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“Biomedical microsystems for interacting at a cellular level”

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Industriales Research Meeting 2016, Madrid, April 20th

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General index

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1.- Introduction: Cells and biomaterials

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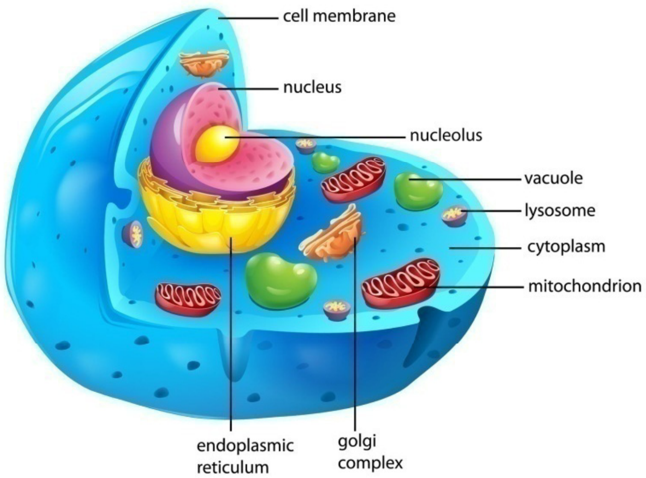
1.1.- The cell: A comple multi-scale and multi-physical/biochemical living system

The eukaryotic cell: The basic unit of life, which operates on the basis of its genetic information and of the complex interactions with the local micro-environment that provides physical and chemical support and signals for survival and regulation (cell niche).



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Stem cells: are defined as cells with self-renewal abilities and with the capability of differentiation into specialized cell types.

These cells are fundamental in tissue repair and regeneration strategies.

The behavior and fate of stem cells is not just dependent on genetic information, but is also regulated by other biochemical and mechanical cues and signals (epigenetic cues), which come from their micro-environment.

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1.- Introduction: Cells and biomaterials

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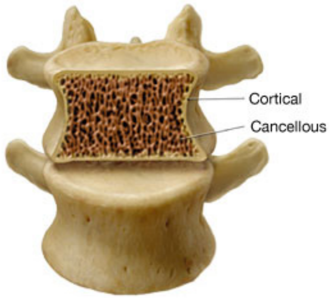
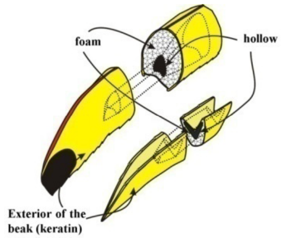
1.2.- Biomaterials and biodevices for interacting with cells and driving their behavior

Natural materials and man-made materials are different in terms of:

- → Elasticity and strength
- → Structure – porosity – morphology
- → Surface topography / texture
- → Fatigue performance
- → Self-healing abilities
- → Aesthetics





Pics. sources: American Medical Association & M.A. Meyers

Current trends for biomimetic and biomechanic solutions:

Design, modeling and manufacture of (bio)materials and related (bio)devices with:
1) porous and lattice geometries; 2) functional gradients of properties;
3) controlled surface topographies; and 4) geometries defined at different scales
(among other trends including surface biofunctionalization, biofabrication…)

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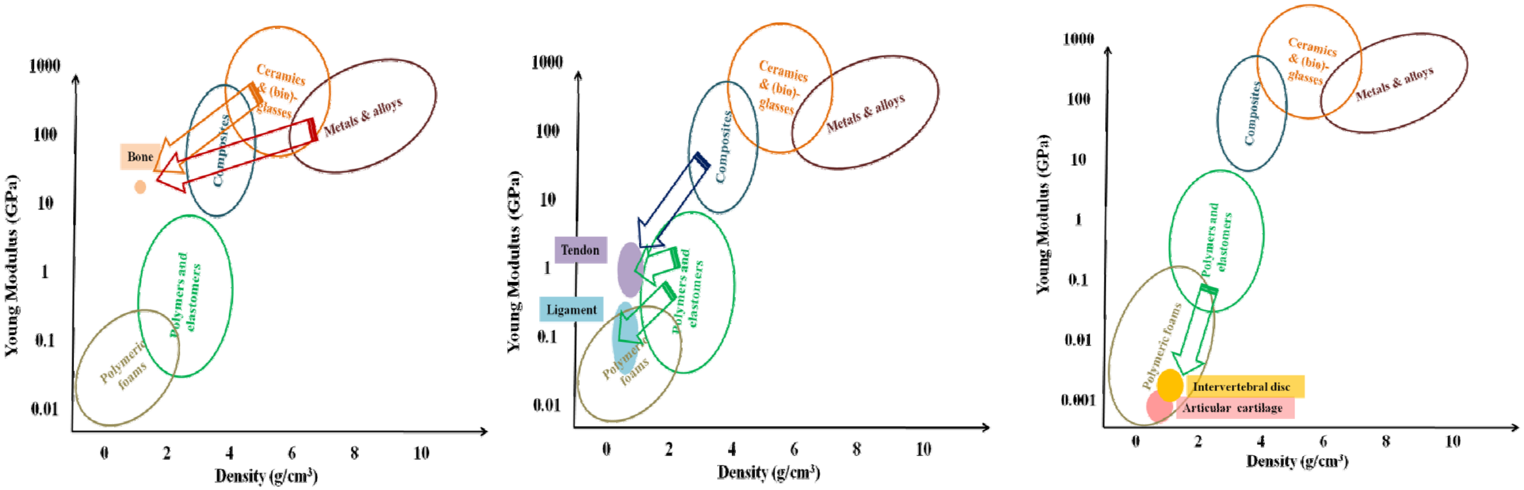
2.- Biomimetic modeling & manufacturing strategies

2.1.- Modeling and manufacturing porous and lattice (bio)materials and (bio)devices

