La reconstruction d'organes par Impression 3D

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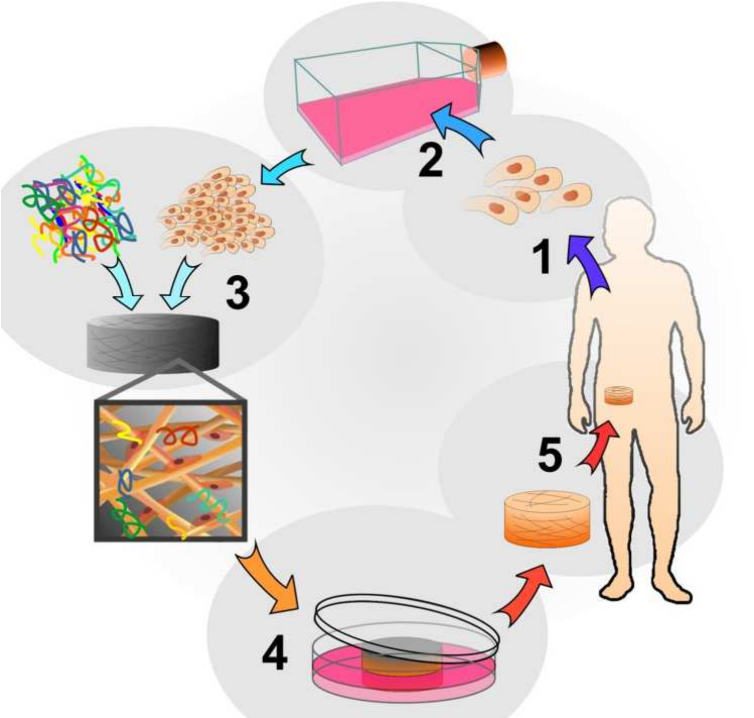
Context: Tissue Engineering



C Blitterswijk, Book Tissue Engineering (2008)

Challenges:

- Tissue Complexity
- Vascularization
- Cost-effectiveness
- Customization
- Skin graft
- Safety
- Regulation

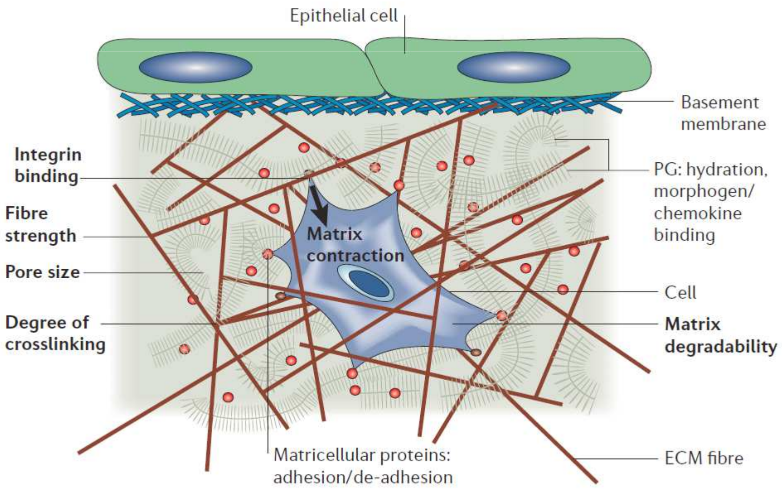
> “Tissue Engineering needs process engineering”

D. Williams, Nature Biotechnology (2005)

Tissue Complexity

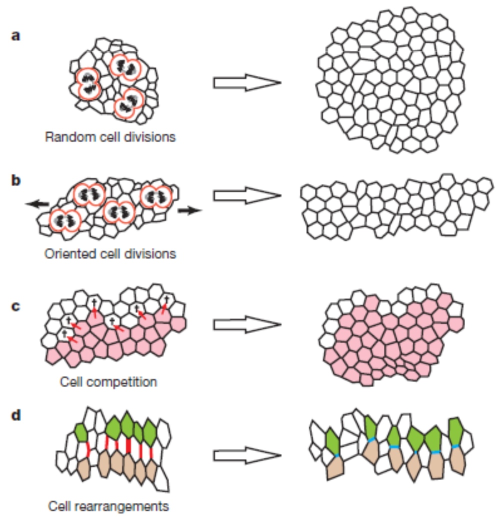
Dynamic interactions between: (stem)-cells, morphogens and extracellular matrix

cell fate



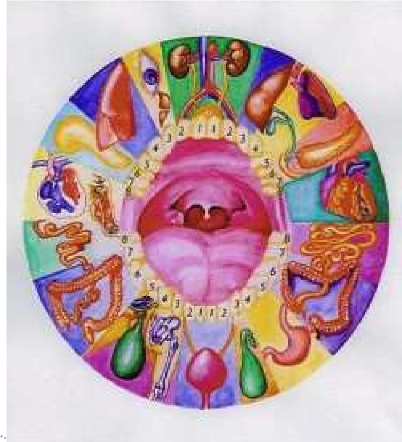
Griffith *et al*. Nature Rev. Mol. Cell Biol, 2009

tissue formation



Lecuit & Le Goff, Nature (2007)

