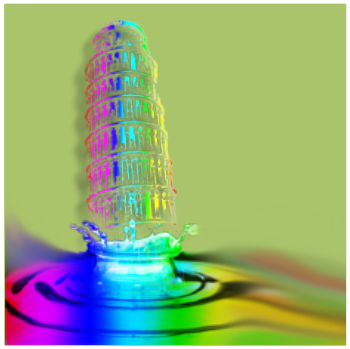
Biofabrication



Centro E. Piaggio
bioengineering and robotics research center

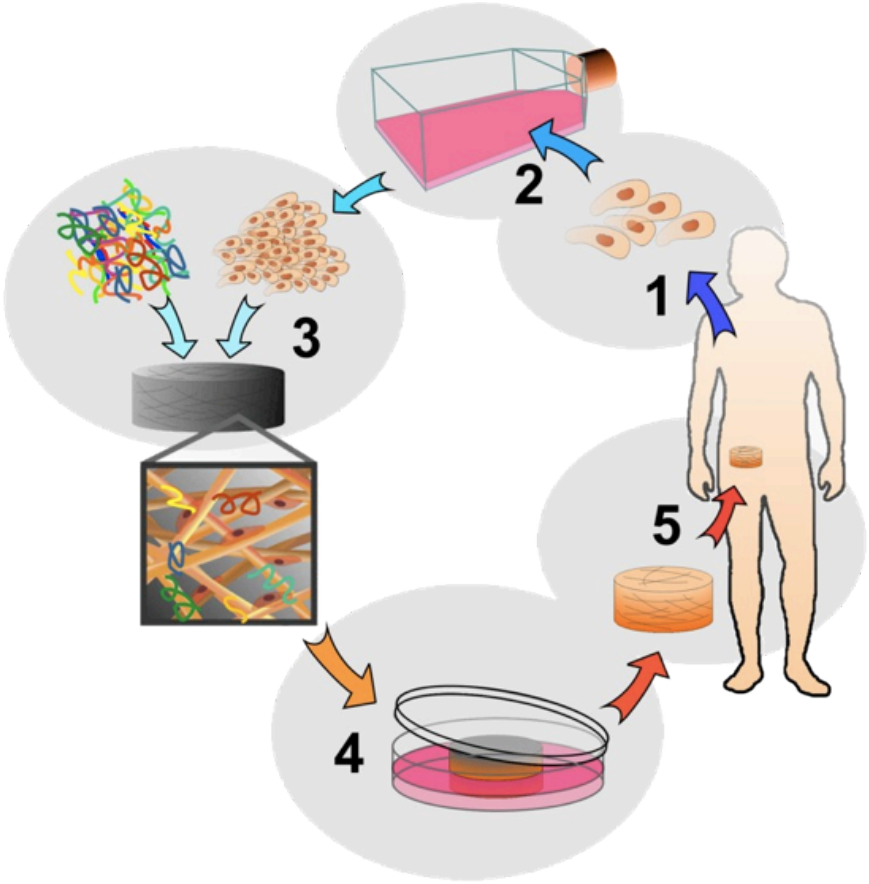
Tissue engineering

- *an interdisciplinary field that applies the principles of engineering and life sciences towards the development of biological substitutes that restore, maintain, or improve biological tissue function or a whole organ*

Langer R, Vacanti JP. *Tissue engineering*. Science 1993, **260**(5110), 920–926

Tissue engineering

- Classic paradigm



Regenerative medicine

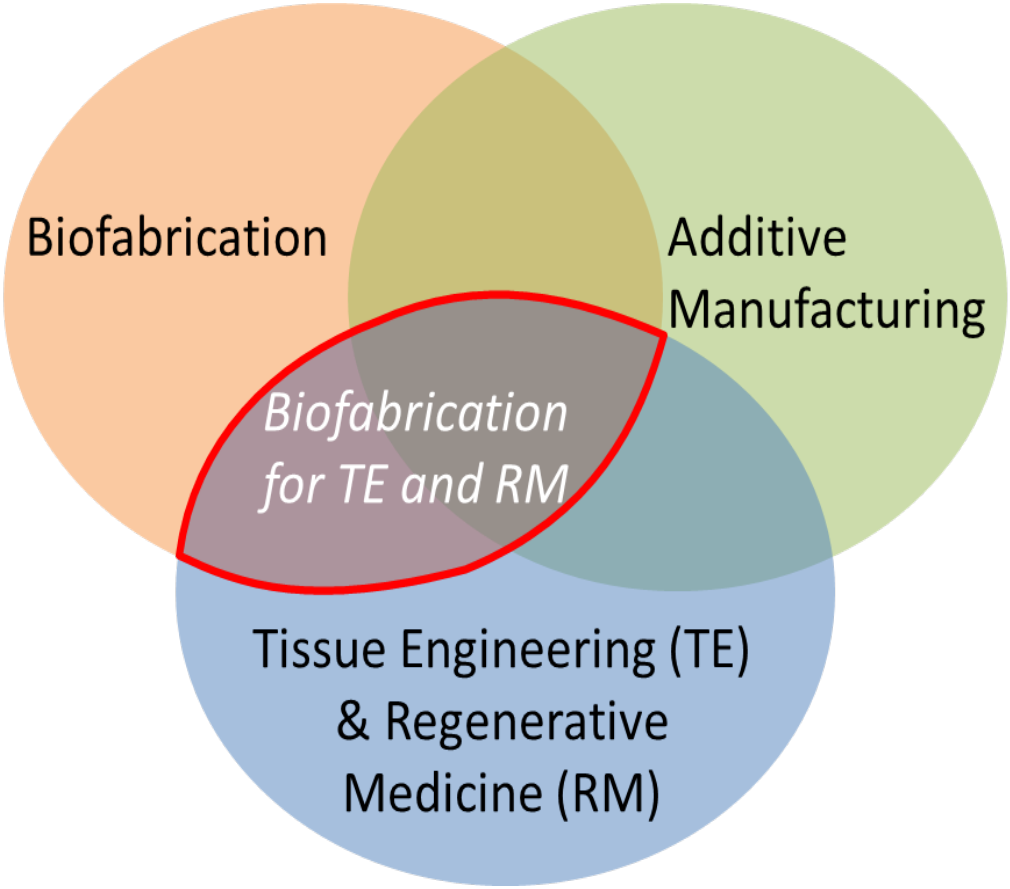
- the application of tissue science, tissue engineering, and related biological and engineering principles that restore the structure and function of damaged tissues and organs

U.S. department of health and human services, 2006: A New Vision - A Future for Regenerative Medicine,

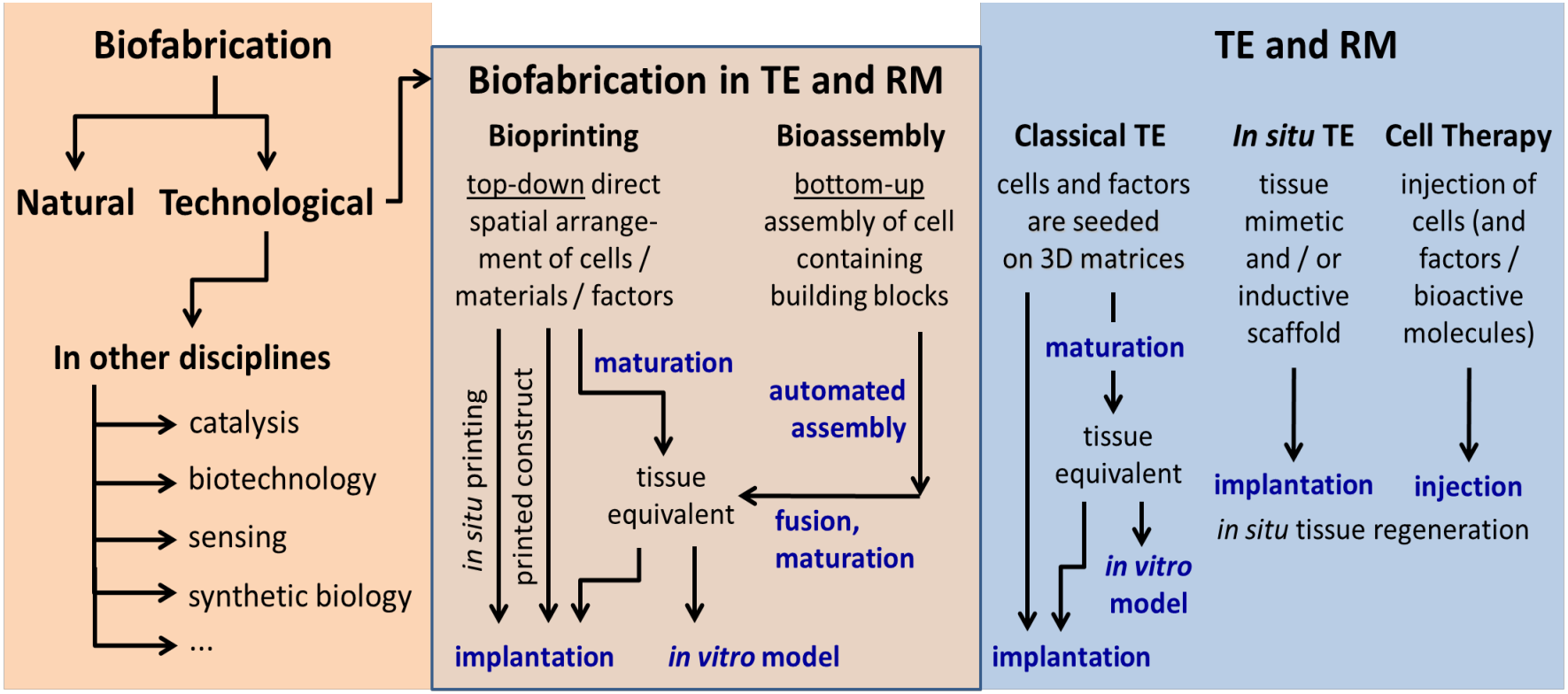
Biofabrication

- *the generation of biologically functional products with structural organization from living cells, micro-tissues or hybrid tissue constructs, bioactive molecules or biomaterials either through top-down (Bioprinting) or bottom-up (Bioassembly) strategies and subsequent tissue maturation processes.*

