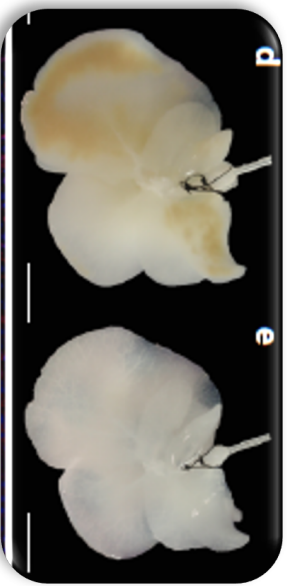


Random Scaffold

Organ processing



Uygun et al, Nature Med, 2010.

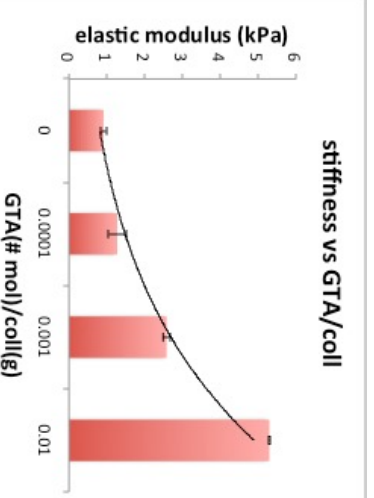
Biomaterial processing



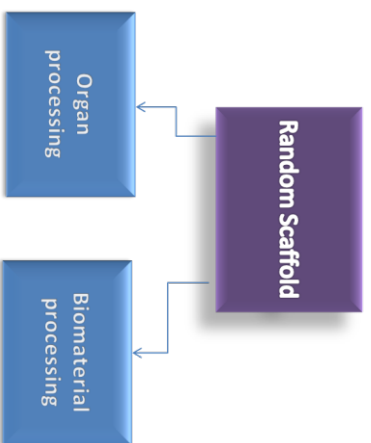
Tirella, Liberto, Ahluwalia, Materials Letters, 74, 58, 2012



Mattei. et al, Biomat. Acta, in press

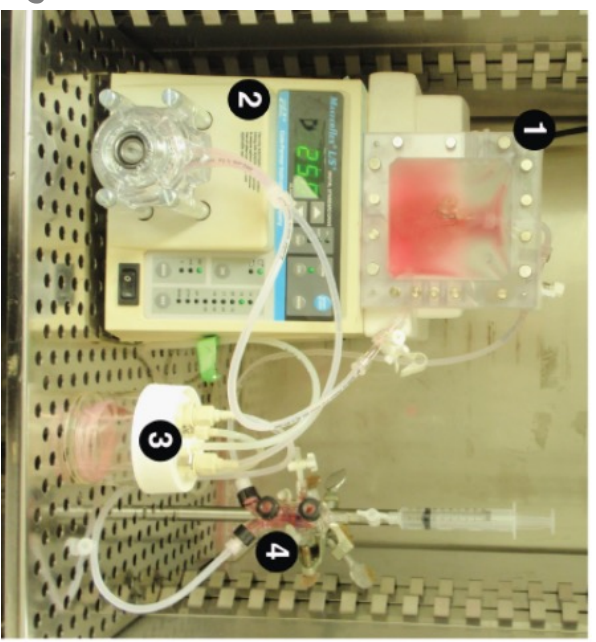


Organ Processing



Whole Organ Perfusion

- Detergents
- Intact microvasculature
- Slow and costly

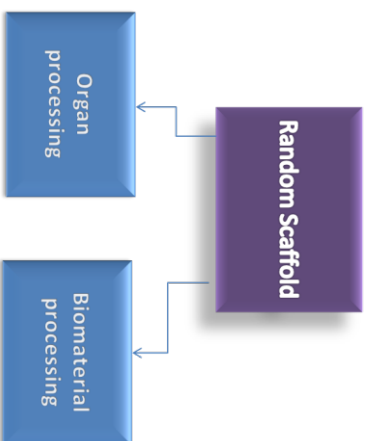


Tissue Decellularization

- Detergents
- Rapid, less wasteful



- Price?*
- Materials?*
- Speed?*
- Repeatability ?*



Biomaterial Processing

- Freeze drying
- Phase separation
- Gas foaming
- Salt leaching

Price?

Materials?

Speed?

Repeatability ?

Random Scaffold

Organ processing

Biomaterial processing

Biomaterial Processing

Freeze drying



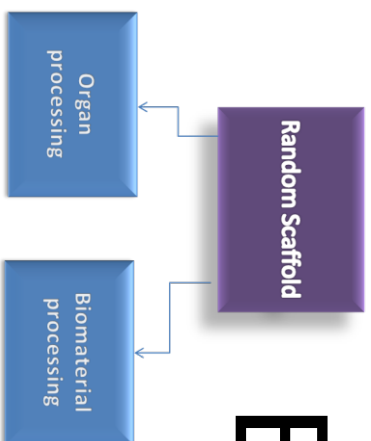
Price?

Materials?

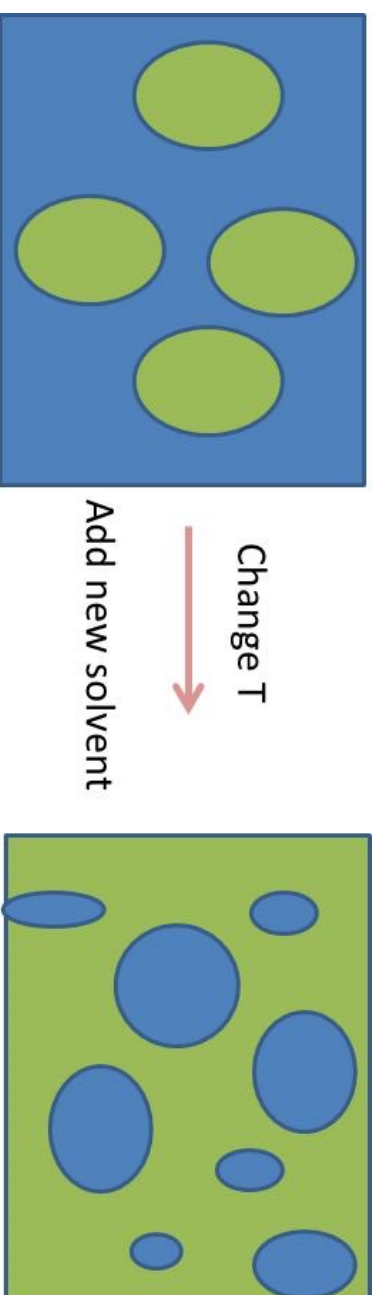
Speed?

Repeatability ?

Biomaterial Processing



Phase separation



Price?

Materials?

Speed?

Repeatability ?

Random Scaffold

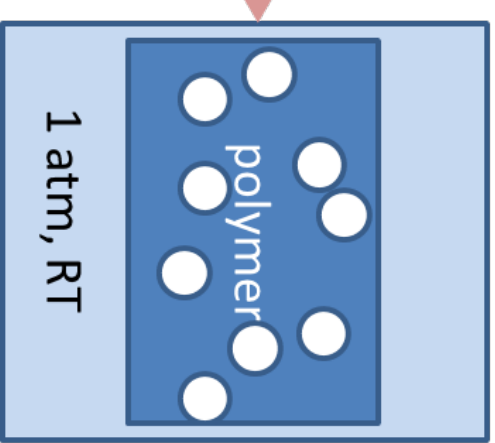
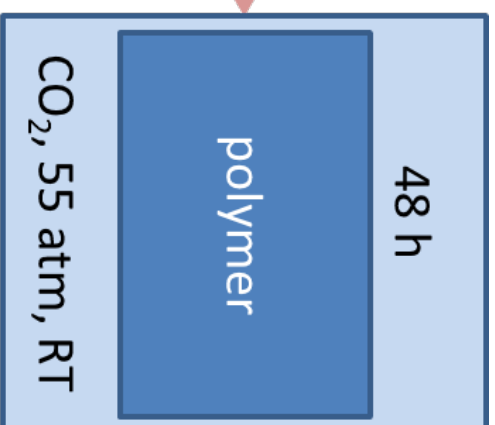
Organ processing

Biomaterial processing

Biomaterial Processing

Gas foaming

polymer



CO₂ dissolves in the polymer

CO₂ forms gas bubbles

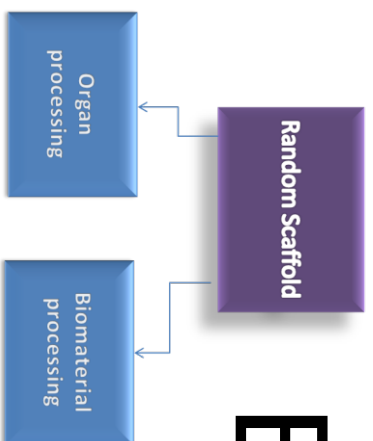
Price?

Materials?

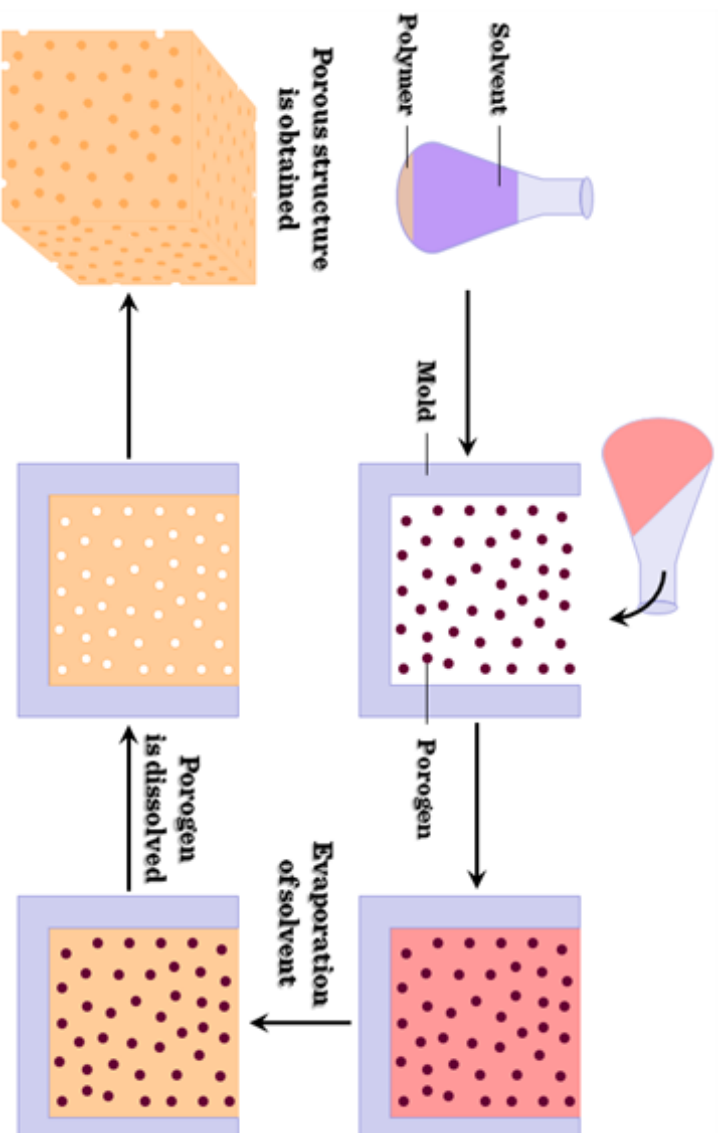
Speed?