Homeostasis



At cell level:

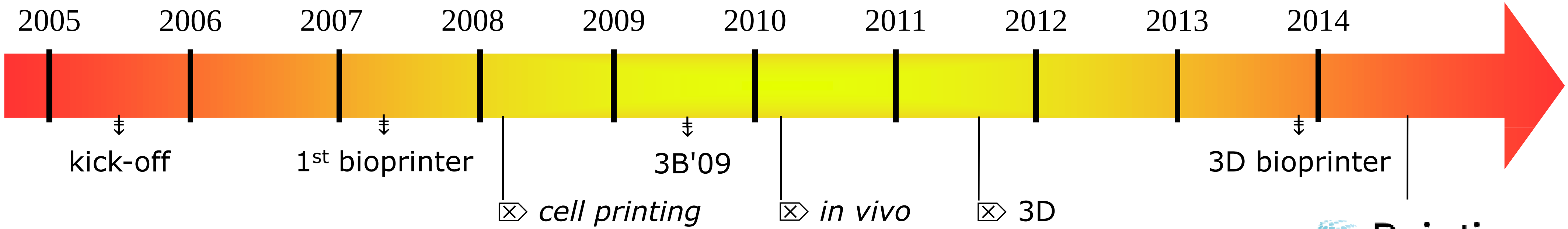
- nanotopography
- stiffness
- ligand density
- growth factors
- cell neighbors
- …

gradients, patterns

At tissue level:

- cell migration
- collective behavior
- cell sorting
- …

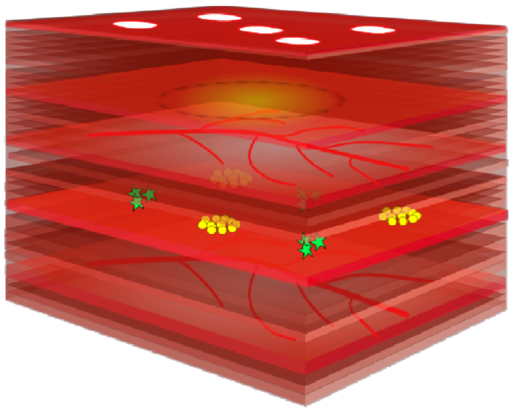
Our approach: dealing with tissue complexity using Bioprinting



