3D Bioprinting of tissues and organs: new technologies aimed at medicine 4.0

Biologization of Technology and Manufacturing

BRAGFOST 2018

Janaina Dernowsek, PhD

Reseacher at CTI Renato Archer

www.biofabricação.com

jadernowsek@gmail.com

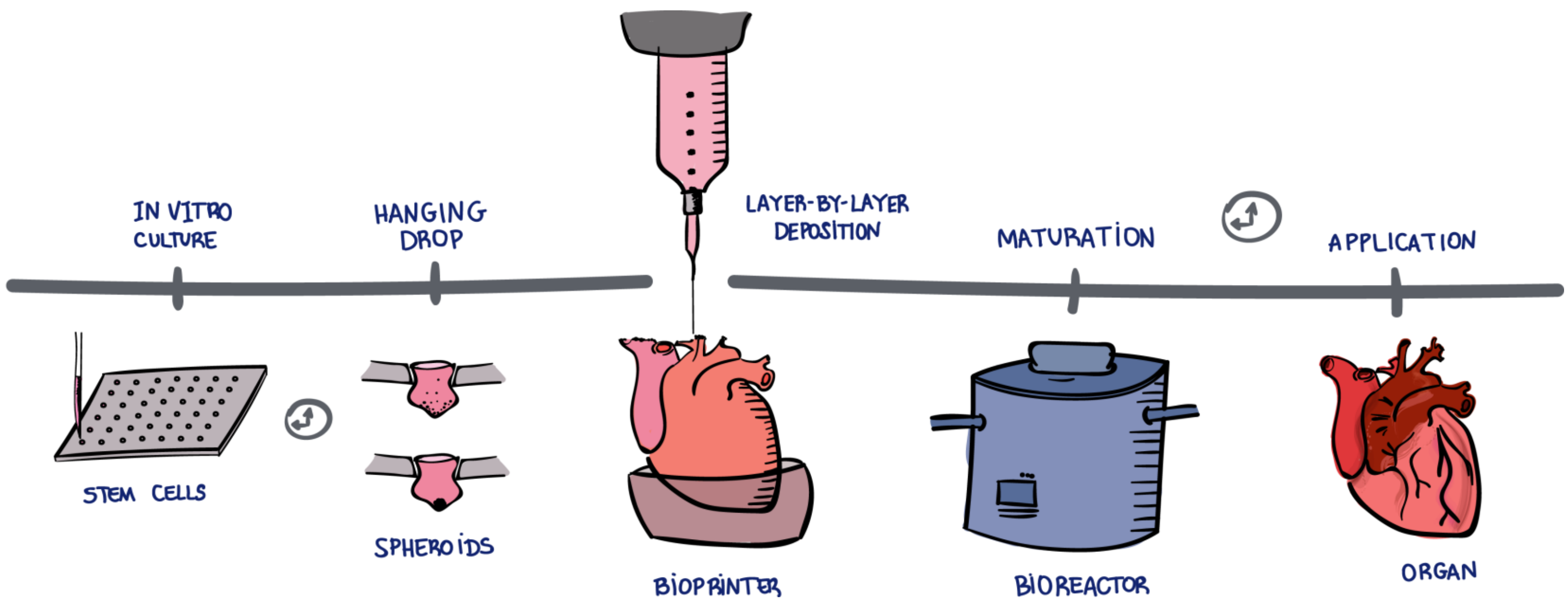
Bio3Data

Founder

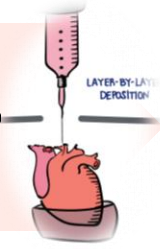
bio3data@gmail.com

Topics

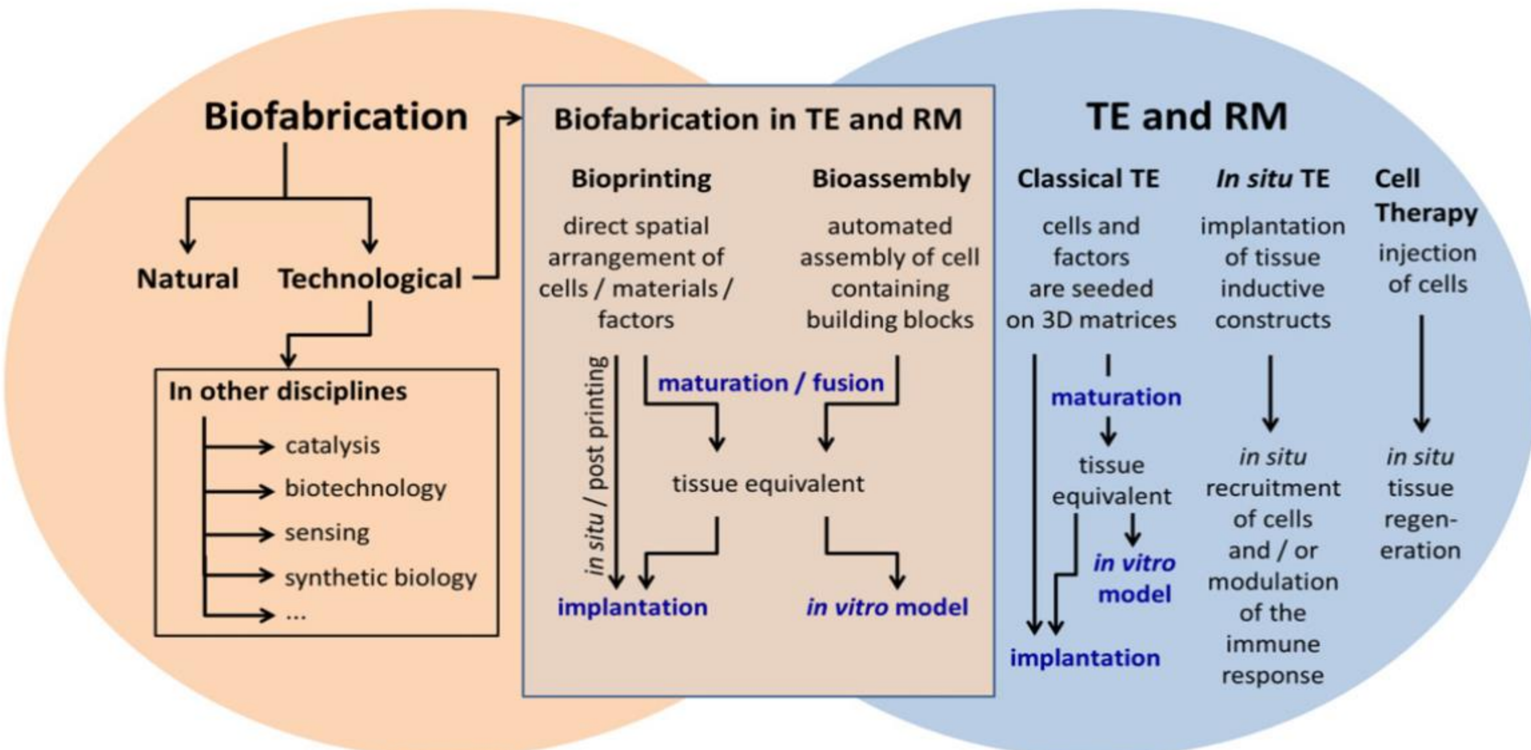
- Biofabrication;
- Bioprinting;
- Technologies;
- Applications;
- Challenges;
- Bioprinters;
- Companies;
- Bioprinting Projects at the CTI Renato Archer and in the world.