Conventional prostheses vs. human materials

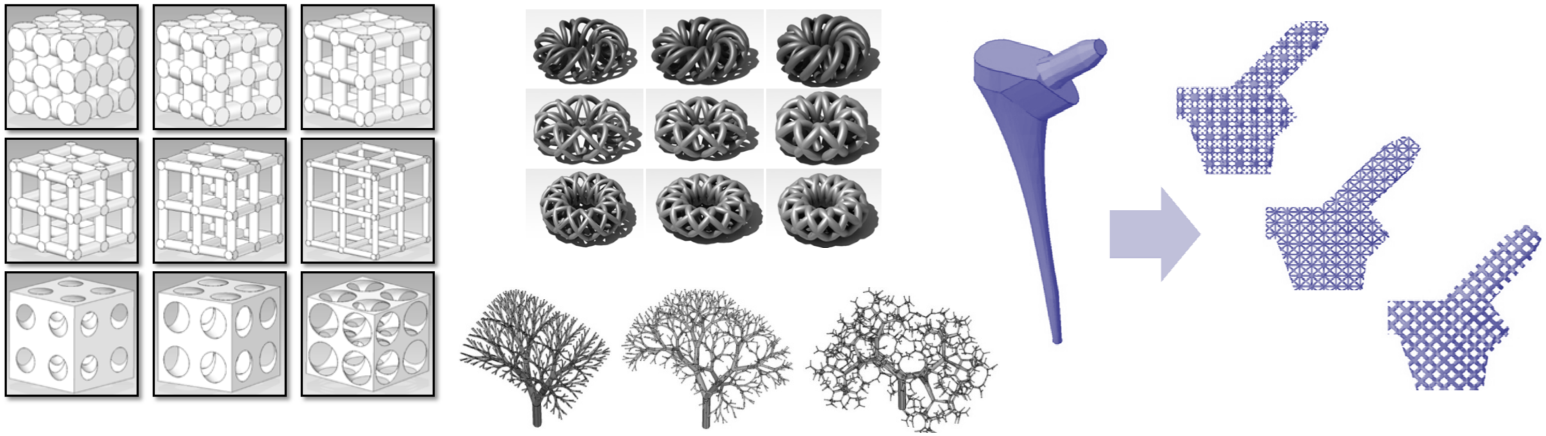


Mechanical mismatches → Inadequate epigenetic cues for cells and tissues
Potential benefits of biomimetic and biomechanical materials for enhanced response

2.- Biomimetic modeling & manufacturing strategies

2.1.- Modeling and manufacturing porous and lattice (bio)materials and (bio)devices

Computer-aided design and engineering of porous and lattice structures



Biomimetic CAD libraries rapidly obtained by means of parametric tools

The use of boolean operations easily promotes connection with final applications

- Díaz Lantada, A.; Lafont Morgado, P..- "Rapid prototyping for biomedical engineering: Current capabilities and challenges". Annual Review of Biomedical Engineering, 14, 73-96, 2012.

- Díaz Lantada, A.; Pareja Sánchez, B.; Gómez Murillo, C.; Urbieta Sotillo, J..- "Fractals in tissue engineering: toward biomimetic cell-culture matrices, microsystems and microstructured implants". Expert Review of Medical Devices, 10(5), 629-648, 2013.

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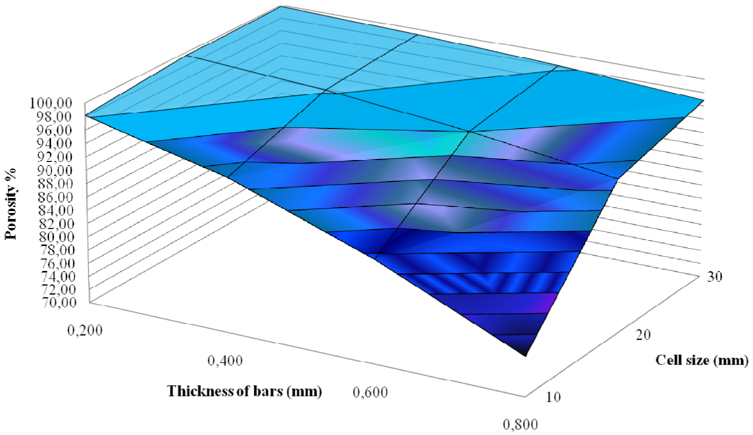
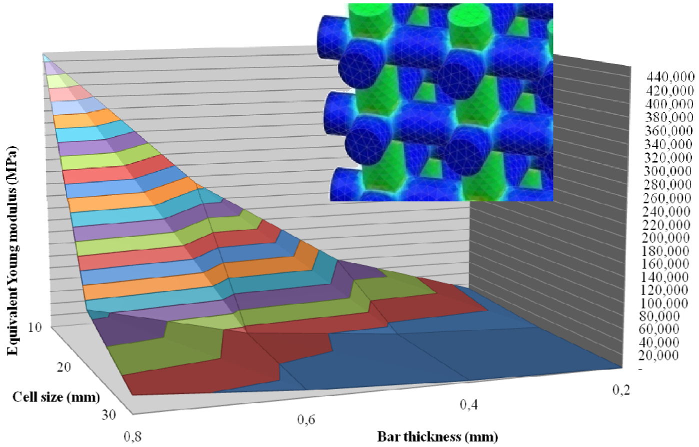
2.1.- Modeling and manufacturing porous and lattice (bio)materials and (bio)devices

Computer-aided design and engineering of porous and lattice structures





Systematically developed CAD libraries + assessment via modeling resources leads to fundamental information regarding the adequacy for final applications

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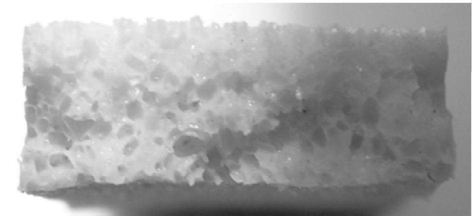
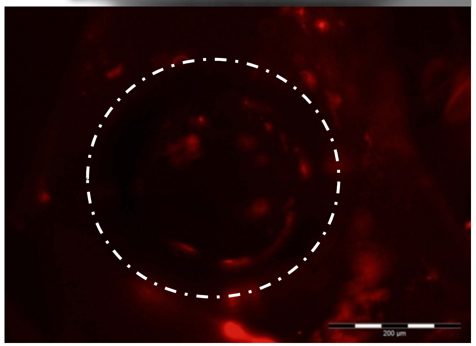
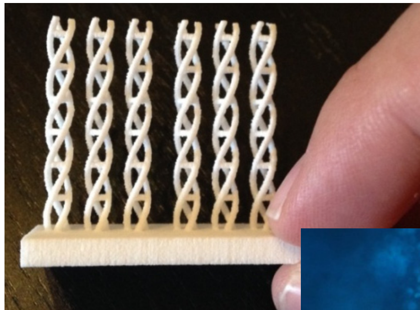
2.1.- Modeling and manufacturing porous and lattice (bio)materials and (bio)devices

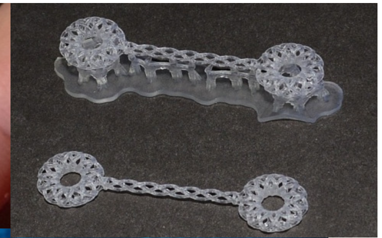
Processes based on phase-separation, particle leaching…

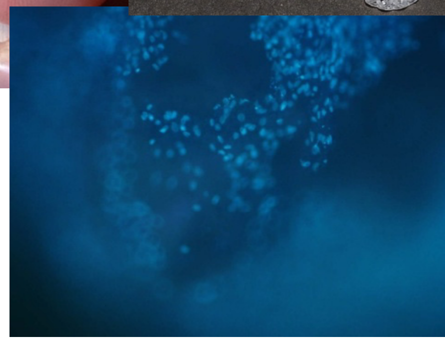




Current trends based on additive manufacturing approaches







Cell cultures & pics. Courtesy of Prof. García-Ruíz, UAM

- Díaz Lantada, A.; Alarcón Iniesta, H.; Pareja Sánchez, B.; García-Ruíz, J.P..- "Free-form rapid-prototyped PDMS scaffolds incorporating growth factors promote chondrogenesis". Advances in Materials Science and Engineering, Vol. 2014, ID 612976, 2014.