Repeatability ?

Biomaterial Processing



Salt leaching



Price?

Materials?

Speed?

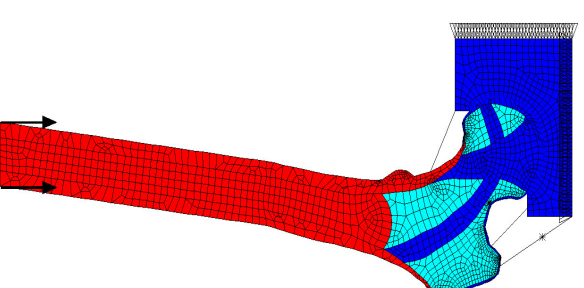
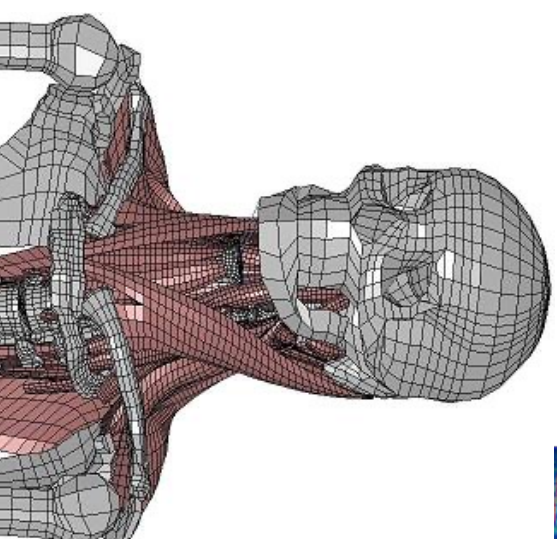
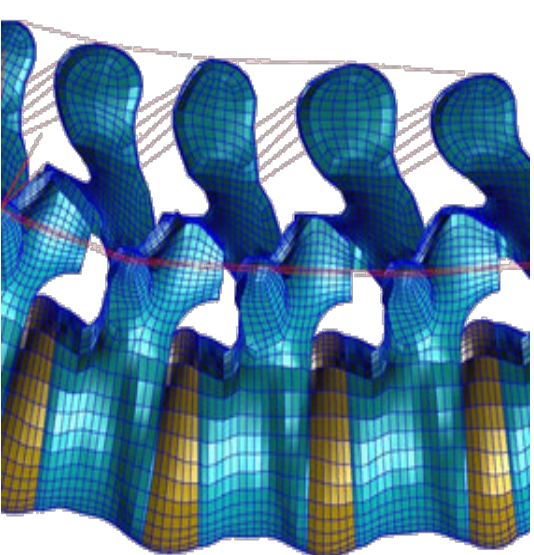
Repeatability ?

Analisi agli elementi finiti

- Metodo per la risoluzione **numerica** di una equazione differenziale, sia essa alle derivate totali o parziali
- Più precisamente si tratta di un metodo per approssimare una equazione differenziale con un sistema di equazioni algebriche

Analisi agli elementi finiti

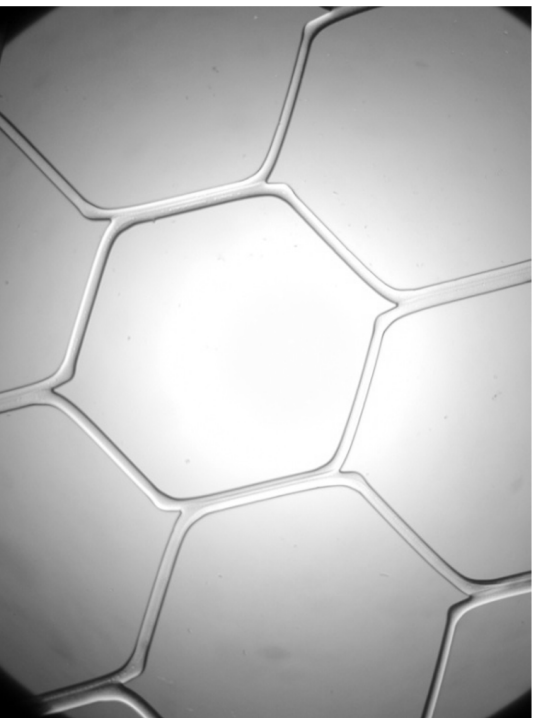
- Elementi
- Nodi
- Funzioni Forma
- Gradi di libertà



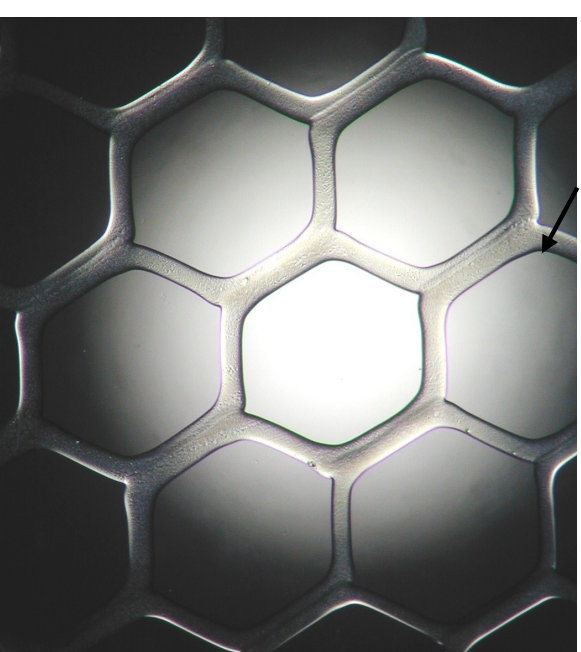
**Is Topology
important for cell functions?**

Topological Stimulus: Neural Tissue

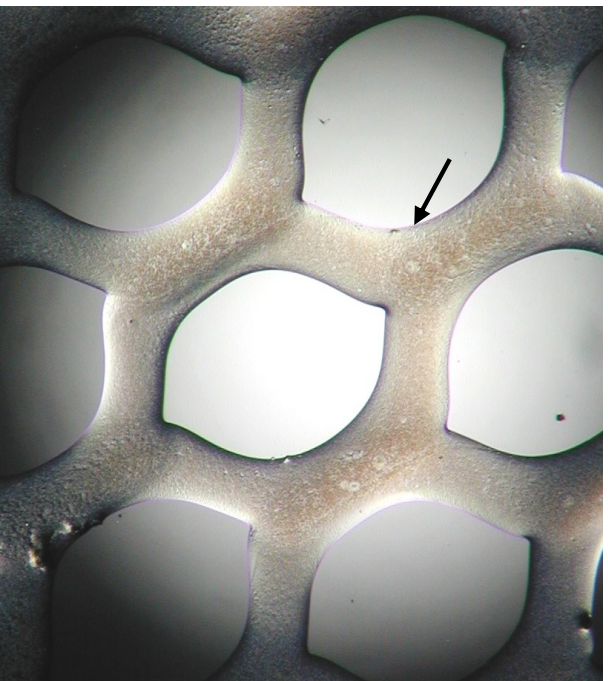
Hexagonal grids with different line width and line length



