Principi Bioingegneristici per lo Sviluppo di Modelli 3d in Vitro in Condizioni Fisiologiche e/o Patologiche

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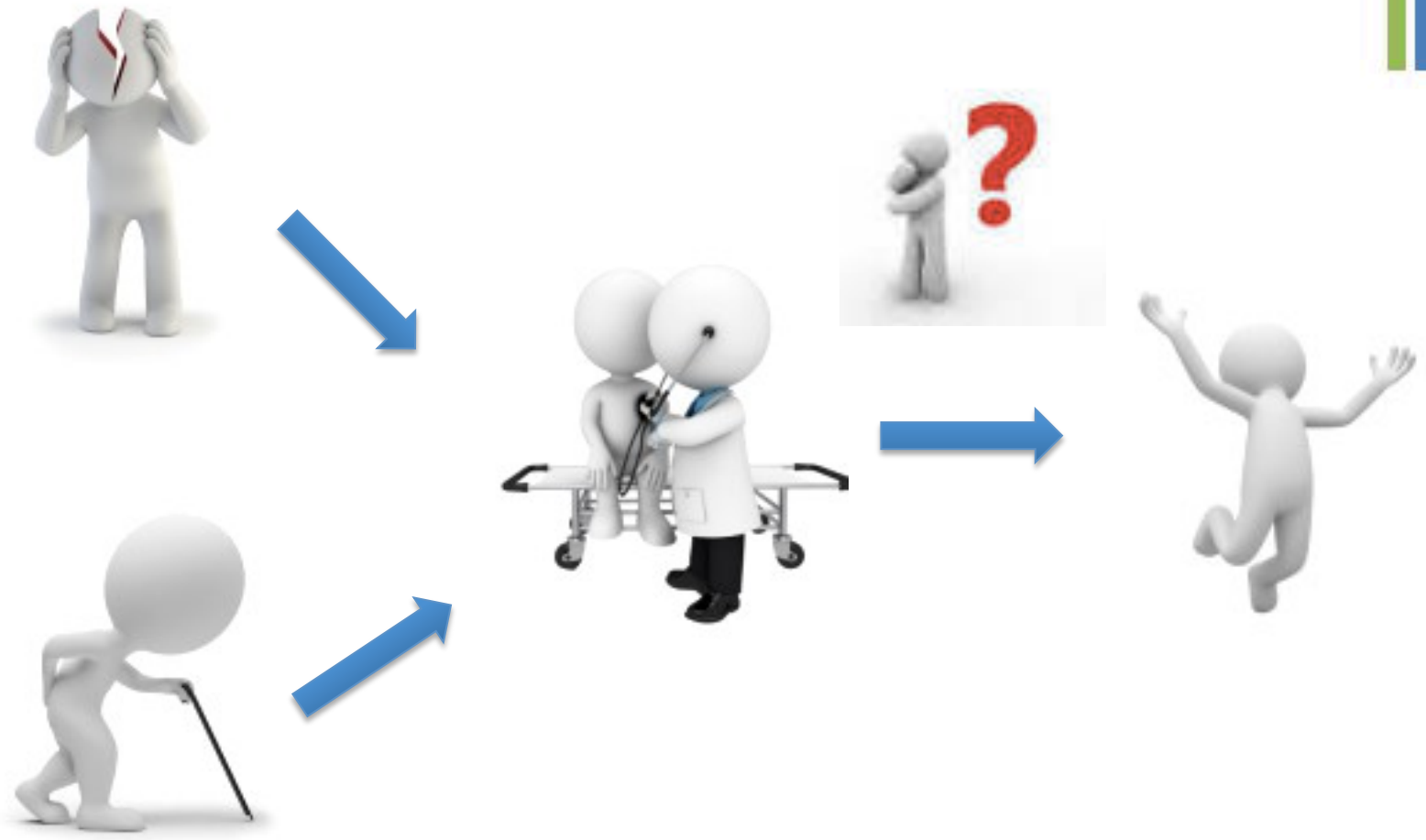
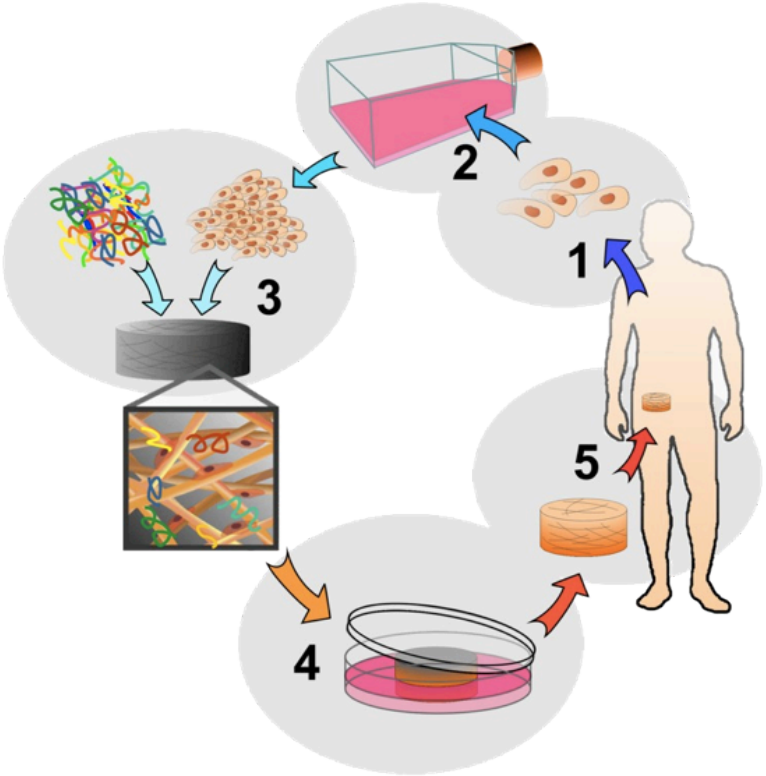