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2.- Biomimetic modeling & manufacturing strategies

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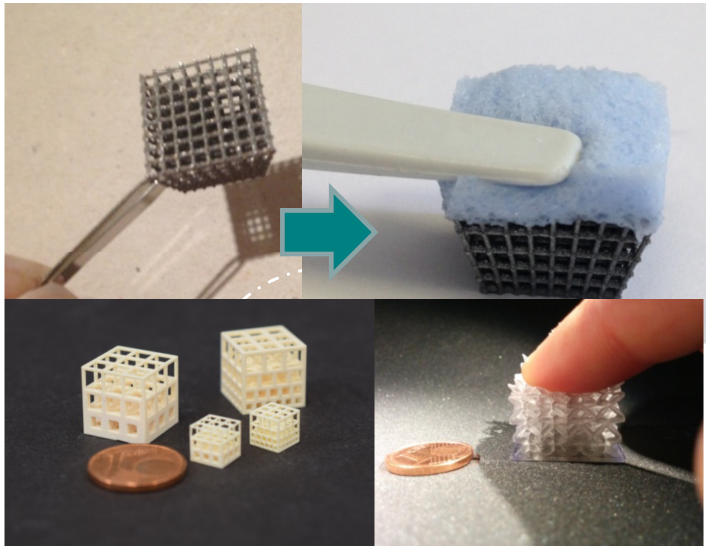
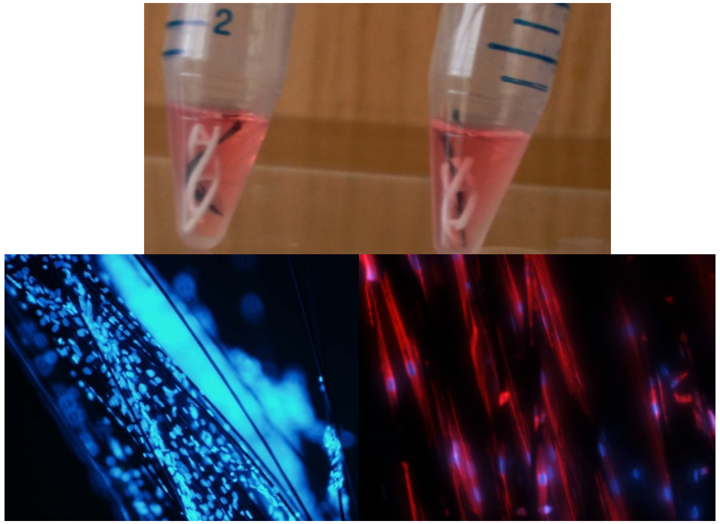
2.1.- Modeling and manufacturing porous and lattice (bio)materials and (bio)devices

Lattices with functional gradients of mechanical properties by AMT



Combined materials and technologies towards biomimetic constructs



Cell culture: Prof. García-Ruíz, UAM

- *Díaz Lantada, A.; Alarcón Iniesta, H.; García-Ruíz, J.P..- "Composite scaffolds for osteochondral repair obtained by combination of additive manufacturing, particle leaching and hMSC-CM functionalization". Materials Science and Engineering C: Materials in Biology and Medicine, 59, 218-217, 2016.*
- *Díaz Lantada, A.; De Blas Romero, A.; Schwentenwein, M.; Jelinek, C.; Homa, J..- "*Lithography-based ceramic manufacture (LCM) of auxetic structures: present capabilities and challenges*". Smart Materials and Structures, 25 (5), 2016.*

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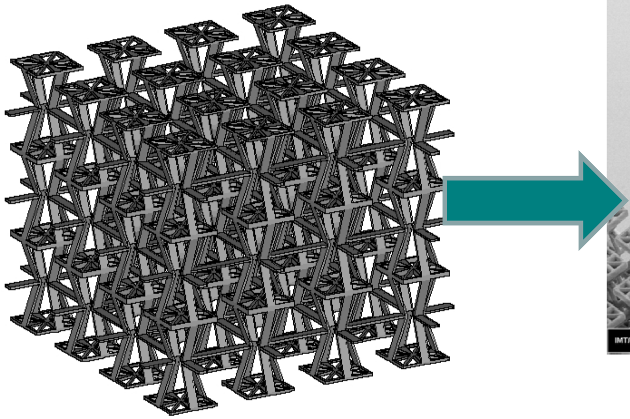
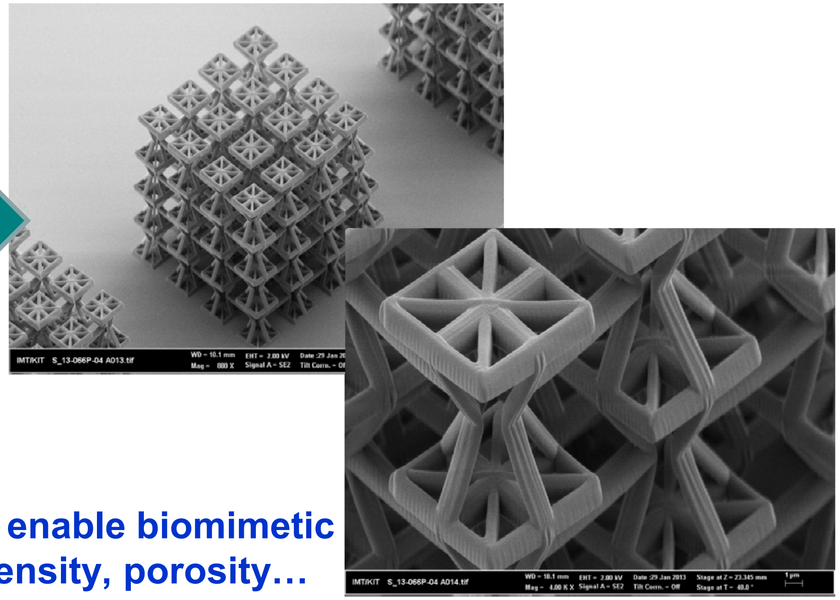
2.2.- Modeling and manufacturing porous and lattice biomaterials and biodevices

Computer-aided design and engineering of lattice and porous structures

Manufacturing resorting to additive apporaches





Different CAD modeling strategies also enable biomimetic gradients of mechanical properties, density, porosity…

- Hengsbach, S.; Díaz Lantada, A..- "Direct laser writing of auxetic structures: Present capabilities and challenges". Smart Materials and Structures, 23, 085033, 2014.