Biofabrication

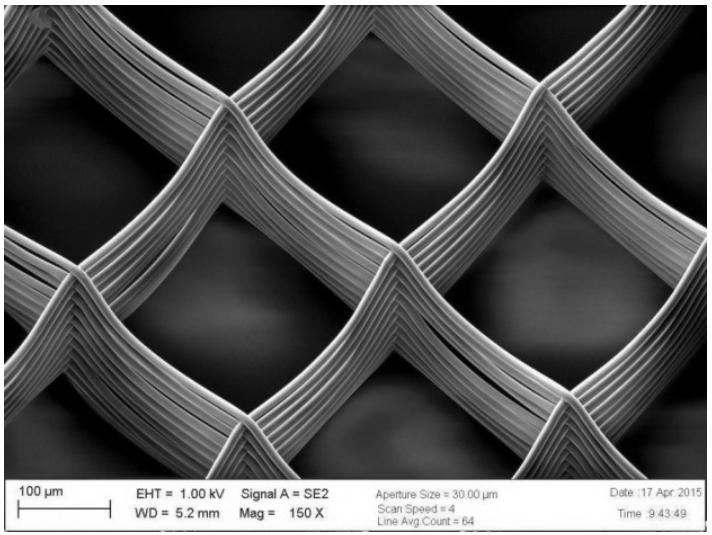


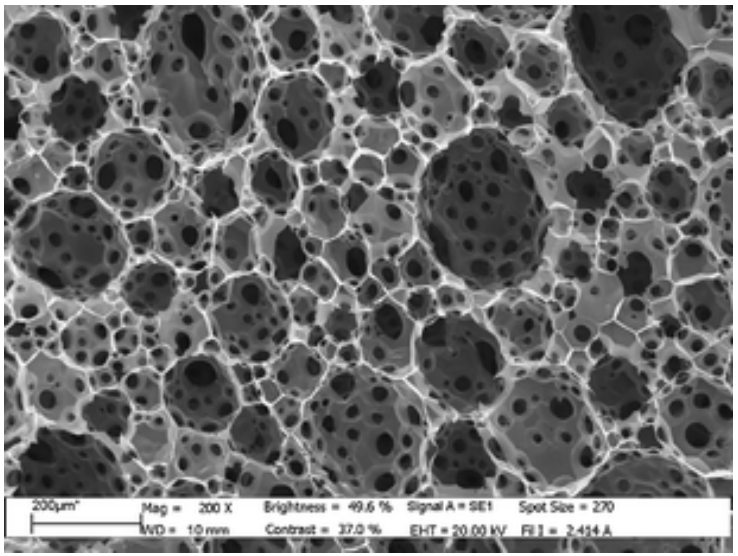
Biofabrication

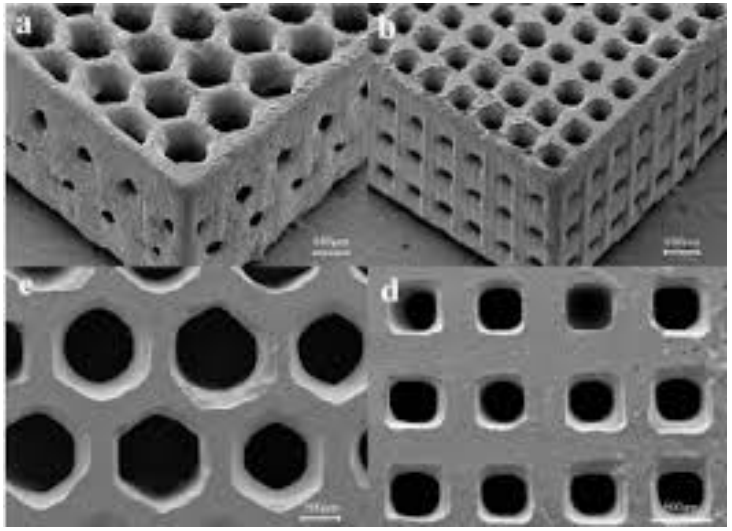


BIOFABRICATION
AT RESEARCH CENTER E. PIAGGIO

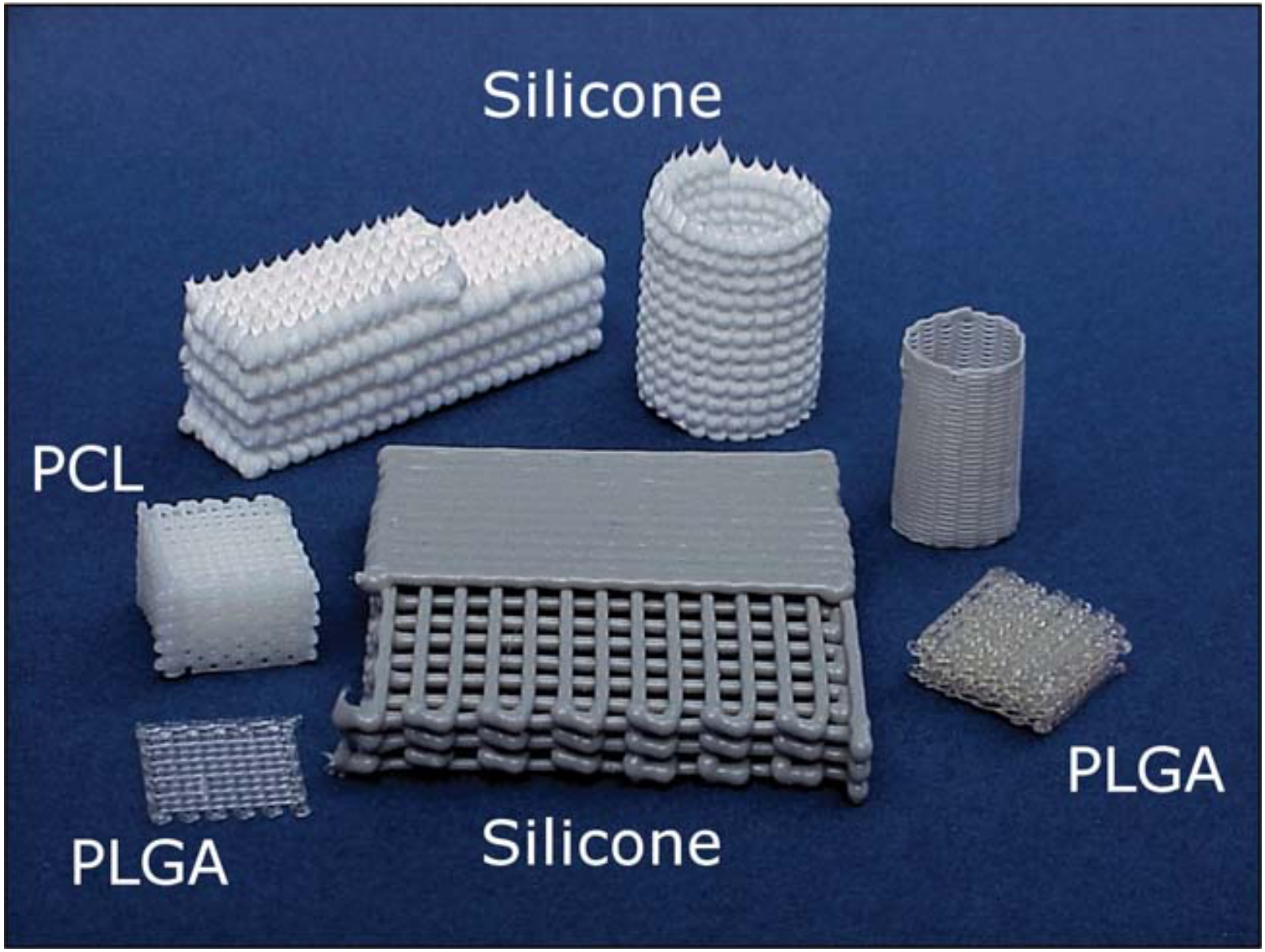
Scaffolds


100 µm
EHT = 1.00 kV
WD = 5.2 mm
Signal A = SE2
Mag = 150 X
Aperture Size = 30.00 µm
Scan Speed = 4
Line Avg Count = 64
Date :17 Apr 2015
Time :9:43:49

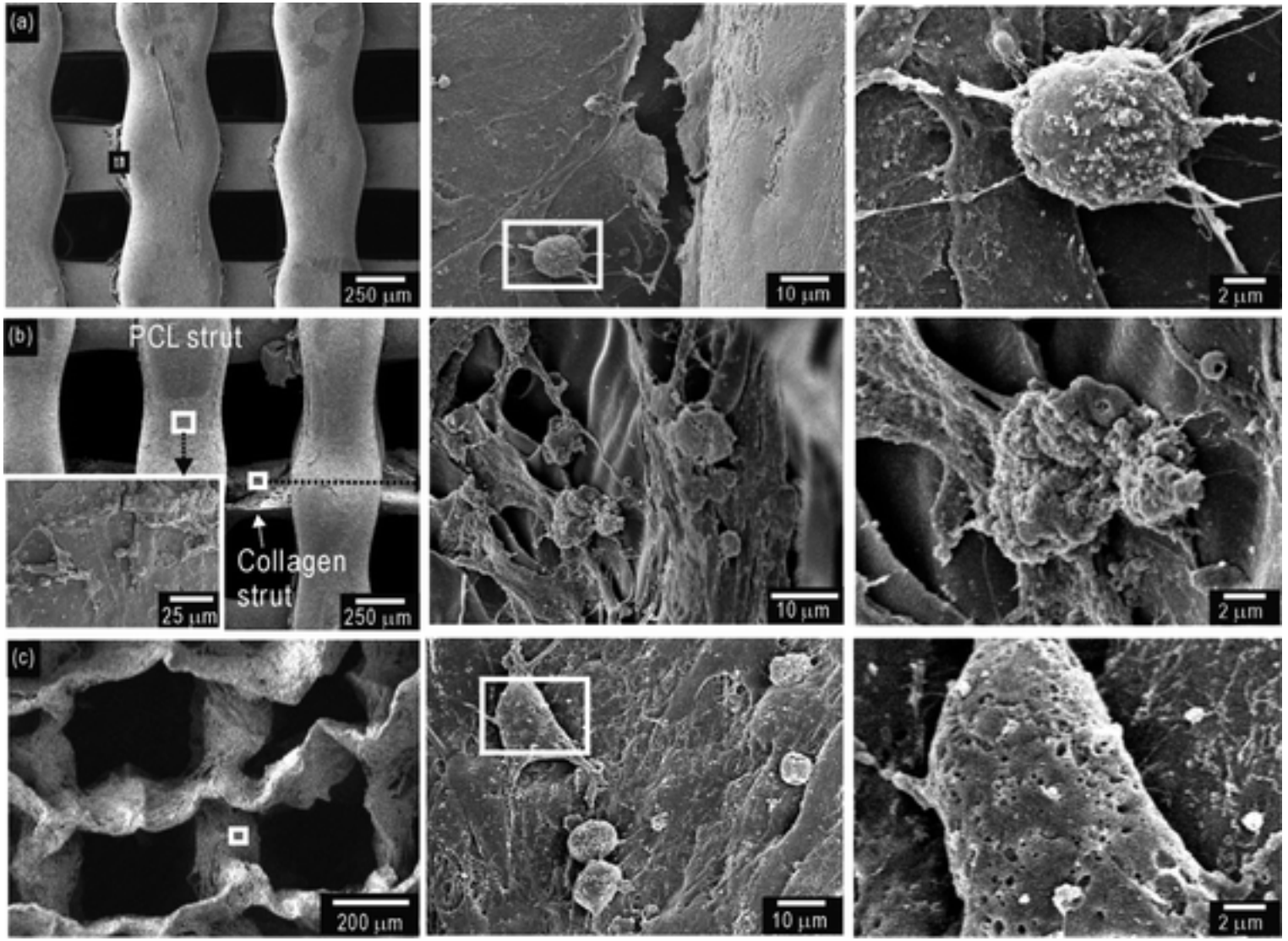

200µm
Mag = 200 X
WD = 10 mm
Brightness = 49.6 %
Contrast = 37.0 %
Signal A = SE1
EHT = 20.00 kV
Spot Size = 270
FI I = 2.414 A


a
b
c
d

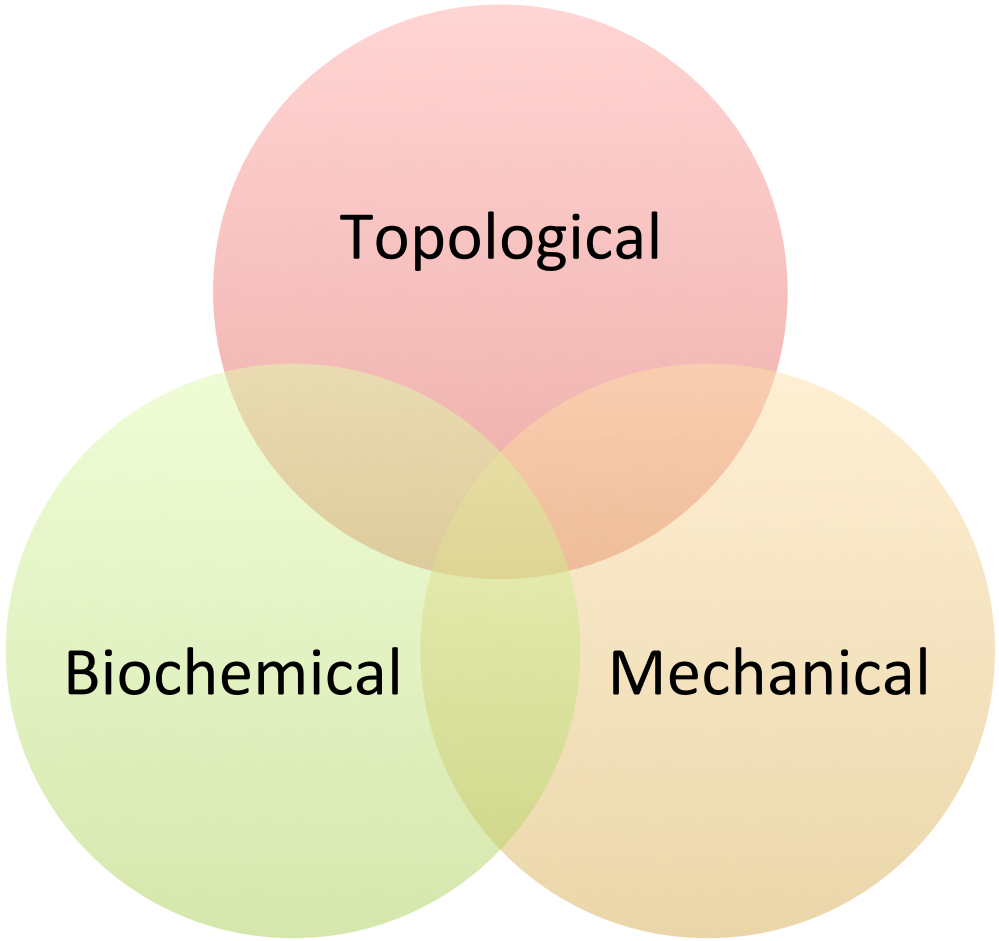
Scaffolds

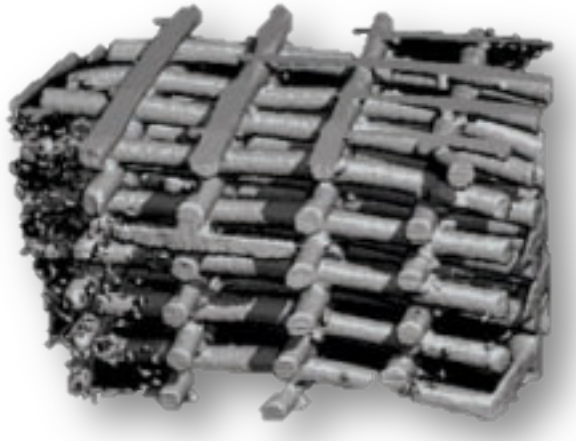


Scaffold

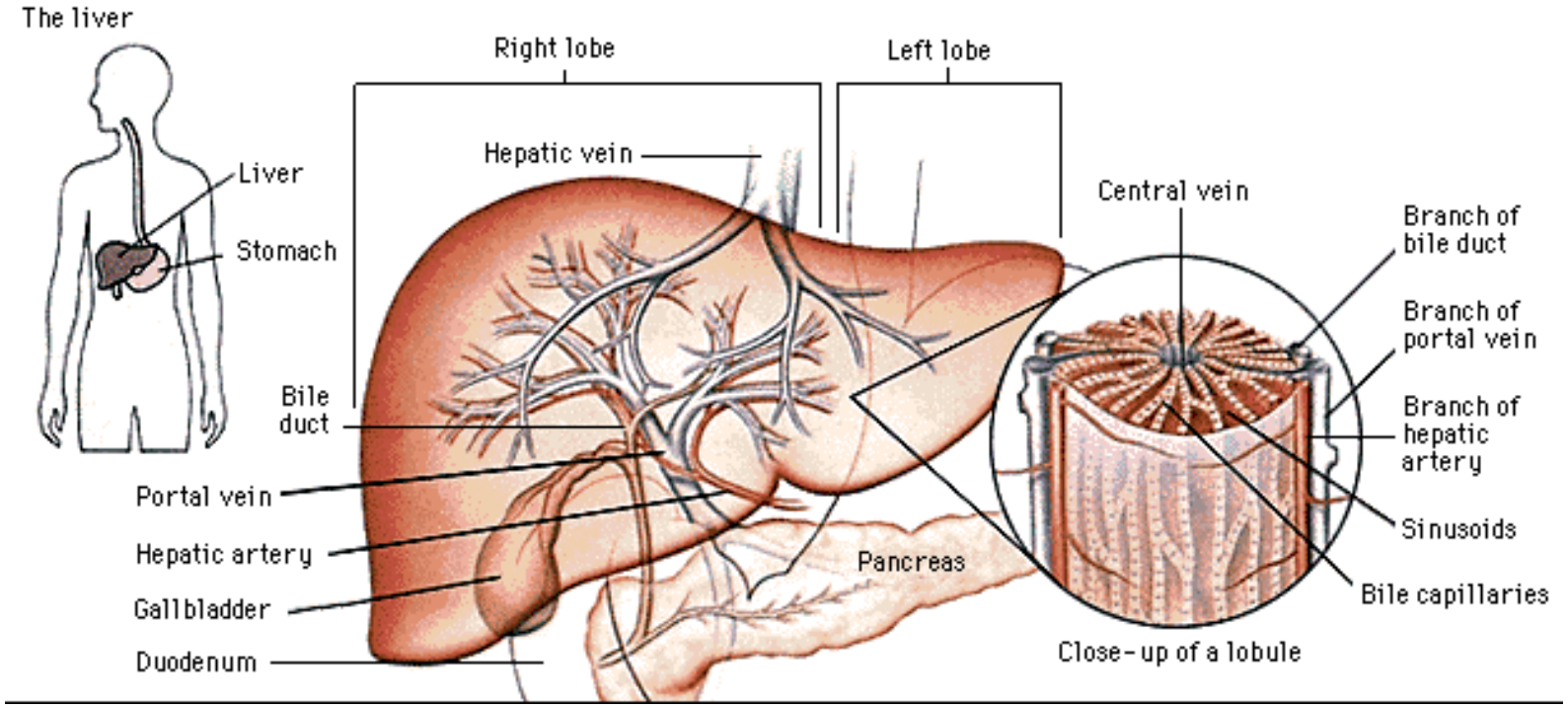

(a)
250 μm
10 μm
2 μm
(b)
PCL strut
25 μm
Collagen strut
250 μm
10 μm
2 μm
(c)
200 μm
10 μm
2 μm

Scaffold cues

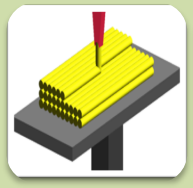
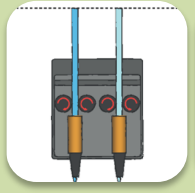




Living tissues: multiscale e multimaterial



Multimaterial Processing

2-Dimensional		3-Dimensional	
	Lithography and Soft-Lithography		PAMSquare
	Soft-Molecular Imprinting		Open-Source FDM
	Electrospinning		Inkjet Printing

