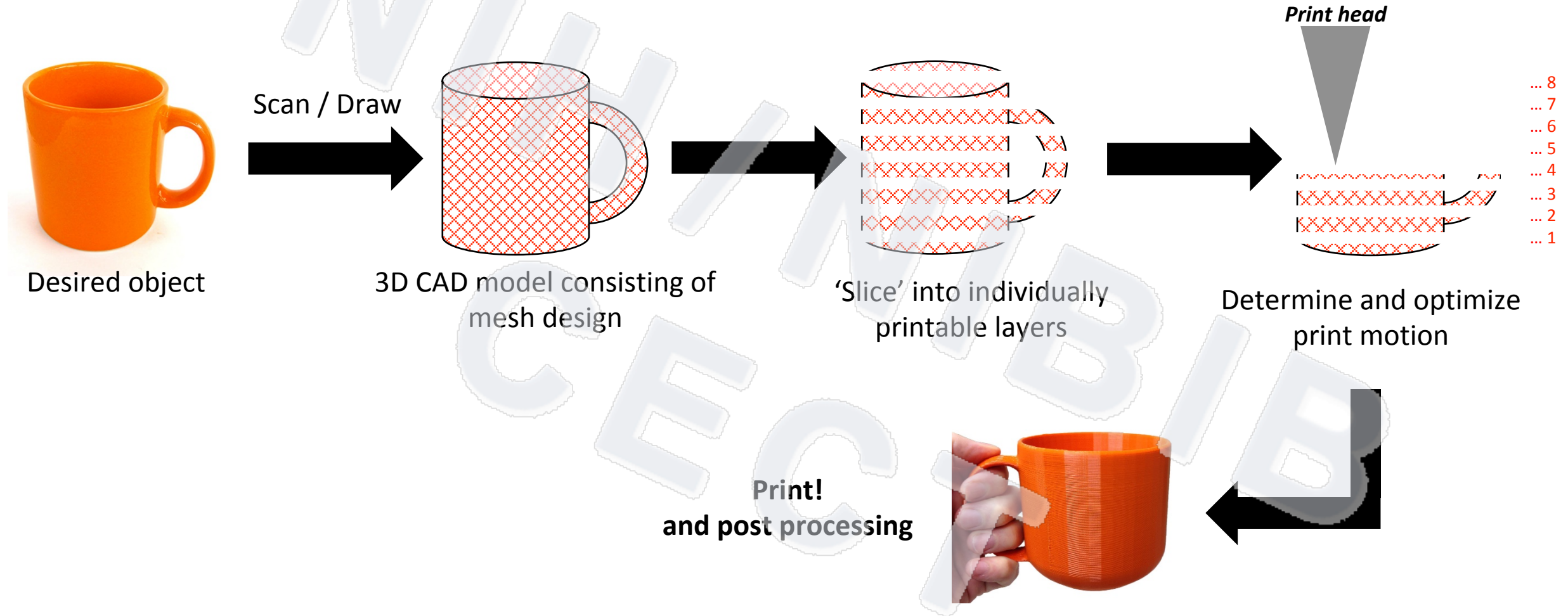
- Paper → CAD → Print
 - Cost
 - Time
 - Frustration



- Early failures



Basic 3D printing process

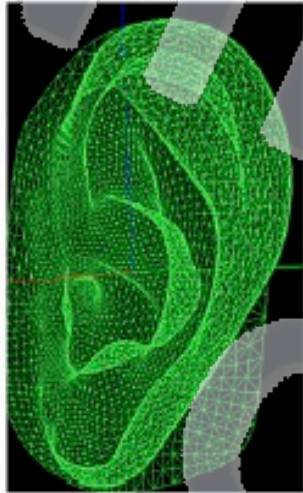


Basic 3D printing process

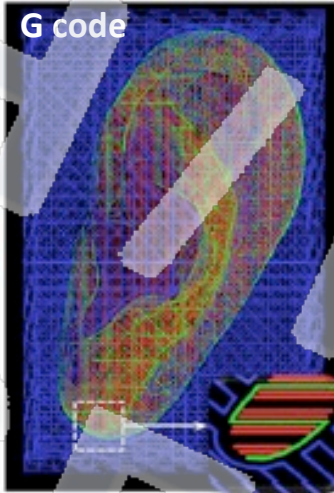
Medical imaging
(CT, MRI)



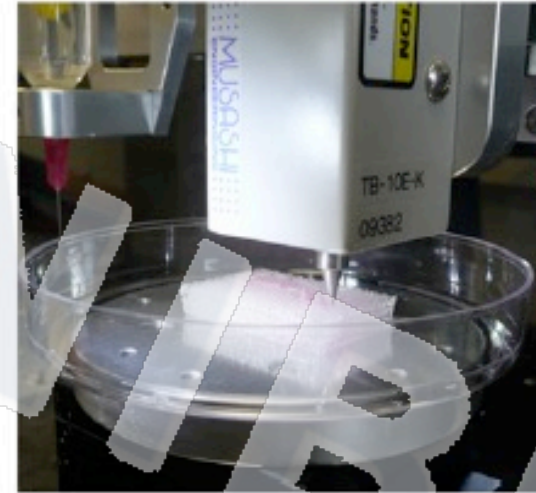
3D CAD model



Visualized motion
program



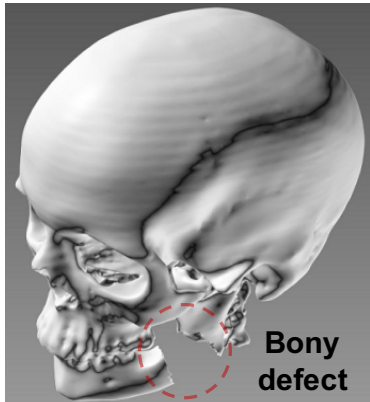
3D printing process



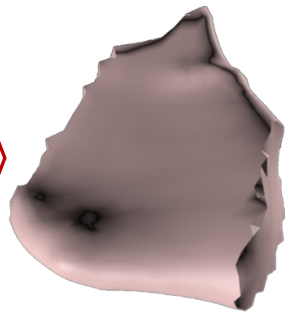
3D bioprinted
tissue product



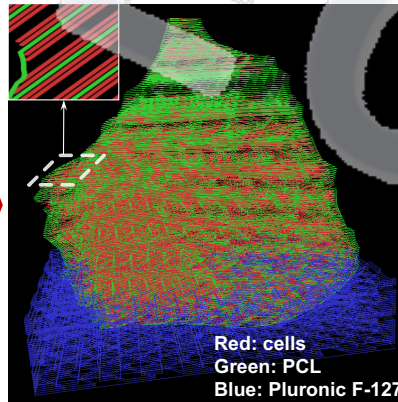
Medical imaging
(CT, MRI, etc.)



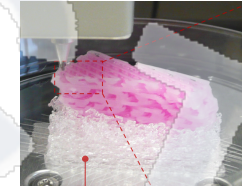
Mirroring



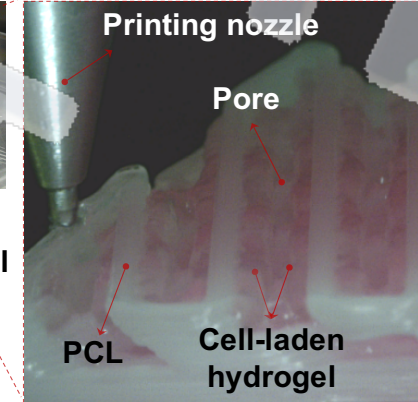
Visualized motion
program



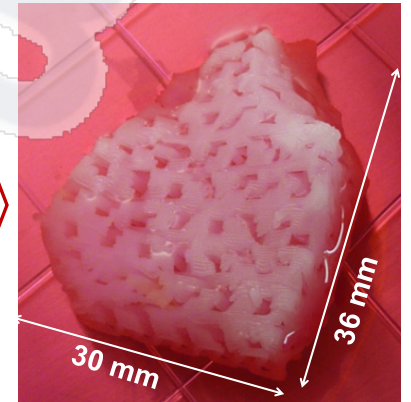
3D printing process



Pluronic
F-127 (sacrificial
material)