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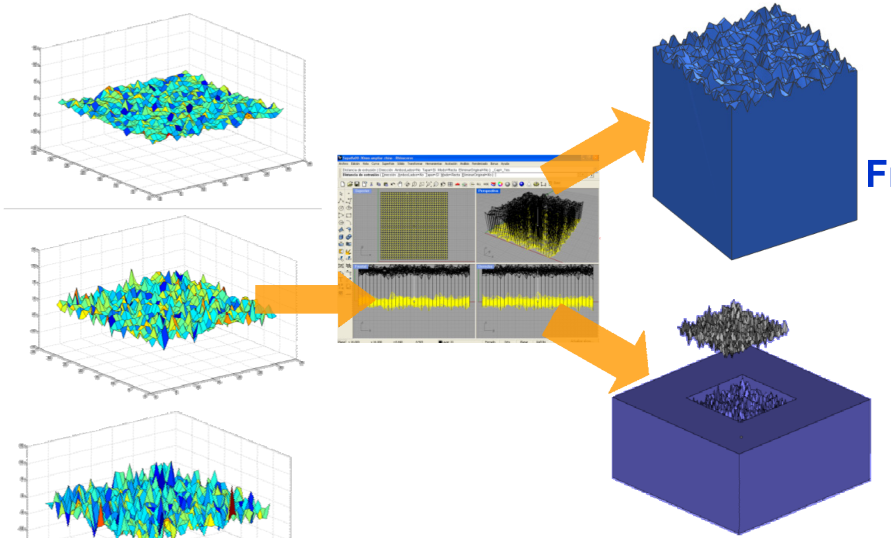
2.- Biomimetic modeling & manufacturing strategies

2.3.- Modeling and manufacturing microtextured (bio)materials and (bio)devices

Computer-aided design and engineering of microtextures and topographies



Fractal models for modeling texture

Brownian surface model with control parameter "alfa"

$$z(x,y) = z_0 + \sum_{k=1}^{\infty} C_k \cdot \lambda^{-\alpha k} \cdot \sin(\lambda^k [x \cdot \cos(B_k) + y \cdot \sin(B_k) + A_k])$$

- Díaz Lantada, A.; Pareja Sánchez, B.; Gómez Murillo, C.; Urbieta Sotillo, J..- "Fractals in tissue engineering: toward biomimetic cell-culture matrices, microsystems and microstructured implants". Expert Review of Medical Devices, 10(5), 629-648, 2013.

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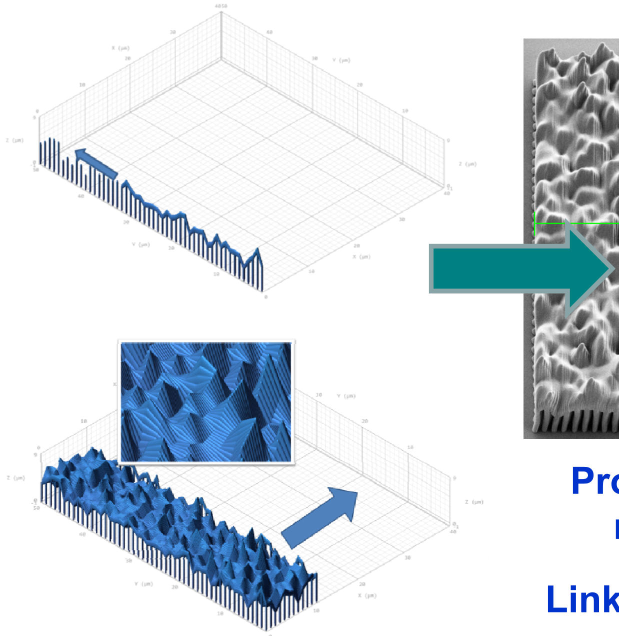
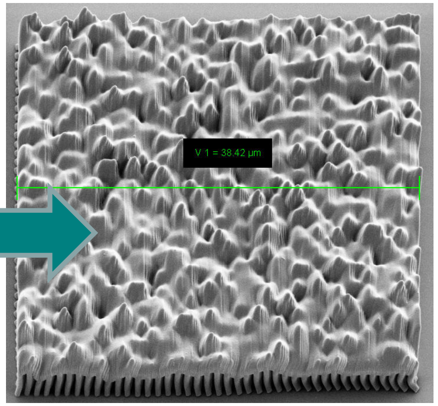
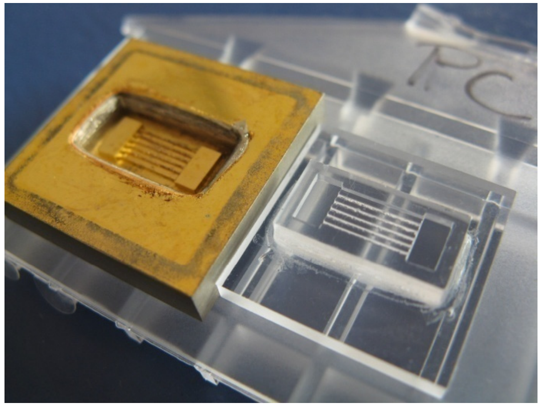
2.3.- Modeling and manufacturing microtextured (bio)materials and (bio)devices

Additive manufacturing applied to obtaining micro-textures and topographies







Prototype of microtextured surface, microtextured mold insert and mass-produced microsystem

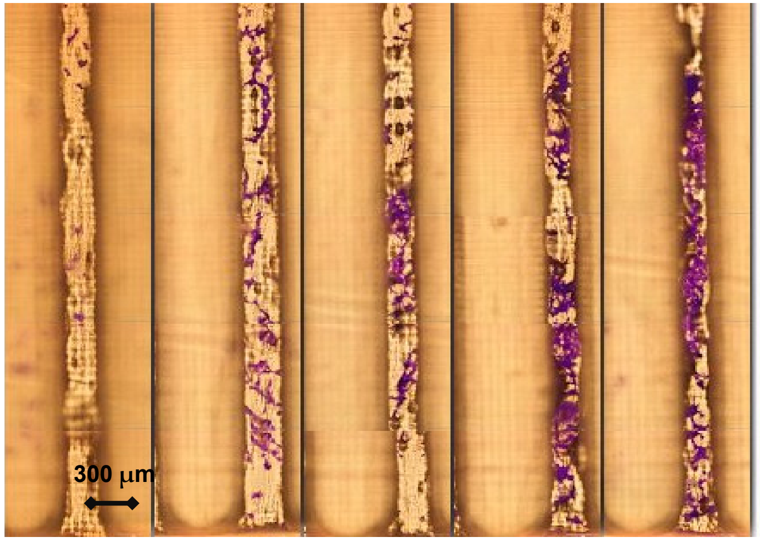
Linking additive manufacturing and mass production