5 μm

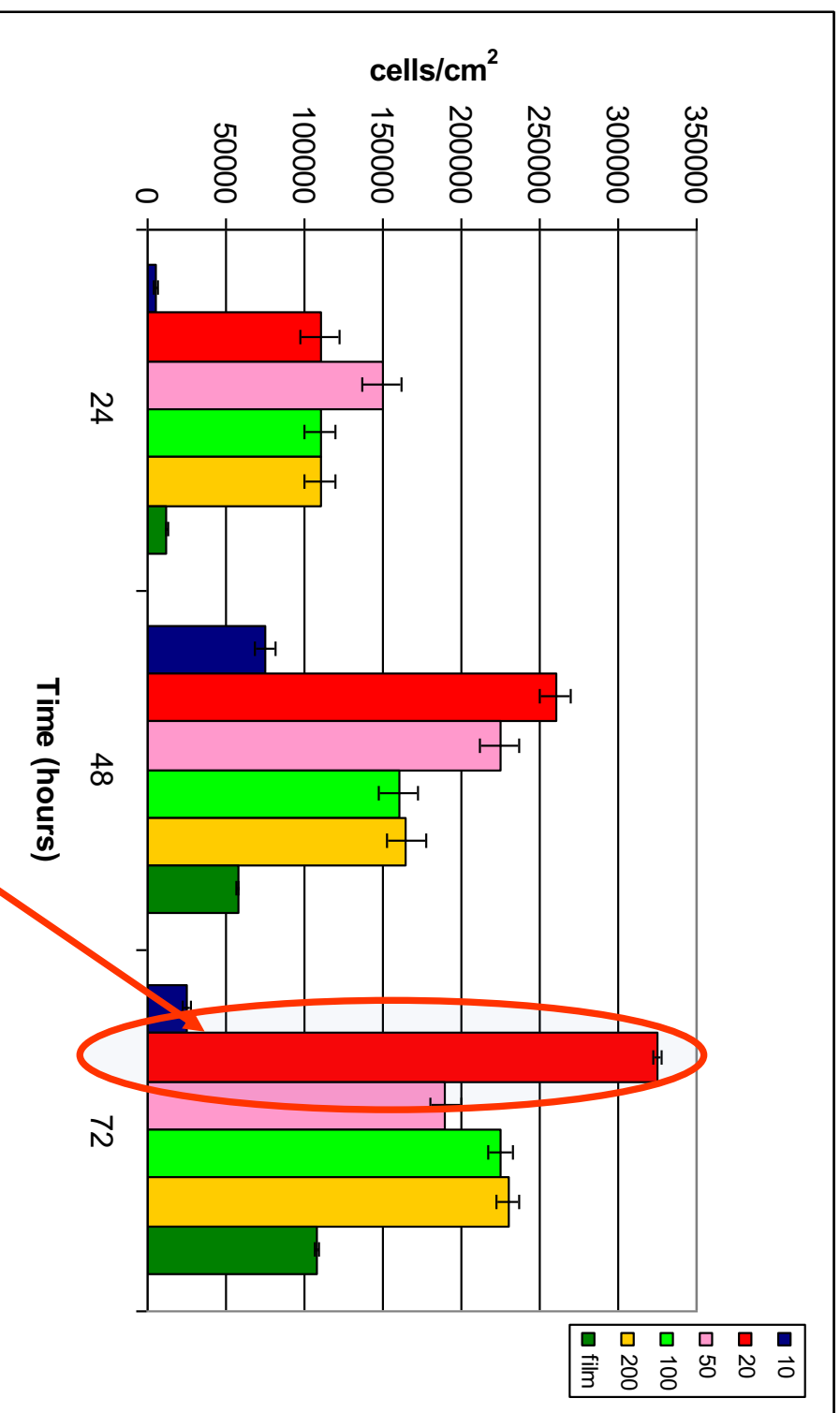


10 μm



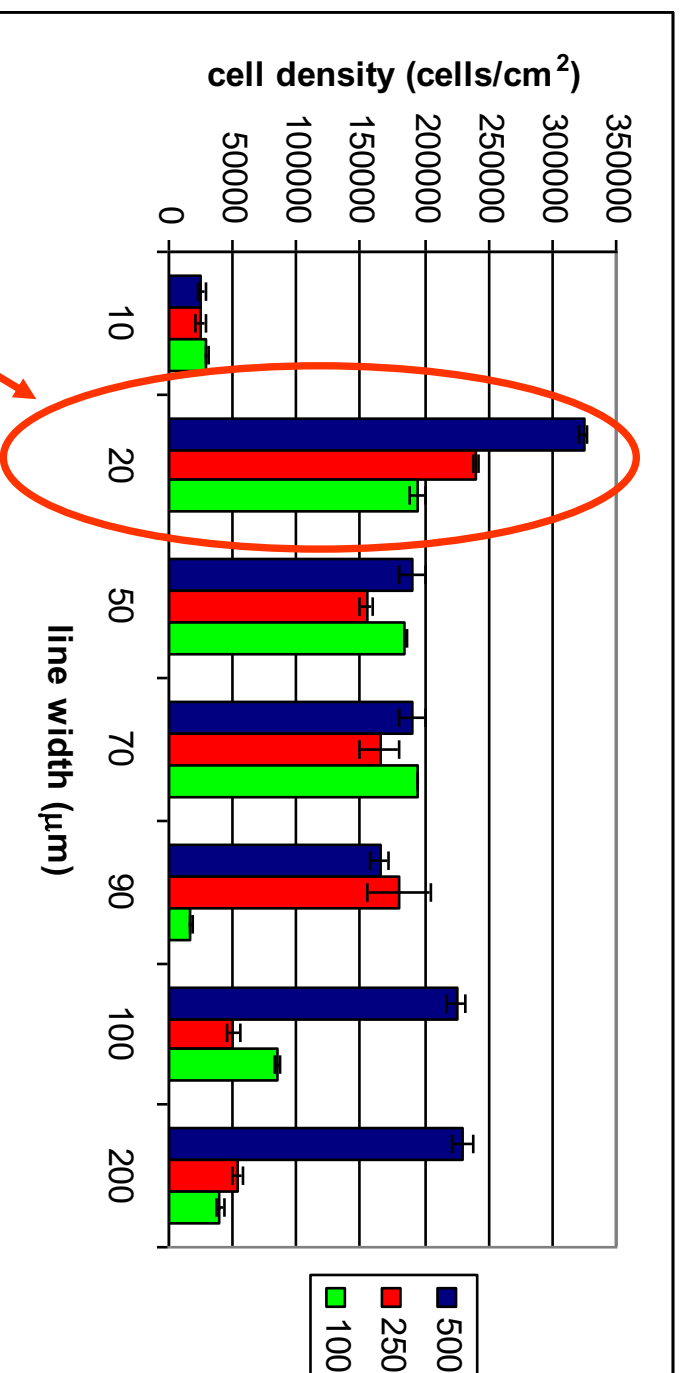
30 μm

Neuronal cells on PAM scaffolds



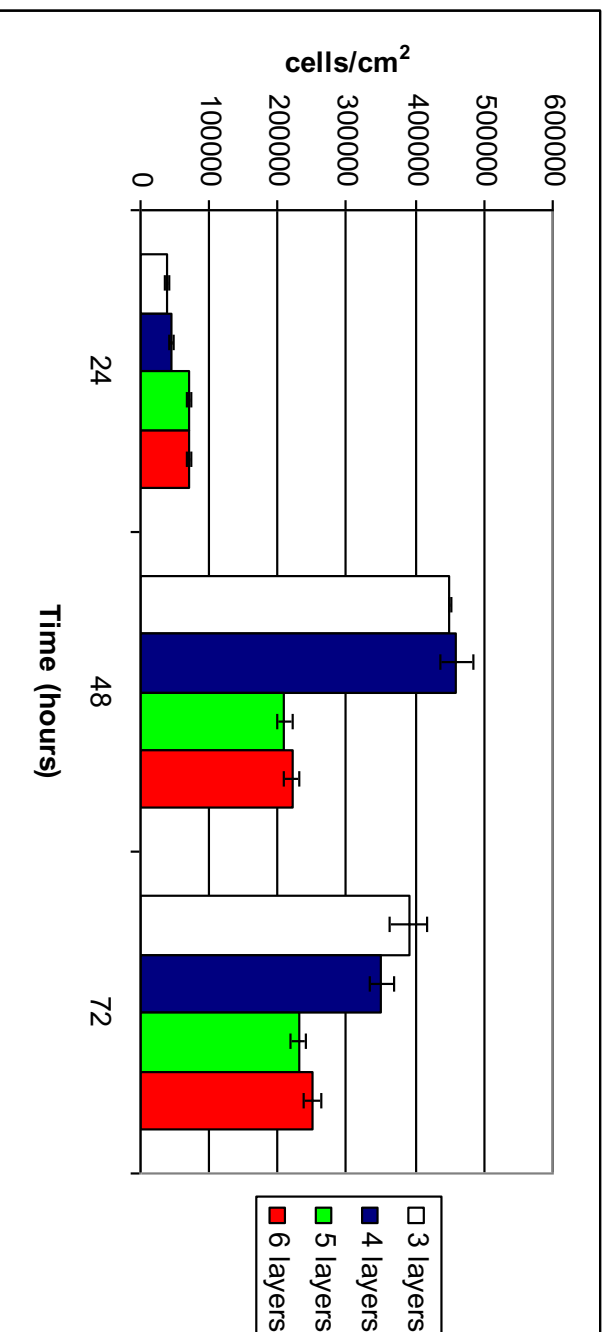
Cell dimension

72h at different line length



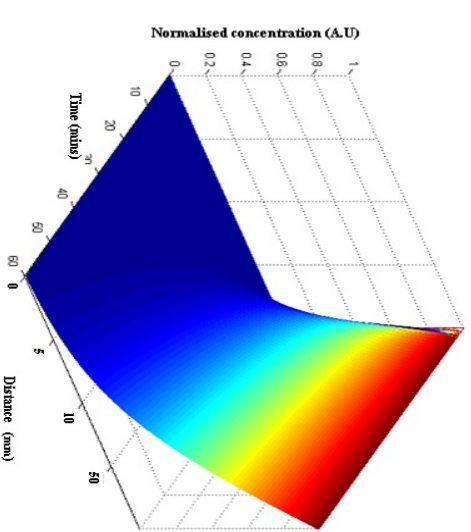
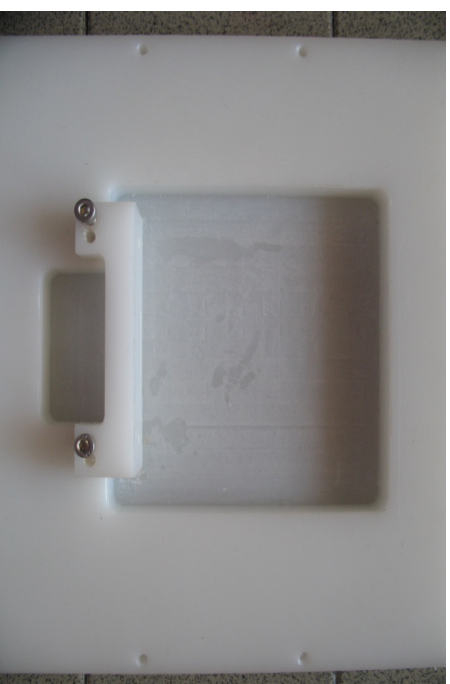
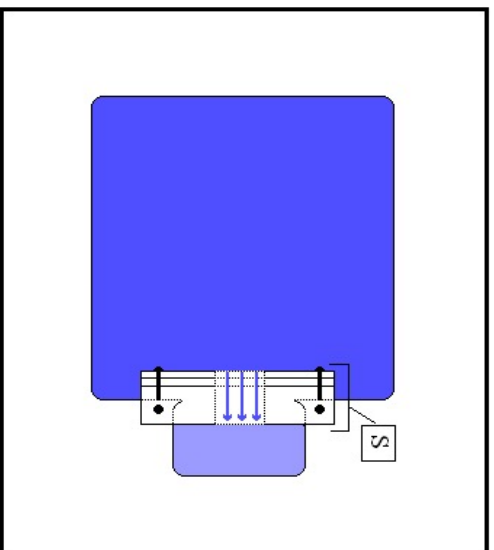
Cell dimension

Neuronal cells on 3D PAM scaffold



Increasing layer number nutrient diffusion is limited

Chemical Gradient Concentration

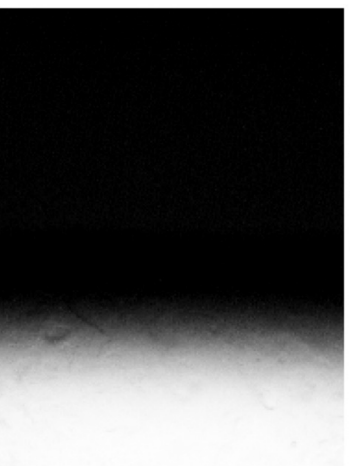
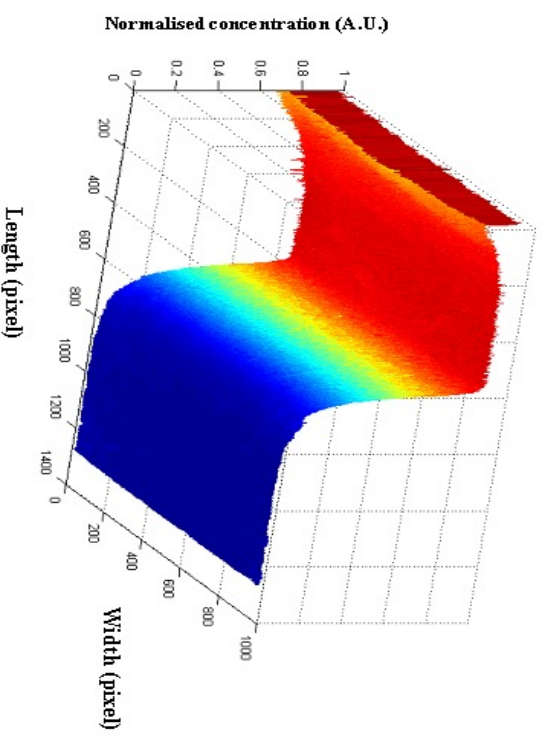