What is Biofabrication and 3D Bioprinting?

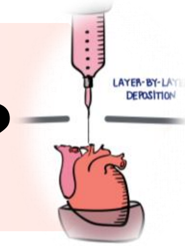


The term biofabrication is used for tissue engineering and 3D printing as
“the automated generation of biologically functional products with the structural organization from living cells, bioactive molecules, biomaterials, cell aggregates or hybrid cell-material constructs, through Bioprinting or Bioassembly”



J Groll et al., *Biofabrication*, 2016

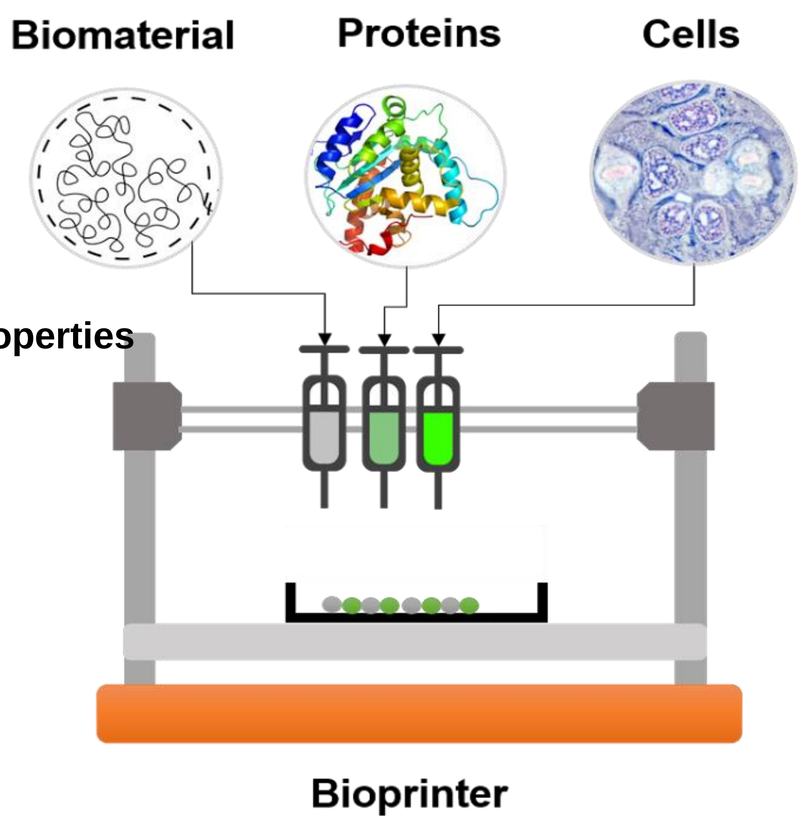
What is Biofabrication and 3D Bioprinting?