- *Hengsbach, S.; Díaz Lantada, A..- "Direct laser writing of fractal surfaces: Strategy to design and manufacture textured materials". Advanced Engineering Materials, 17(2), 172-180, 2015.*
- *Díaz Lantada, A.; Piotter, V.; Plewa, K.; Barié, N.; Guttmann, M.; Wissmann, M..- "Towards mass production of microtextured microdevices: Linking rapid prototyping with microinjection molding". Int. Journal of Adv. Manufacturing Tech., 2014, Sept. 2014.*

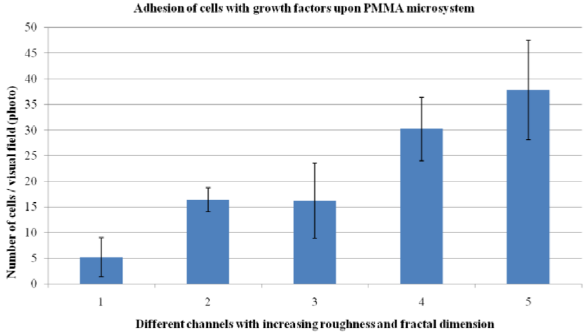
2.- Biomimetic modeling & manufacturing strategies

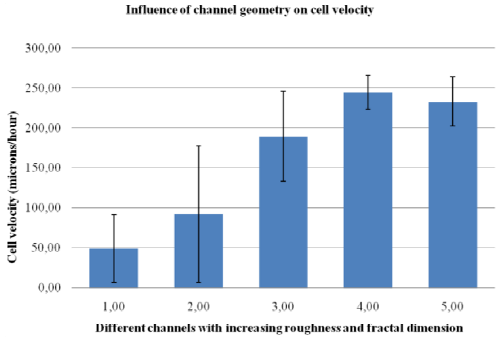
2.3.- Modeling and manufacturing microtextured (bio)materials and (bio)devices

Additive manufacturing applied to obtaining micro-textures and topographies



Cell cultures & pics.
Courtesy of Prof. García-Ruíz, UAM





-Díaz Lantada, A.; Alarcón Iniesta, H.; García-Ruíz, J.P..- "Multi-channeled polymeric microsystem for studying the impact of surface topography on cell adhesion and motility". Polymers, 7(11), 2371-2388, 2015.

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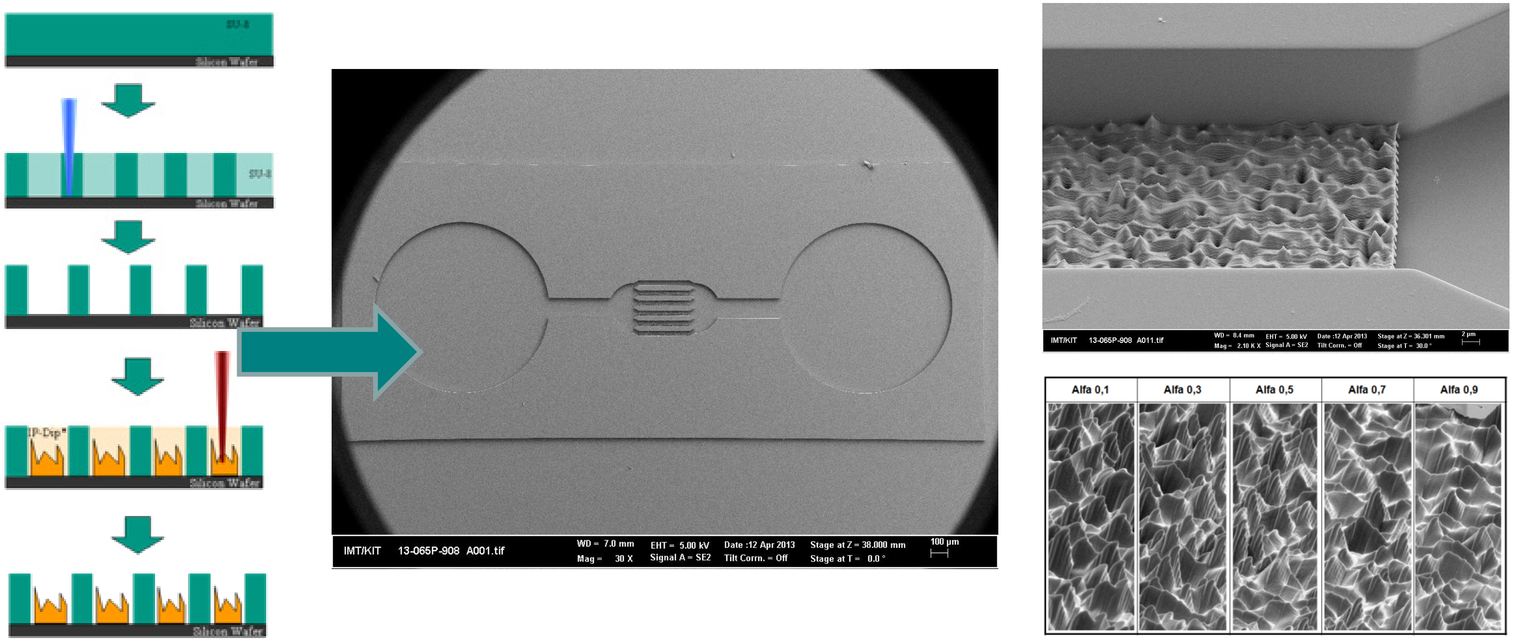
2.4.- Modeling and manufacturing multi-scale (bio)materials and (bio)devices

Combined manufacturing processes applied to obtaining multi-scale geometries



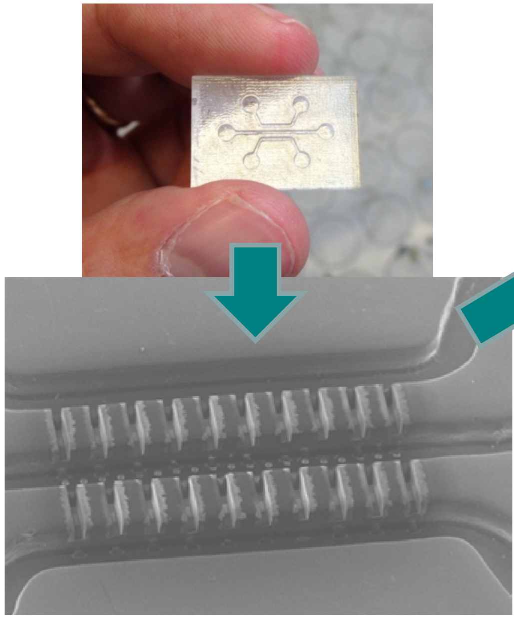
- Hengsbach, S.; Díaz Lantada, A..- "Rapid prototyping of multi-scale biomedical microdevices by combining additive manufacturing technologies". Biomedical Microdevices, 16(4), 617-627, 2014.