Chemical Gradient Concentration



100 μm

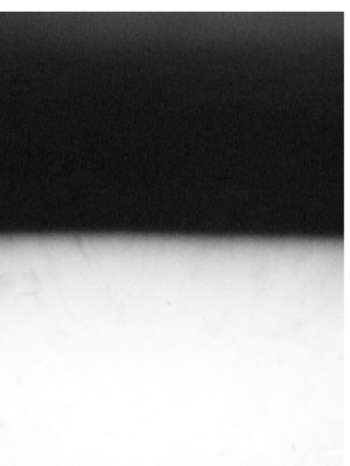
(b)



red channel



green channel

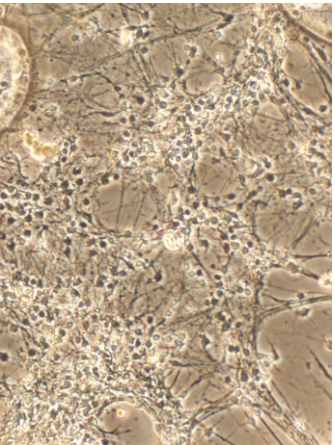


blue channel

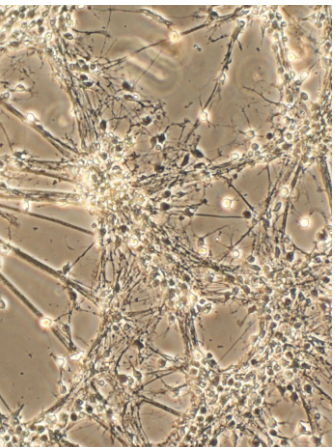
Chemical Gradient Concentration

(a)

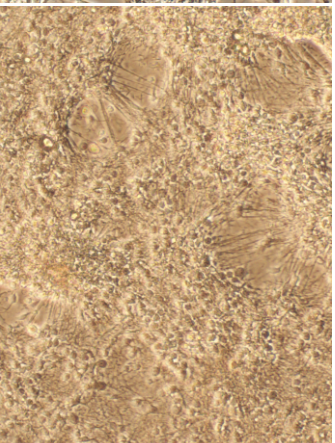
25 $\mu\text{g/ml}$



50 $\mu\text{g/ml}$

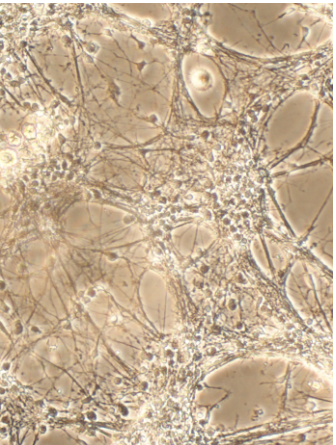


100 $\mu\text{g/ml}$

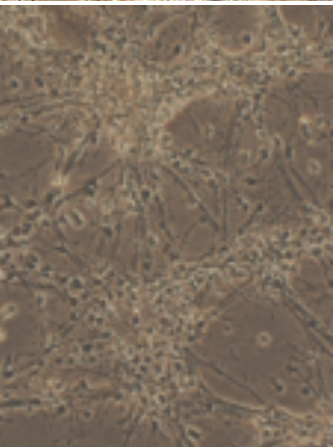


(b)

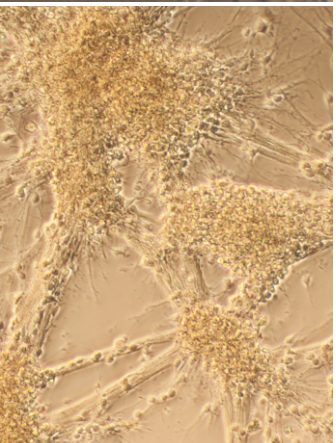
25 $\mu\text{g/ml}$



50 $\mu\text{g/ml}$



100 $\mu\text{g/ml}$



Conductive hollow fibers

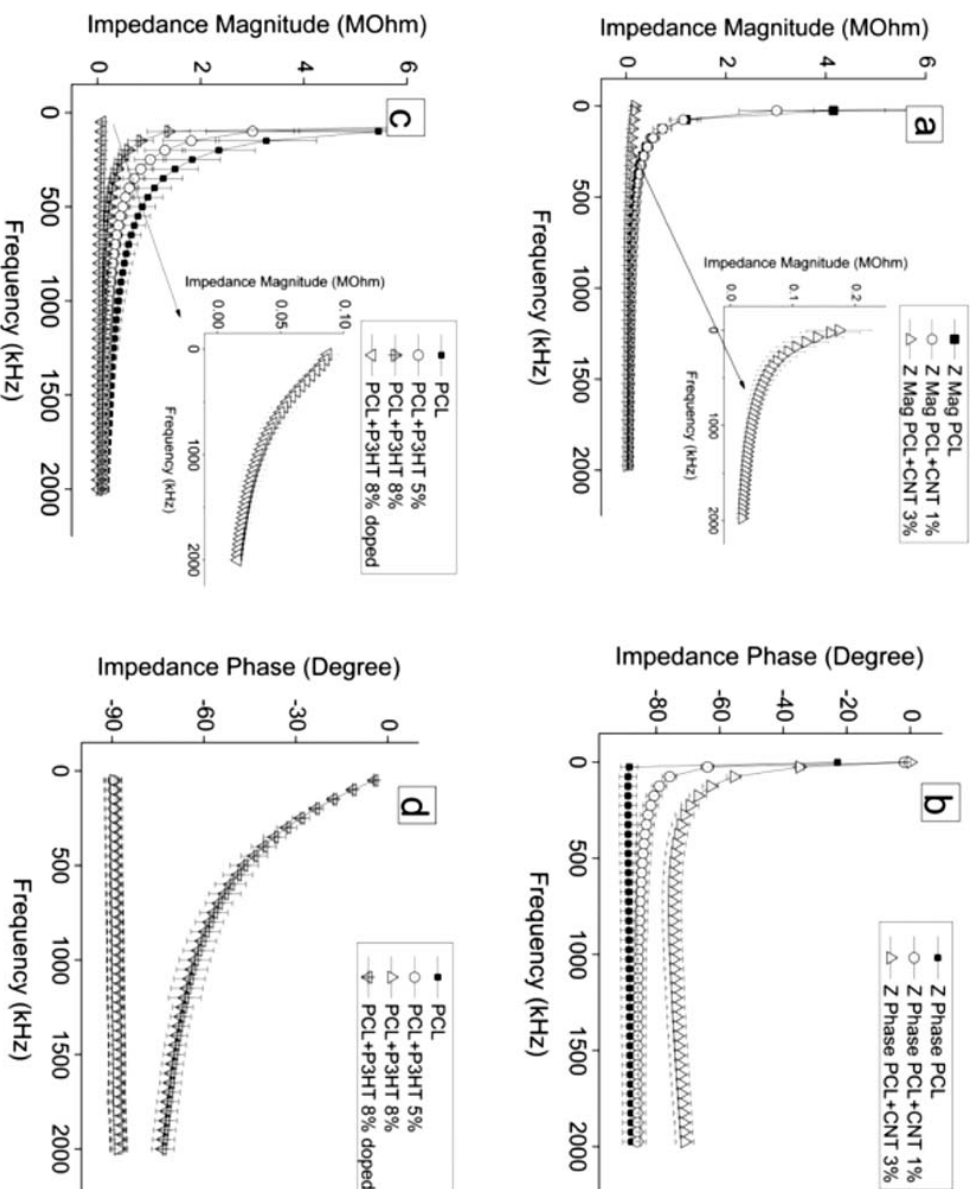
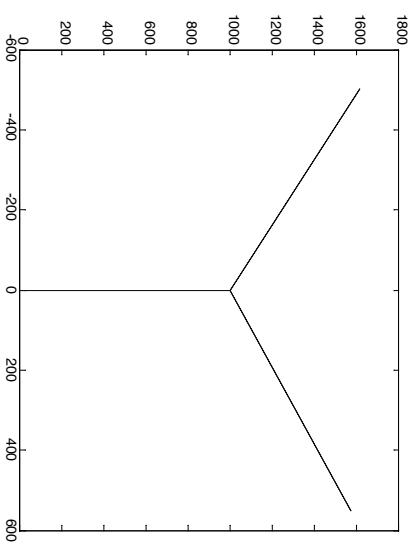


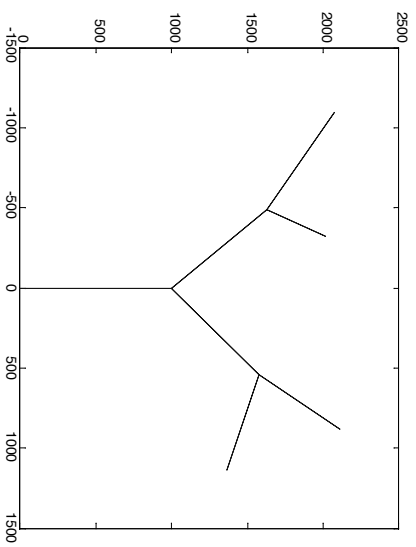
FIGURE 4. Impedance (a) magnitude and (b) phase profiles of CNT/PCL hollow fiber and (c) magnitude (d) phase profiles of P3HT/PCL hollow fiber.