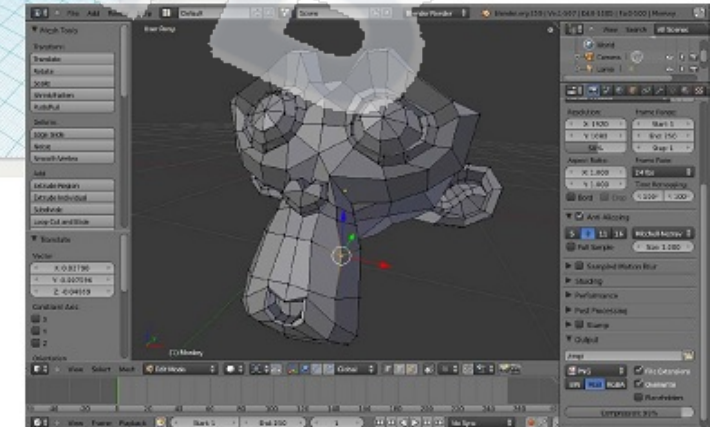
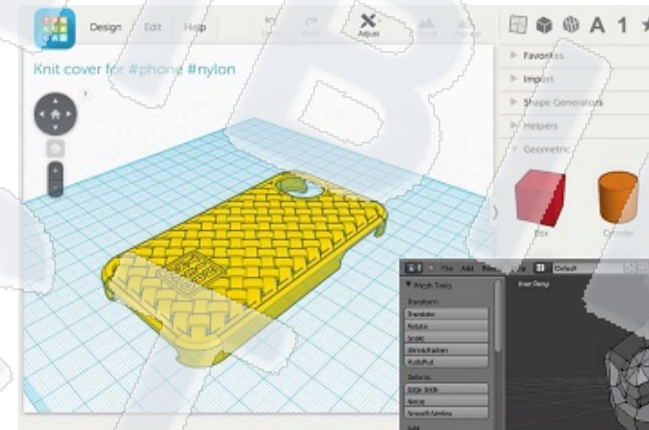
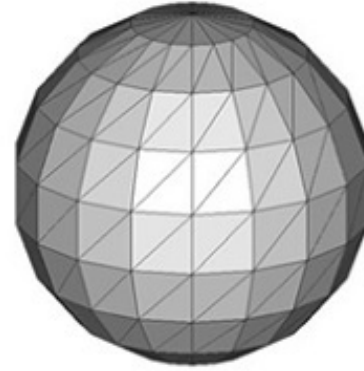
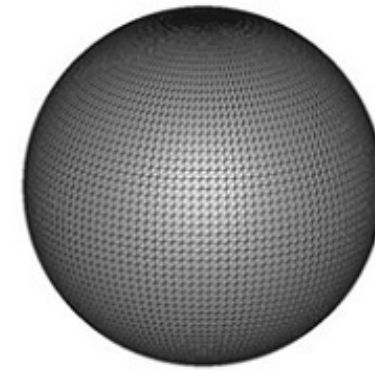


3D bioprinted bone
construct



Print file optimization

- Variations in stl file origins might impact final outcomes
- Resolution
- Autocorrection of shells, mesh size, etc.

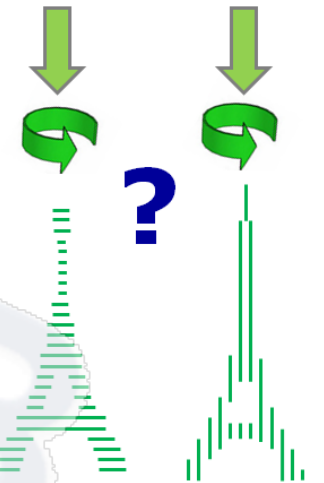
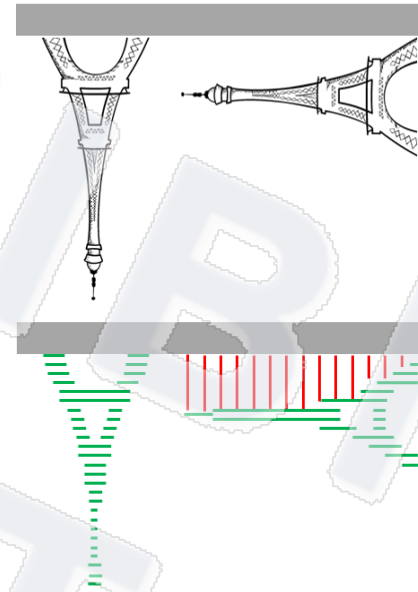


Printing orientation

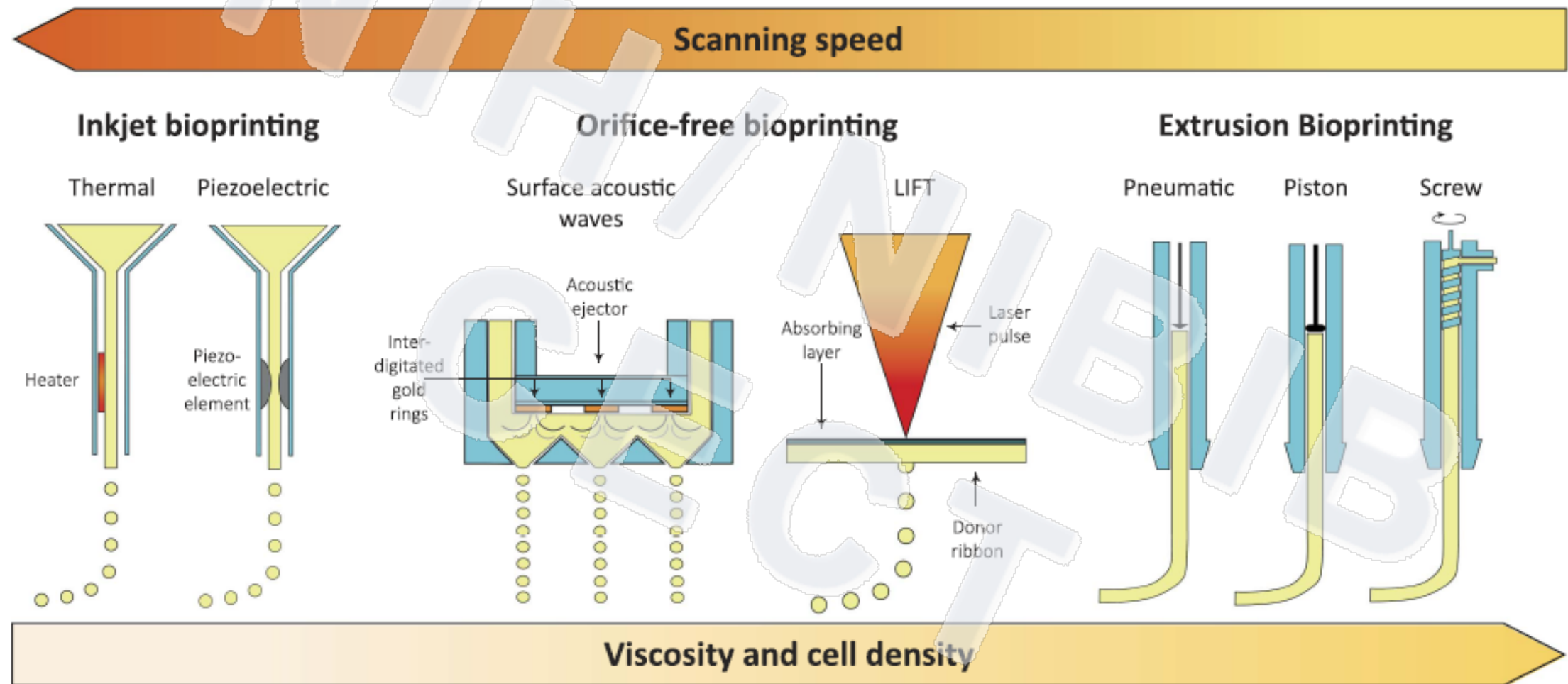
- Effect of orientation of print design on its properties
 - Mechanical strength
 - Structural stability
 - Print accuracy