Combination of 2D and 3D Technologies

Lithography and Soft-Lithography

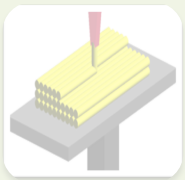
2-Dimensional

Lithography and Soft-Lithography

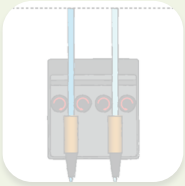
Soft-Molecular Imprinting

Electrospinning

3-Dimensional



PAMSquare



Open-Source FDM

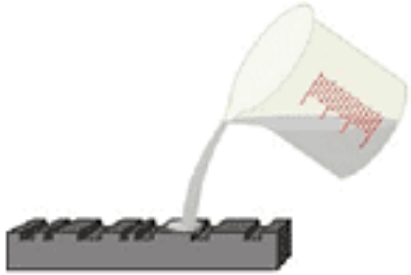
Inkjet Printing

Combination of 2D and 3D Technologies

Soft-lithography process

Silicon master

PDMS solution

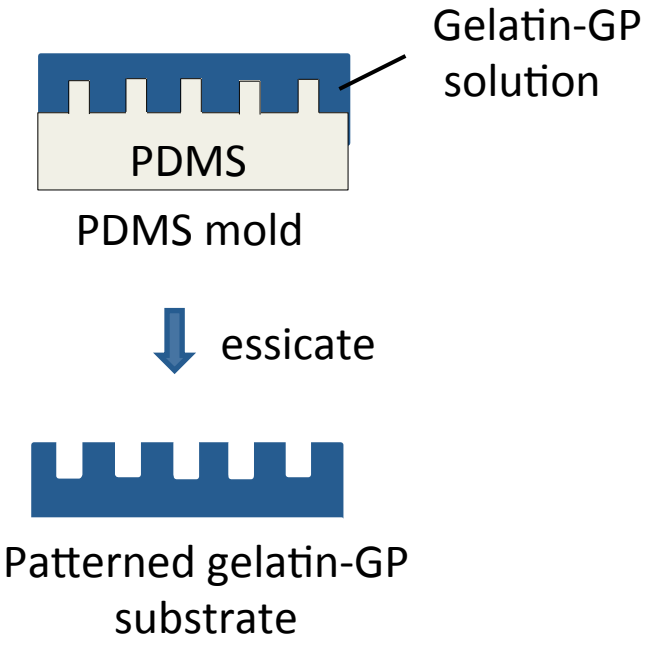


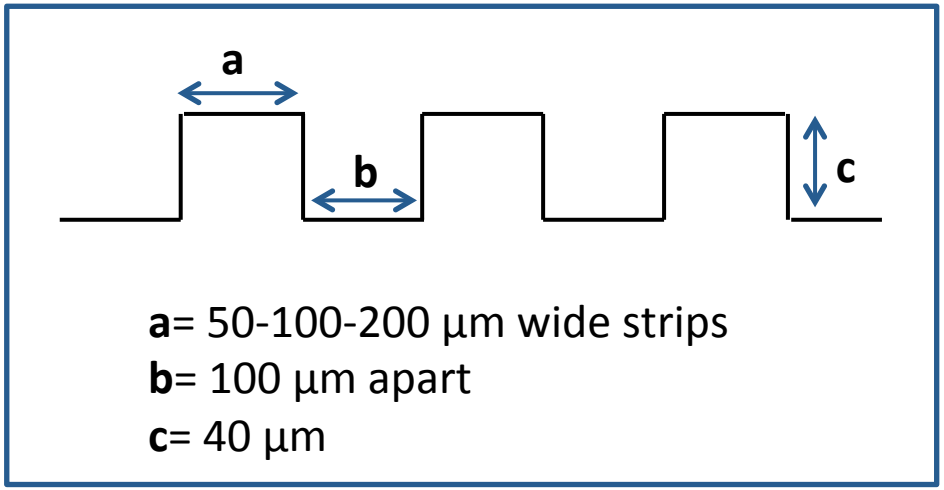
Casting

Lift-off of mold

PDMS mold

Micro-pattering of gelatin-GP scaffolds

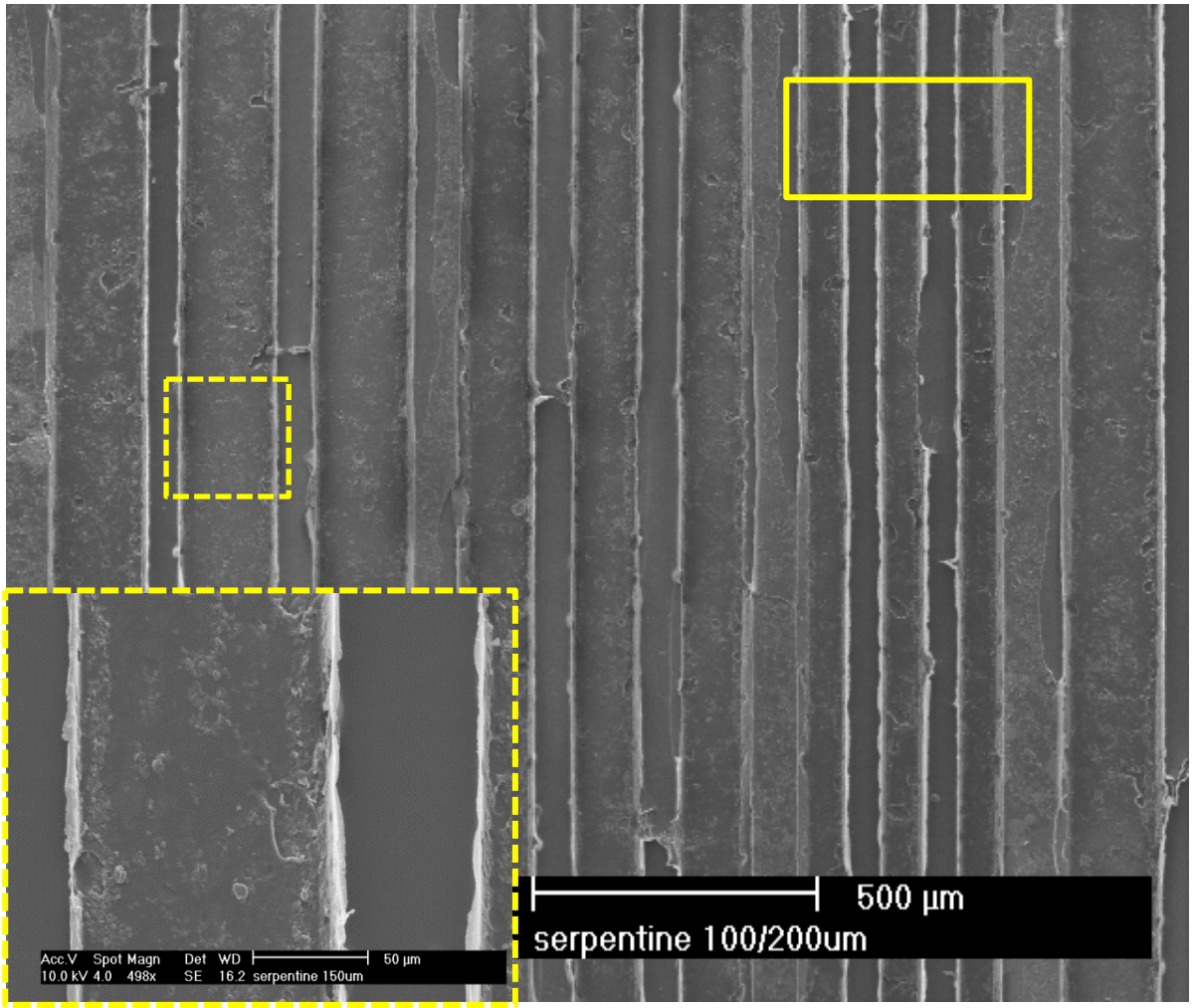




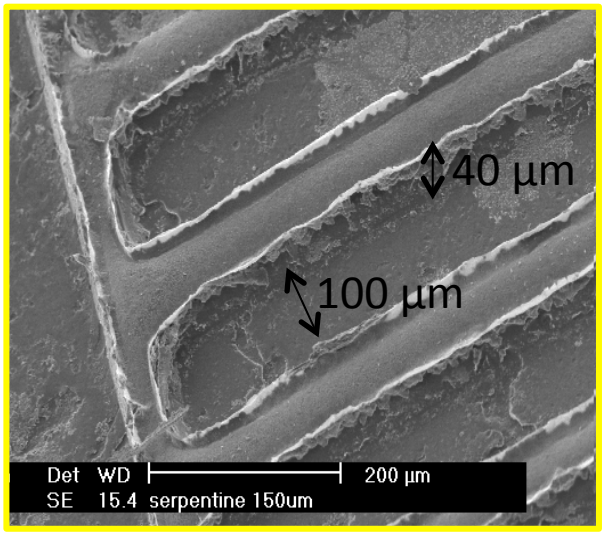
Micro-pattering of gelatin-GP scaffolds

Graded patterned substrates were used to follow myoblasts and myotubes orientation

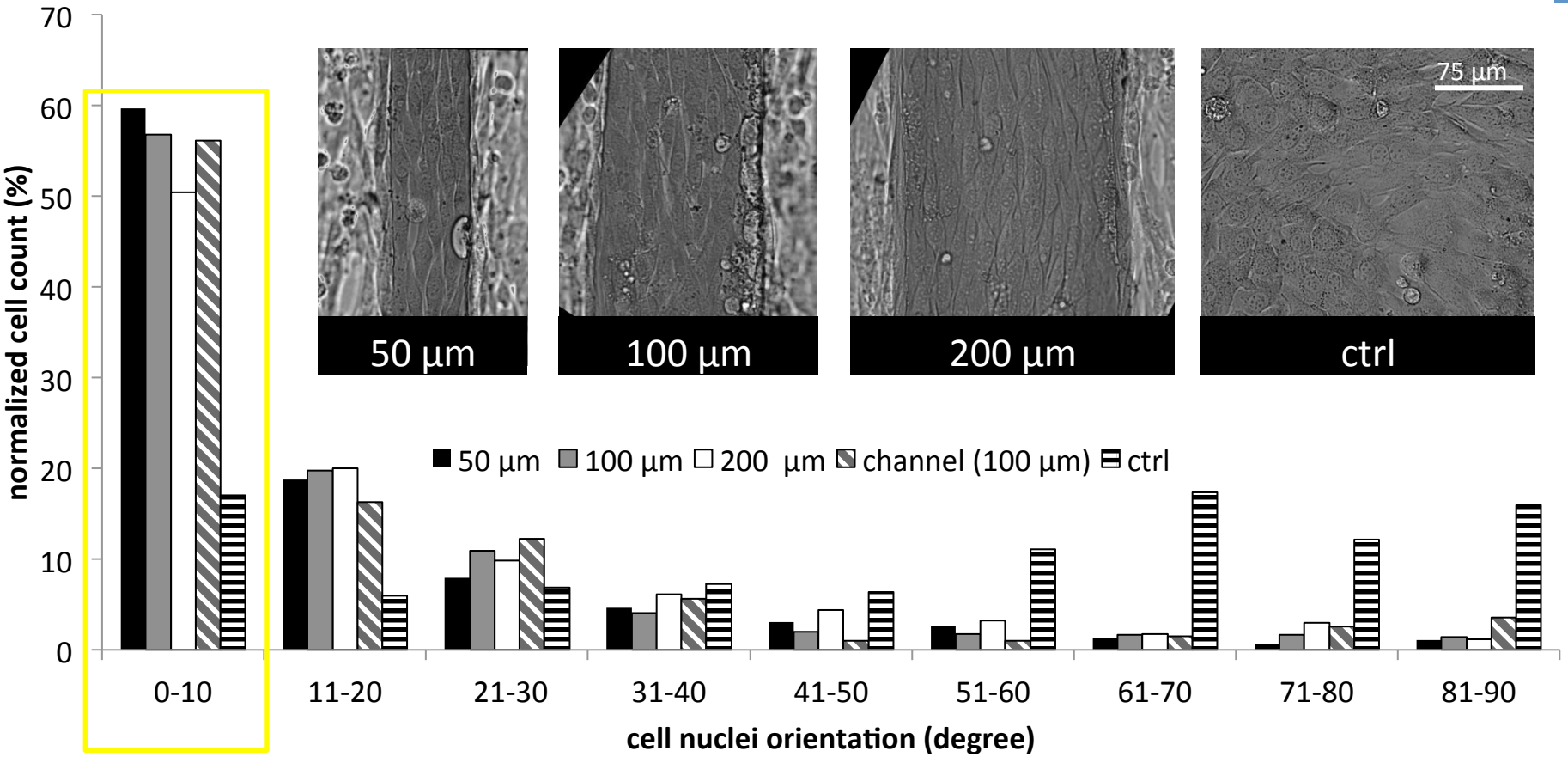
200 µm 100 µm 50 µm



LATERAL VIEW

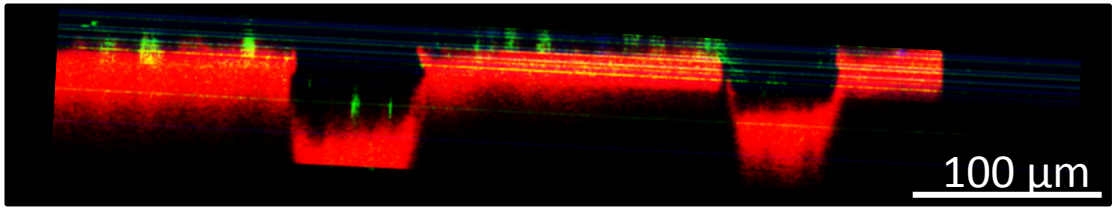


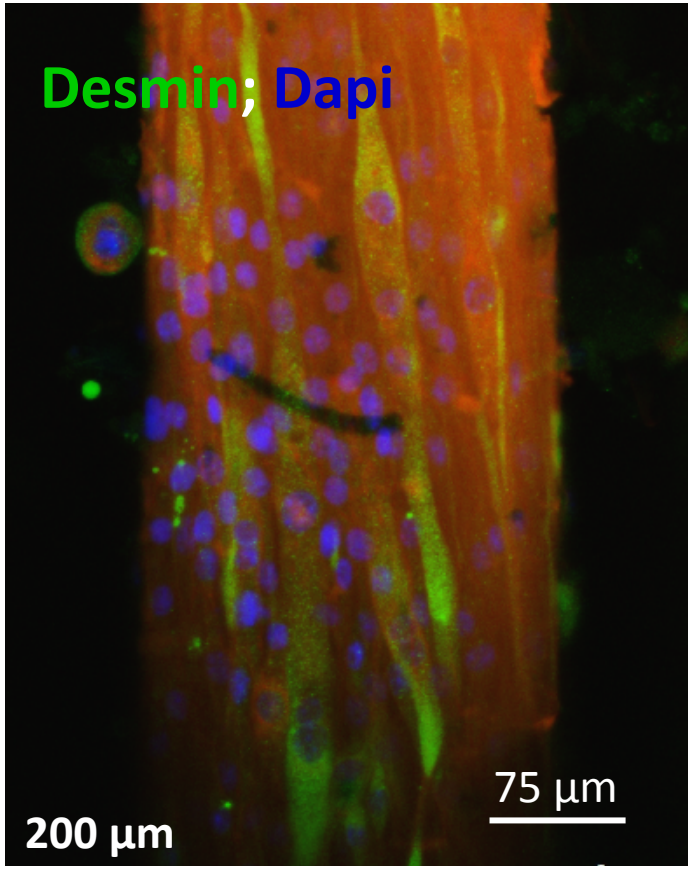
C212 myoblasts orientation on patterned structures