Tissue engineering

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

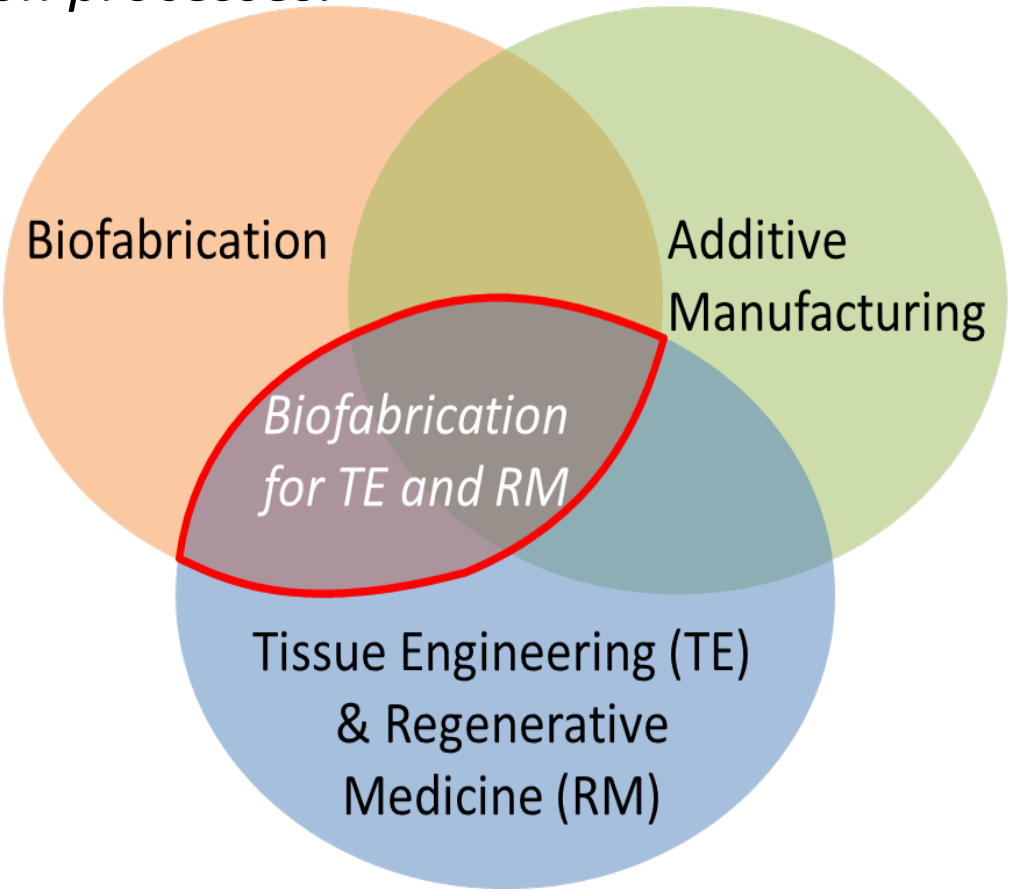
Regenerative medicine

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,

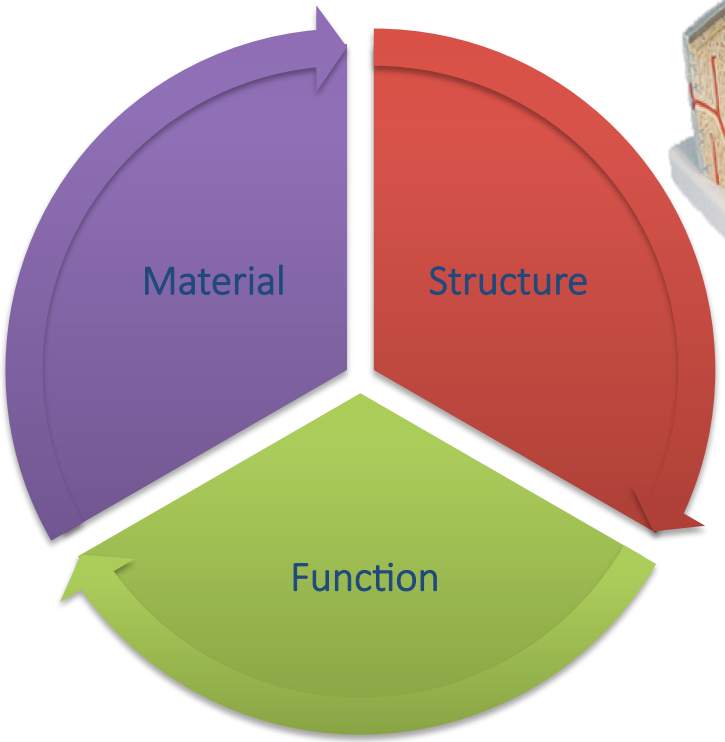
Biofabrication

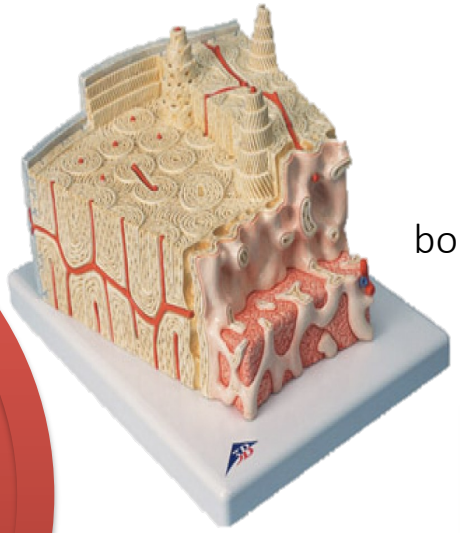
the generation of biologically functional products with structural organization from living cells, micro-tissues or hybrid tissue constructs, bioactive molecules or biomaterials either through top-down (Bioprinting) or bottom-up (Bioassembly) strategies and subsequent tissue maturation processes.



Living tissues

- Multiscale and multimaterial structure



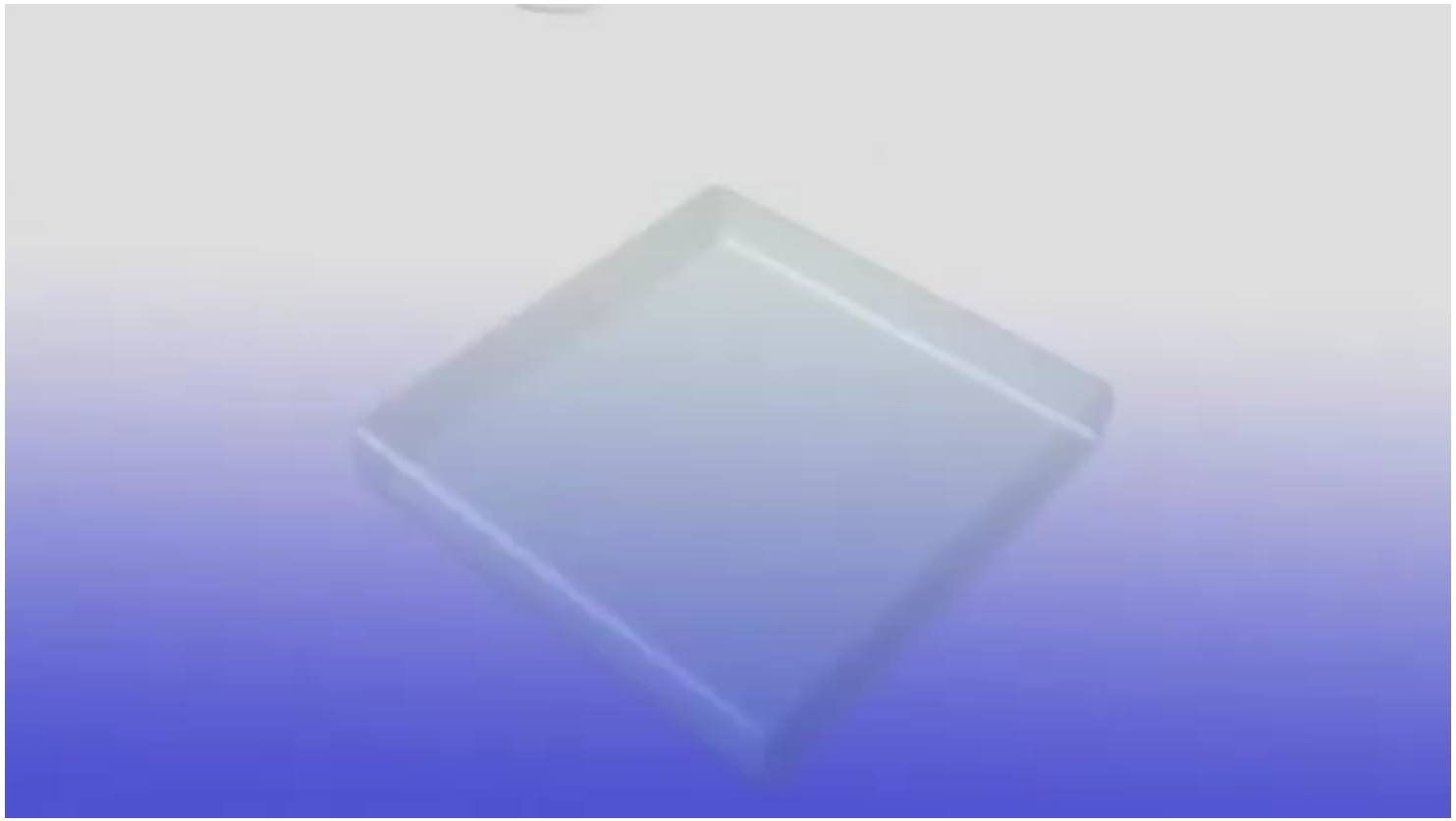


bone

retina

blood vesses

Vozzi G and Ahluwalia A. *Microfabrication for tissue engineering: rethinking the cells-on-a scaffold approach*, J Mat Chem 17 (13), 1248-1254