Poietis
makes tissue real

→ controlling 3D distribution of cells and cues using Laser-Assisted Bioprinting

→ driving tissue self-organization (4th D) to produce functional tissues

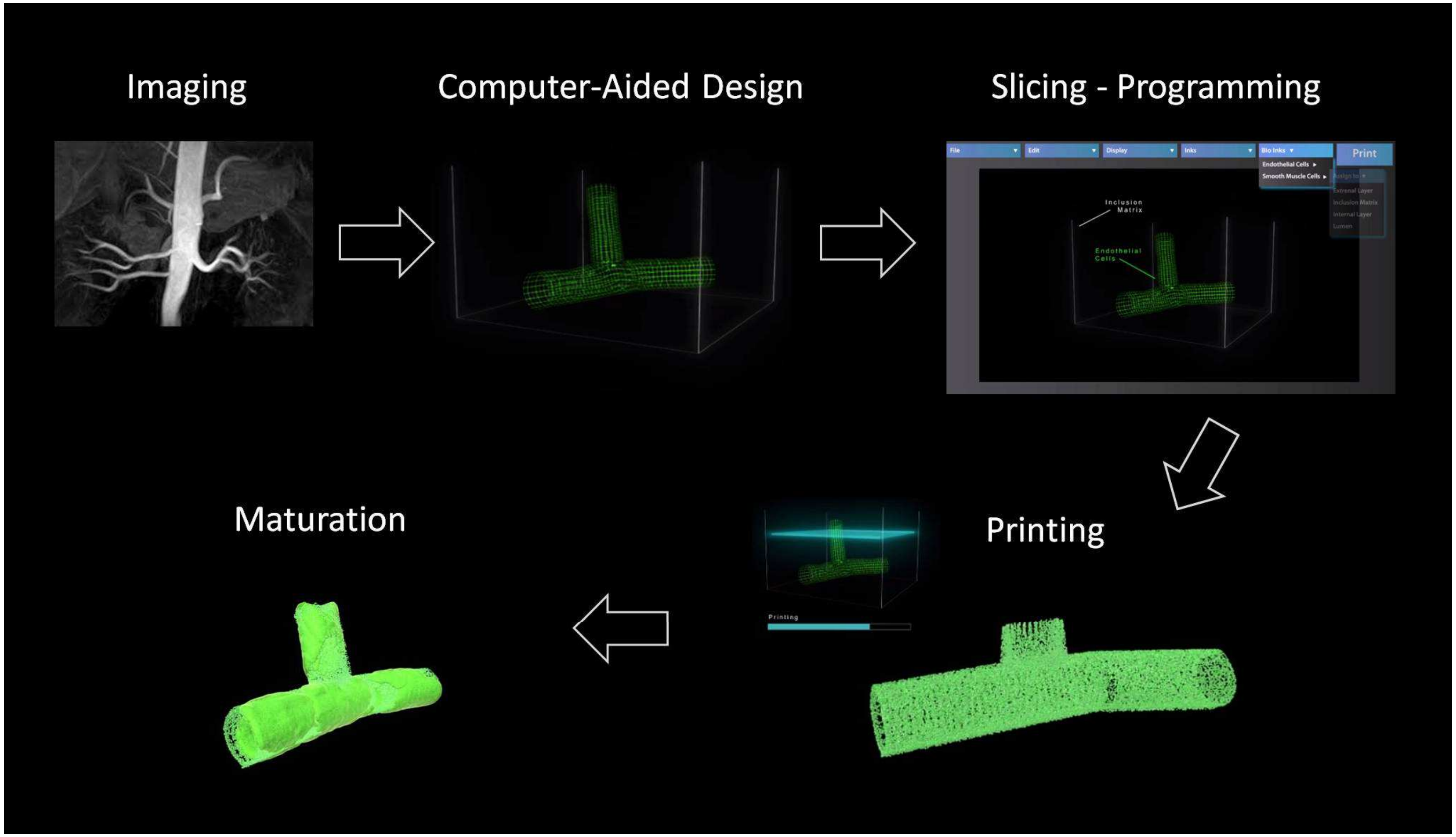


B. Guillotin & F. Guillemot, Trends in Biotechnology (2011)

3D Printing + Biology = Bioprinting

"Transformational technology"

Gartner Institute, 2012



Duality digital - biology ➡ Robotized fabrication of complex, personalized tissues

Bioprinting: an old story

Experimental Cell Research 179 (1988) 362–373

Cytoscribing: A Method for Micropositioning Cells and the Construction of Two- and Three-Dimensional Synthetic Tissues

ROBERT J. KLEBE

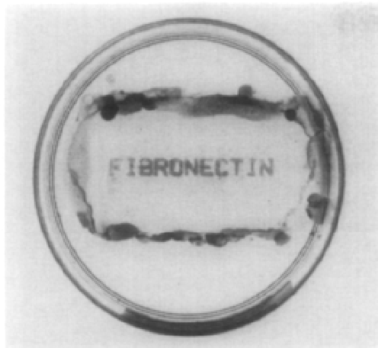
Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, Texas 78023

In the present study, a technique, termed cytoscribing, is described which enables one to establish precise spatial interrelationships between cells. In essence, cytoscribing involves the use of a computer for the high-precision positioning of cells. It is demonstrated that either an ink jet printer or a graphics

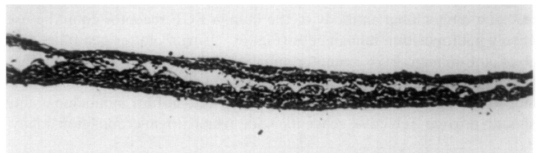
Deposition of fibronectin on substrata. Cytoscribing was carried out with either a Hewlett Packard 2225C Think Jet ink jet printer or a Hewlett Packard 7470A graphics plotter. In this study, the word "fibronectin" was cytoscribed in fibronectin (a) by using the word processing package, Displaywrite 3, in conjunction with the ink jet printer or (b) by using a plotter controlled by a simple BASIC program.