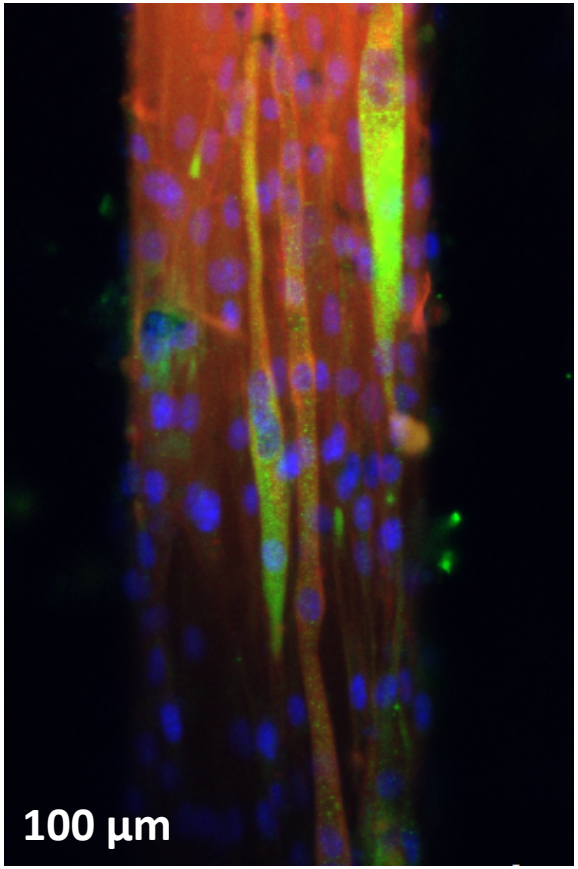


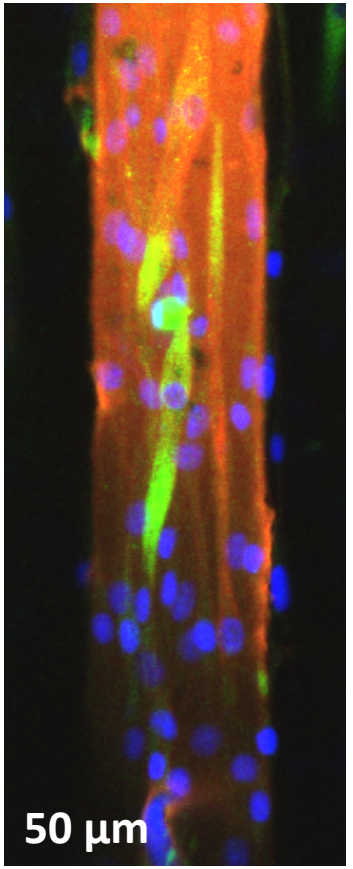
C2C12 myoblasts orientation is preferentially restricted within 10° relative to the direction of the structure