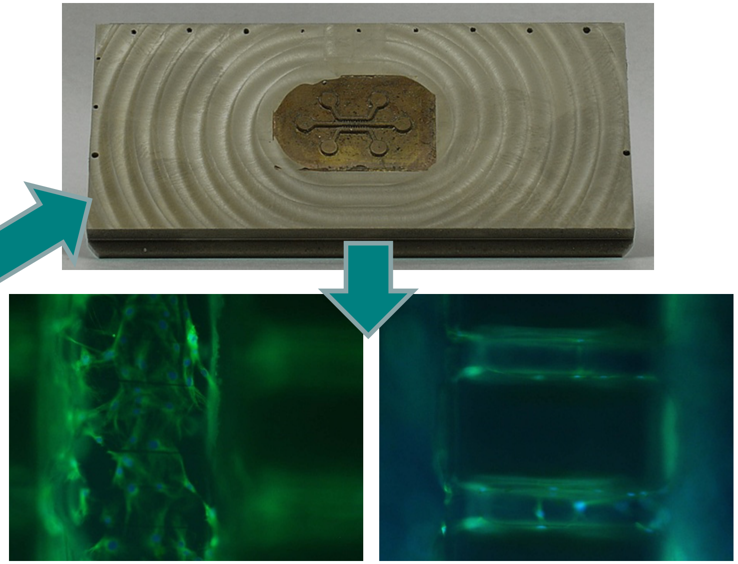
2.- Biomimetic modeling & manufacturing strategies

2.4.- Modeling and manufacturing multi-scale (bio)materials and (bio)devices

Combining additive manufacturing, laser ablation and metallization towards mass production via micro-injection molding: Application to organs-on-chips

Liver-on-chip device





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- Díaz Lantada, A.; Begasse, G.; Morss Clyne, A.; Hengsbach, S.; Piotter, V.; Smyrek, P.; Plewa, K.; Guttmann, M.; Pfleging, W..- "Towards reliable organs-on-chips and humans-on-chips". Spriger's Handbook on Biomedical Microdevices for Interacting at a Cellular Level. In press, 2016.

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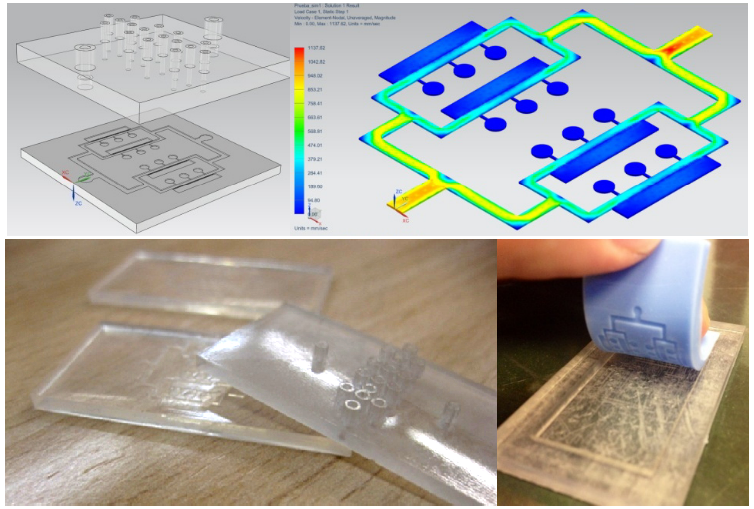
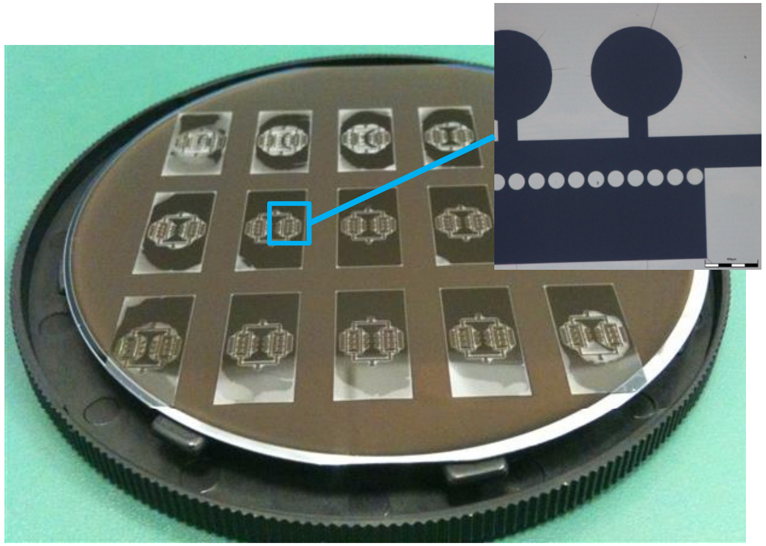
2.- Biomimetic modeling & manufacturing strategies

2.4.- Modeling and manufacturing multi-scale (bio)materials and (bio)devices

Combining additive manufacturing, laser ablation and metallization towards mass production via micro-injection molding: Application to organs-on-chips