Topological Stimulus: Angiogenesis

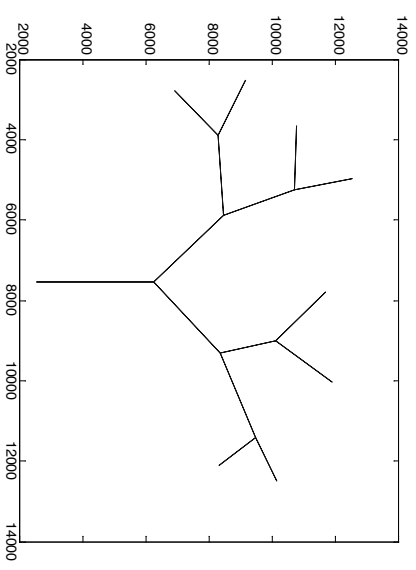
2



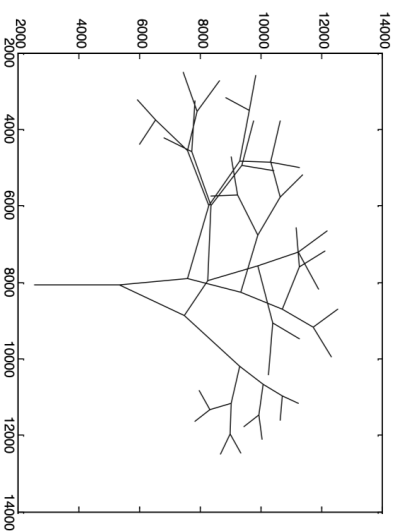
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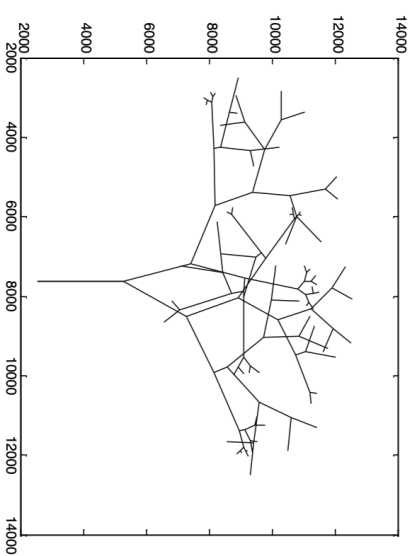
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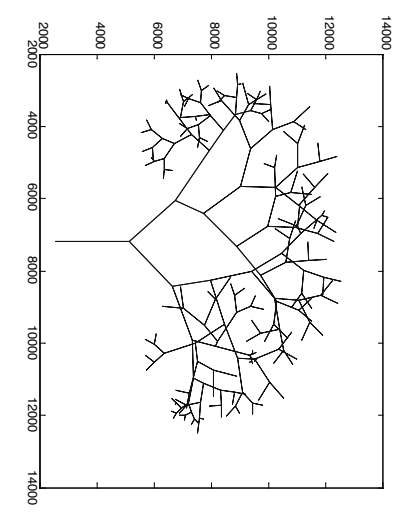
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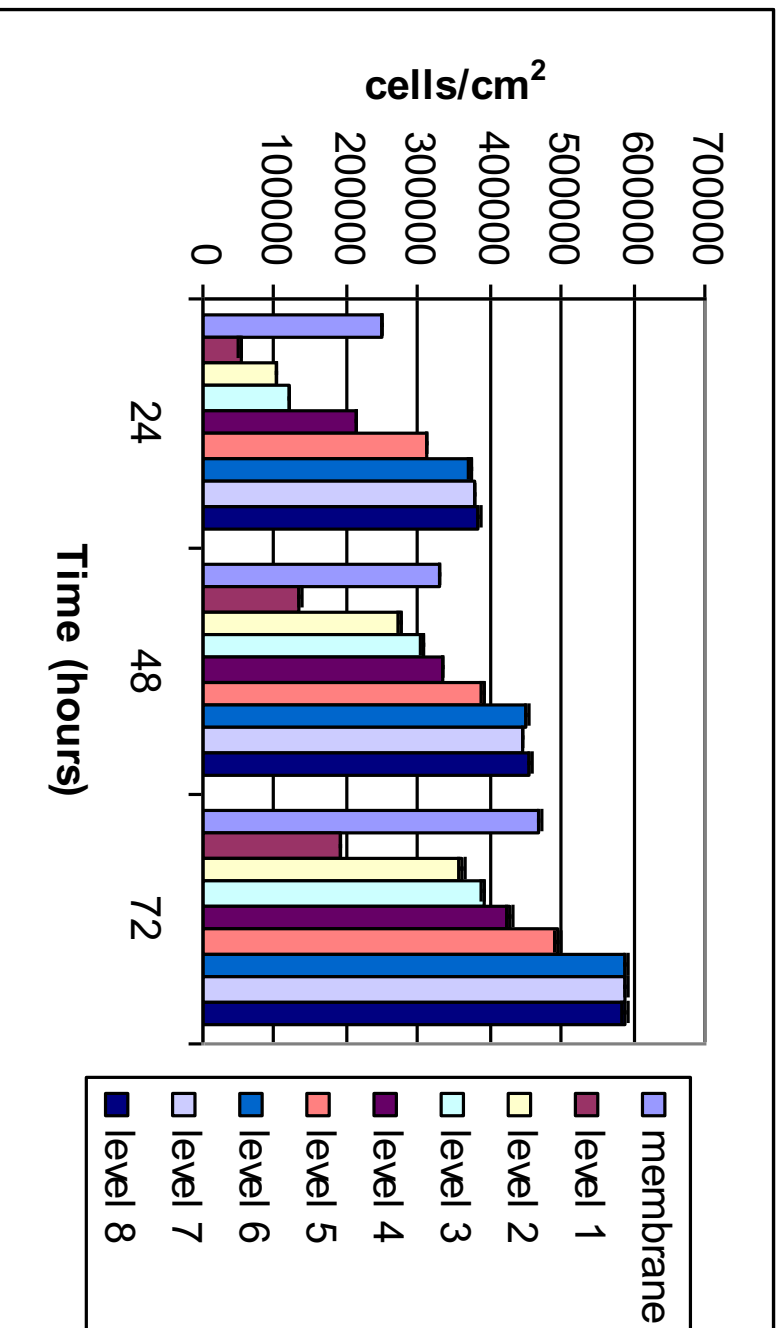
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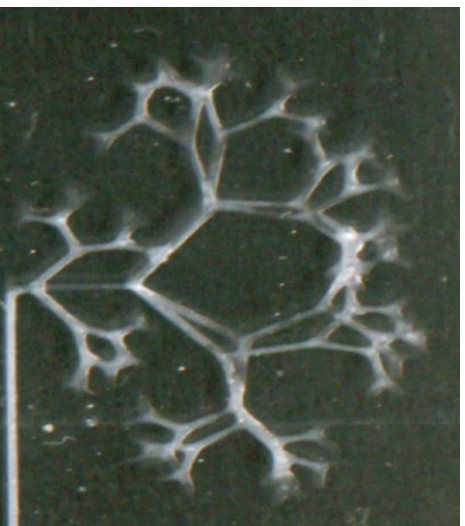
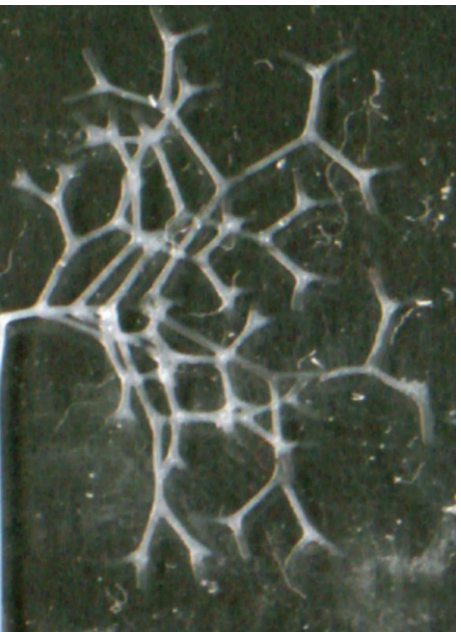
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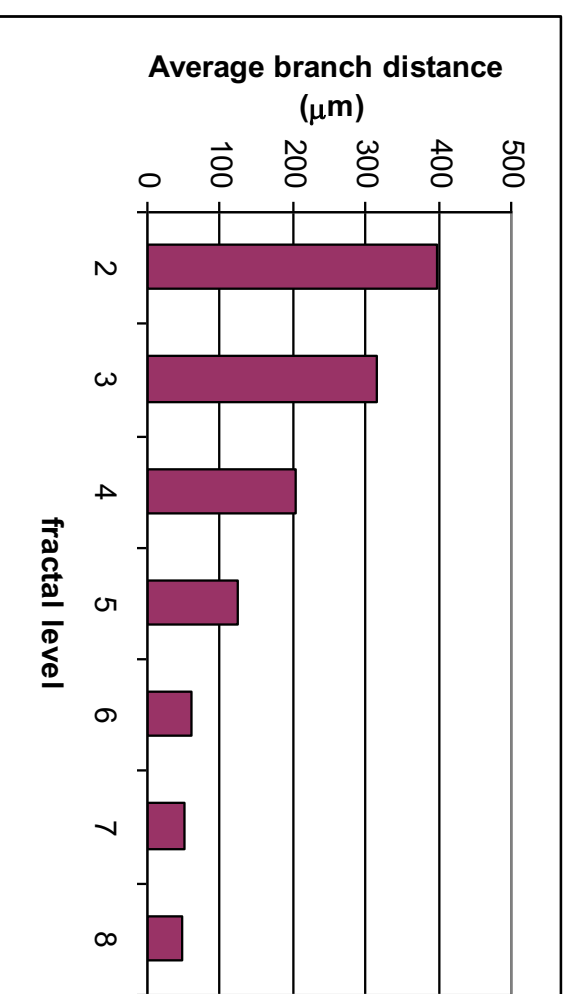
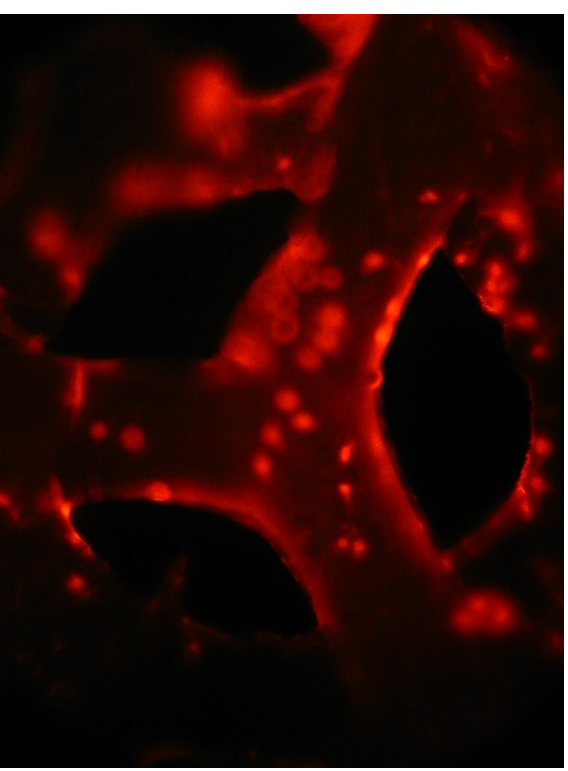
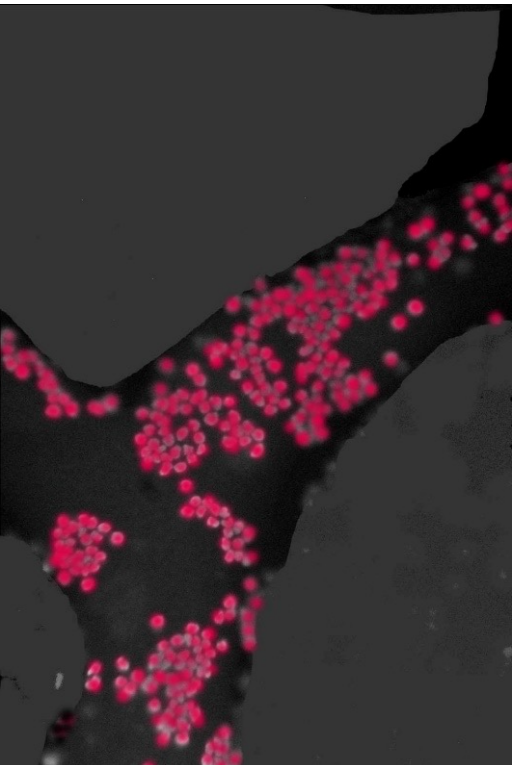
Results