C212 myoblasts orientation on patterned structures



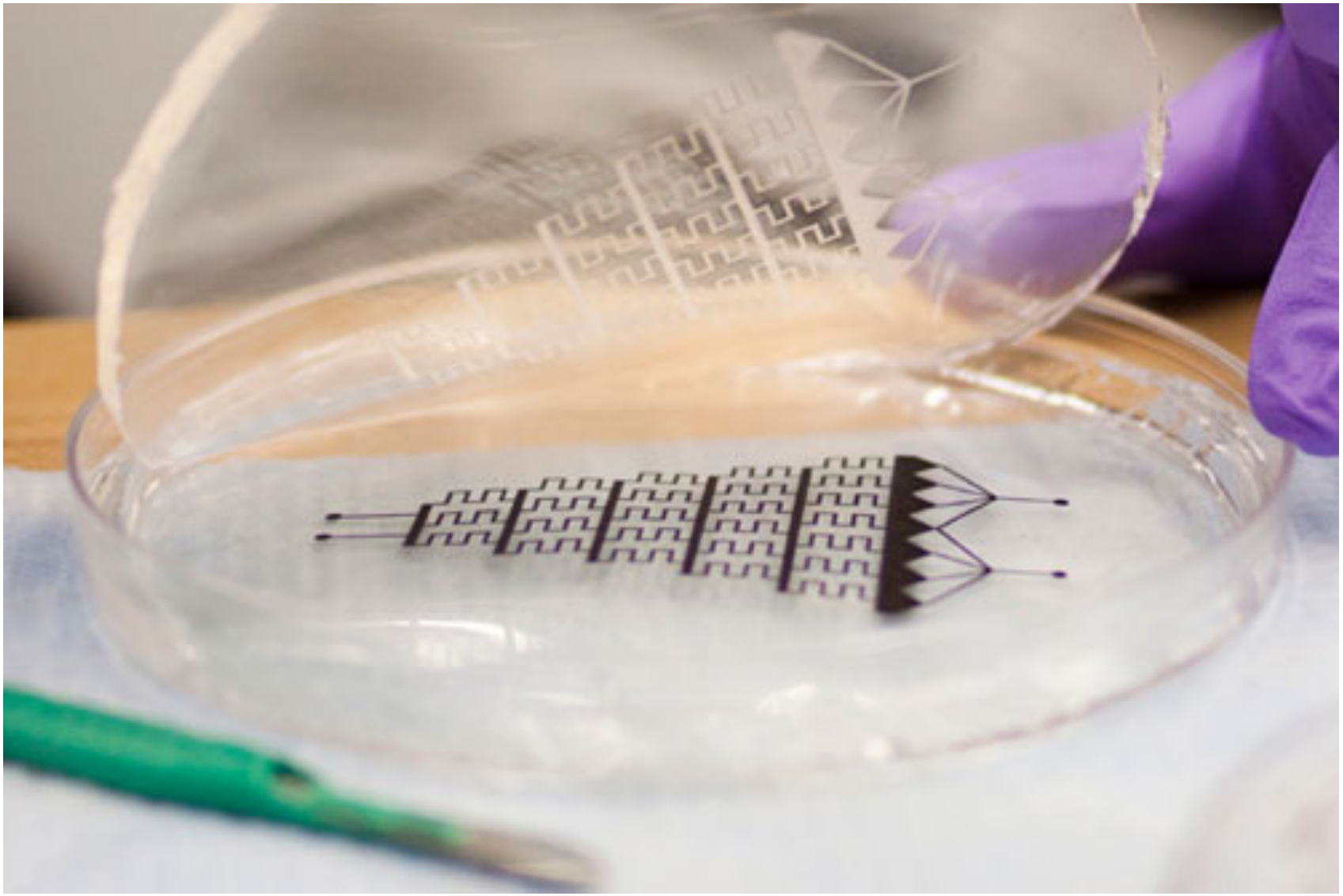




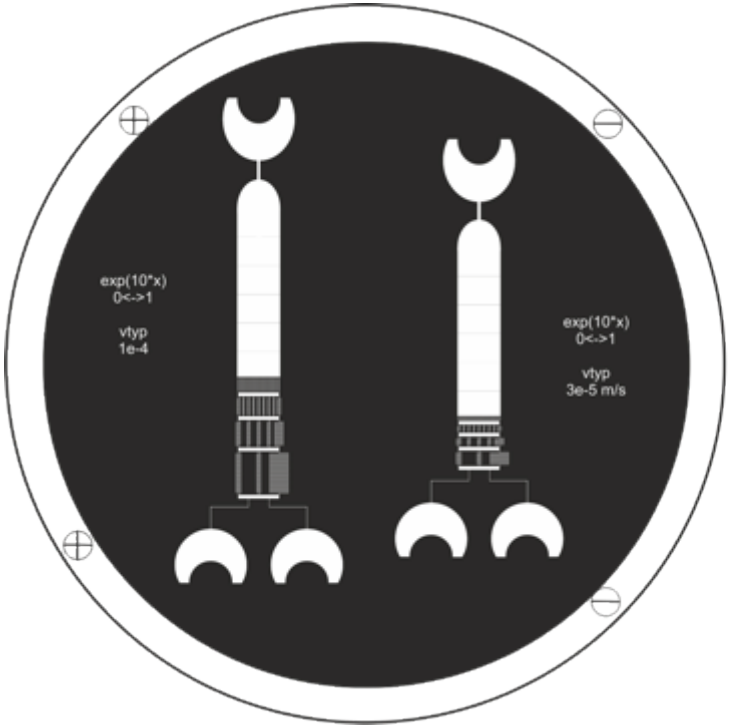


C2C12 myotubes are orientated on micropatterned substrates

Microdevice fabrication

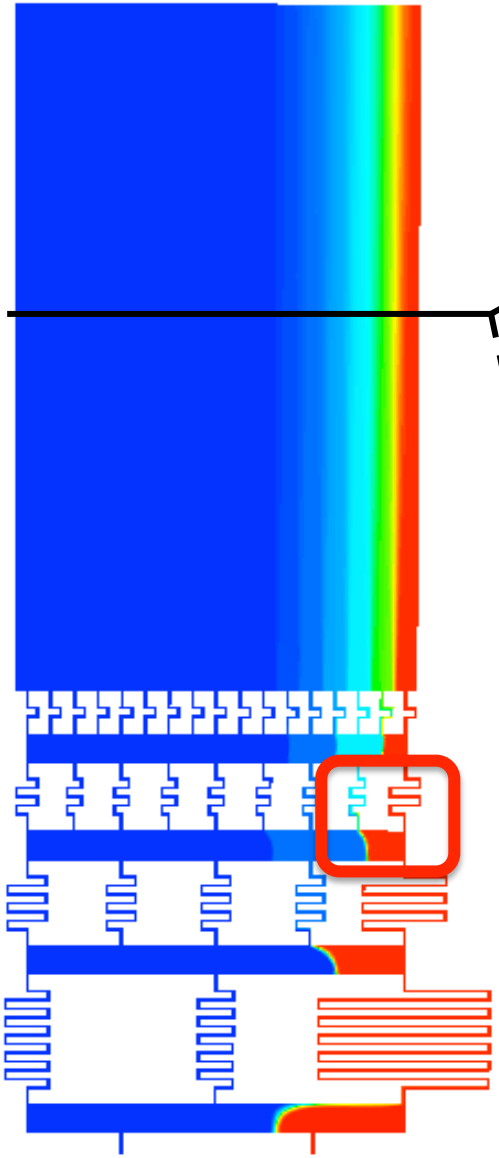


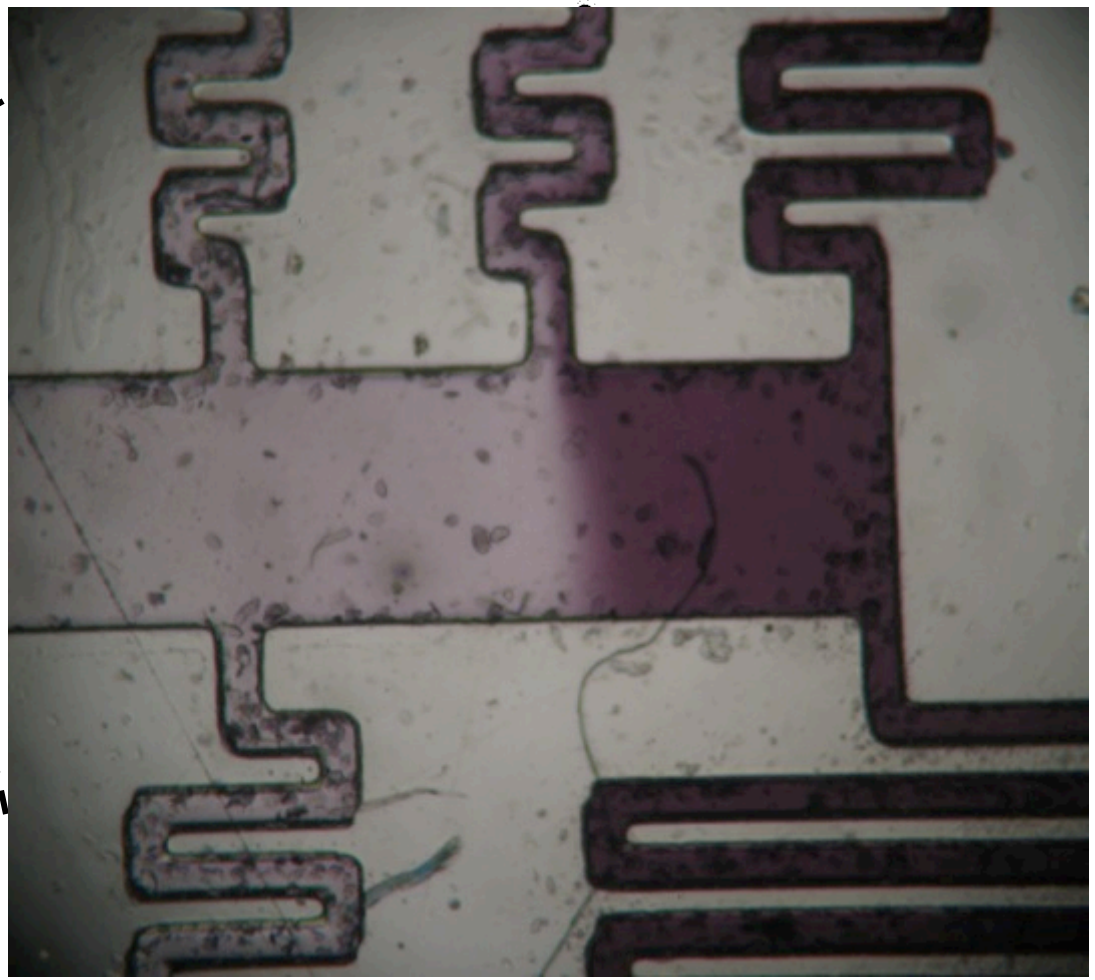
Microdevice fabrication



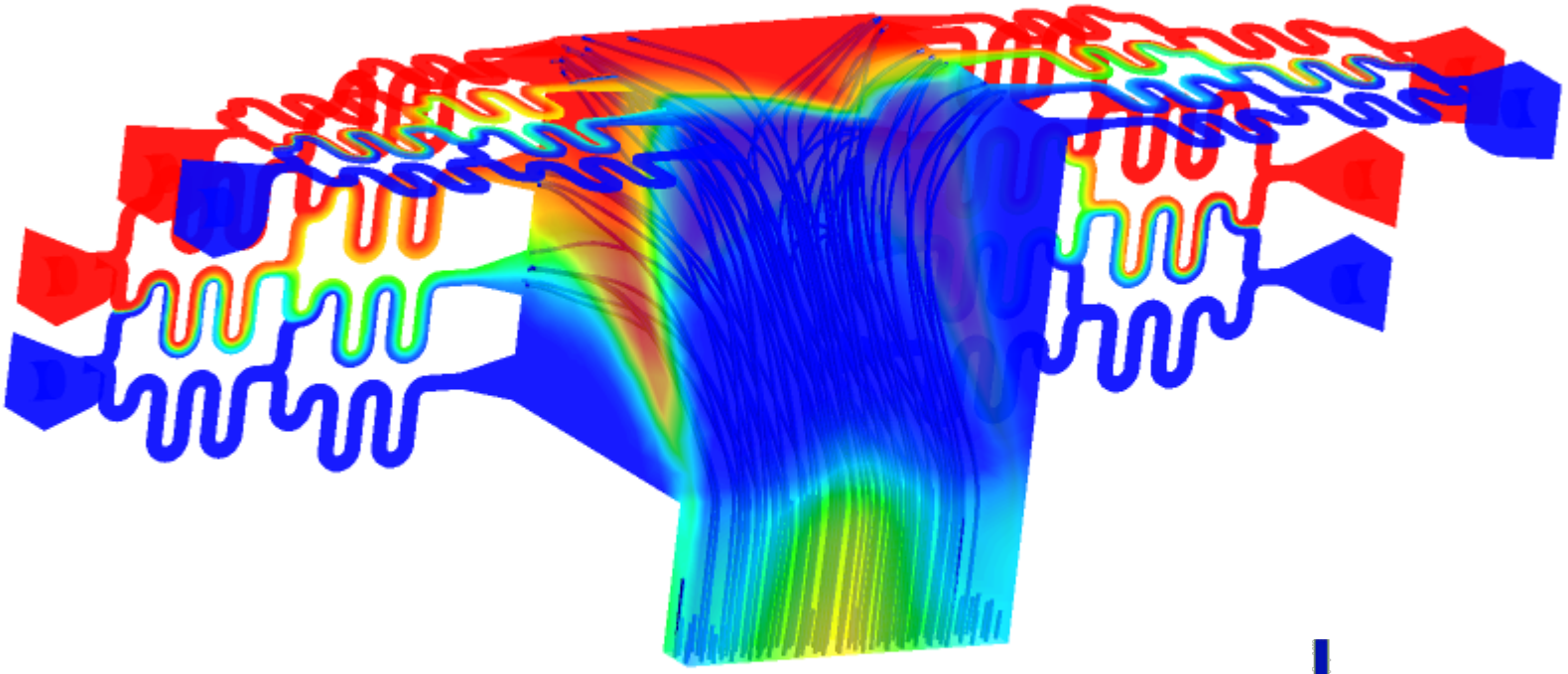
Silicon Wafer with SU-8 structure

Experimental vs simulated



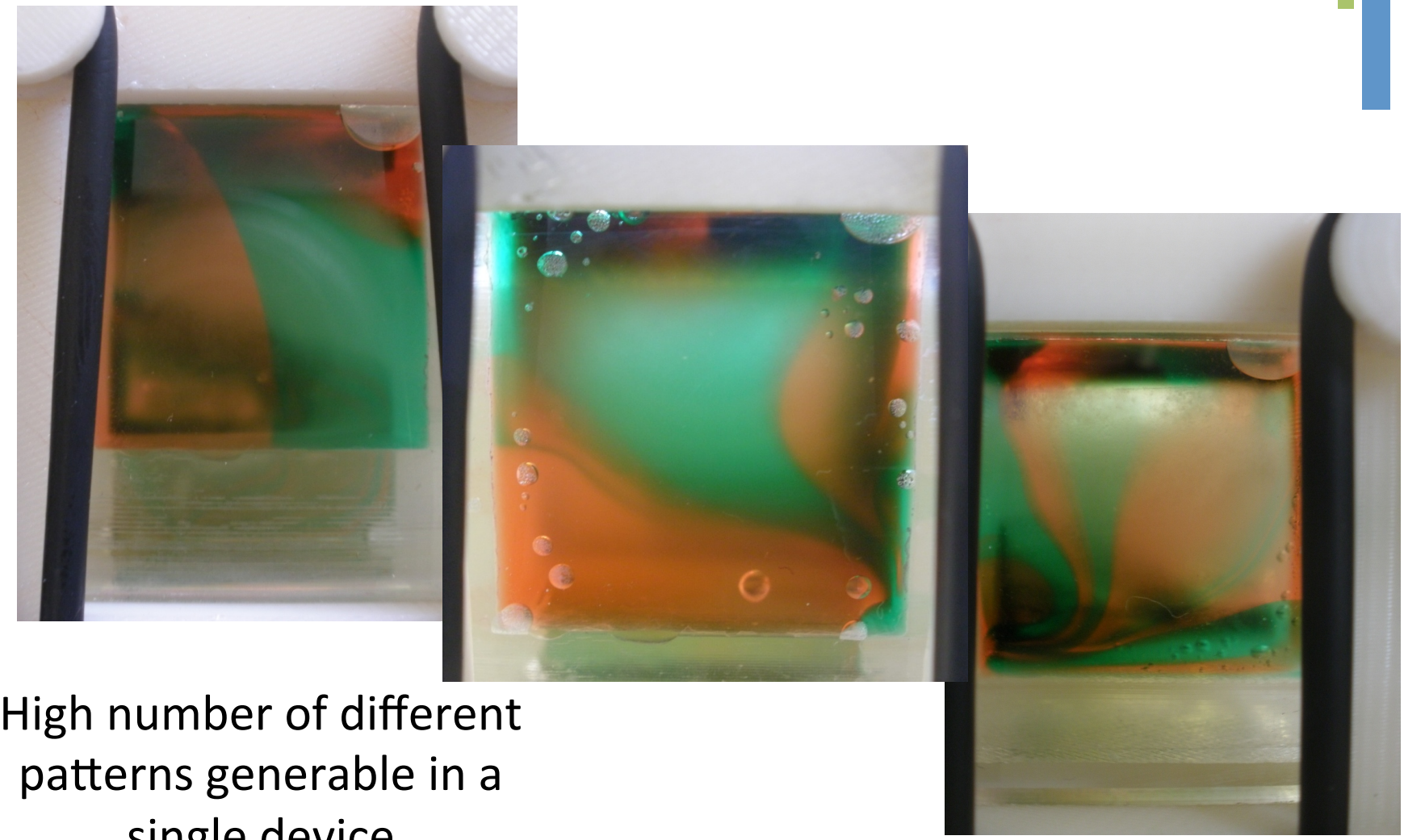


3D Concentration gradient maker



LINARI Engineering
Biomedical division

Graded stiffness substrates



High number of different patterns generable in a single device

Soft-MI

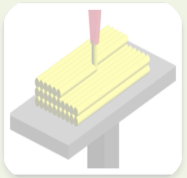
2-Dimensional

Lithography and Soft-Lithography

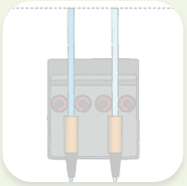
Soft-Molecular Imprinting

Electrospinning

3-Dimensional



PAMSquare



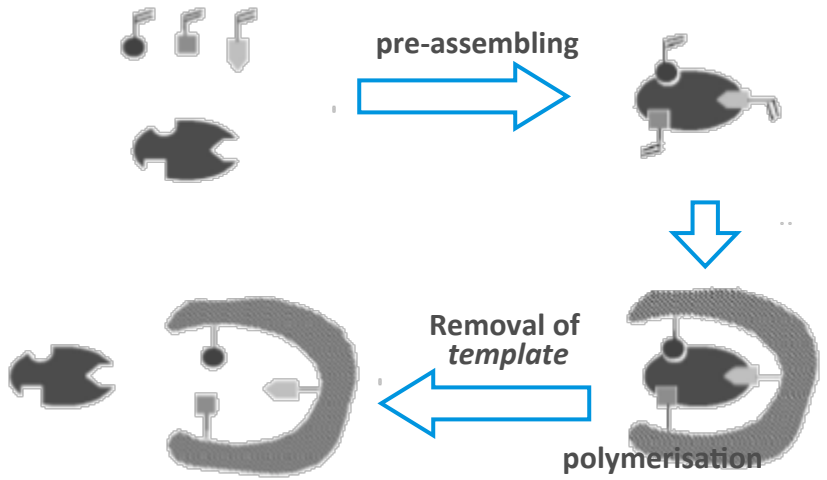
Open-Source FDM

Inkjet Printing

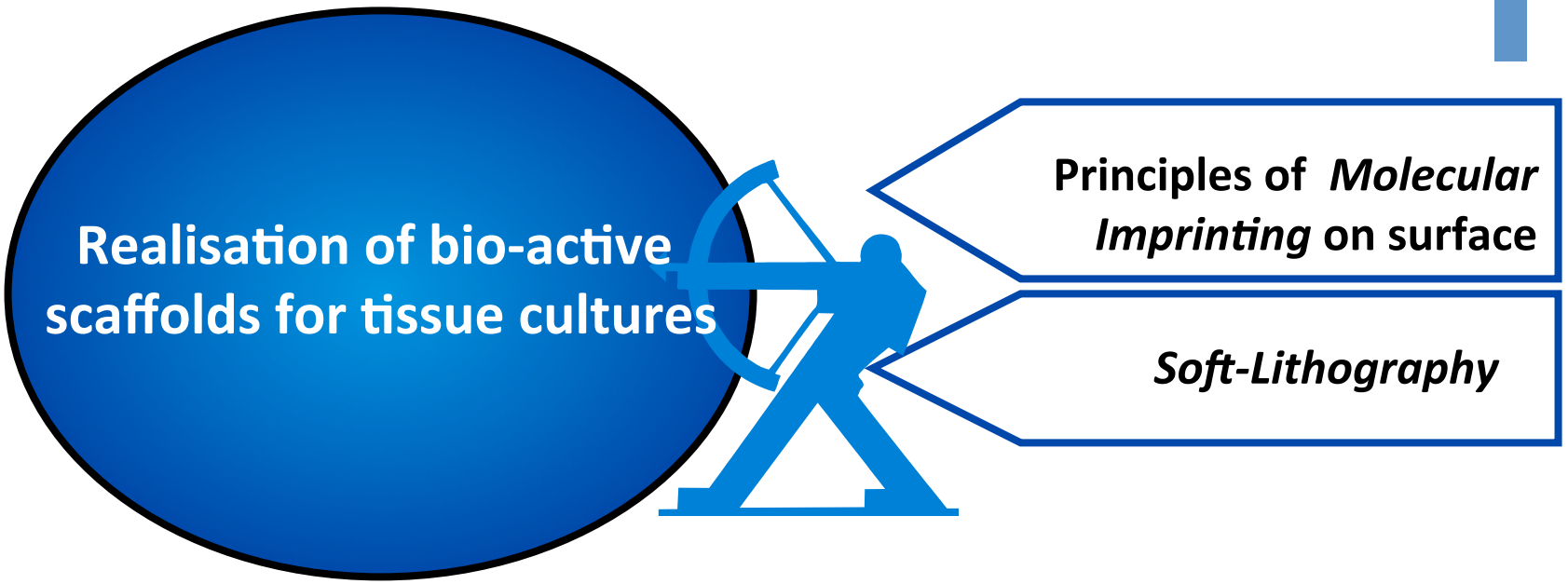
Combination of 2D and 3D Technologies

Molecular Imprinting

- Molecular Imprinting is a technology that allows to realise matrix or surface, usually made of organic polymers, with specificic and selective sites of recognition of a selected molecule (template) thanks to the steric and chemical complementarity
  - covalent interactions
  - reversible not covalent interactions



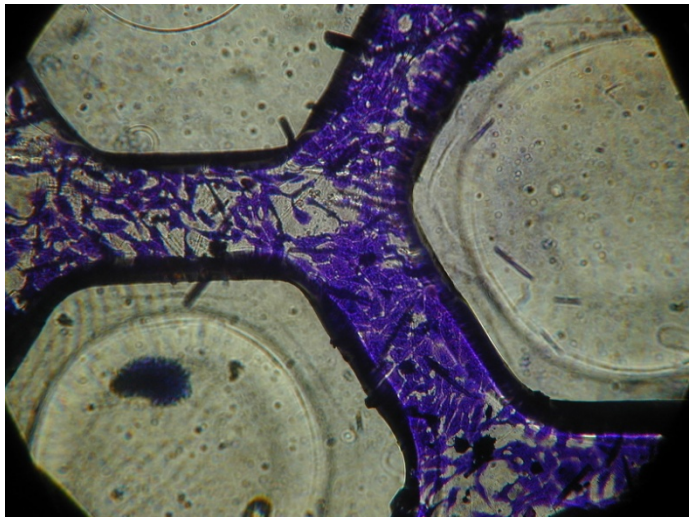
SOFT-MI



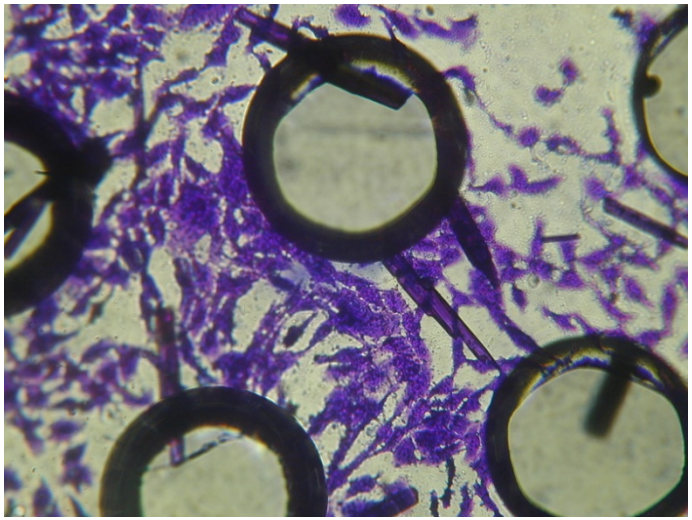
1. Fabrication of PDMS mold
2. modification of its superficial chemical properties
3. functionalisation of its surface
4. cell culture test

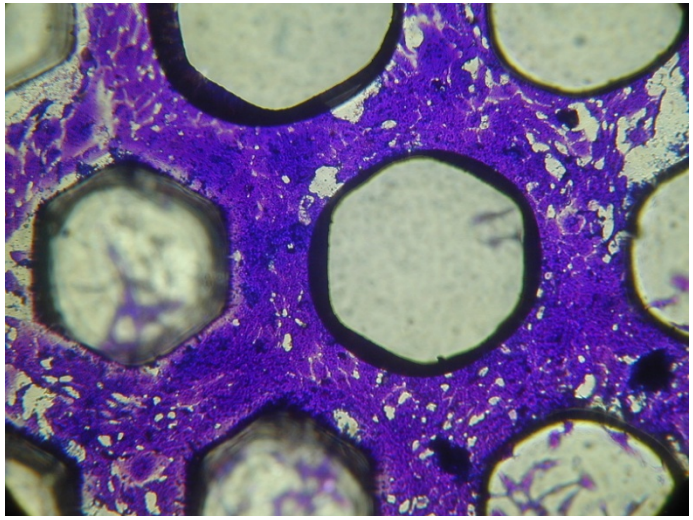
Vozzi G et al Biotechnol Bioeng. 2010;106(5):804-17.