With the aid of the methods described here, a three-dimensional tissue form could be constructed by stacking two-dimensional tissues in layers. Thus, cytoscribing provides a facile means of establishing precise spatial arrangements within large populations of cells and, thereby, permits new approaches to be made toward understanding the mechanisms involved in morphogenesis. Development of the technology described here should aid in the production of artificial tissues [8, 26] which resemble natural tissues and organs.

inkjet



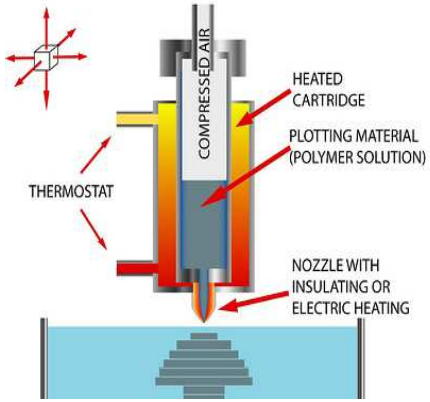
graphics plotter



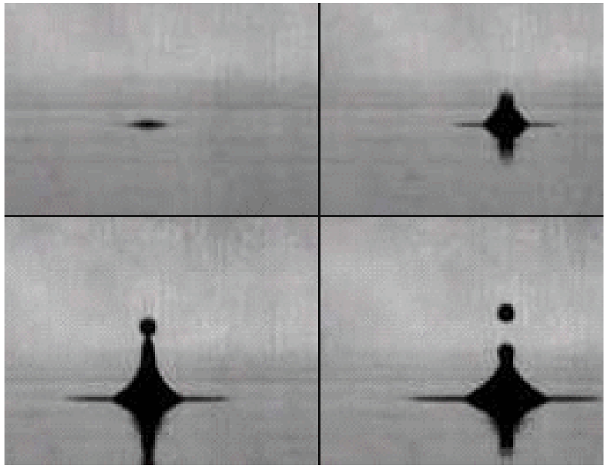
First 3D assembly : 2 layers of collagen

Bioprinting technologies

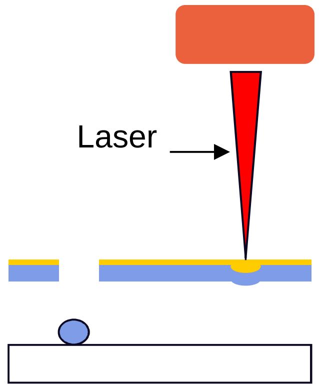
Inkjet (thermal, piezo)



Bioplotting
(extrusion through syringe)