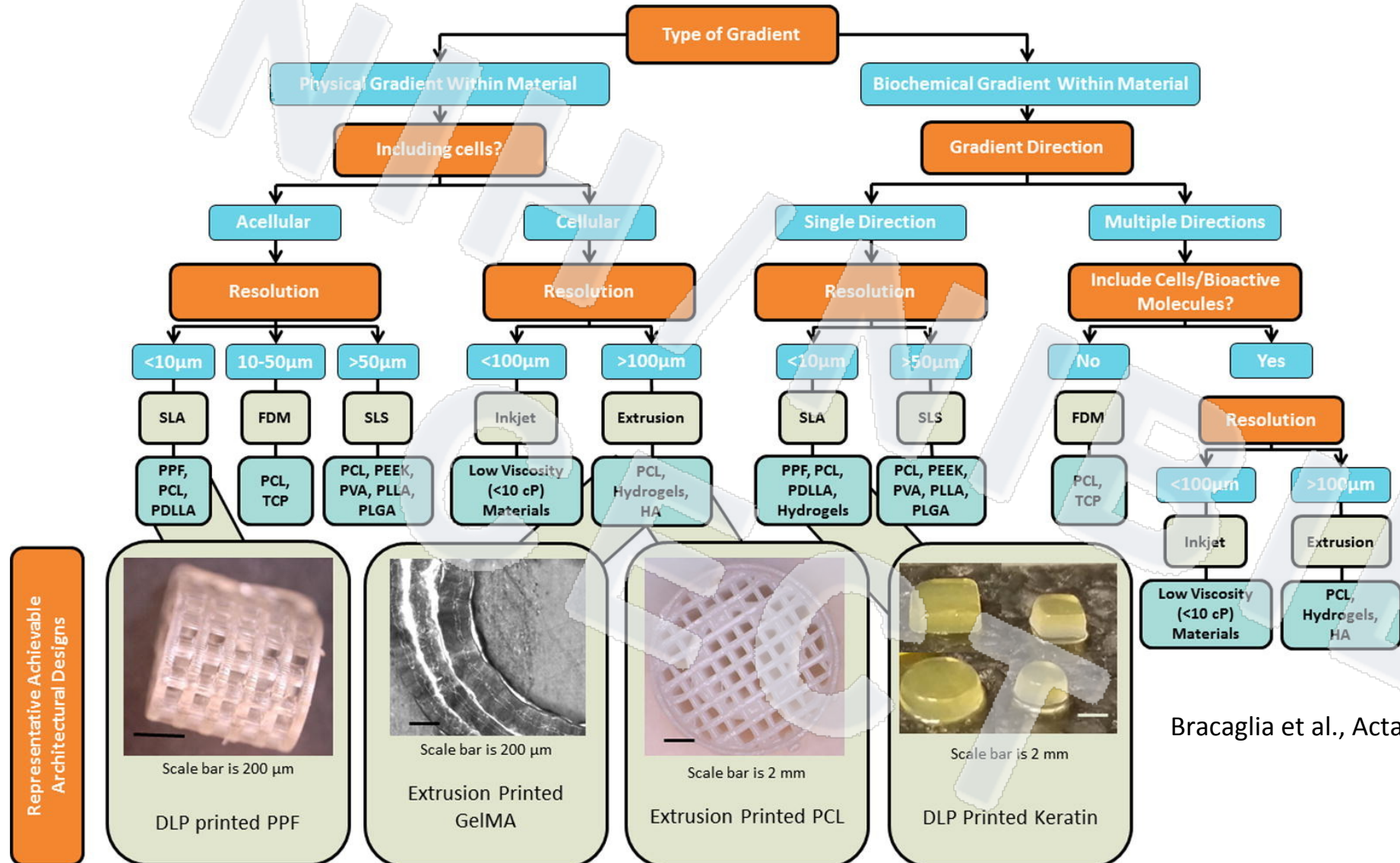
Image: <http://www.3ders.org/articles/20131210>



Choosing a 3D Printing Technique



Choosing a 3D Printing Technique



Bracaglia et al., Acta Biomaterialia, 2017

Material selection

- Dictated by printer selection (done in tandem)
- What is the **function** of the part?
- What are the downstream applications?
- Cost
- Available metals
 - Ceramics
 - Metals
 - Thermoplastics
 - Resins
 - Hydrogels

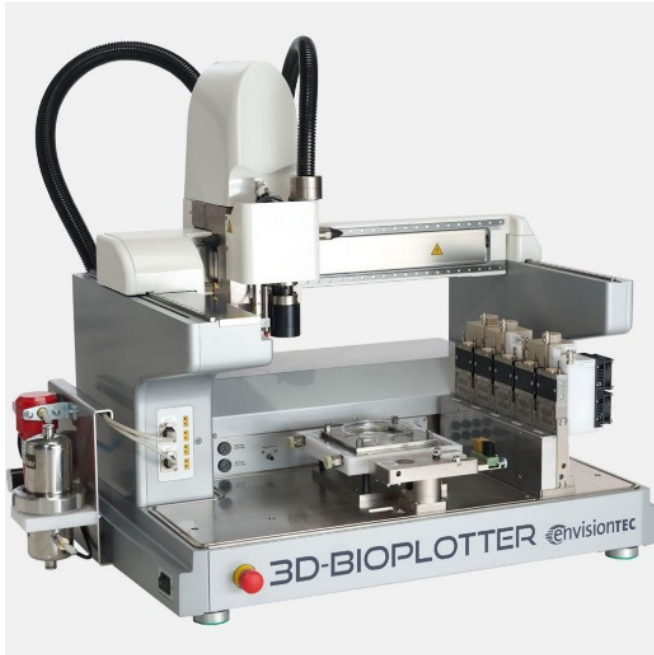


DLP printer: EnvisionTEC Perfactory



- Light-based crosslinking
 - UV
 - Visible
- Photosensitive materials
 - Eshell 300
 - Keratin
 - PEG-based
- Orientation matters

Microextrusion: 3D Bioplotter



- 4 bioinks at a time
 - 2 high temp (RT-160°C)
 - 2 low temp (4°C – RT)
- UV crosslinking
- Controlling internal architecture
- Extrudable materials
 - PCL, PLA, PLGA, etc.
 - Alginate, gelatin, pluronic, etc.

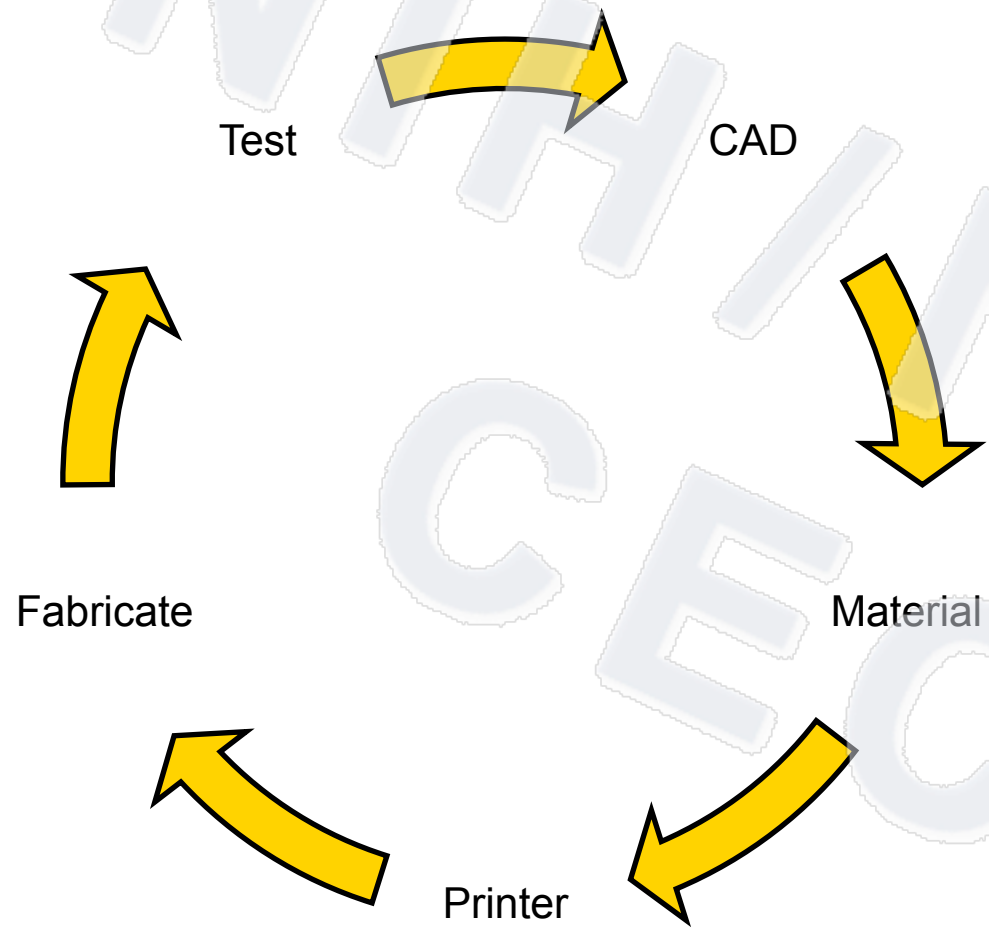
Microextrusion: BioAssemblyBot



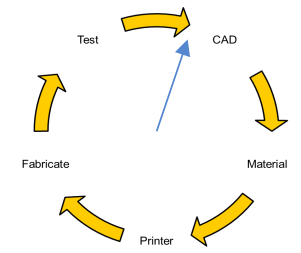
<https://3dprint.com/230675/3d-fab-opens-up-new-possibilities-for-medical-3d-printing/>