Endothelial cells



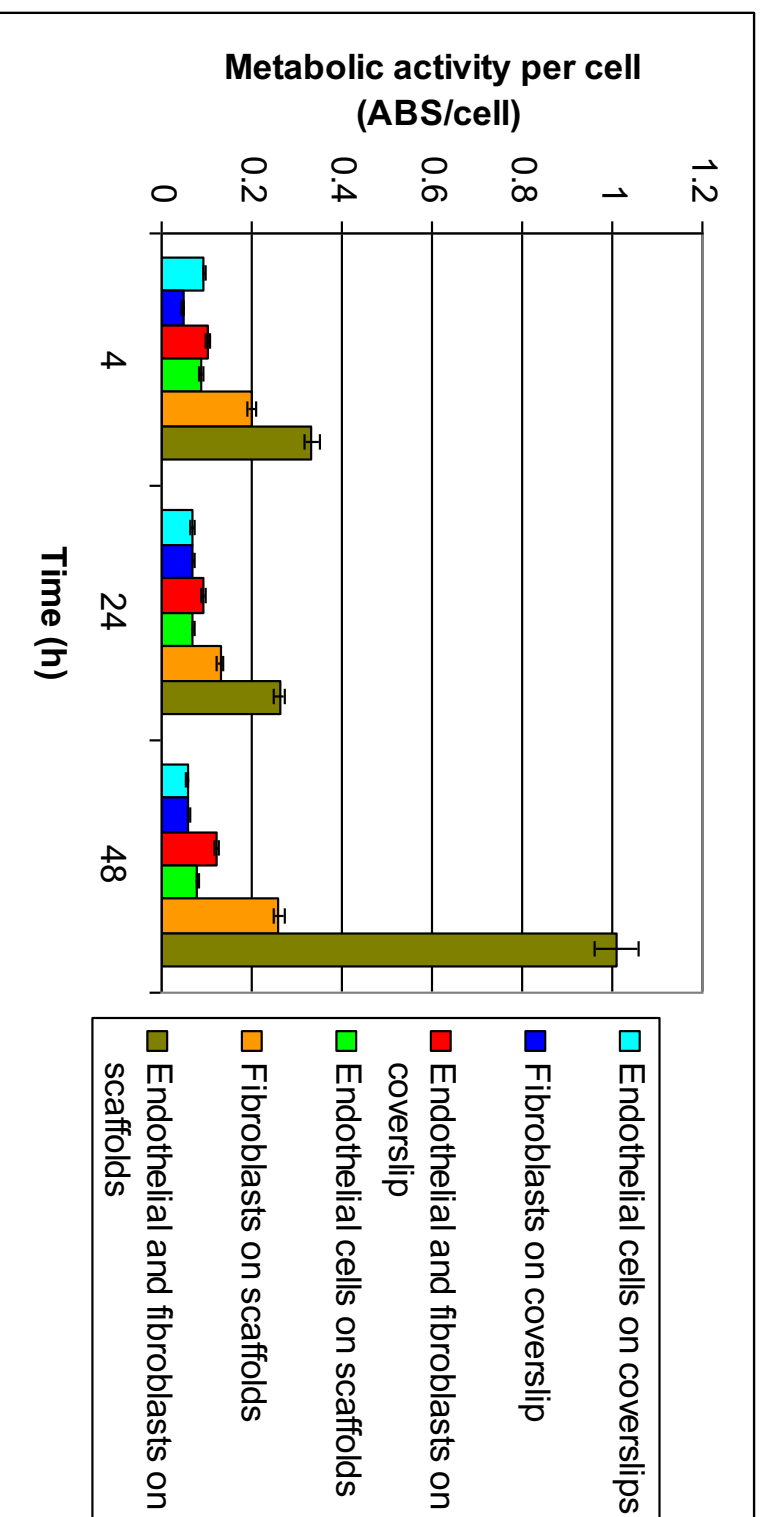
Results



**Is biochemical stimulus
important for cell functions?**

Biochemical stimulus: Angiogenesis

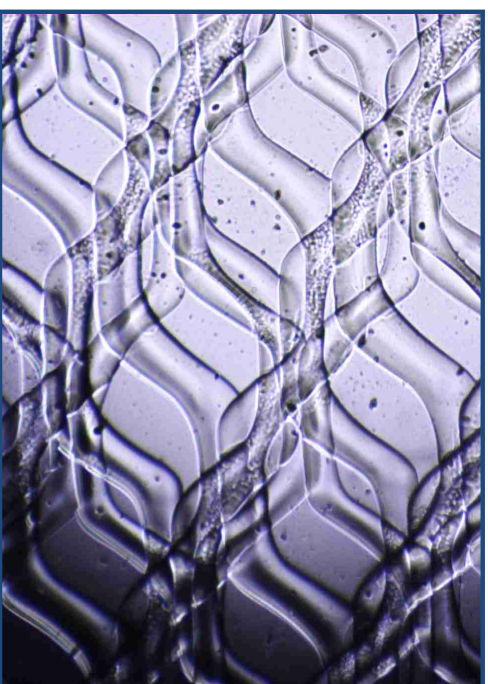
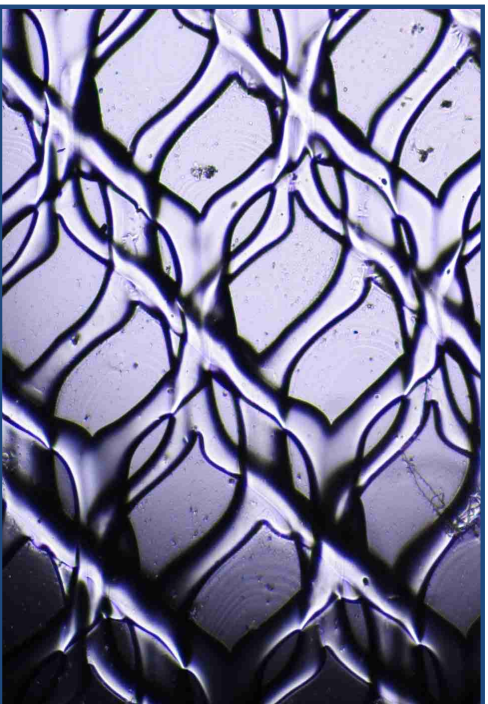
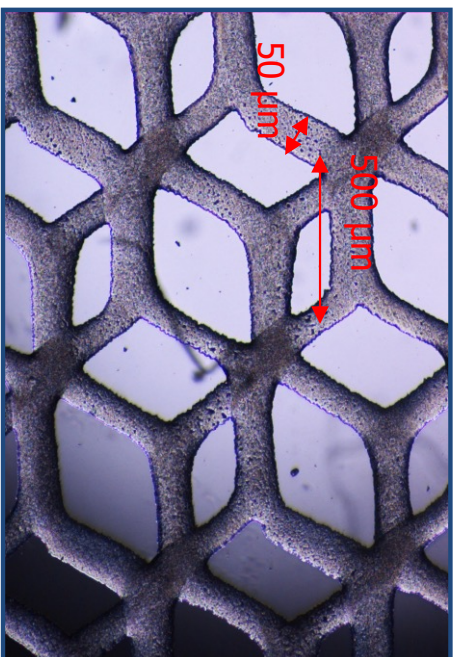
- 6 th fractal level PAM Scaffold
- Co-culture of endothelial cells and fibroblasts
- Metabolic activity for cell



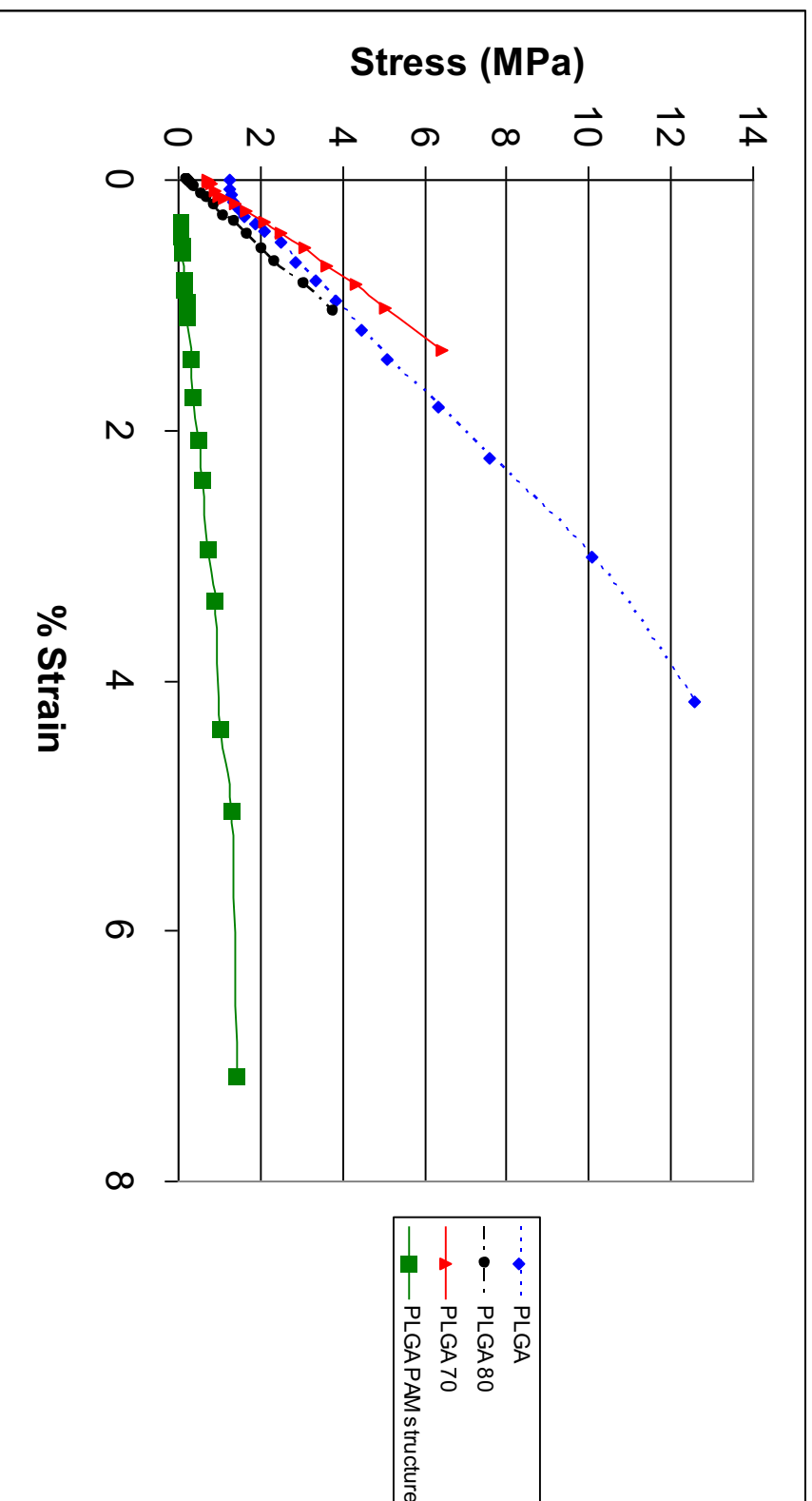
Two stimuli apparently not related interact synergically in order to boost cell organisation and differentiation