Blood-brain barrier on chip





Laser stereolithography + soft lithography

Direct laser writing for enhanced precision

3.- Current challenges and future proposals

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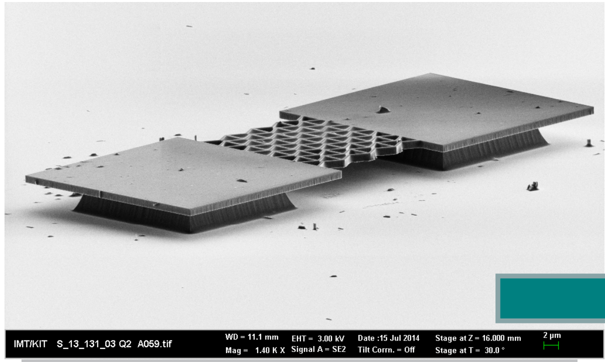
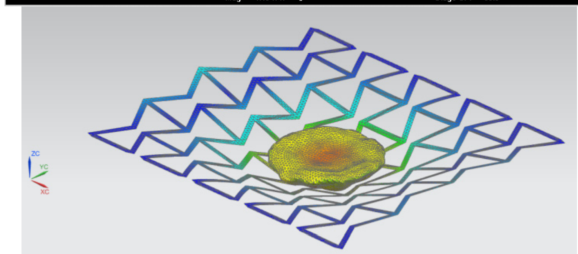
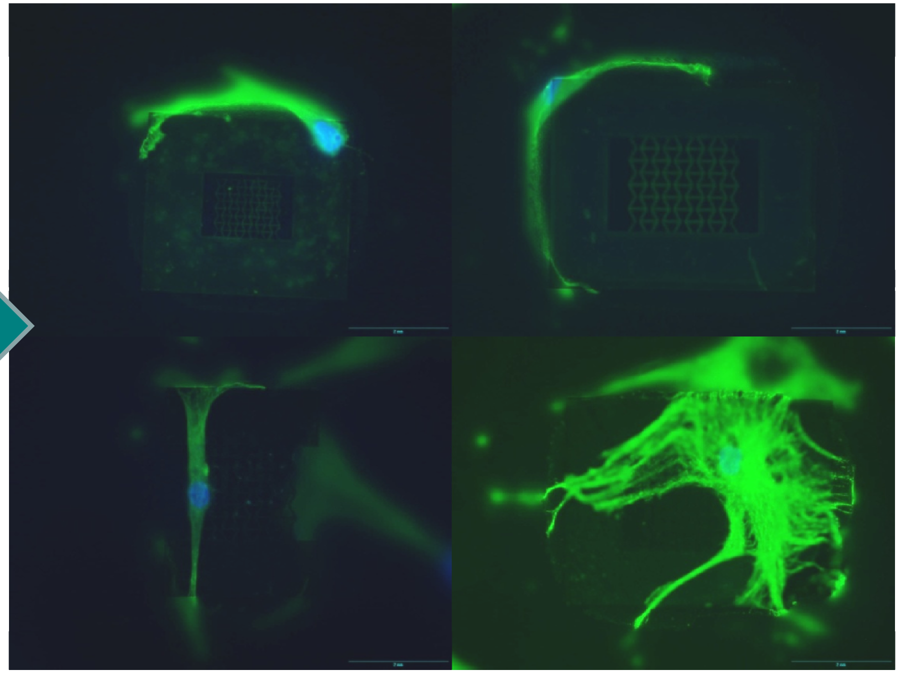
3.1.- Current technological limits and challenges

Multi-scale modeling and manufacturing processes are needed

Precision and part size are linked in micro-/nano-manufacturing technologies







- Díaz Lantada, A.; Muslija, A.; García-Ruíz, J.P..- "Auxetic tissue engineering scaffolds with nanometric features and resonances in the megaHertz range". Smart Materials and Structures, 24, 2015.

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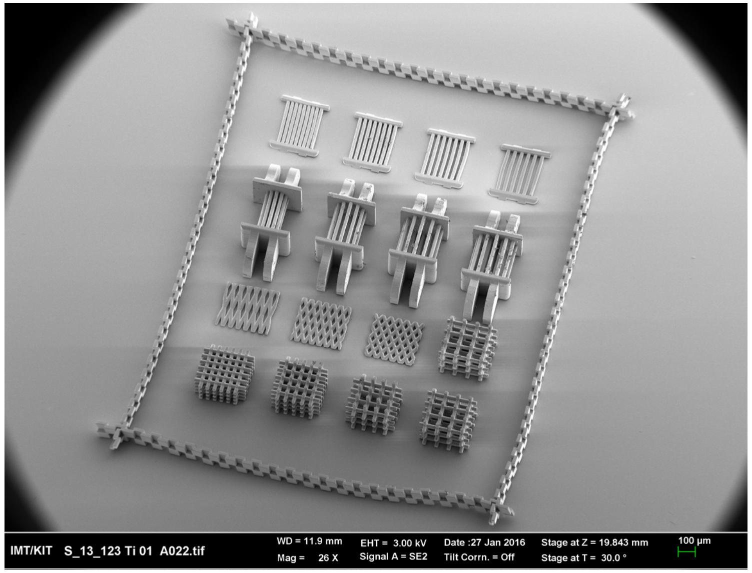
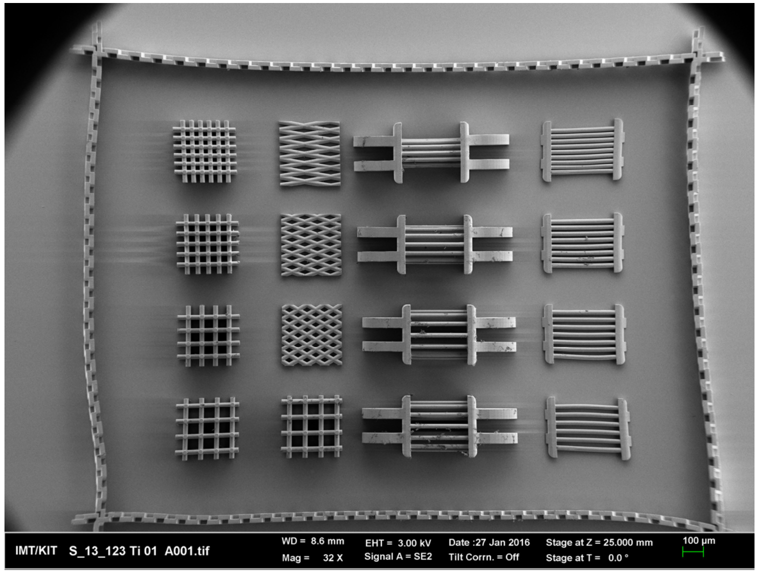
3.- Current challenges and future proposals

3.1.- Current technological limits and challenges

Multi-scale modeling and manufacturing processes are needed

Precision and part size are linked in micro-/nano-manufacturing technologies





Nano "playground" for cells: Multi-culture platform for studying the impact of several extracellular matrices on cell behavior in a single experiment