EPSON

In vitro model

- Requirements
  - Availability (storage)
  - easiness of use
  - cost

- Norms
  - "Three Rs": Replacement, Reduction and Refinement
  - Directive 2010/63/EU

- Opportunities given by biofabrication
  - high customization (printing patient's cells)
  - increase complexity
  - increase reproducibility

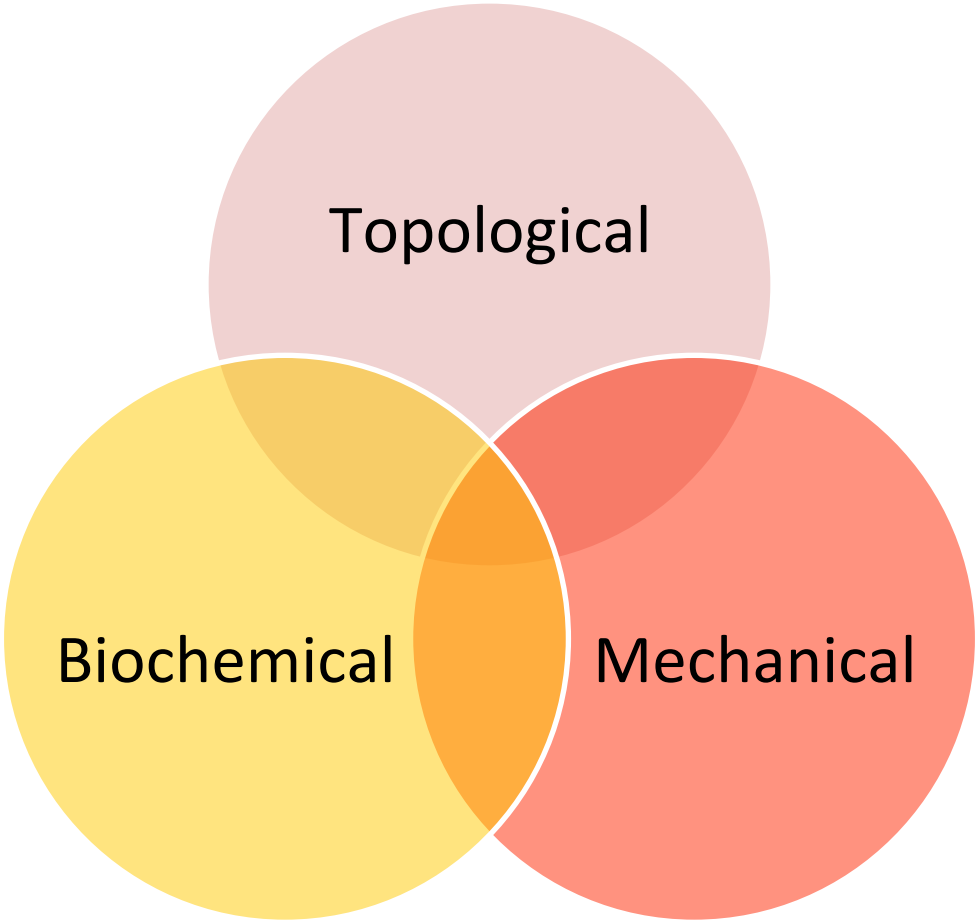
- Weakness
  - limited functions
  - not a single model but a family of models

Abd E. et al. *Skin models for the testing of transdermal drugs* Clin Pharmacol. 2016 Oct 19;8:163-176.

Flaten GE et al., *In vitro skin models as a tool in optimization of drug formulation*. Eur J Pharm Sci. 2015 Jul 30;75:10-24.

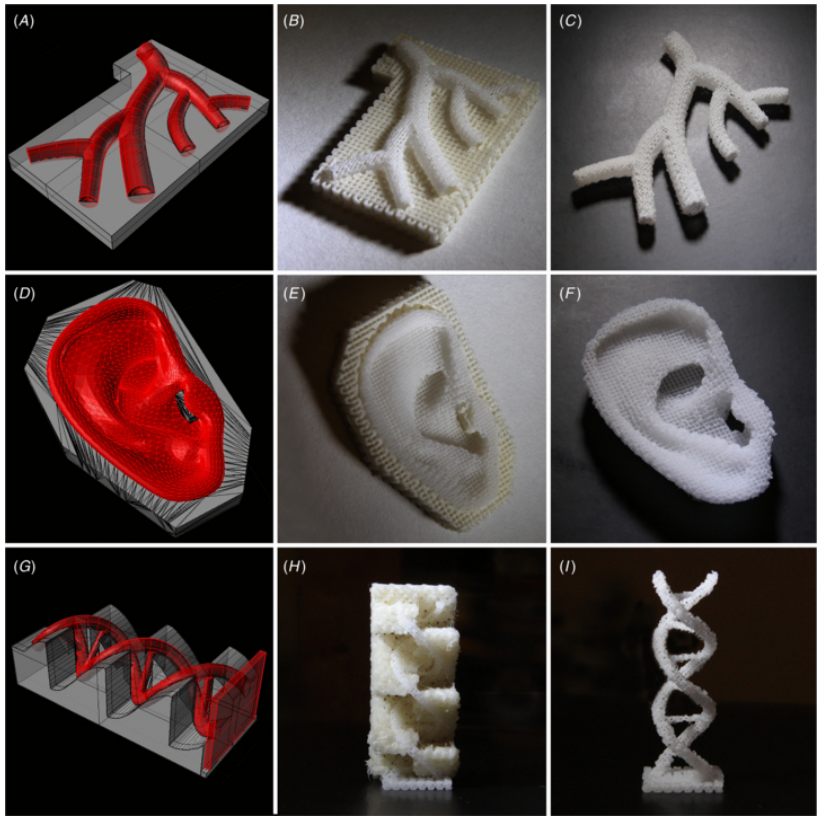
How we may mimic natural tissue?

Three main simuli



What is a scaffold?

Polymeric structure topogically well-defined and modulating biochemical and mechanical signals typical of natural tissue, i.e. ***a 3D structure which supports 3D tissue growth***



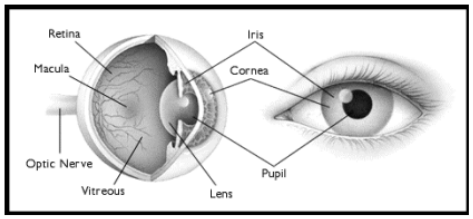
What are the features of an ideal scaffold?