- Non-planar printing
- 6 print heads
 - 1 high temp
 - 1 low temp
 - 1 UV
 - 1 mixer
 - 2 RT
- Scanner

Example – DLP Bioreactor

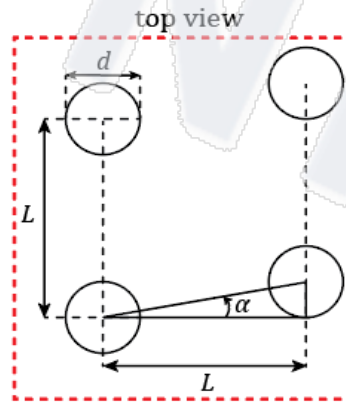
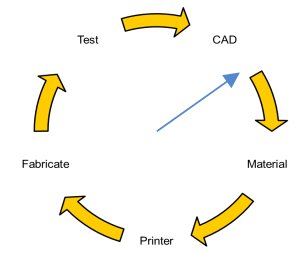


Design: Background



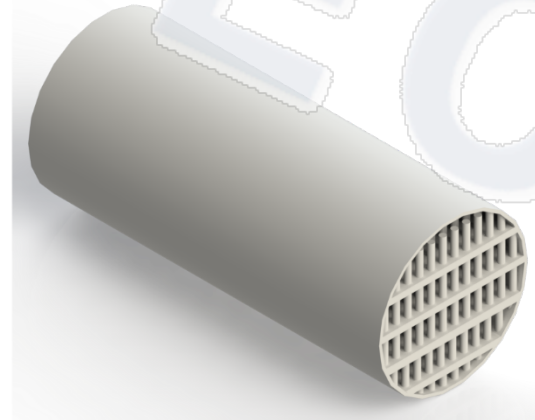
- Design Criteria
 - Perfusion flow
 - Non-cytotoxic
 - Compact
 - Control of shear stress
 - Clear
 - Impactful 3D geometry
- Design Utilized
 - Pillared array
 - Round – to fit inside tubing
 - DLP Technology – E-Shell 300

CAD Generation



Imaging

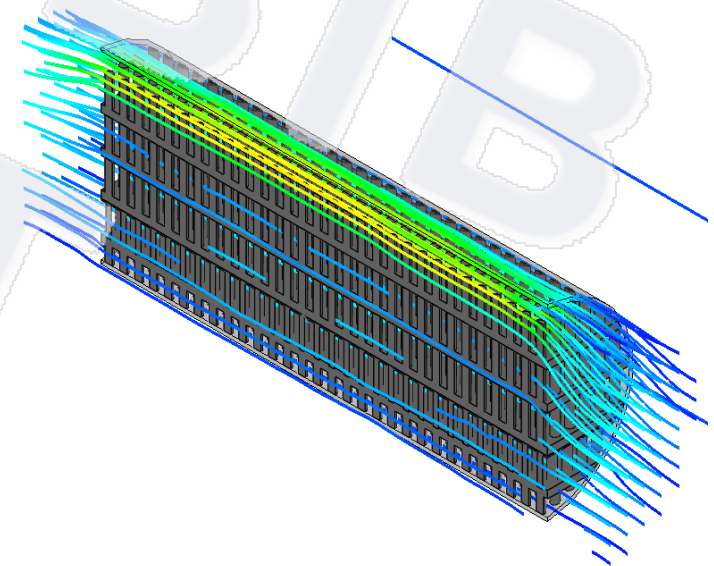
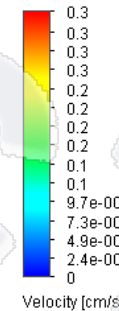
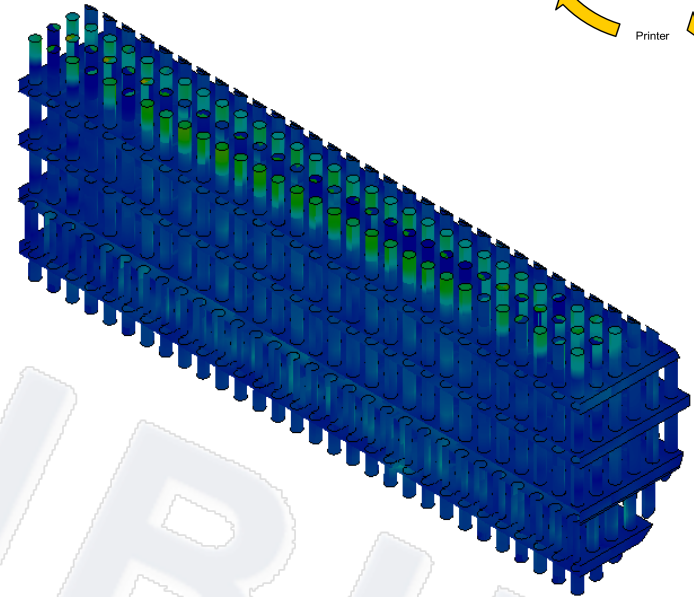
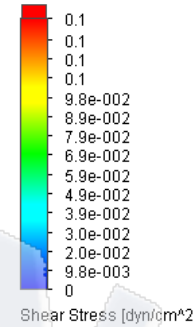
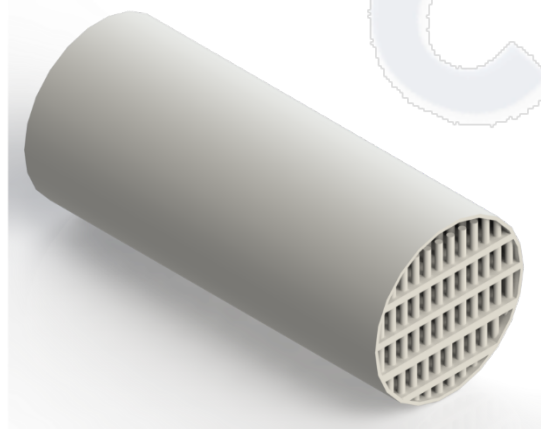
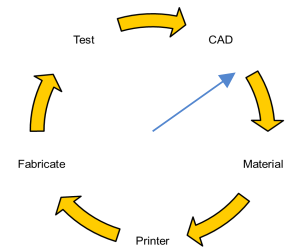
Cell expansion



- Application based design
 - Single layer for imaging studies
 - Multilayered for flask replacement

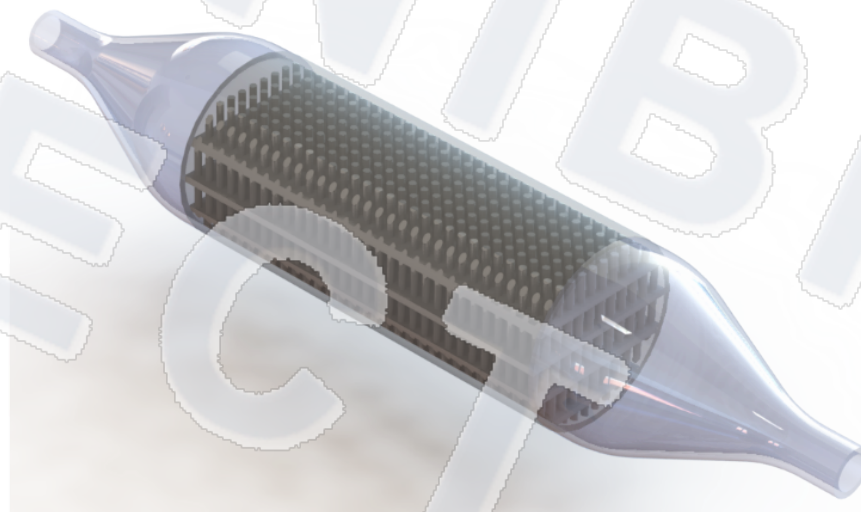
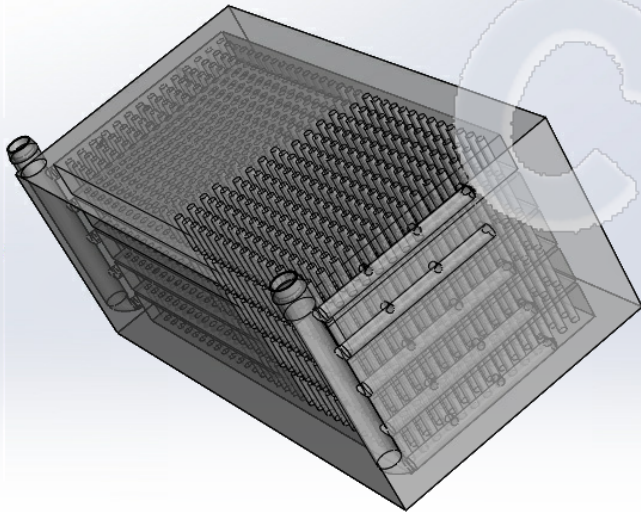
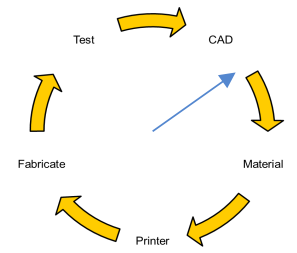
Design Verification