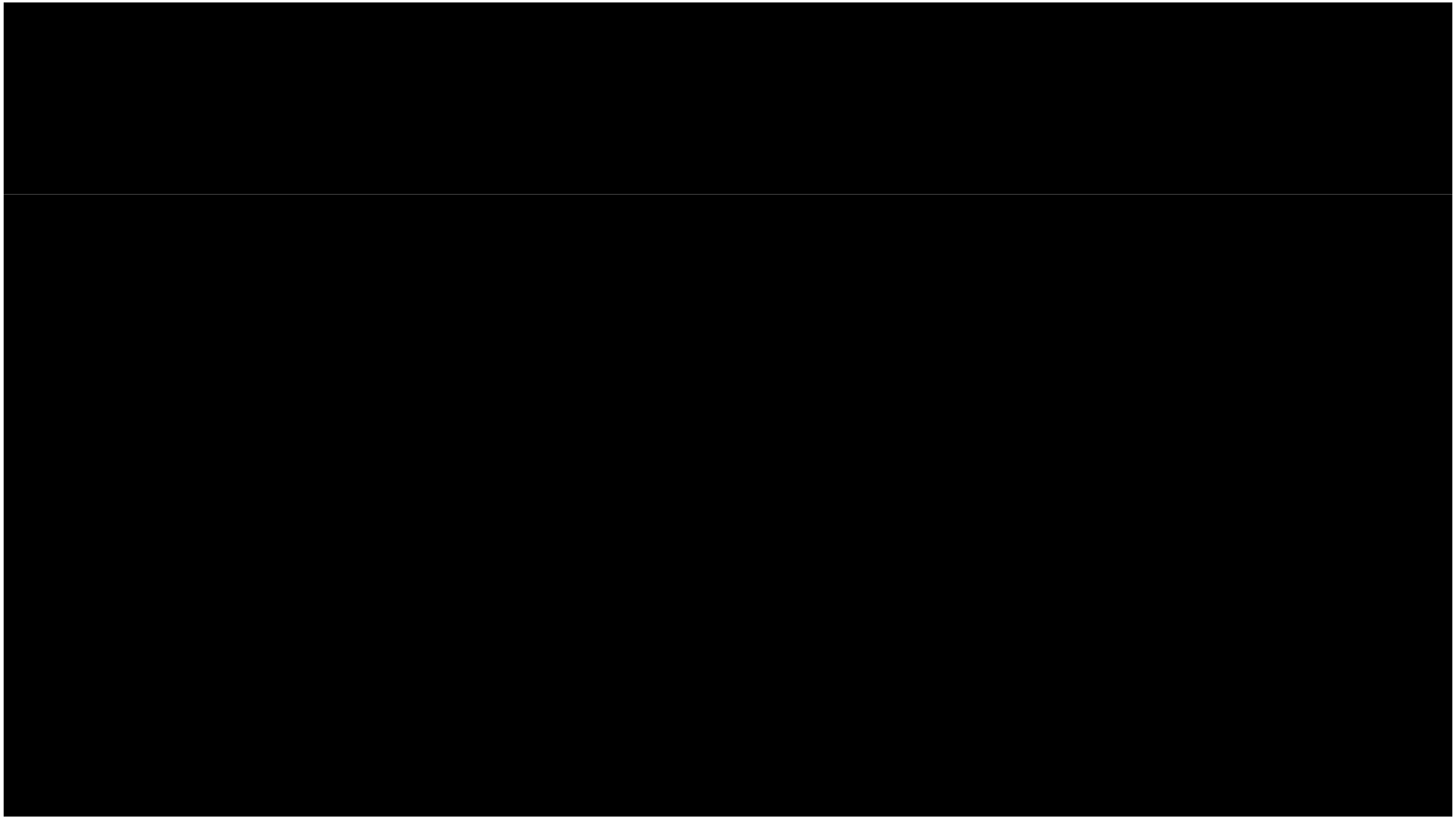


Acoustic Droplet Ejection



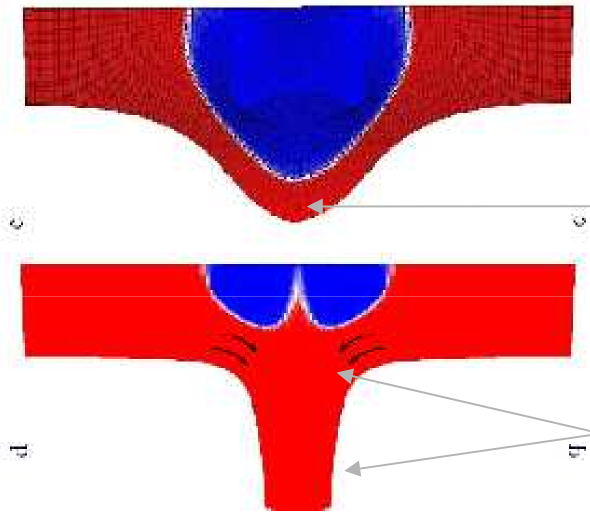
Laser - Assisted Bioprinting

Laser-Assisted Bioprinting (principle)



Numerical modeling of jet formation

Hydrocode CHIC (CELIA)



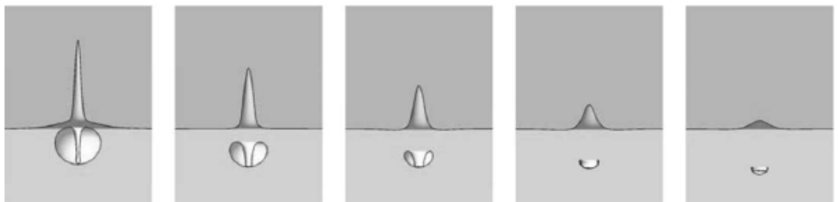
High pressure in the apex area (singular point)

2 jets are created:
→ bubble collapsing
→ droplet ejection

Mezel *et al*. Phys. Plasma (2009)

Interaction of the bubble with the free surface:

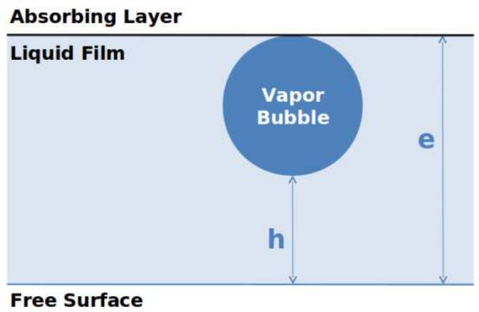
by analogy to studies on cavitation → dimensionless coefficient:



(a) $\gamma = -0.45$. (b) $\gamma = -0.65$. (c) $\gamma = -0.80$. (d) $\gamma = -1.00$. (e) $\gamma = -1.30$.

$$\Gamma = h / R_{max}$$

- h → film thickness
- R_{max} → E, viscosity



(Pearson, Engineering Analysis with Boundary Elements, 2004)