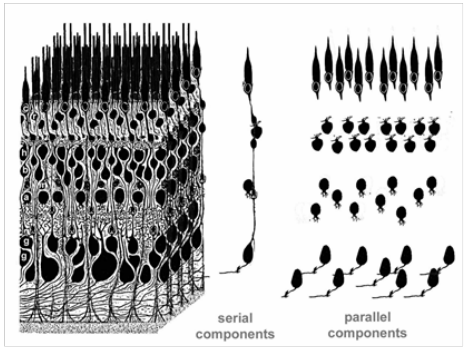
- Biocompatible, cell adhesive, bioerodable and *bioactive*
- Mechanical properties *similar* to those of natural tissue
- Optimal meso, micro and nano pores
- Well-defined, or *quantifiable* topology at meso- micro- and nanoscales

Designer or Random?

Structure ⇄ **Function**

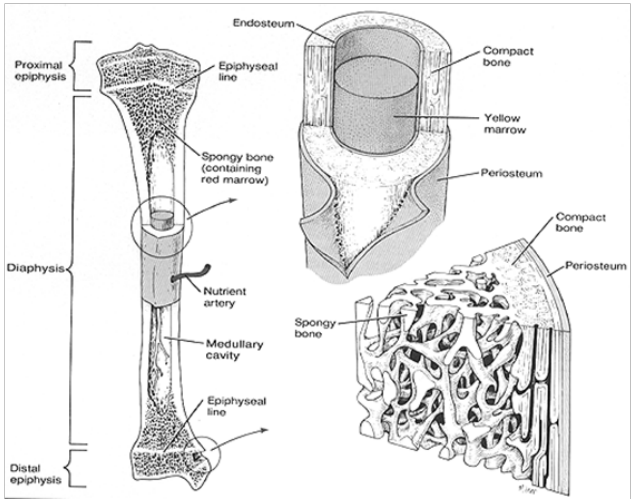
Retina





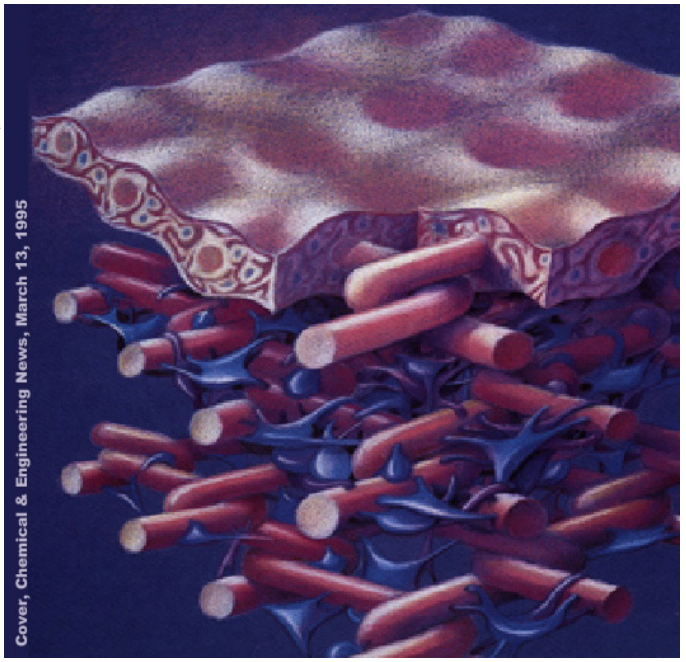
Liver

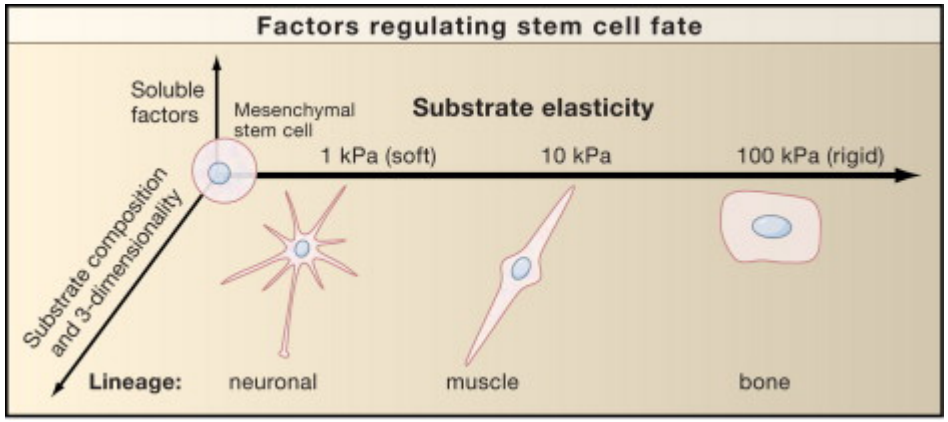
Bone



Biochemical stimuli in scaffolds

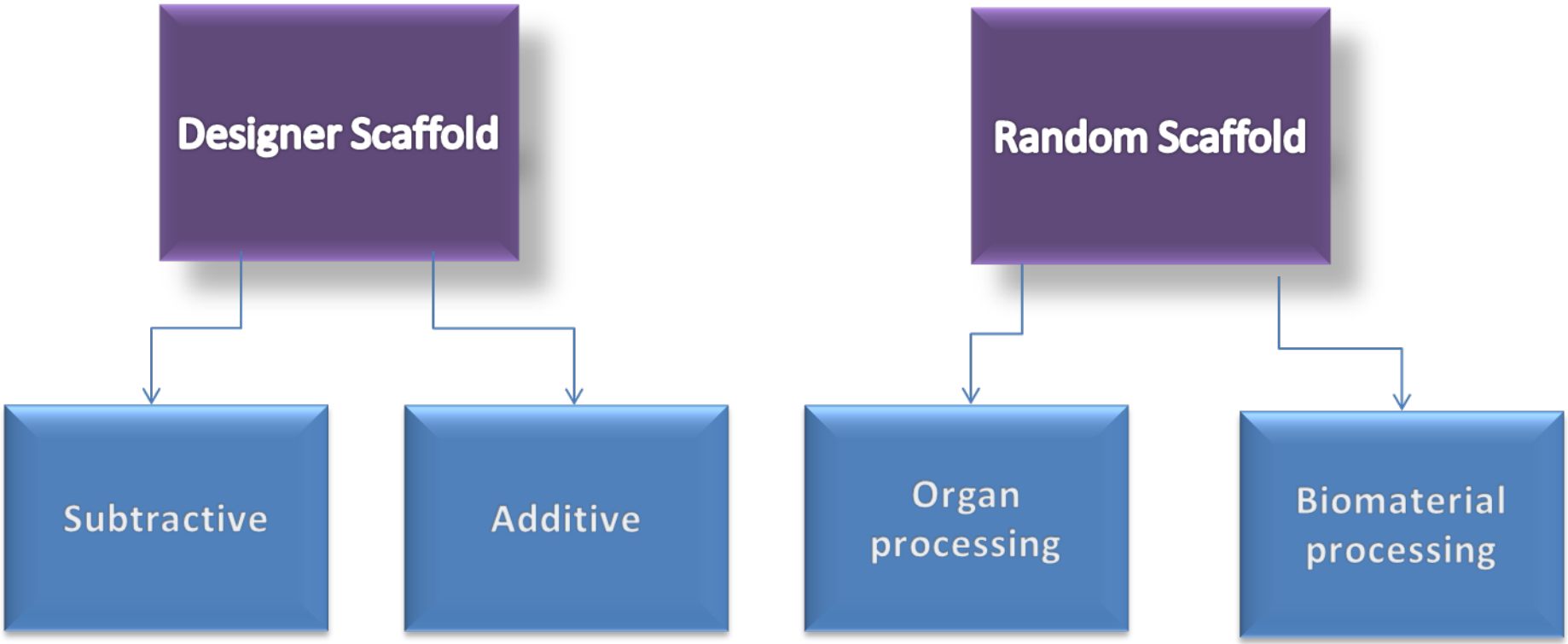
- Synthetic biomaterials with ligands
- Natural biomaterials
- Decellularized Tissue