- Computational modeling of design
- CFD informed flow, pillar array

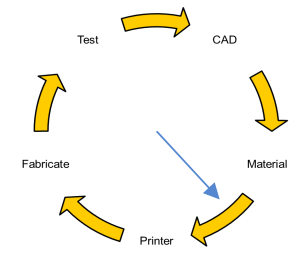


Design Improvements

- Increased volume array
- Compact structure
- Improved connections



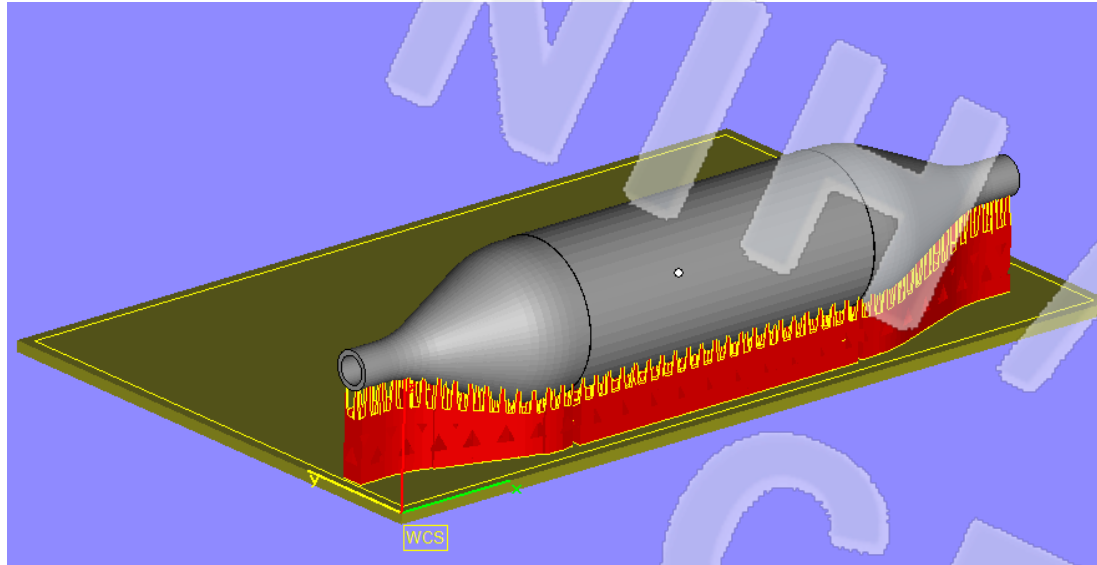
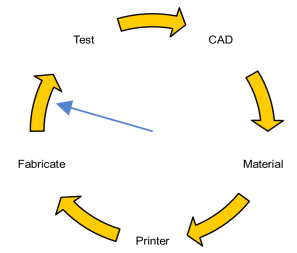
DLP Printer and Material Selection



- EnvisionTEC Perfactor 4 DLP System
 - Owned
 - Material dependent resolution (15-100 μm)
- Material options
 - All proprietary
 - Several now available
 - Limited at the time to E-shell 300



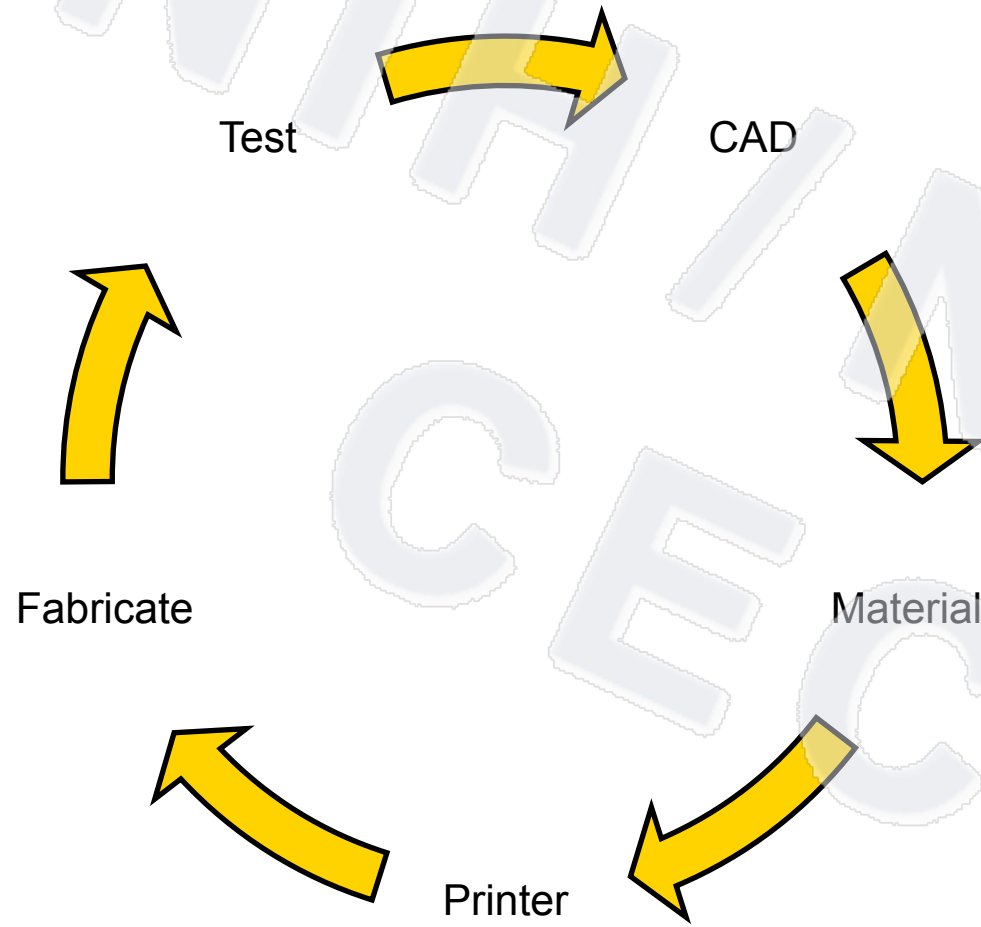
DLP Fabrication



- Orient Parts
 - Support scaffold
 - Material outflow
 - Layer generation favorability
- Inspect internal pillars
- Attach to bioreactor system