Development of Laser-Assisted Bioprinters

1st bioprinter: delivered in 2007
(a collaboration with NovaLase S.A.
(Canéjan, France))

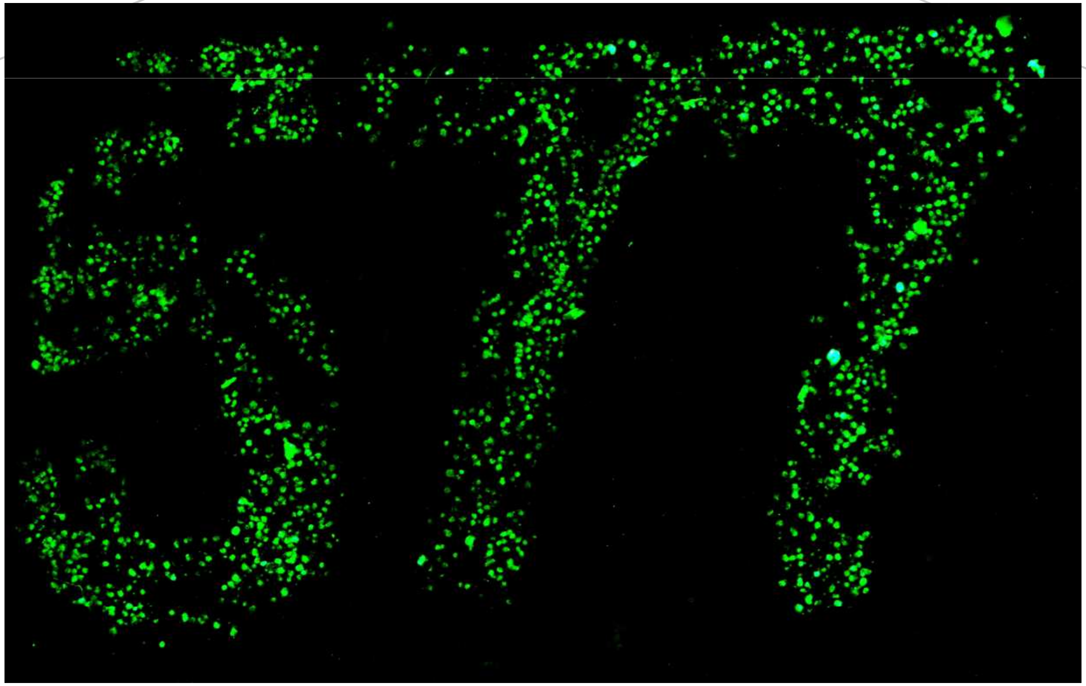
2nd bioprinter: delivered end-2013
(a collaboration with Alphanov (Talence, France)

Cell printing: main focus

Cell function

Viability

Resolution



Multicolor printing

Speed / high throughput

Critical parameters for controlling cell viability

Cell injuries may be associated with:

i) bioink composition (e.g.: glycerol),

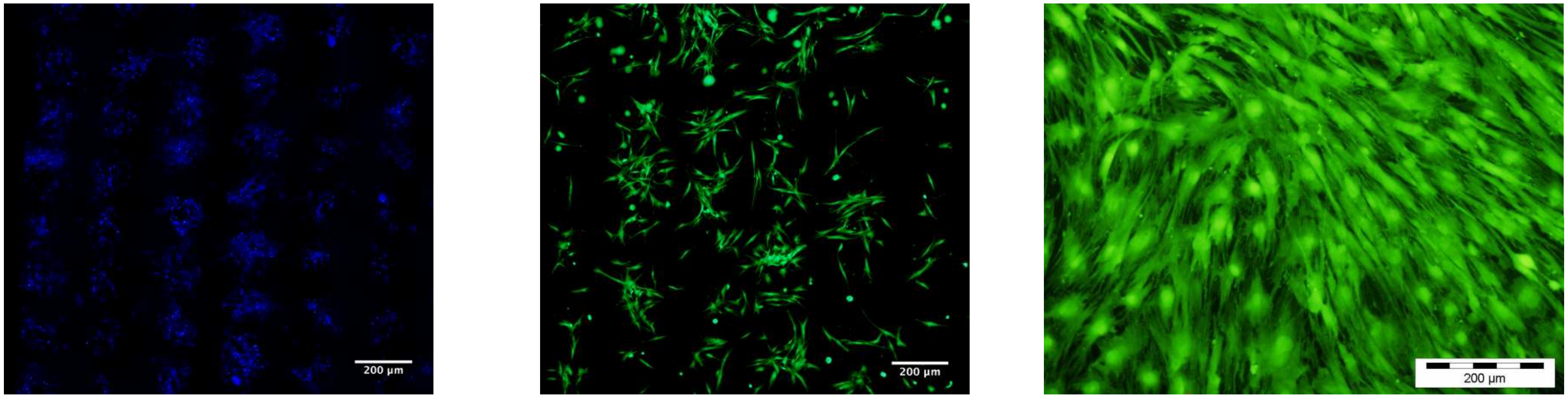
ii) interactions of cellular components with light (UV → DNA),