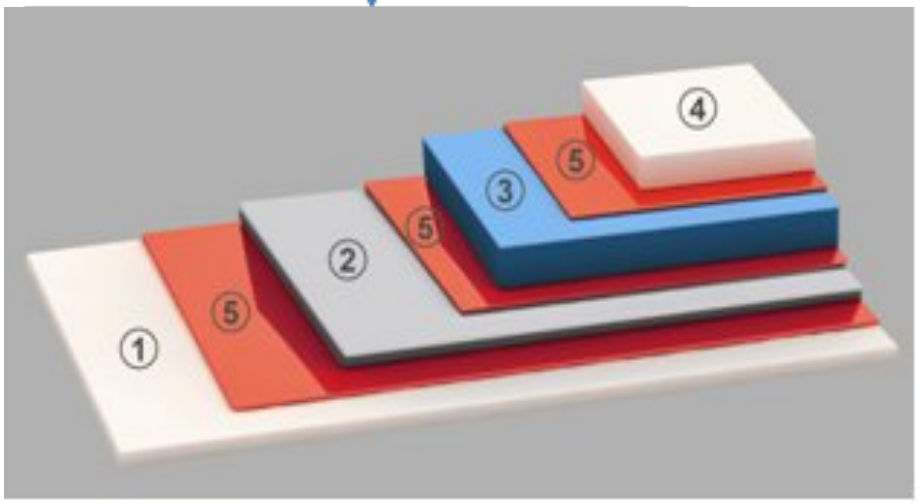


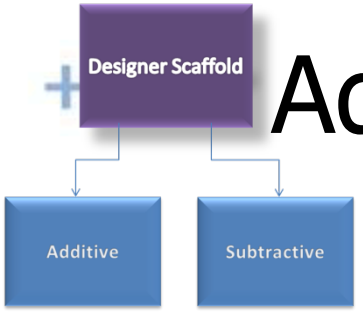
Even-Ram s et al, Matrix Control of Stem Cell Fate, Cell. Volume 126, Issue 4, 25 August 2006, Pages 645–647