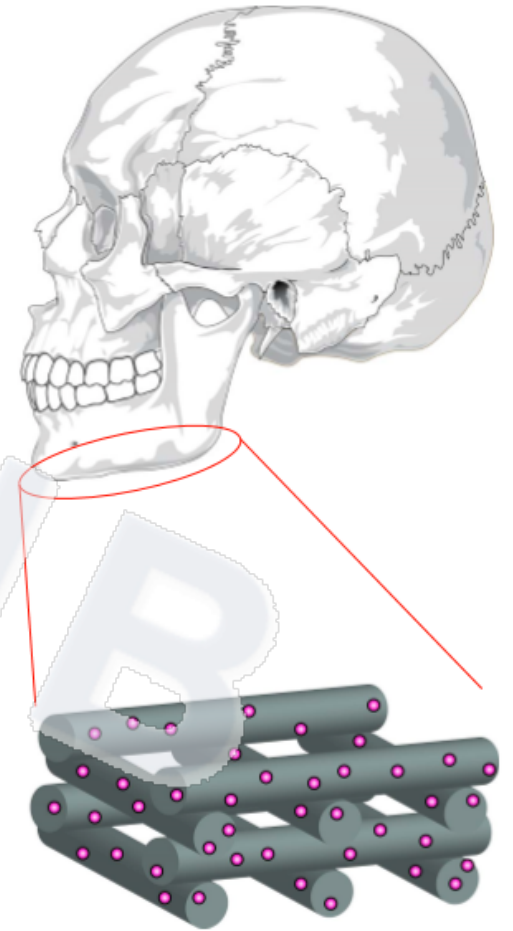


Example – Biomimetic Shaped Implant



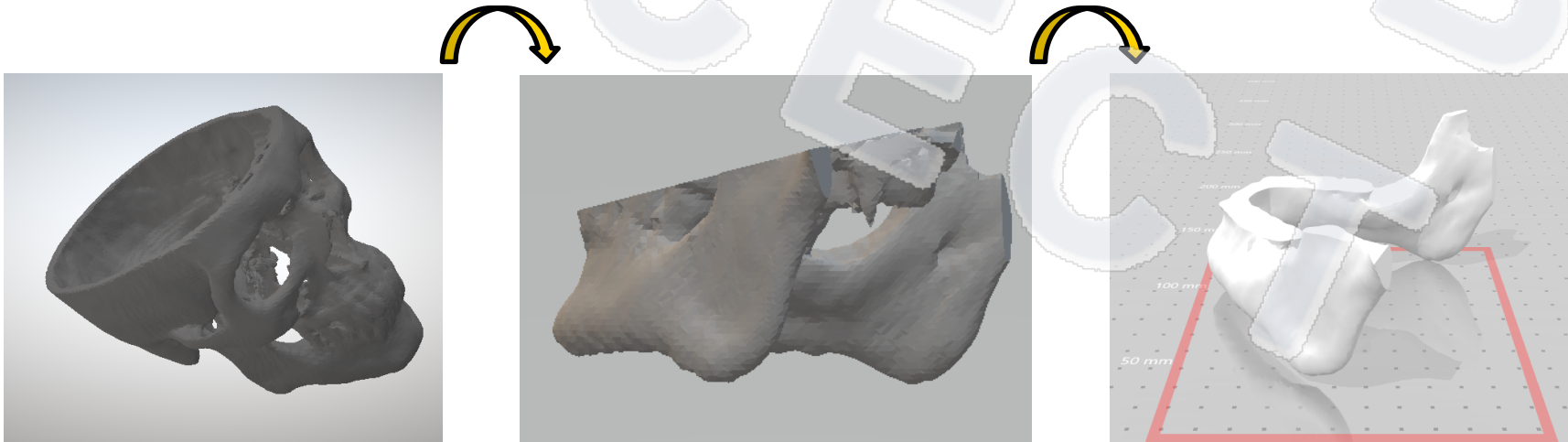
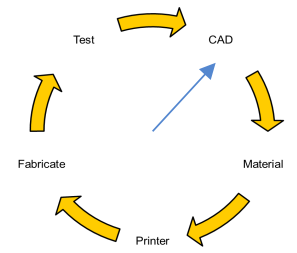
Background and Motivation

- Implantable craniofacial repair material
 - High structural complexity
 - Non-cytotoxic
 - Biodegradable
 - Vascularization
- Biomimetic driven
 - CT



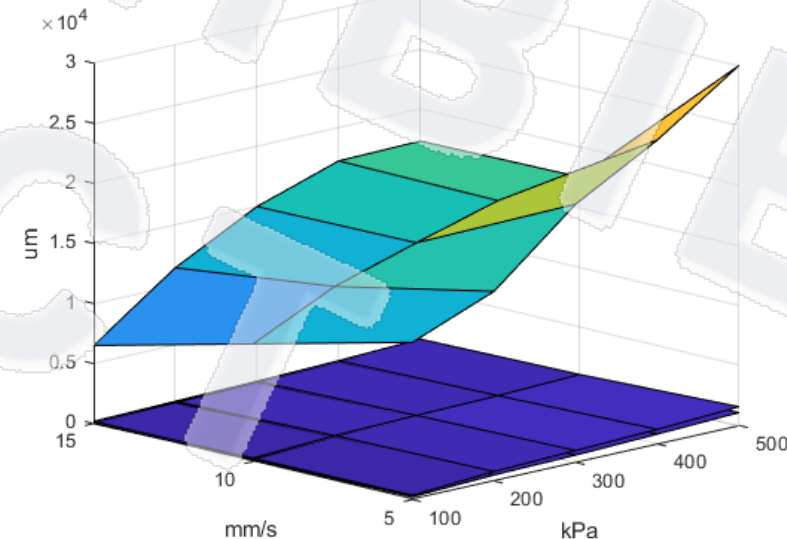
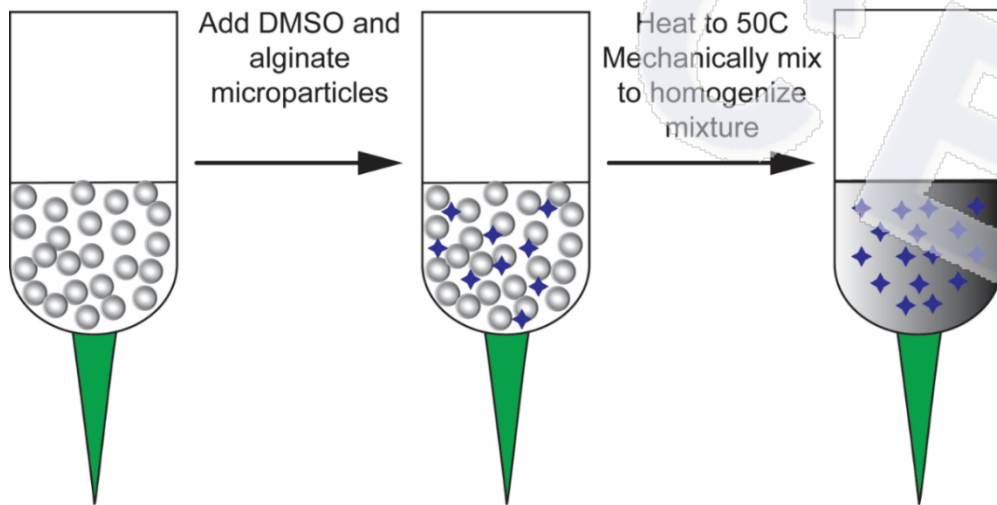
STL generation

- Use CT scan from NIH 3D Print Exchange
- Modify part to remove excess fragments
- Rescale

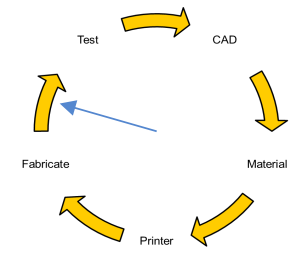


Biomimetic Shape – Material Tuning

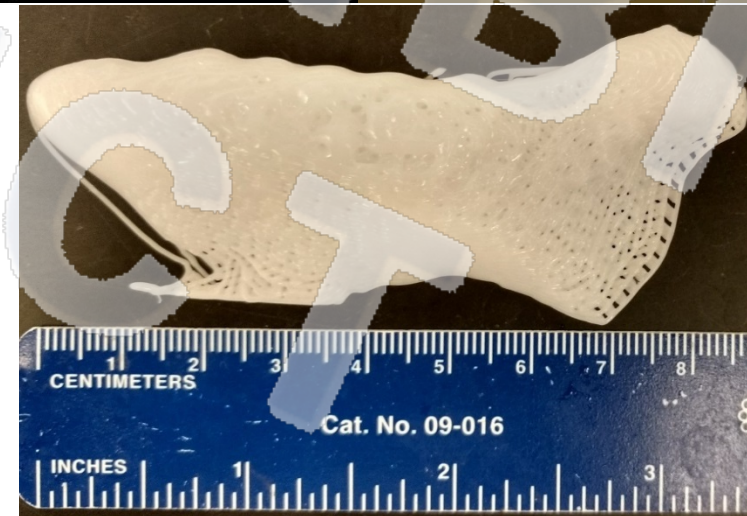
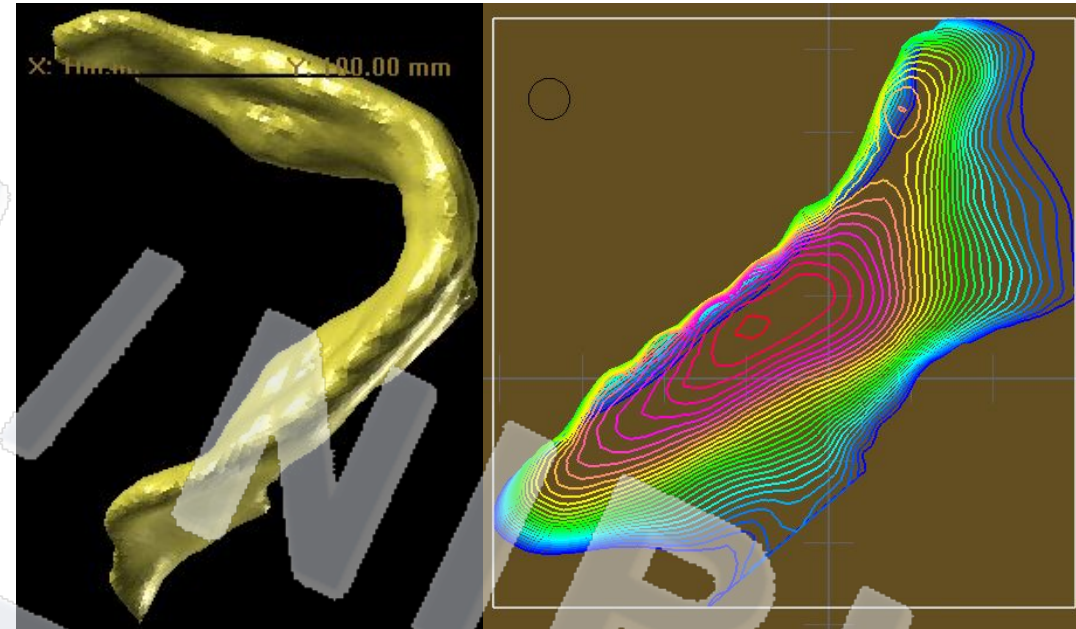
- Develop new material
 - Compounding method
 - Printing method
 - Repeatability