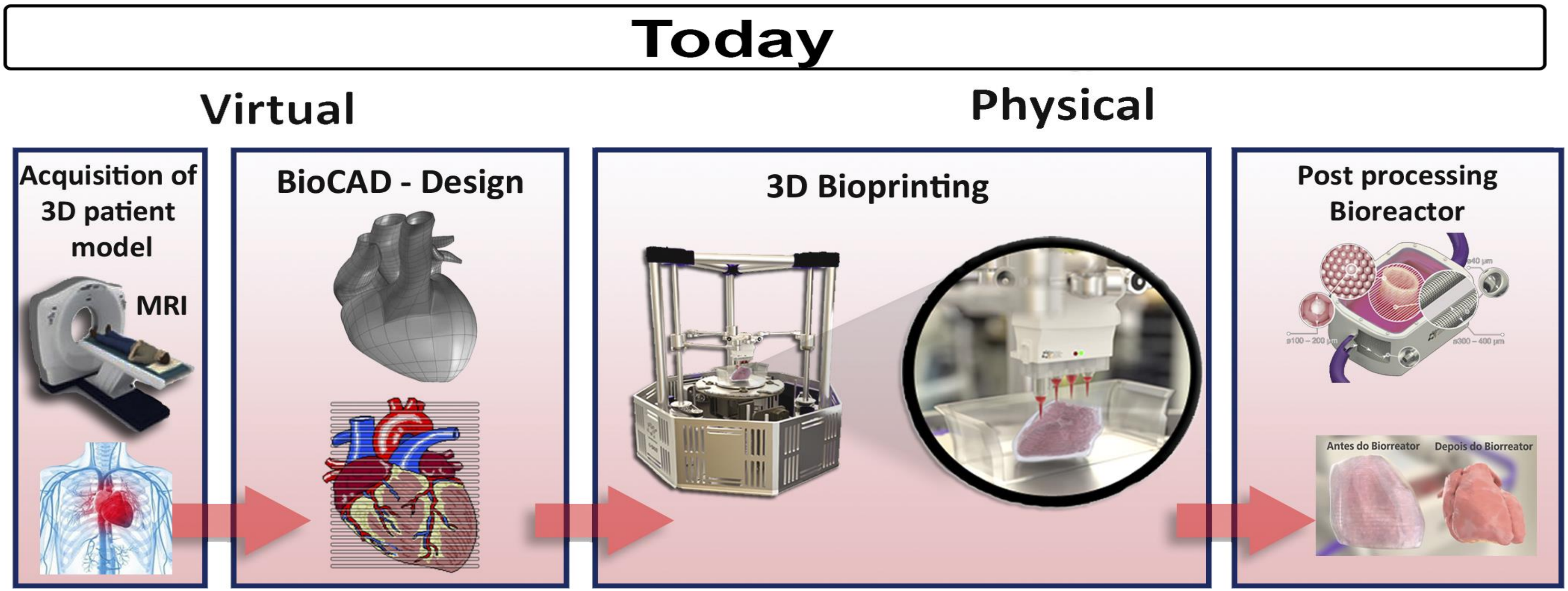
And Bioprinting….