Imprinting cells

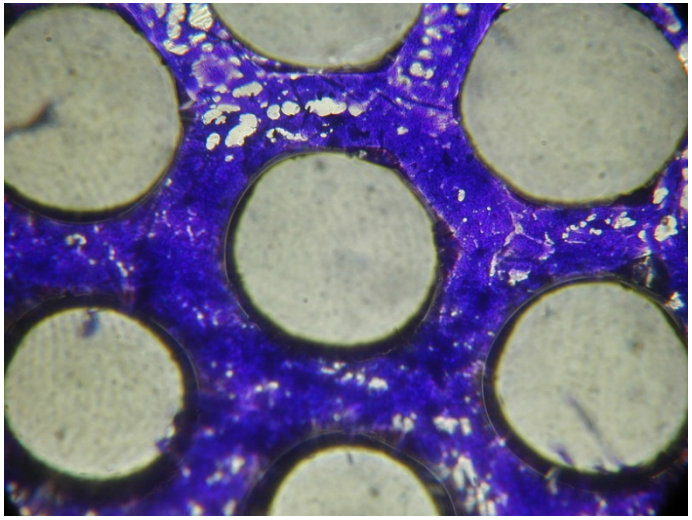


48h





72h



Electrospinning

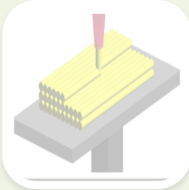
2-Dimensional

Lithography and Soft-Lithography

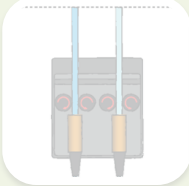
Soft-Molecular Imprinting

Electrospinning

3-Dimensional



PAMSQUARE

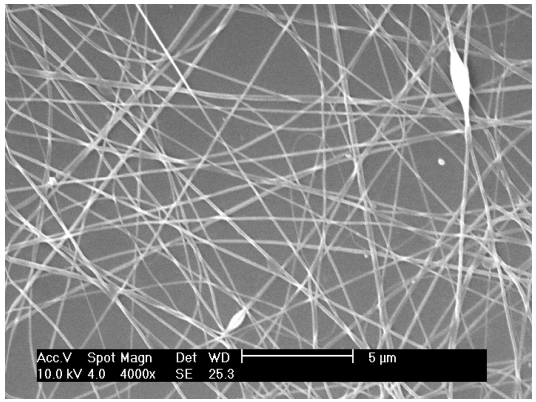


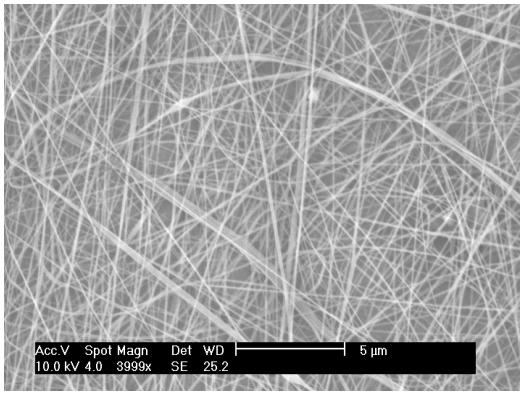
Open-Source FDM

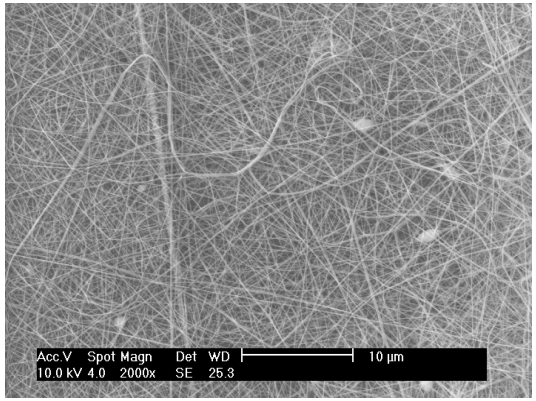
Inkjet Printing

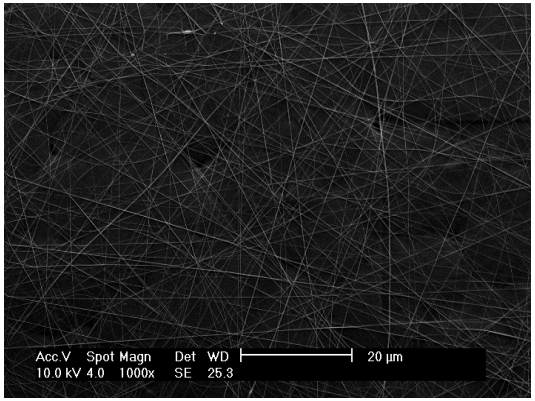
Combination of 2D and 3D Technologies

Electrospinning

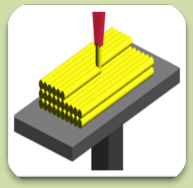
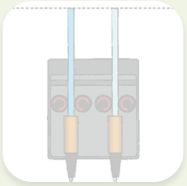








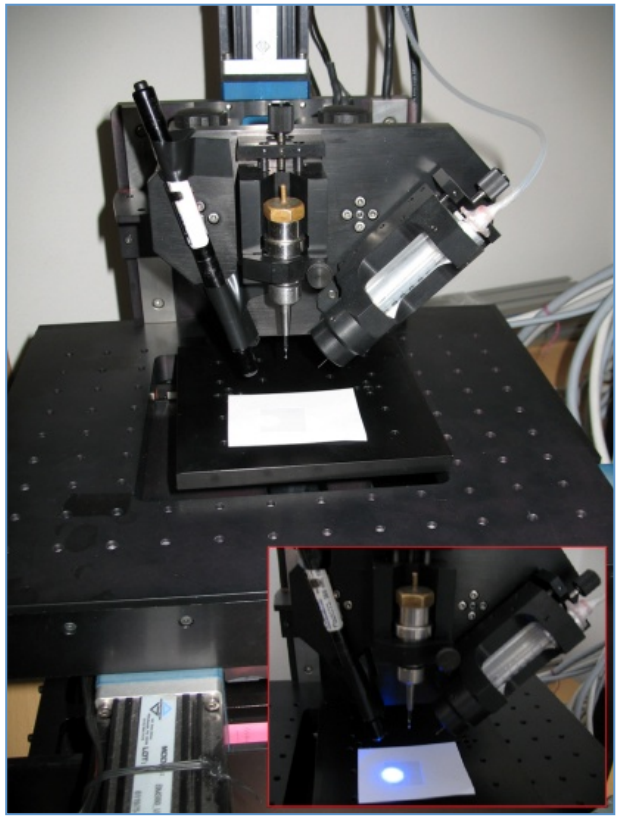
PAMsquare

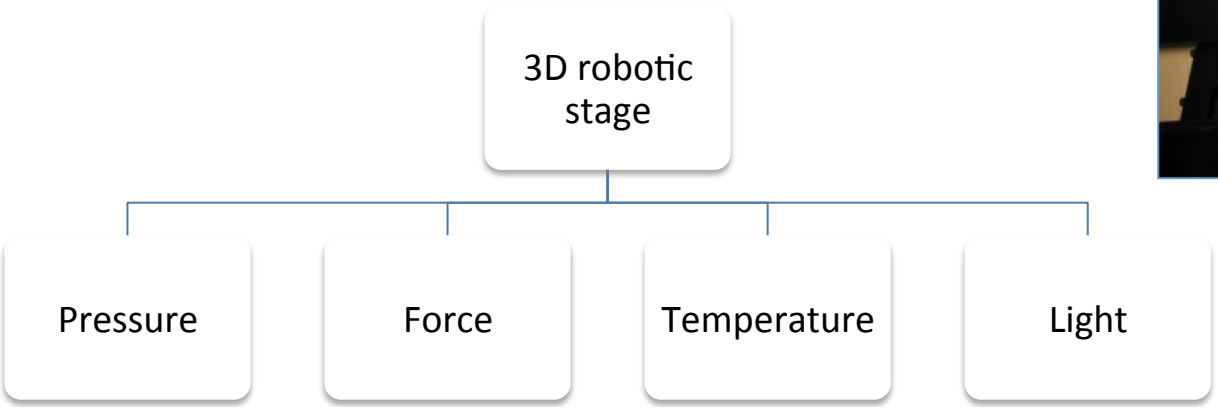
2-Dimensional		3-Dimensional	
	Lithography and Soft-Lithography		PAMsquare
	Soft-Molecular Imprinting		Open-Source FDM
	Electrospinning		Inkjet Printing

Combination of 2D and 3D Technologies

PAM²

- Modular CAD/CAM system
- A 3-axes robotic stages:
  - position ±50 mm;
  - velocity 0-15 mm/s;
  - resolution 1 µm;
  - different extrusion modules;
  - layer-by-layer processing.

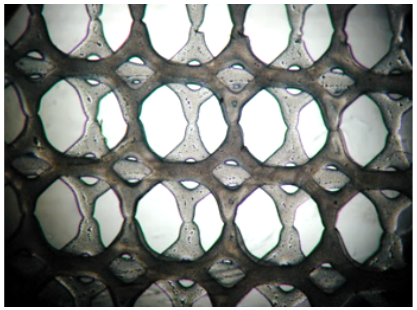
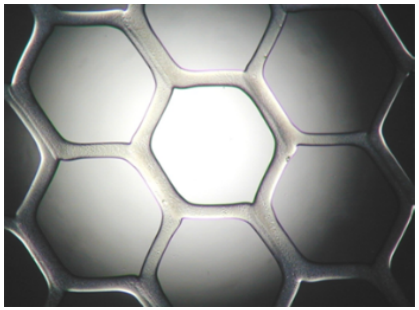
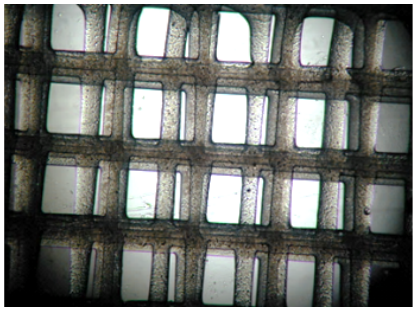




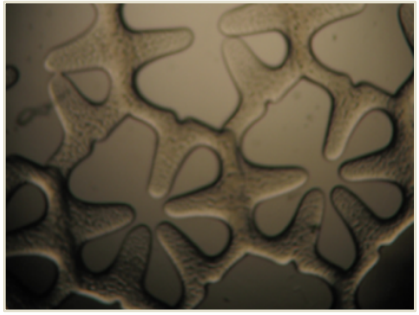
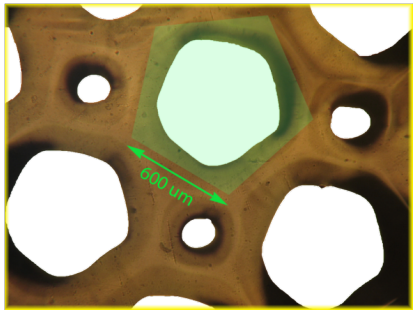
Tirella A, De Maria C, Criscenti G, Vozzi G, Ahluwalia A. The PAM² system: a multilevel approach for fabrication of complex three-dimensional microstructures. Rapid Prototyping J 2012;18(4):5-5

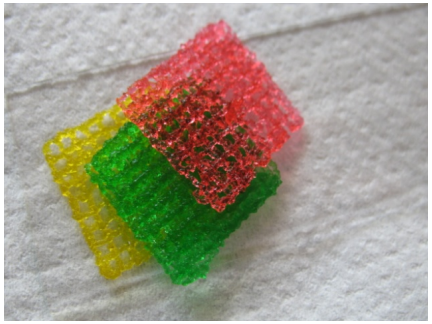
PAM²

Polyester structures

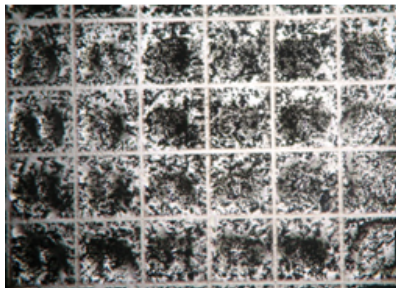
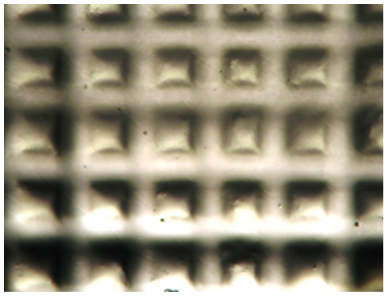