Biomimetic Shape – Print

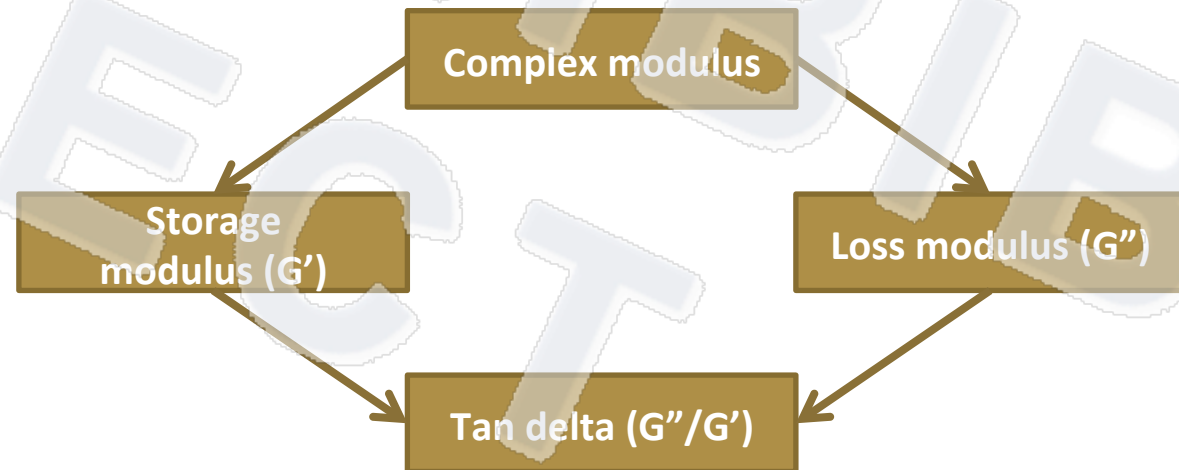


- Process STL
 - Remove unwanted sections
 - Orient for printer
- Slice print file
 - Material properties
 - Overall shape
 - Generate G-code
- Post processing
- Test
 - Elution data
 - Yield and modulus
 - Cytotoxicity

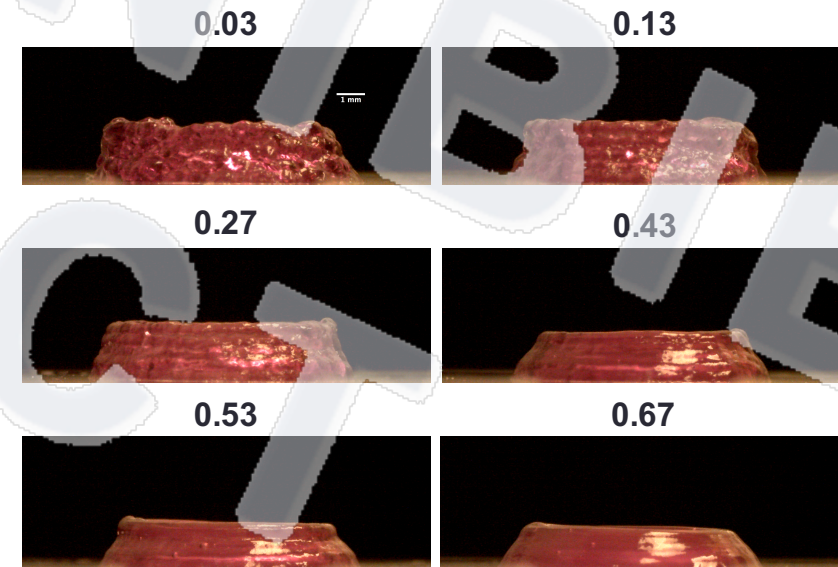
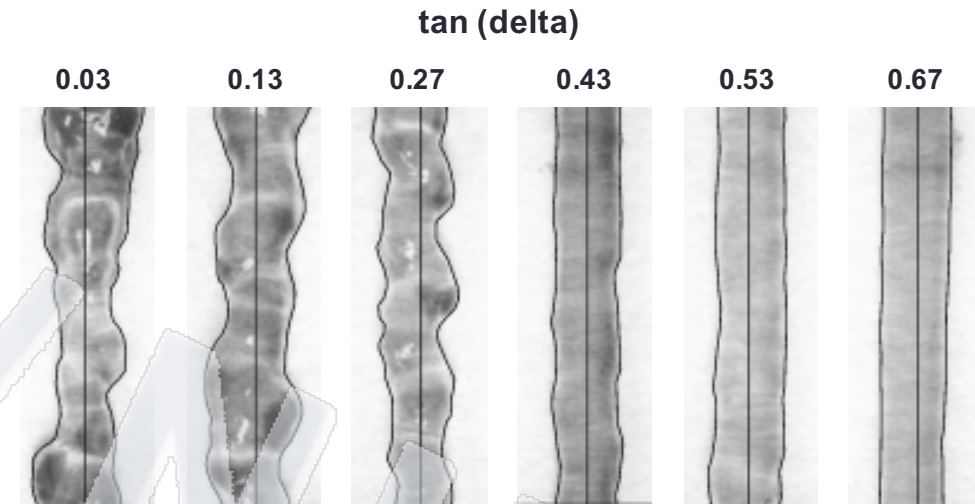
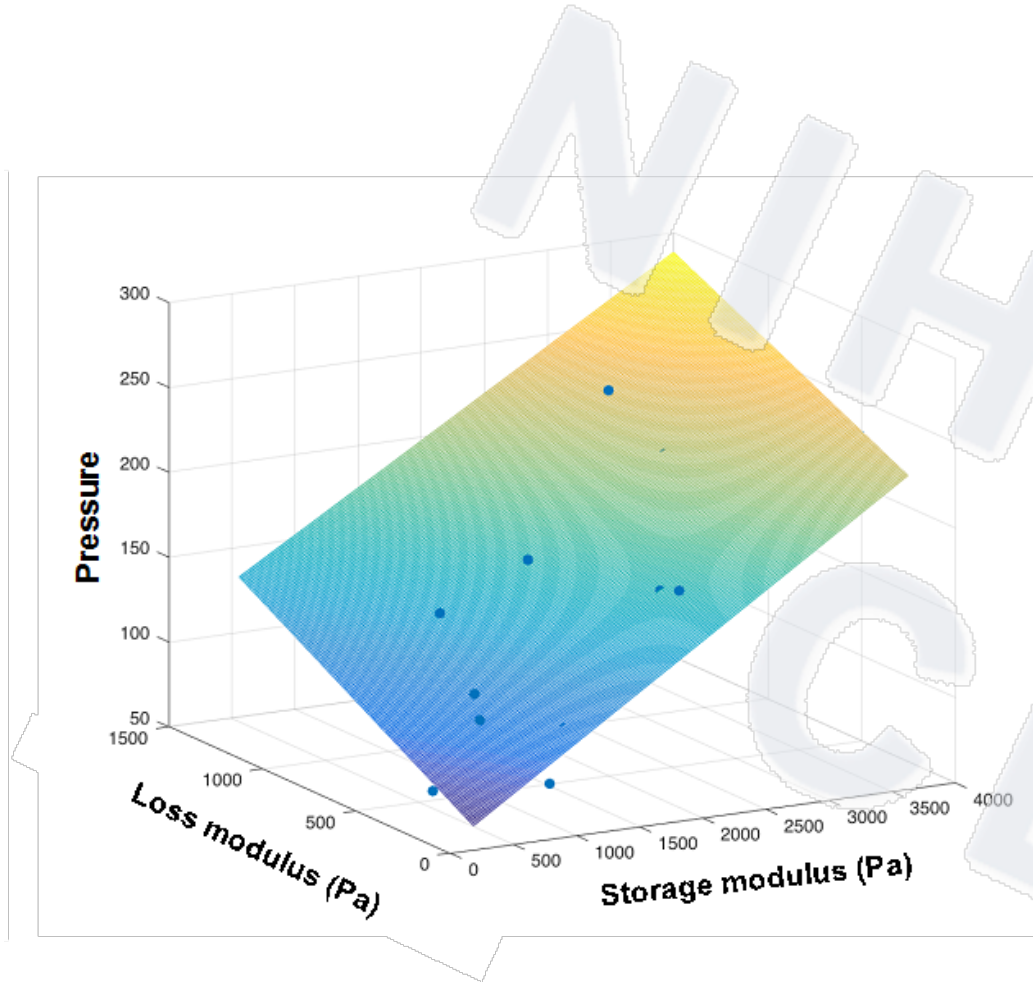