iii) thermal effect

iv) pressure generated during bubble growth,

v) shear stress within the jet (viscosity, jet speed)

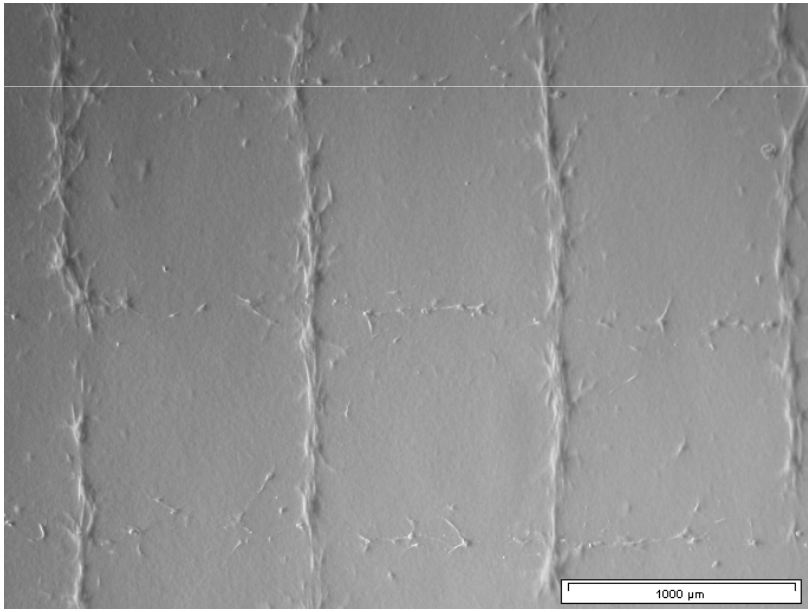
vi) landing conditions (hydrogel thickness + ink viscosity)

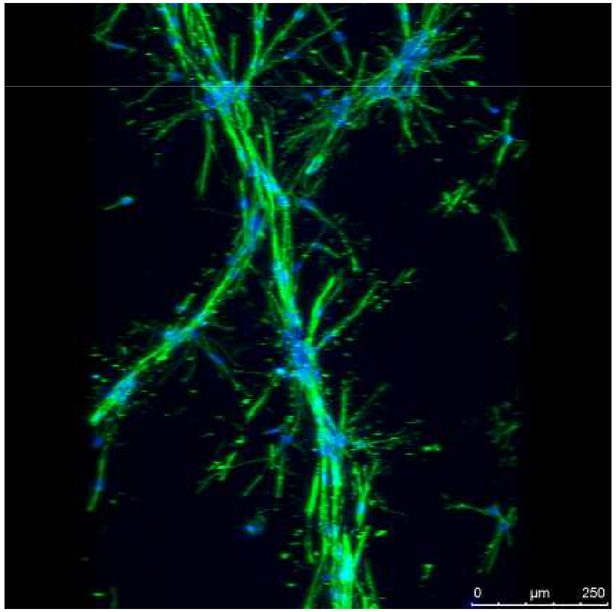


Day 0 Day 2 Day 15

Viability of Human Osteoprogenitors (HOP) after printing (Live/dead assay)