Methods for generating MS stimuli in scaffolds

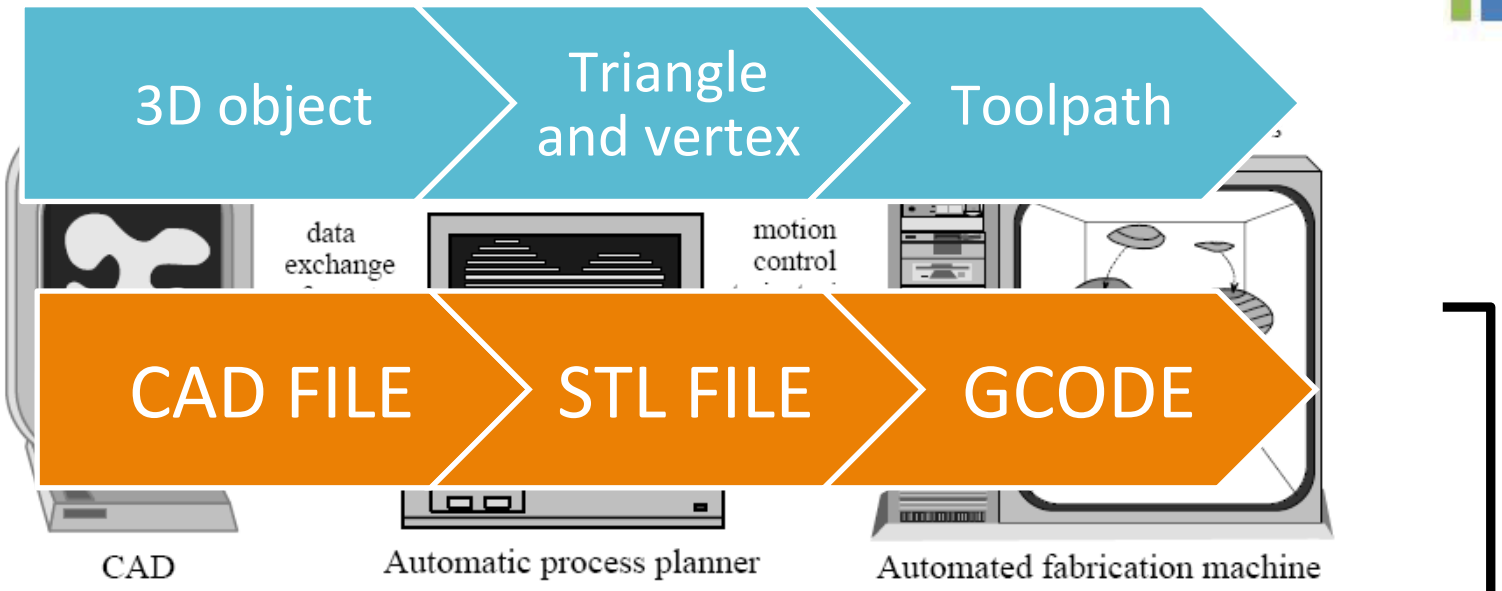


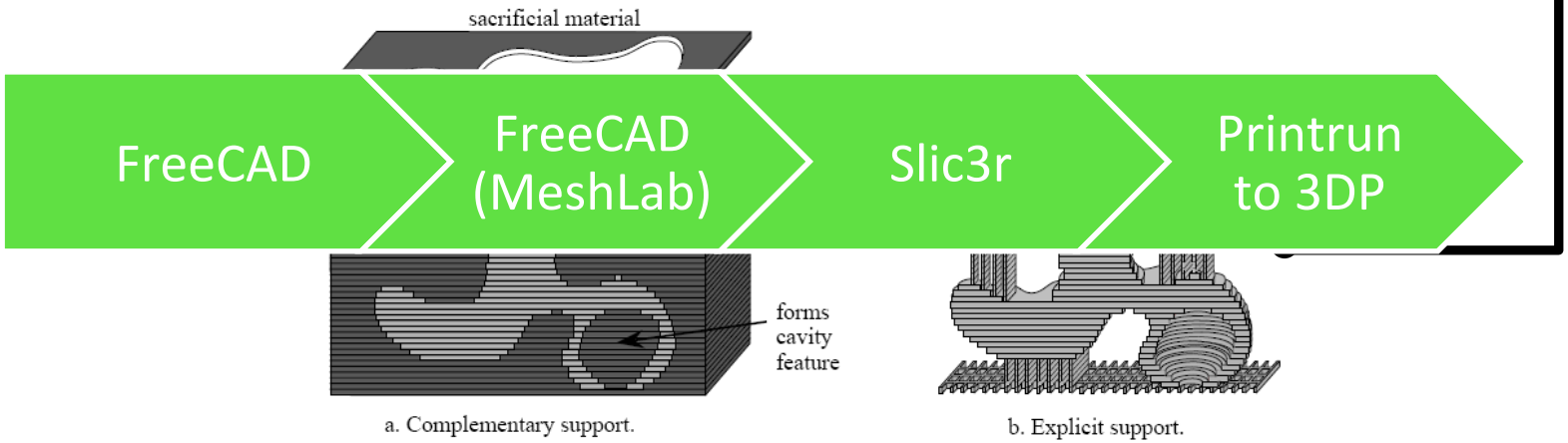
Designer Scaffold

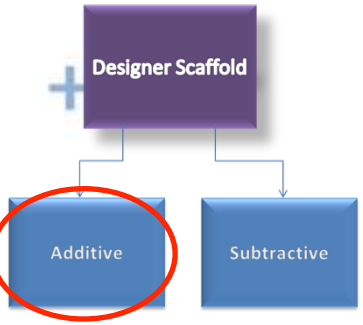




Additive = rapid prototyping



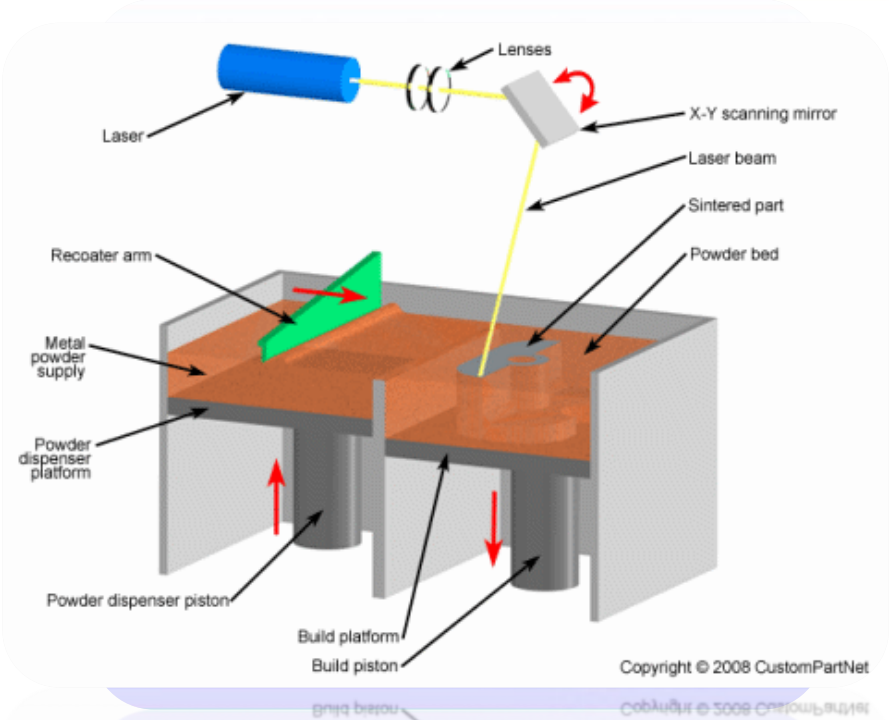




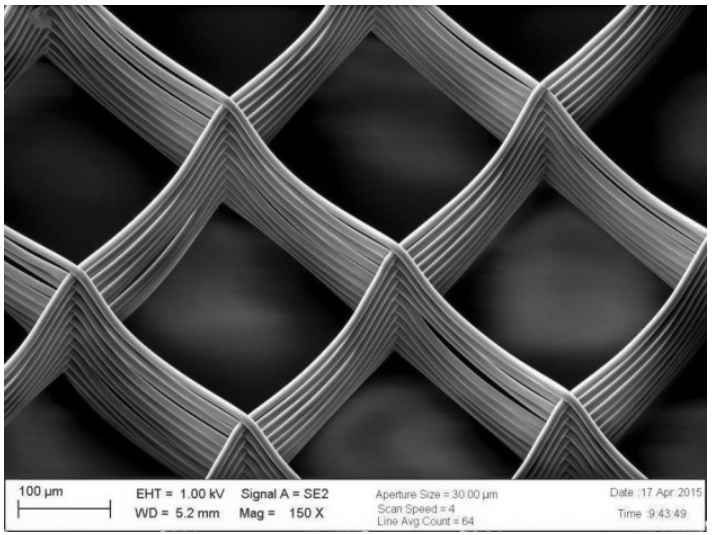
Designer Scaffold

Three main groups:

- laser systems
- nozzle based systems
- direct writing systems



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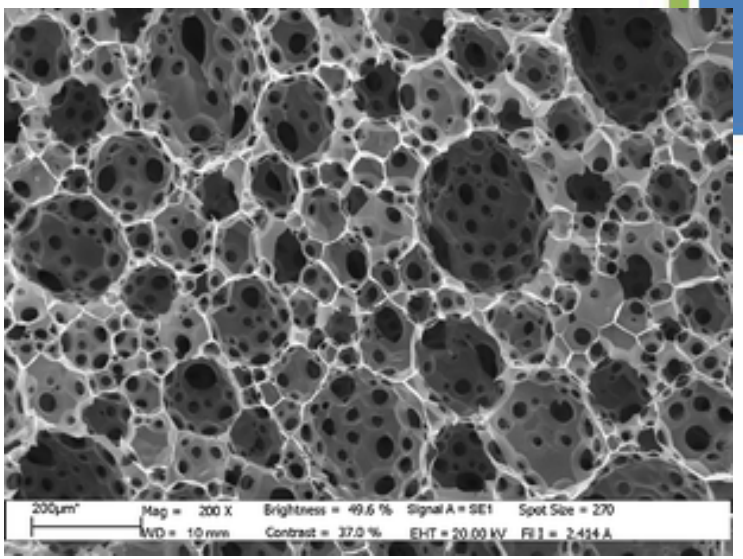
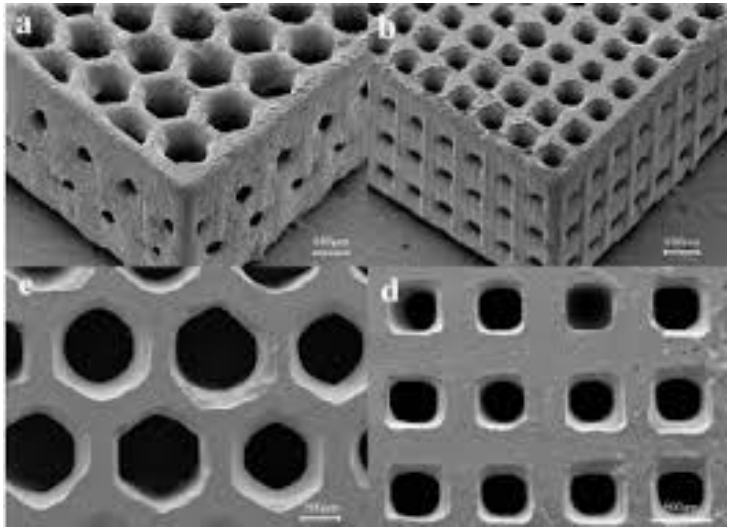
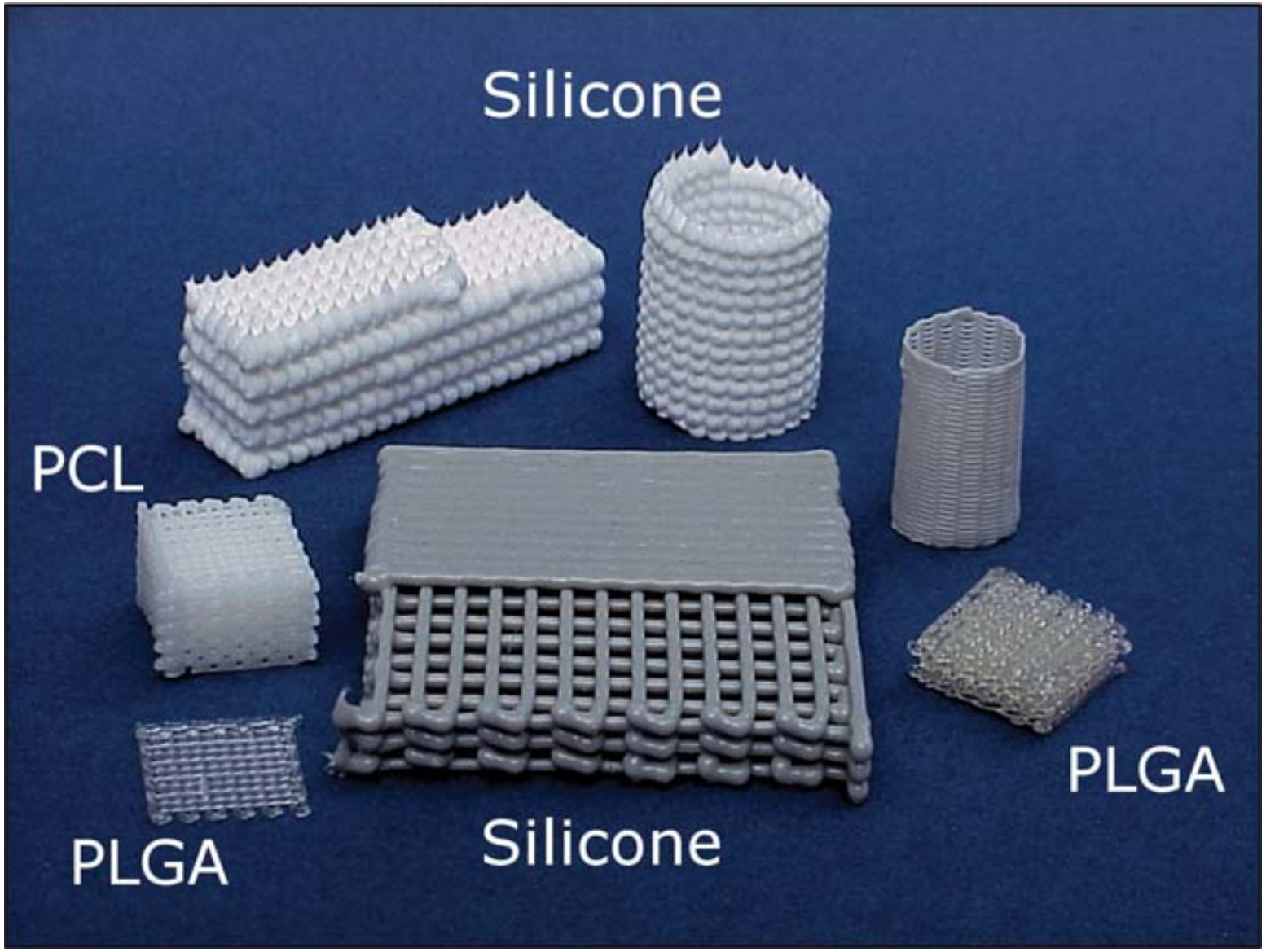
Mag = 150 X
Aperture Size = 30.00 µm
Scan Speed = 4
Line Avg Count = 64
Date :17 Apr 2015
Time :9:43:49