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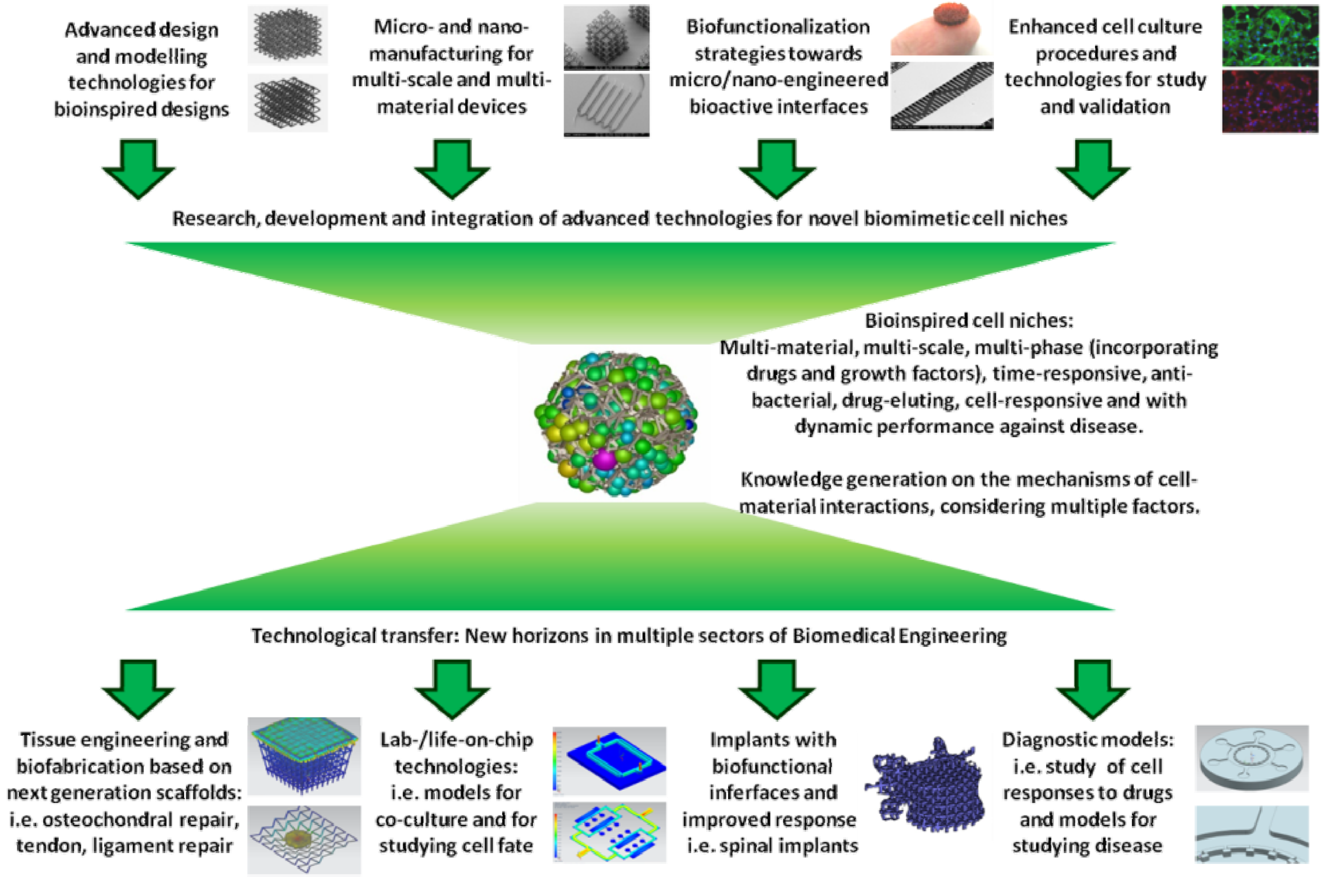
3.- Current challenges and future proposals

3.2.- Future proposals and research directions



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4.- Main conclusions

Main conclusions:

-Designing, modeling and manufacturing biomimetic materials may enhance the performance of several types of biomedical devices.

-Strategies for taking into account the common porosities, hierarchical geometries and textures of biomaterials have been described.

-Computer aided design and engineering resources help to model and assess the potential performance of the proposed biomaterials, even integrated into complex devices.

-Combining advanced manufacturing resources constitutes a very adequate approach for the development of new biomaterials and their integration into biomedical microdevices for enhanced performance.

-Solutions developed on the basis of biomimetic approaches have impact in several industries, inlcuding: health, transport, energy, space.

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5.- Personal note

Acknowledgements:

Machines Engineering Division, Product Development Lab, ETSI Industriales UPM:
Pilar Lafont, Pilar Leal, Socorro Martín, Silvia Ortega, Juan Manuel Muñoz, José Luis Muñoz, Javier Echavarri, Enrique Chacón, Julio Muñoz, Pedro Ortego, Antonio Sillero, Adrián de Blas, Alejandro Abou-Assali, Ely Dannier V. Niño

Karlsruhe Nano-Micro Facility, Helmholtz Research Facility, Karlsruhe Institute of Technology:
Dieter Maas, Stefan Hengsbach, Alban Muslija, Volker Piotter, Klaus Bade, Markus Guttmann, Wilhelm Pfleging, Klaus Plewa, Markus Wissmann, Peter Smyrek, Nicole Barie, Thomas Schaller, Jürgen Mohr, colleagues from KNMF & KIT

Molec. Biology Dpt., Univ. Autónoma de Madrid:
Josefa Predestinación García Ruíz, Hernán Alarcon Iniesta

Institute of Materials Science and Technology, Tech. Univ. of Viena: Jürgen Stampfl

Lithoz GmbH:
Johannes Homa, Martin Schwentenwein

Vascular Kinetics Lab. Drexel University:
Alisa Morss Clyne

SENTI, University of Cranfield:
José Luis Endrino

H2020 Tomax Project:
Tool-less manufacture
of complex geometries

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Biomedical microsystems for interacting at a cellular level

THANKS FOR YOUR ATTENTION

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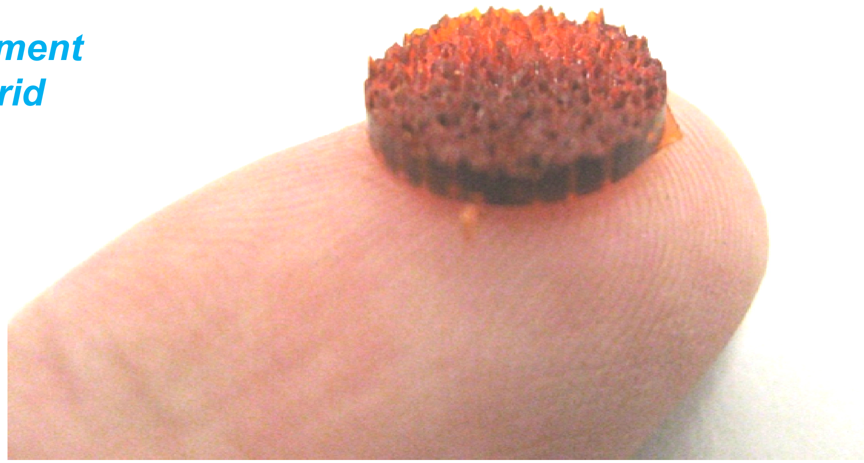

Industriales Research Meeting 2016, Madrid, April 20th