**Are mechanical properties
important for cell functions?**

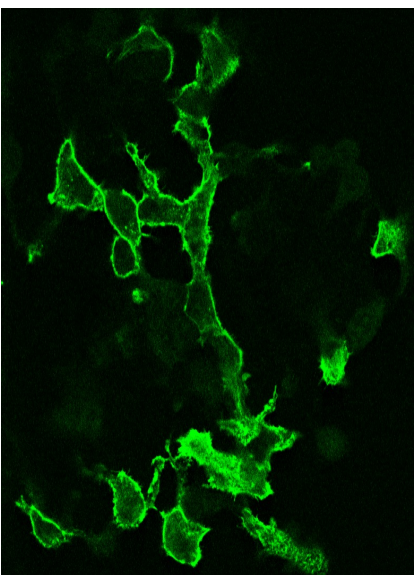
Comparison between a 3D PAM scaffold and a PLGA sponge



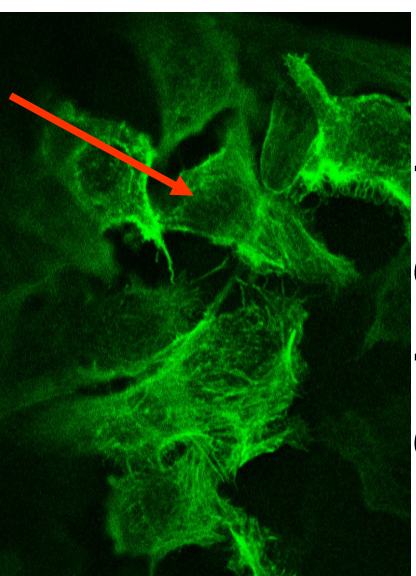
Results



Results

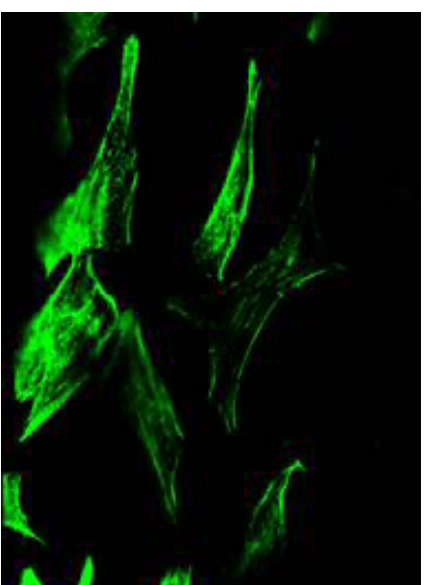


NCTC 2544 keratynocytes dyed with fluorescent phalloidin (actin filaments) cultured on PLGA salt-leached sponge (original magnification x400)

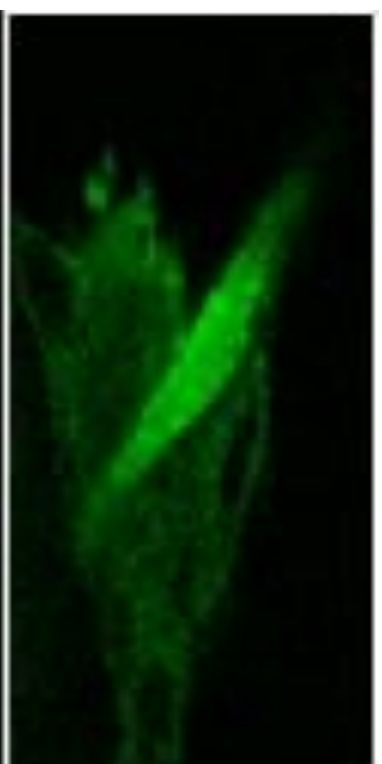


PAM (original magnification x600). There is a better cell-cell and cell-substrate adhesion

Results

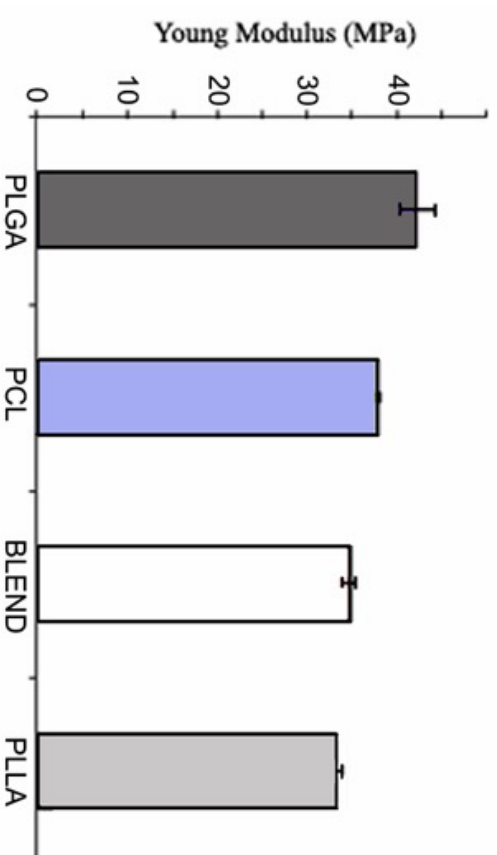
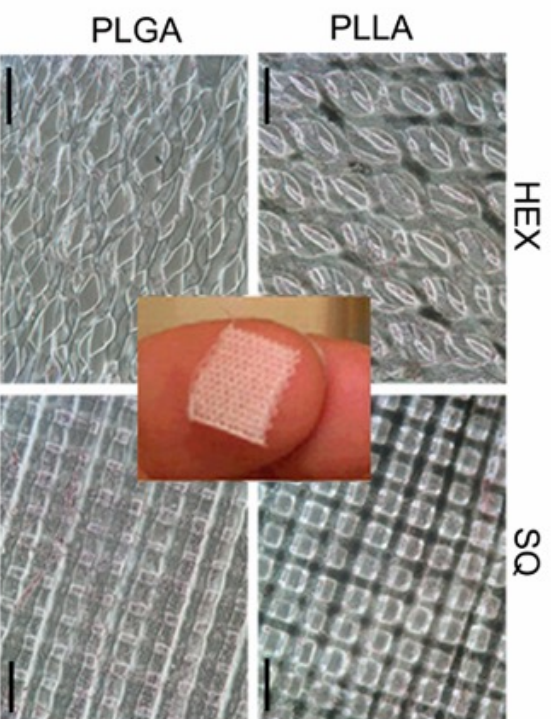


MG 63 osteoblasts dyed with fluorescent phalloidin (actin filaments) cultured on PLGA salt-leached sponge. Cells are more arranged and better adhered on substrate (original magnification x400) .

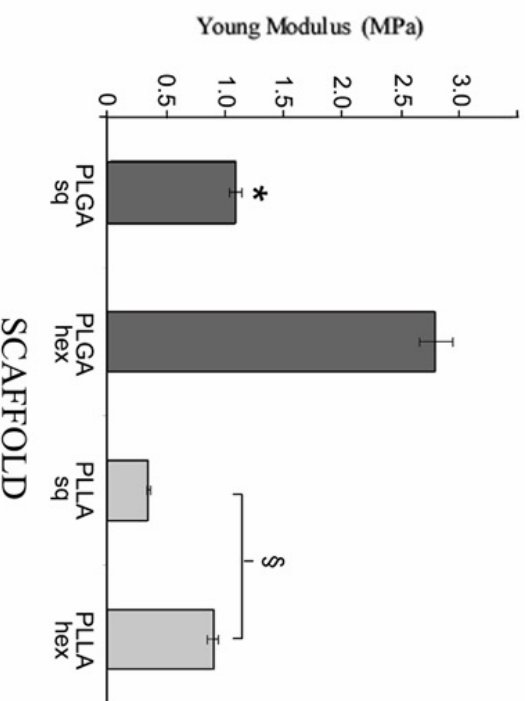


The cell adhesion on PAM scaffold is reduced

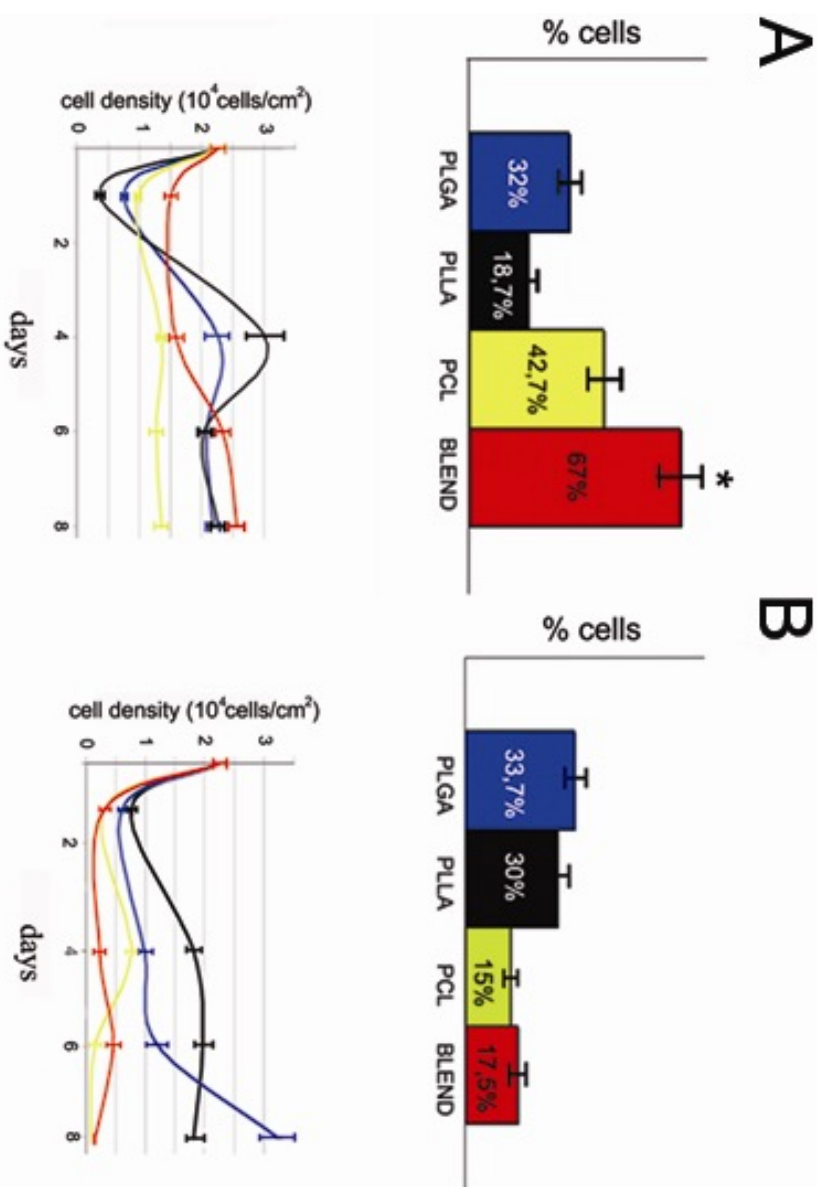
Mechanical and topological stimuli: heart regeneration