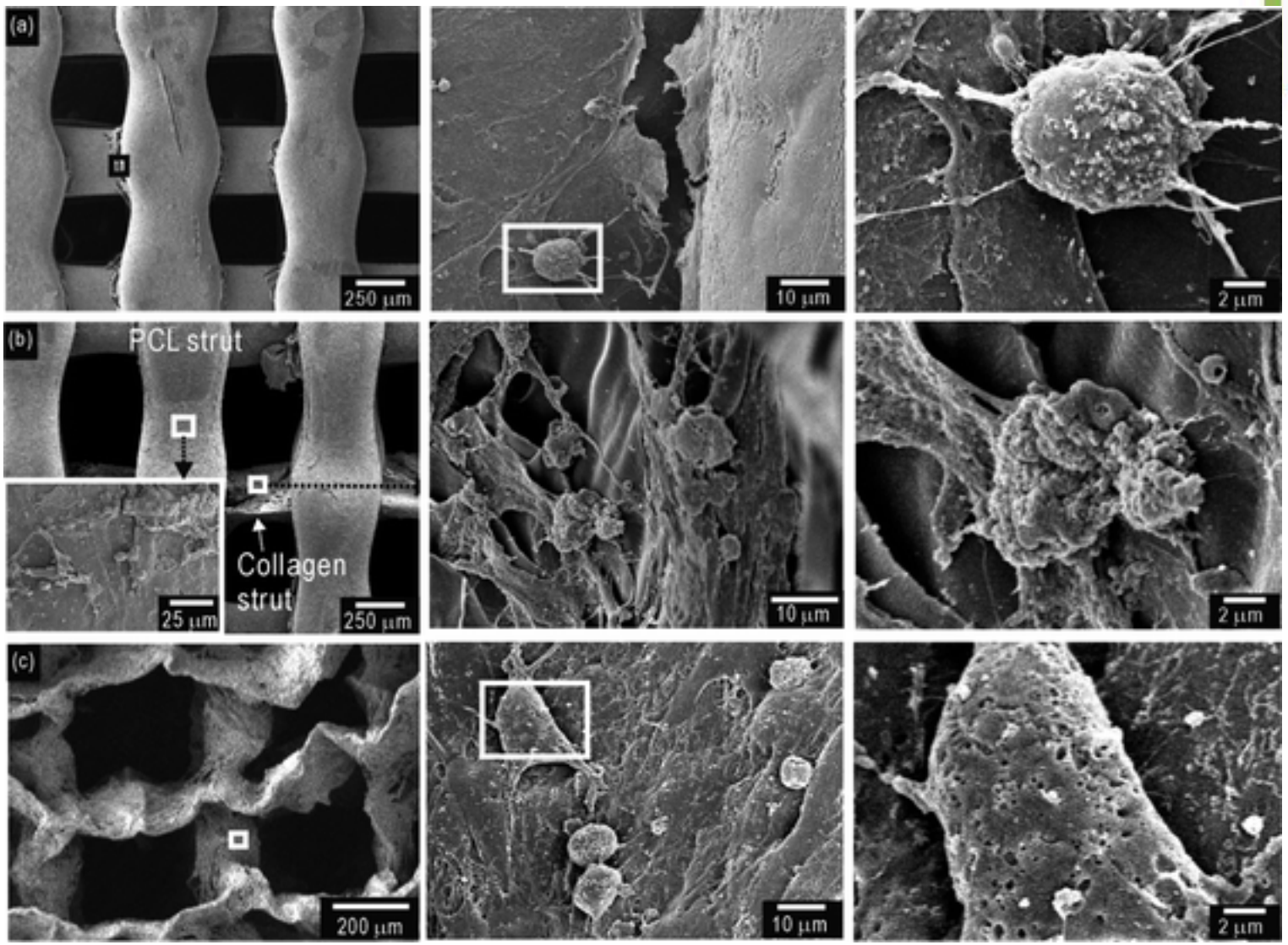

200µm
Mag = 200 X
WD = 10 mm
Brightness = 49.6 %
Contrast = 37.0 %
Signal A = SE1
EHT = 20.00 kV
Spot Size = 270
FI I = 2.414 A