Natural polymer hydrogel structures

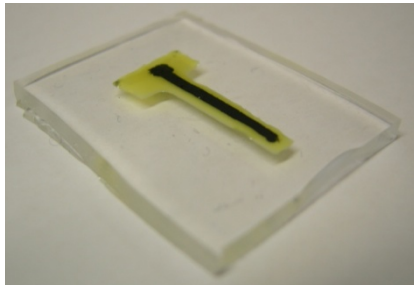





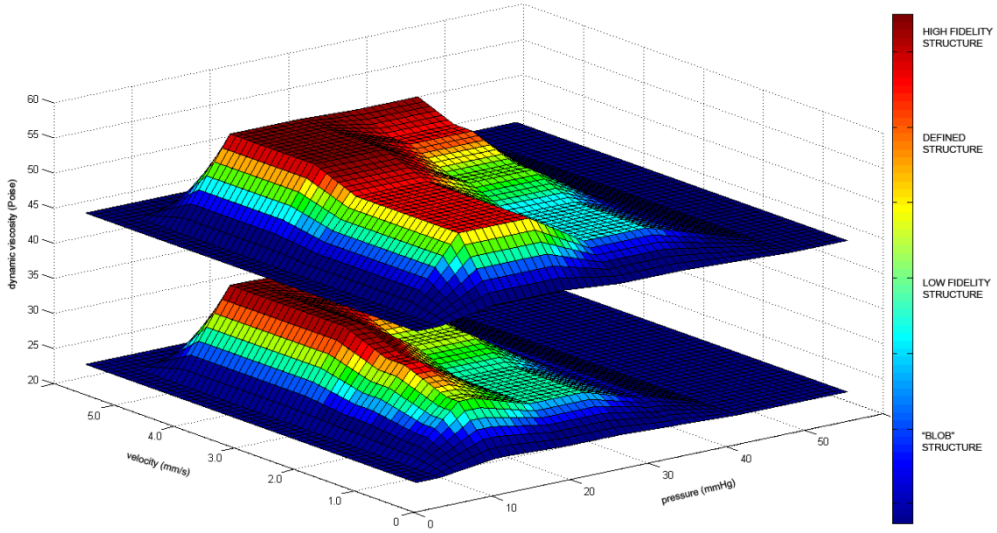
Laser ablation dry and wet structures

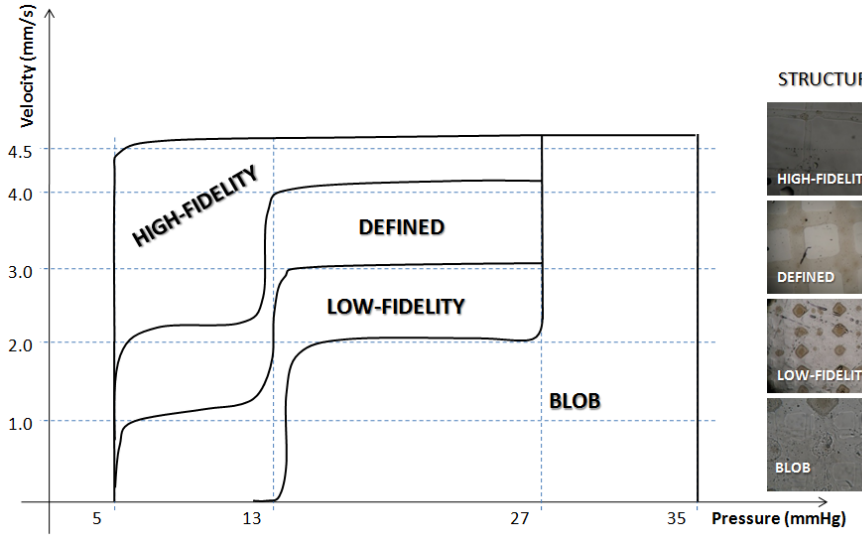



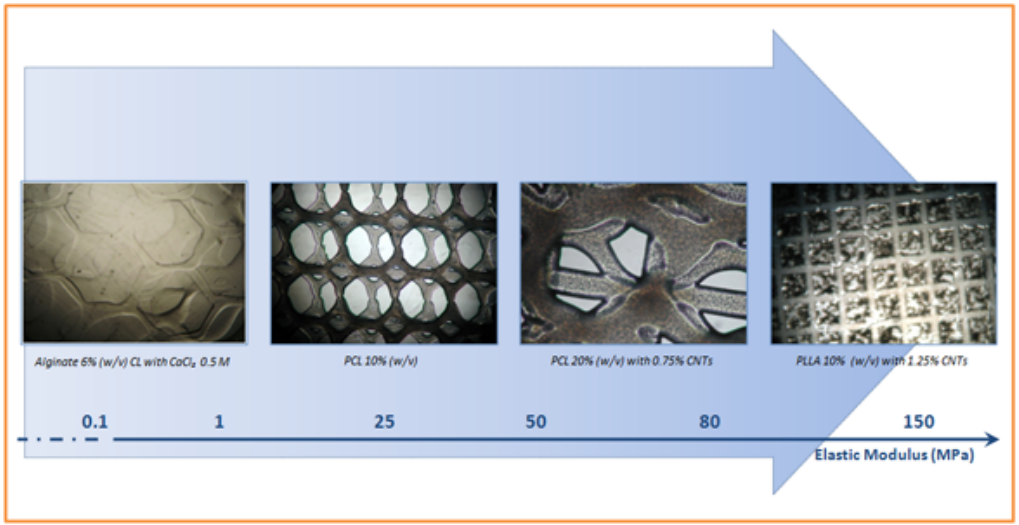
Polymeric actuators

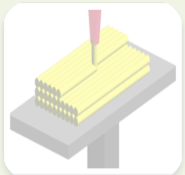
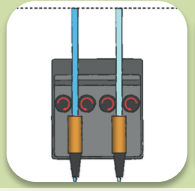
Multi-tuning Bioactive scaffold





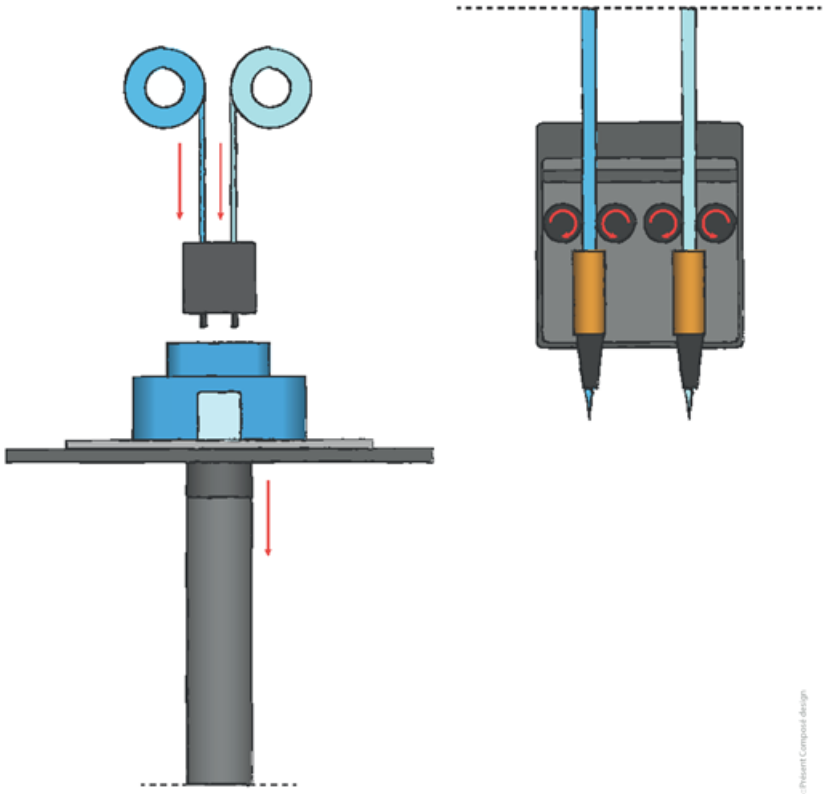


Open-Source FDM

2-Dimensional		3-Dimensional	
	Lithography e Soft-Lithography		PAMsquare
	Soft-Molecular Imprinting		Open-Source FDM
	Elettrospinning		Inkjet Printing

Combination of 2D and 3D Technologies

Fused Deposition Modeling



Polymeric structures for bacterial cell growth for cellulose production

IPL instituto politécnico de leiria

CHALMERS :: BBV

FABLAB PISA THE IDEAS FACTORY

Inket Printing

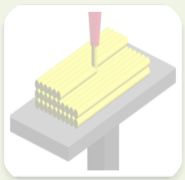
2-Dimensional

Lithography and Soft-Lithography

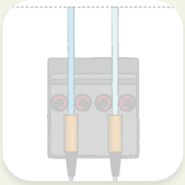
Soft-Molecular Imprinting

Electrospinning

3-Dimensional



PAMSquare

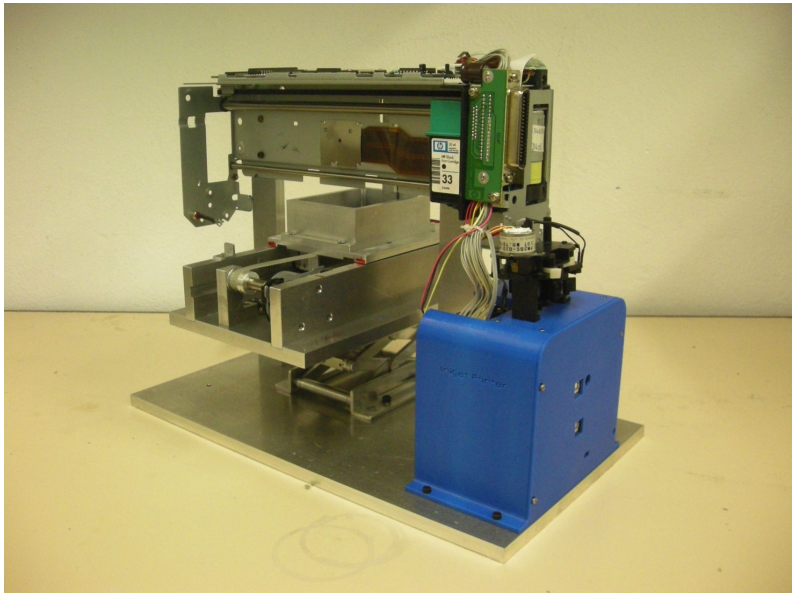


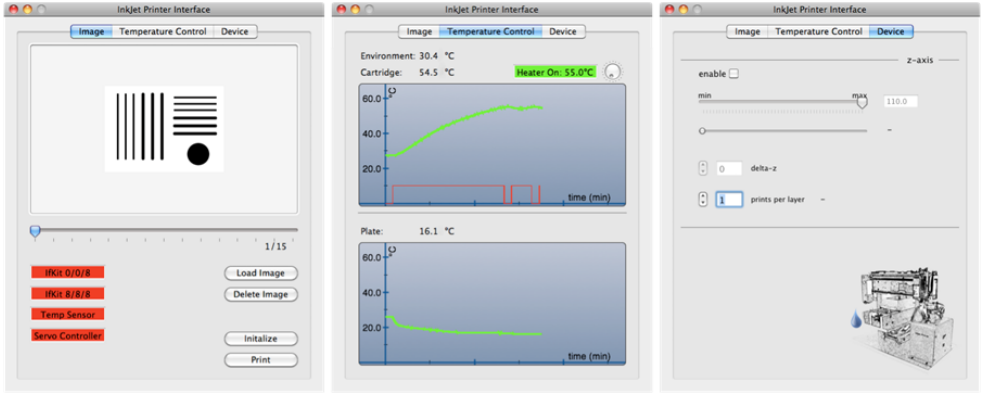
Open-Source FDM

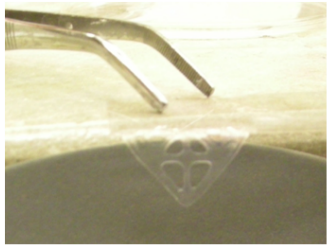
Inkjet Printing

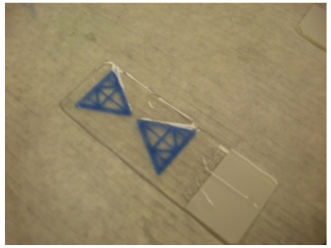
Combination of 2D and 3D Technologies

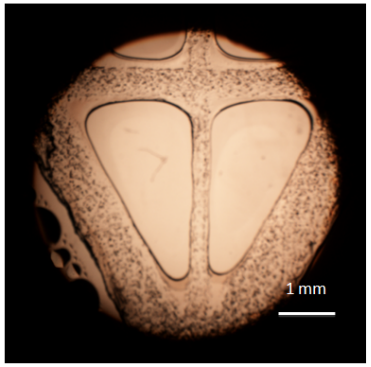
Penelope Ink-Jet printer



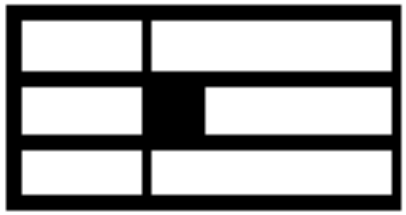








Printable Smart Scaffolds

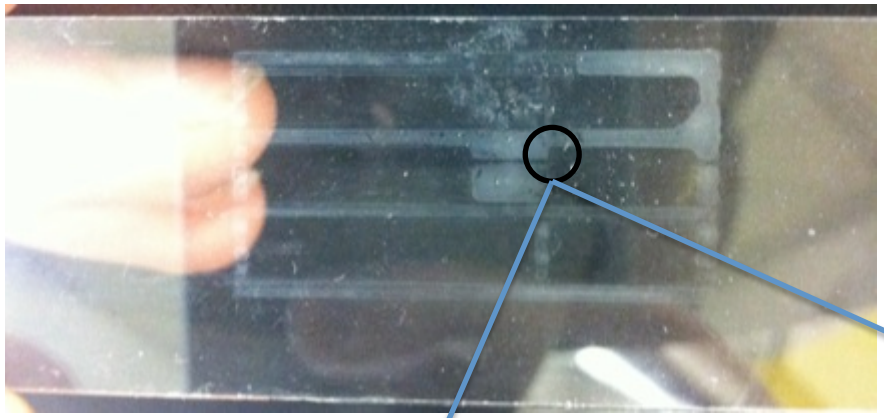


Structure not altered by 24 h at 60°C in water.

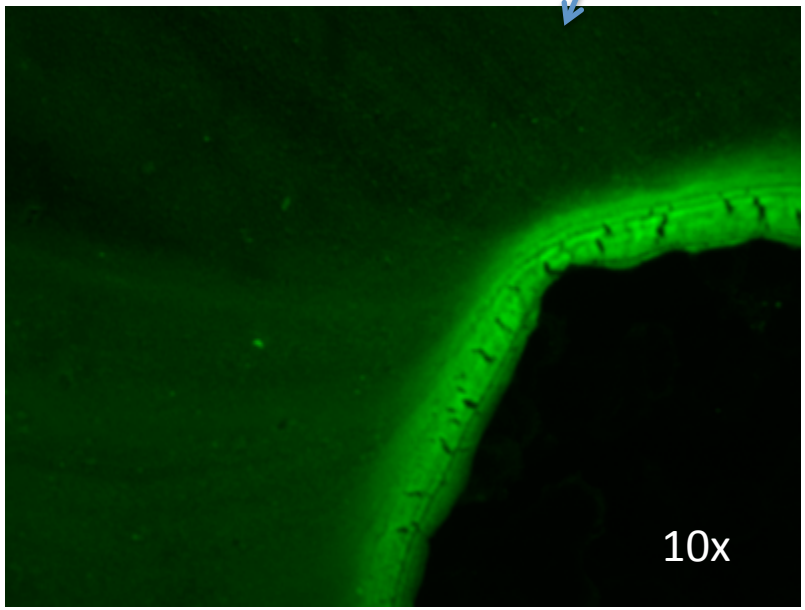
Also GPTMS silanol groups are able to bond to glass, so delamination is unlikely.

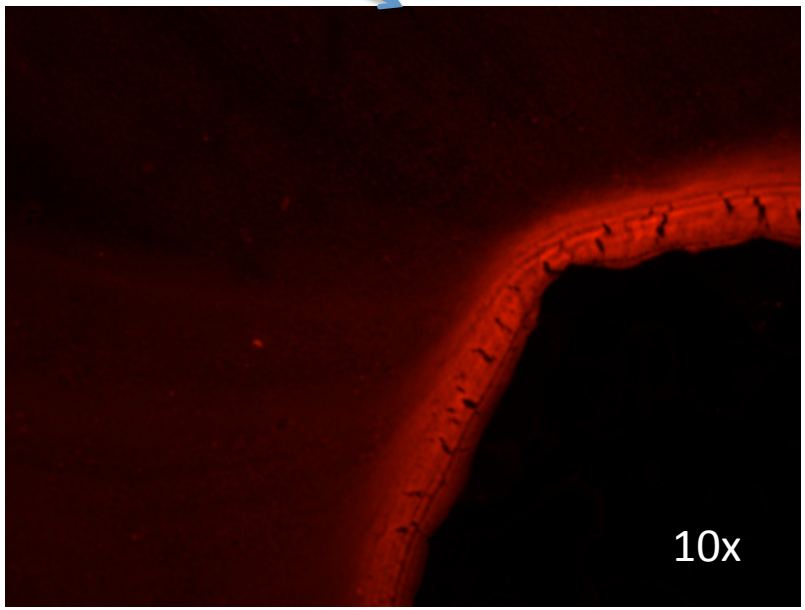
Swelling effects are minimal.