Biomaterial rheology

- Material properties under deformation and flow
- Printability affected by several factors
 - Temperature; Pressure; Needle size; Flow rate
- Rheological characteristics
 - Viscosity
 - Shear-thinning properties



Extrudability and Structural stability



Nuances of bioink selection and properties

Extrusion status

Under-gelation








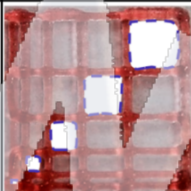
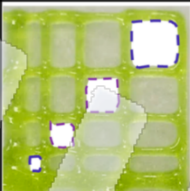
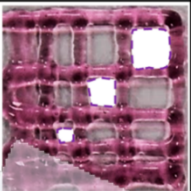
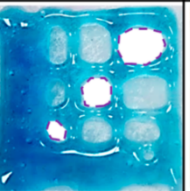






Proper-gelation



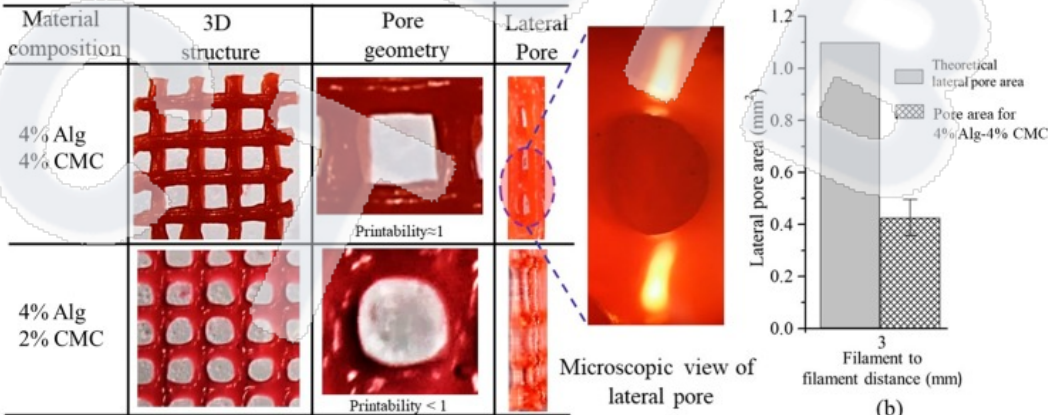
Over-gelation



Ouyang et al. 2016, Biofabrication

	Material concentration (w/v)				
	4% Alg-4% CMC	4% Alg-3% CMC	4% Alg-2% CMC	4% Alg-1% CMC	4% Alg
Gelation status	 Proper gelation	 Proper gelation	 Proper gelation	 Under gelation	 Under gelation
Macro pore					
Lateral view					

4 mm

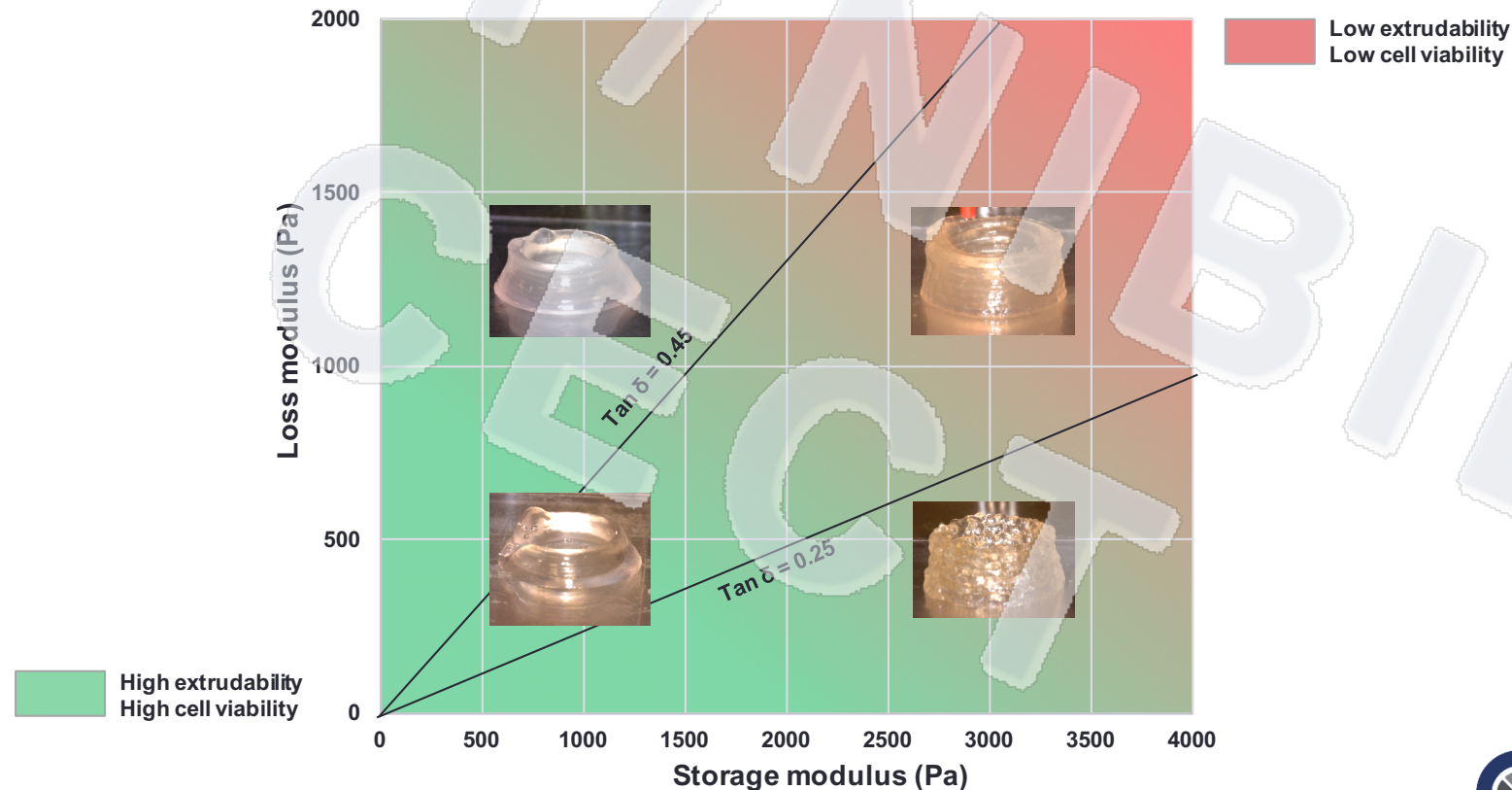


(a)

(b)

Optimal printing properties

- Looking beyond viscosity
- Complicated with effects of T, P, presence of cells, etc.



Questions?