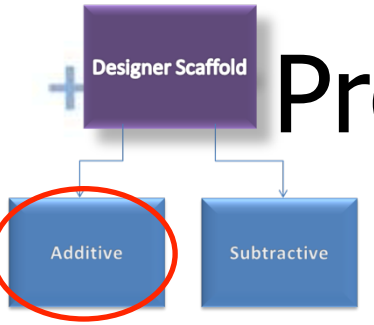

a
b
c
d

Scaffolds



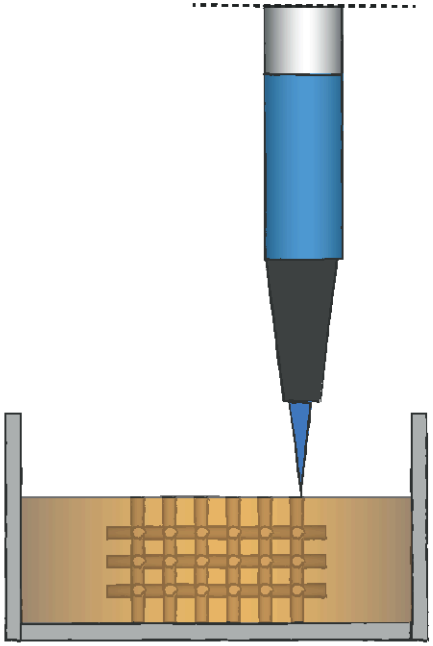
Scaffold


(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

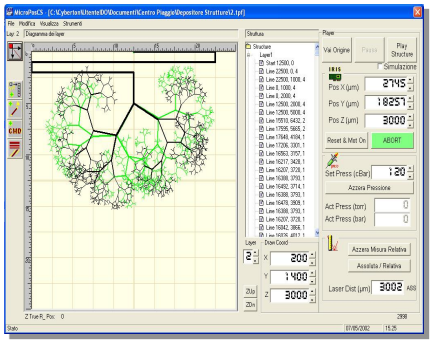


Pressure Assisted Microsyringe (PAM)

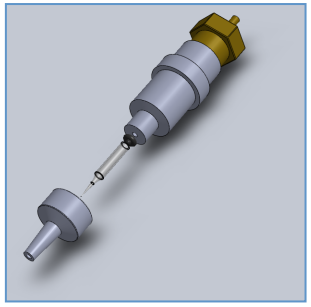
Regulated air flow



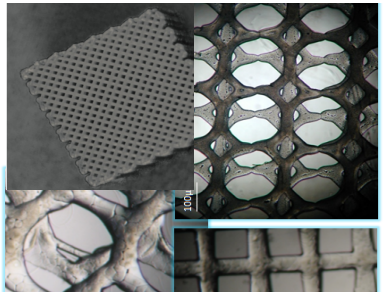
PAM system



Software

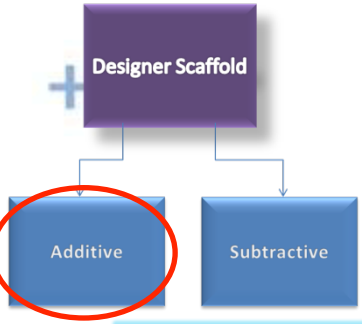


Syringe design

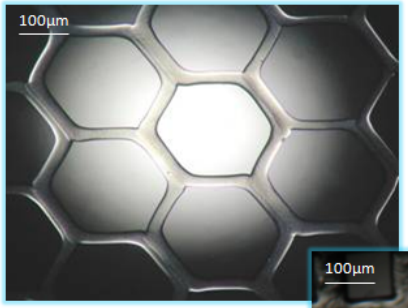


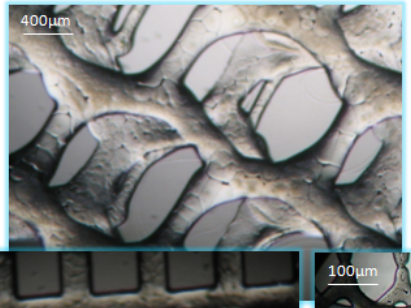
Software

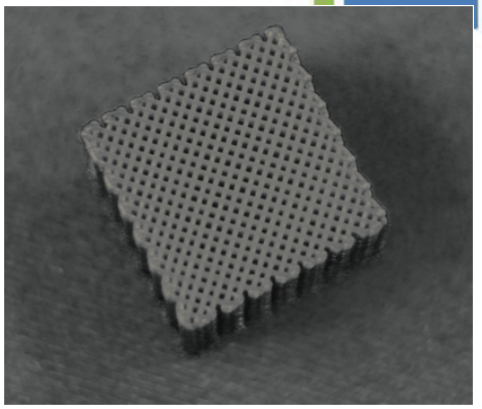
Vozzi, Previti, De Rossi,. Tissue Engineering, 8, 34, 2002. Vozzi , Flaim, Ahluwalia, Bhatia , Biomaterials, 24, 2533, 2003

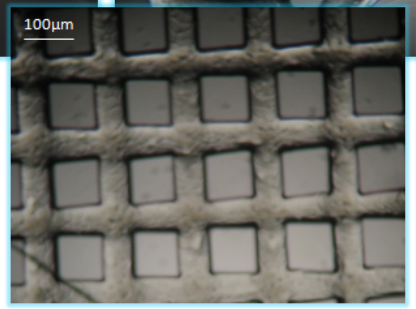


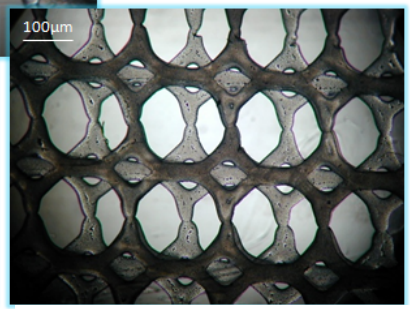
Scaffolds with PAM

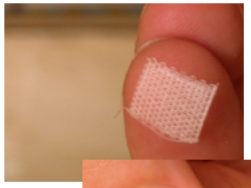


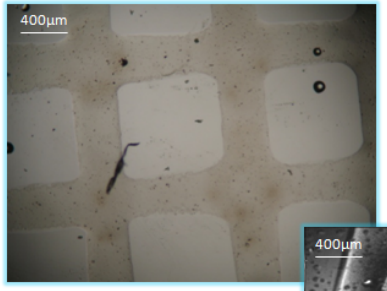


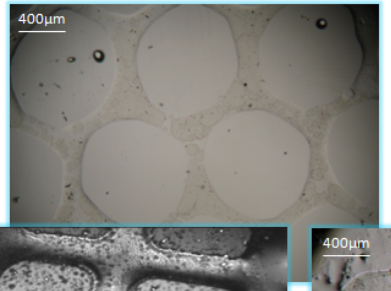


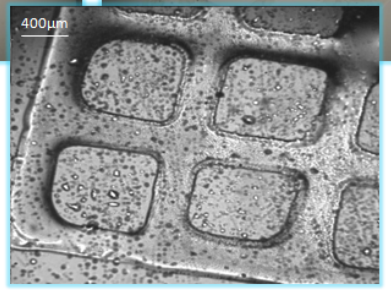


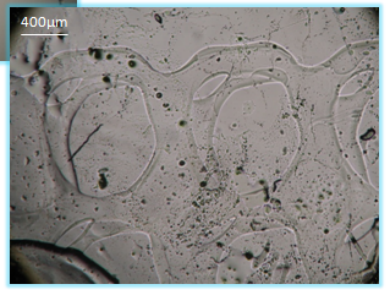












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Mariani et al., Tissue Eng. 12, 547, 2006.
Bianchi et. Al. JBMR 81, 462, 2007.