Printable Smart Scaffolds



Both Red and Green fluorescence detected in the structure

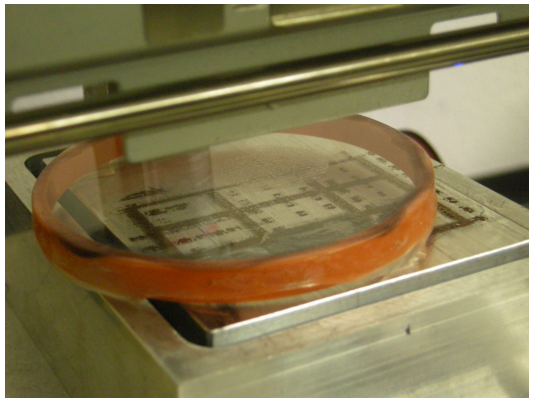


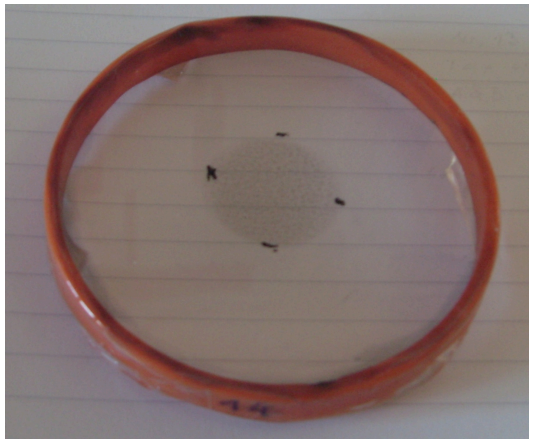


Nanoparticles are within the gel, even after 24 h at 60 degrees.

Inkjet printer - application

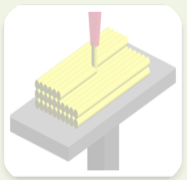
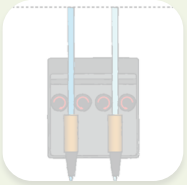
- CNTs for compliant and transparent electrodes for polymeric actuators
  - 0.01 SWNTs in 1% SDS in water
  - Problems with surfactants





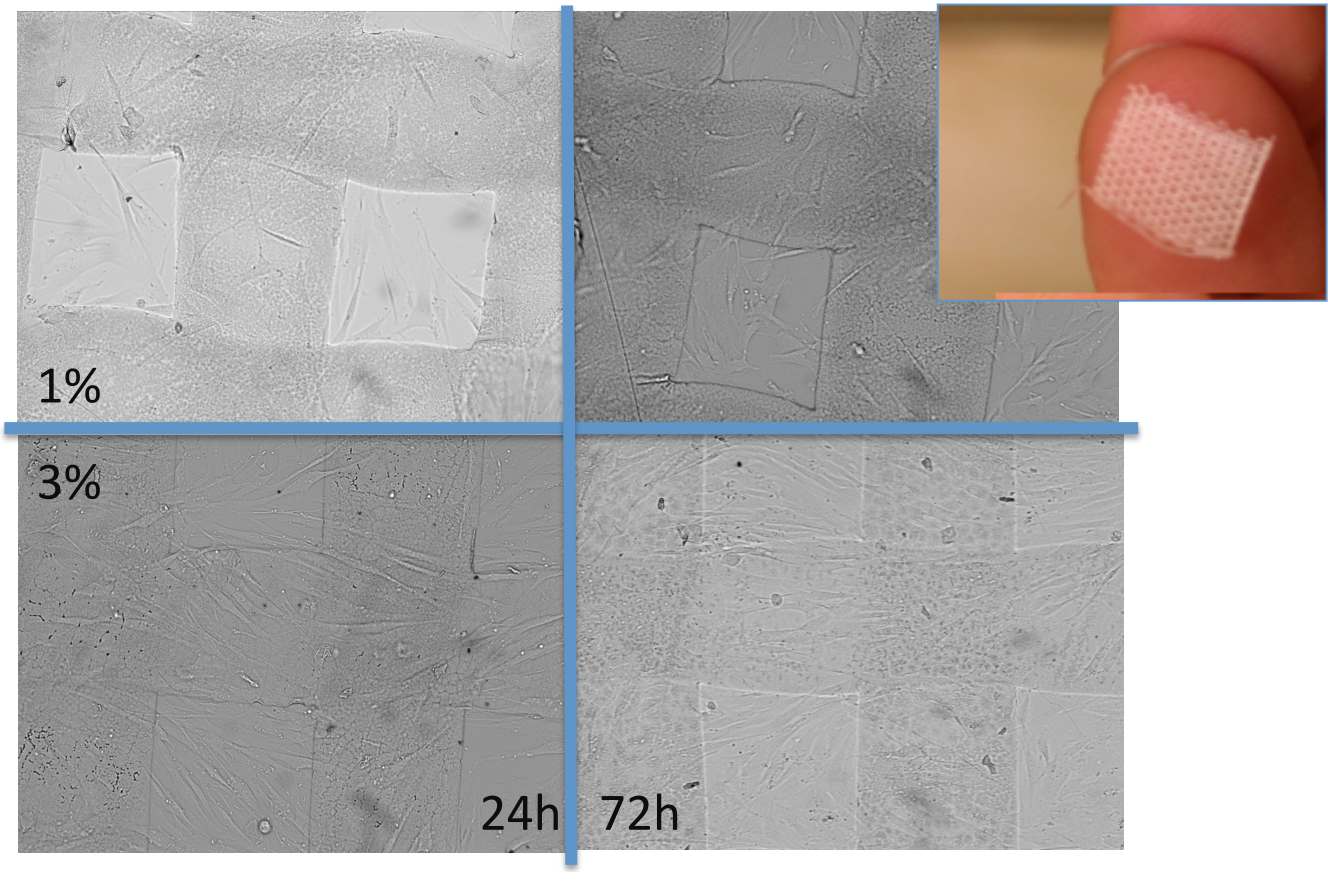
In collaboration with Eng. Carpi's group

Combination of 2D and 3D Technologies

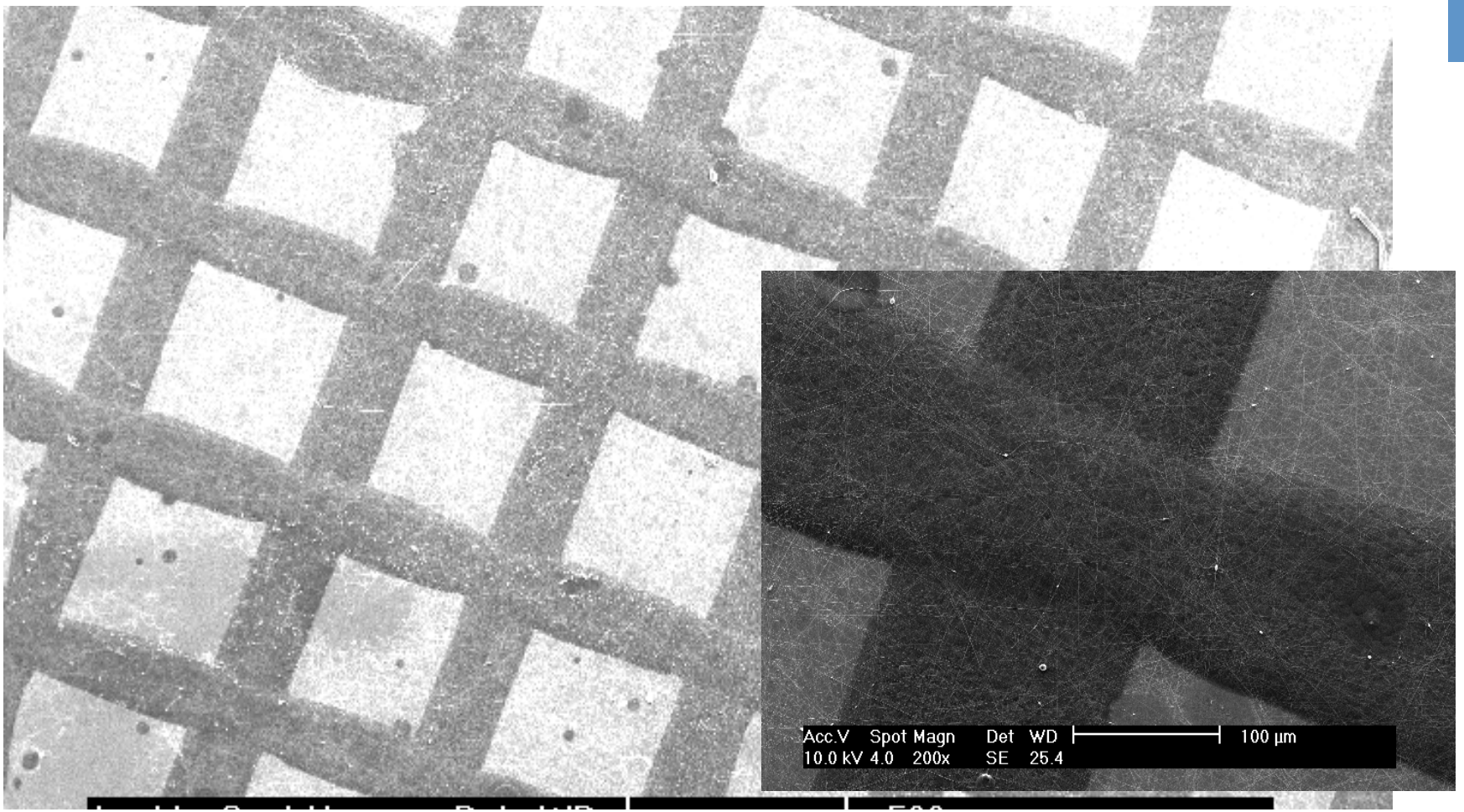
2-Dimensional		3-Dimensional	
	Lithography e Soft-Lithography		PAMsquare
	Soft-Molecular Imprinting		Open-Source FDM
	Electrospinning		Inkjet Printing

Combination of 2D and 3D Technologies

PAM & Inkjet

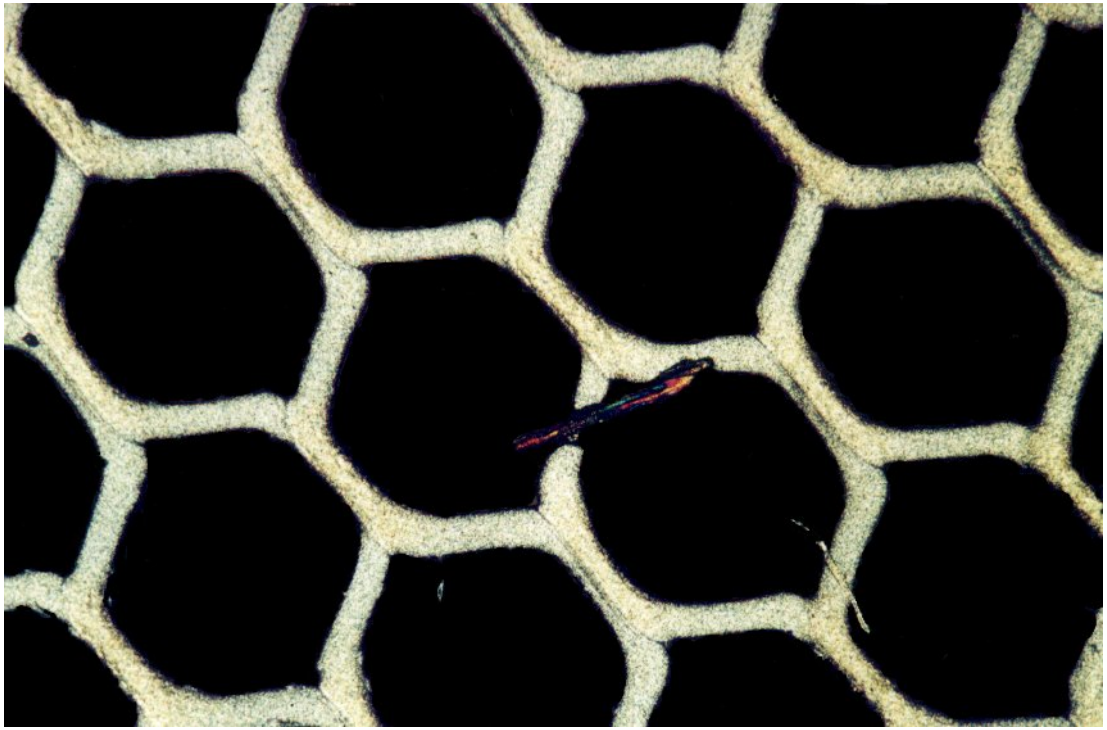


PAM^2 & Electrospinning



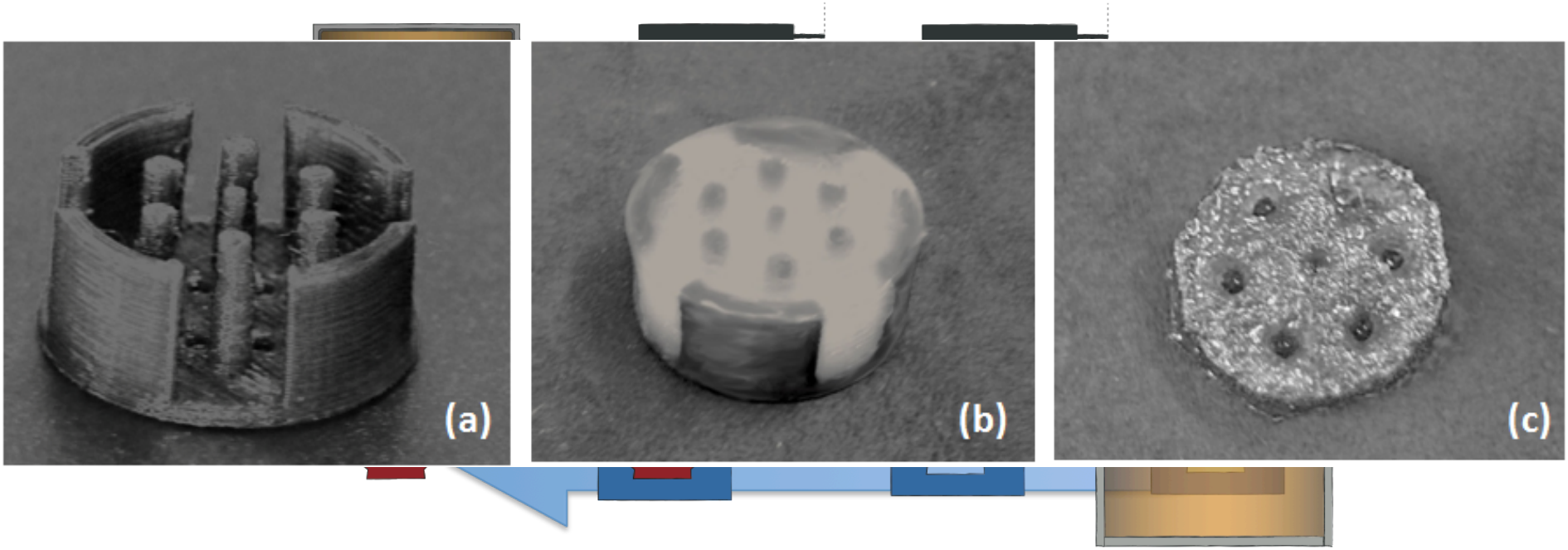
In combination with inkjet printing

SOFT MI & PAM



Indirect Rapid Prototyping (iRP)

- Molds realised with RP devices (CAD/CAM)
- Casting of the desired (bio-)material
- Extraction of the final object



SCAFFOLD CHARACTERISATION

Scaffold Characterisation

- Mechanical Characterization
  - Zwick Roell Uniaxial Testing Machine
  - Trasduttori isometrico e isotonico Ugo Basile
- Surface Characterization
  - Kelvin Probe
  - Contact Angle
- Rheological Characterization
  - Rheometer Rheostress
- Optical Microscopy
- Finite Element Modelling


KEEP
CALM
AND USE
THE
FORCE