C

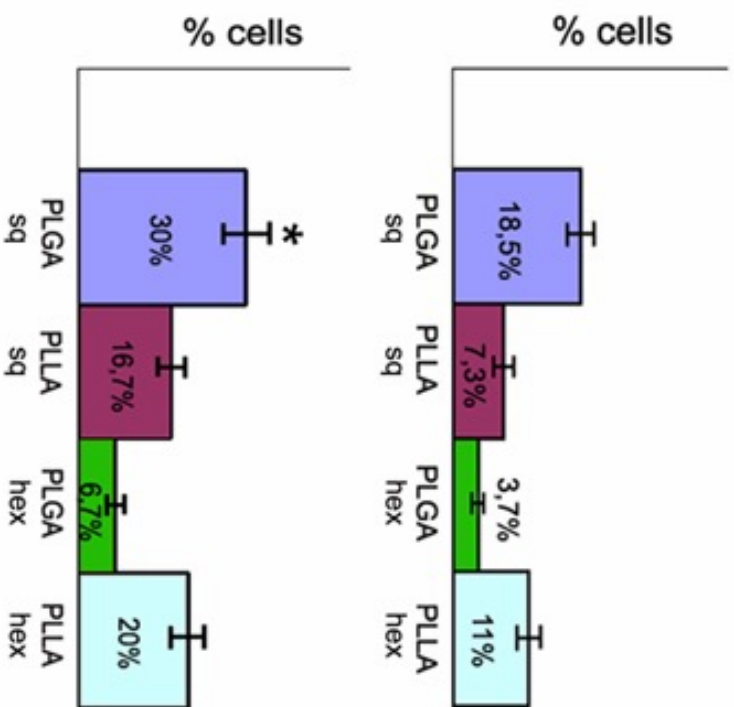


Mechanical and topological stimuli: heart regeneration

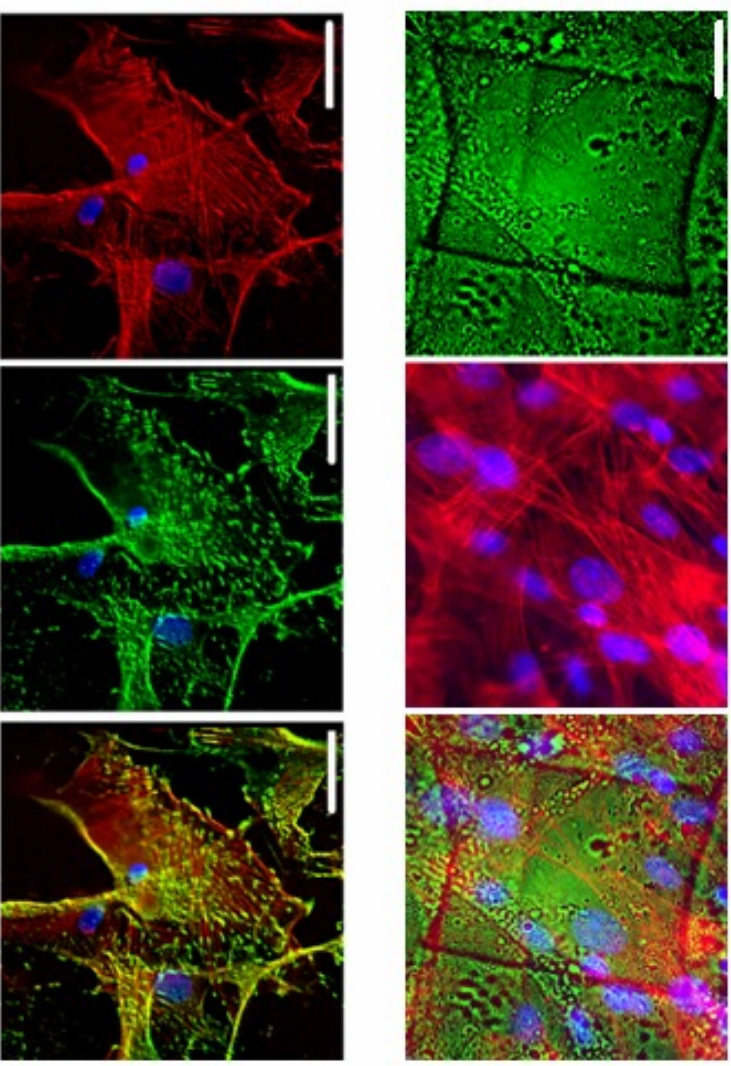


(A) MSC and **(B) CPC** adhesion (top) and proliferation (bottom) ability on PLGA, PLLA, PCL and BLEND 2D films

A Mechanical and topological stimuli: heart regeneration

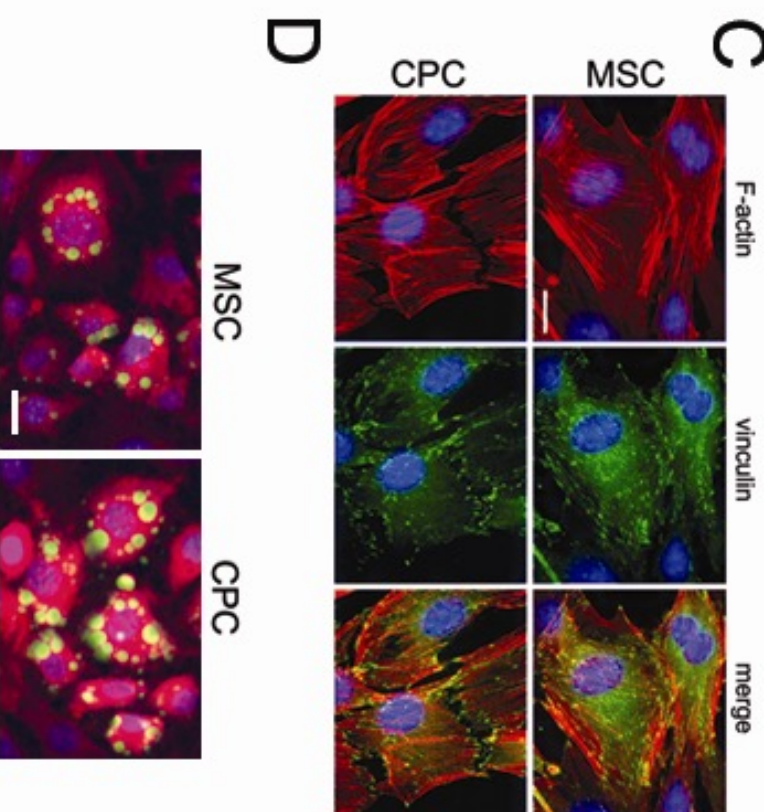


C



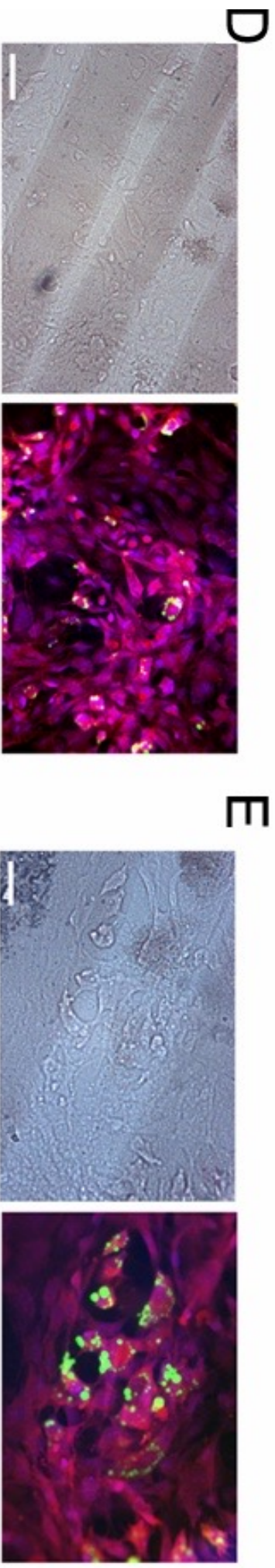
- Progenitor cell response to 3D scaffold geometry and stiffness. **(A)** MSC (top) and CPC (bottom) adhesion fraction on 3D scaffolds, as evaluated 24h after cell seeding.
- Immunofluorescence **(B)** and confocal **(C)** image of CPC exhibiting the expression of F-actin (red), vinculin (green), and related merge (yellow) within square pore PLLA scaffolds.

Mechanical and topological stimuli: heart regeneration



- **(C)** MSC and CPC cytoskeletal organization (F-actin, red) and expression of adhesion proteins (vinculin, green) on PLLA films. Equivalent results were obtained after cell seeding on PLGA, PCL and BLEND films.
- **(D)** MSC and CPC retain multipotency on all the polymers tested (representative pictures of MSC and CPC differentiation on PLLA), as shown by the presence of lipid droplets (yellow) after cell treatment with adipogenic medium. MSC and CPC display distinct adhesive and proliferative responses in respect to the film chemical composition. No significant differences in cell adipogenic potential were detected.

Mechanical and topological stimuli: heart regeneration



(**D**) Adipocytic differentiation of MSC and (**E**) CPC cultured on 3D square PLLA scaffolds. Equivalent results were obtained on the other 3D scaffolds tested. MSC and CPC display distinct adhesive ability, while retaining multipotential attitude on all 3D scaffolds evaluated.