Current project: 3D bioprinting of human cornea



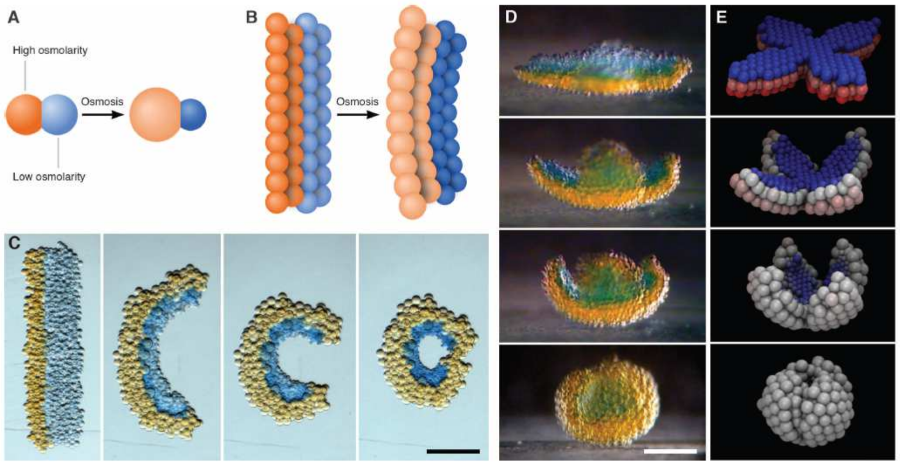


→ Bioprinting human keratocytes

4D Bioprinting: 4th Dimension is self-organisation

".. to create objects that can change after they are printed, making them self-adapting. The act of printing is no longer the end of the creative process but merely a waypoint."

S. Tibbits (MIT)



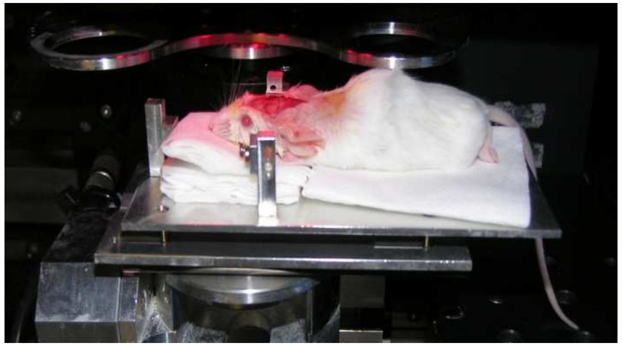
G. Villar *et al*., Science (2013)

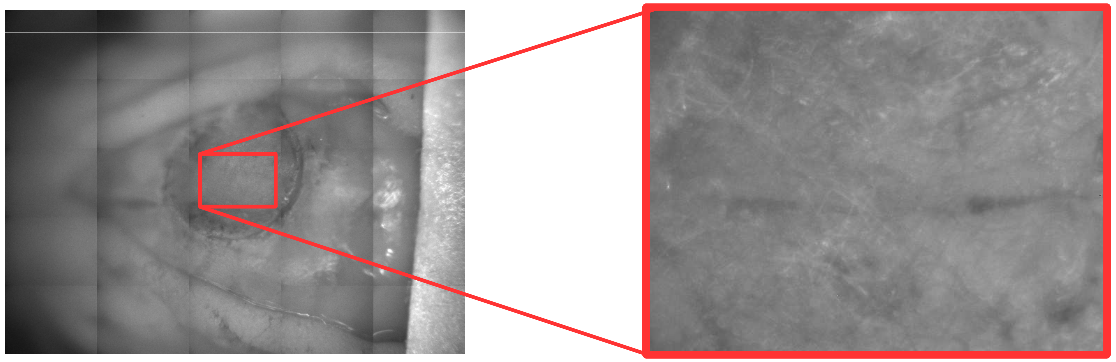
Mesenchymal stem cells onto collagen

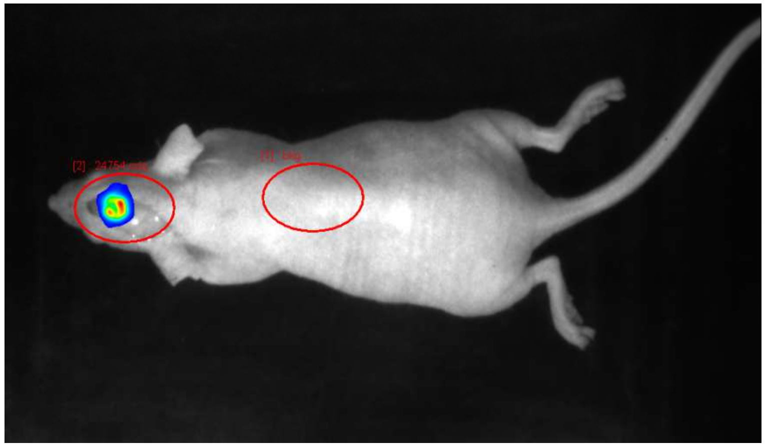
Bioprinting *in vivo*, *in situ*

Aim: demonstrating feasibility of bioprinting *in vivo*

→ Bioprinting mesenchymal stem cells into mouse critical size bone calvaria defect







Start-up

On demand fabrication of human tissues for:

- research (pharma and cosmetic industry)
- Personnalized medicine
- grafting (regenerative medicine)

Emergence, 2012

La reconstruction d'organes par impression 3D

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