“the automated generation of cell-comprising structure through the spatially-controlled deposition of cells and/or cell containing materials in user defined, geometric patterns”

- **Biocompatible**
- **Degradation**
- **Rheology**
- **Bioprintable**
- **Mechanical properties**

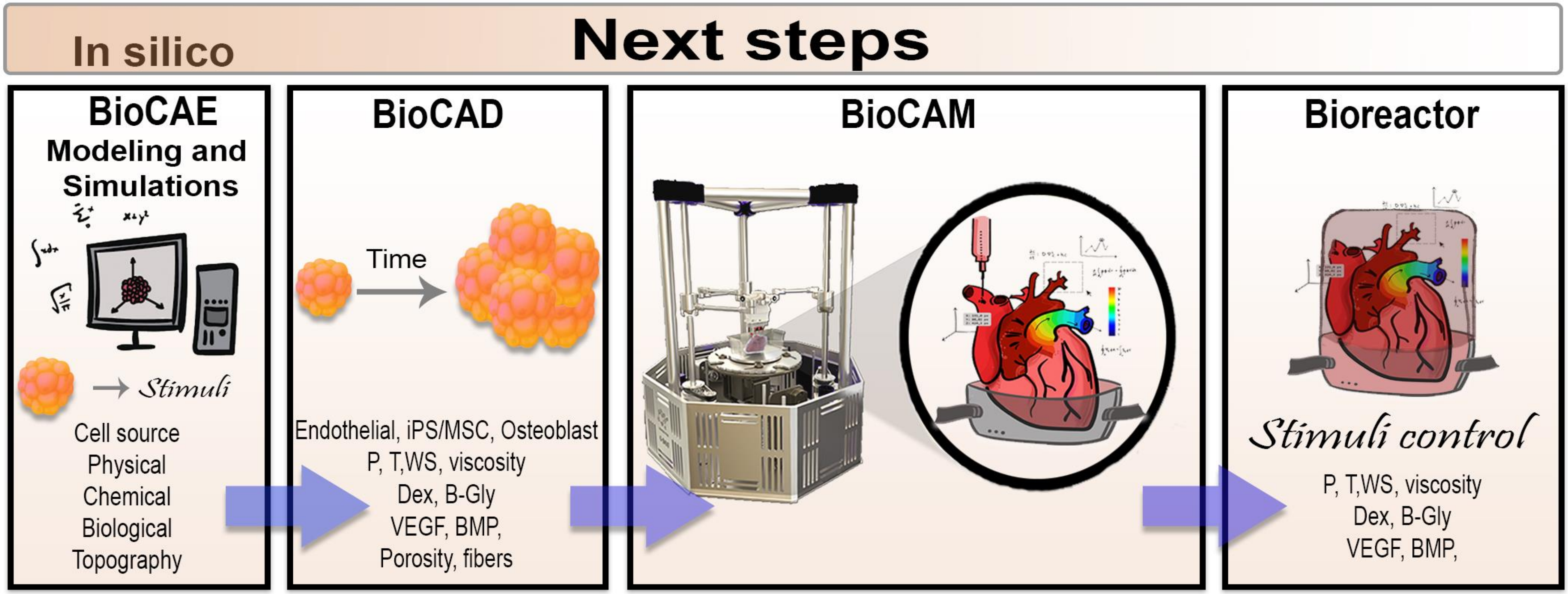


Bioprinting processes



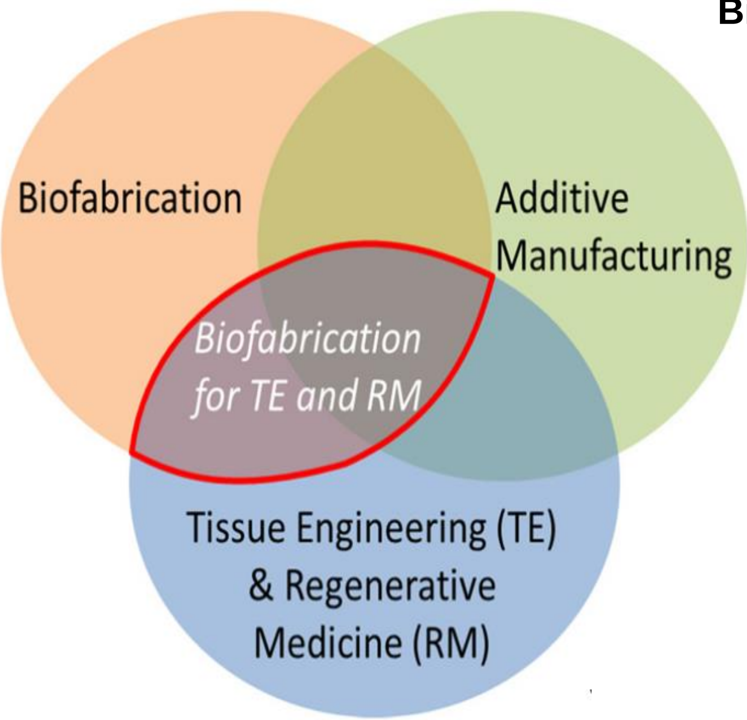
DICOM images → STL file

Bioprinting processes

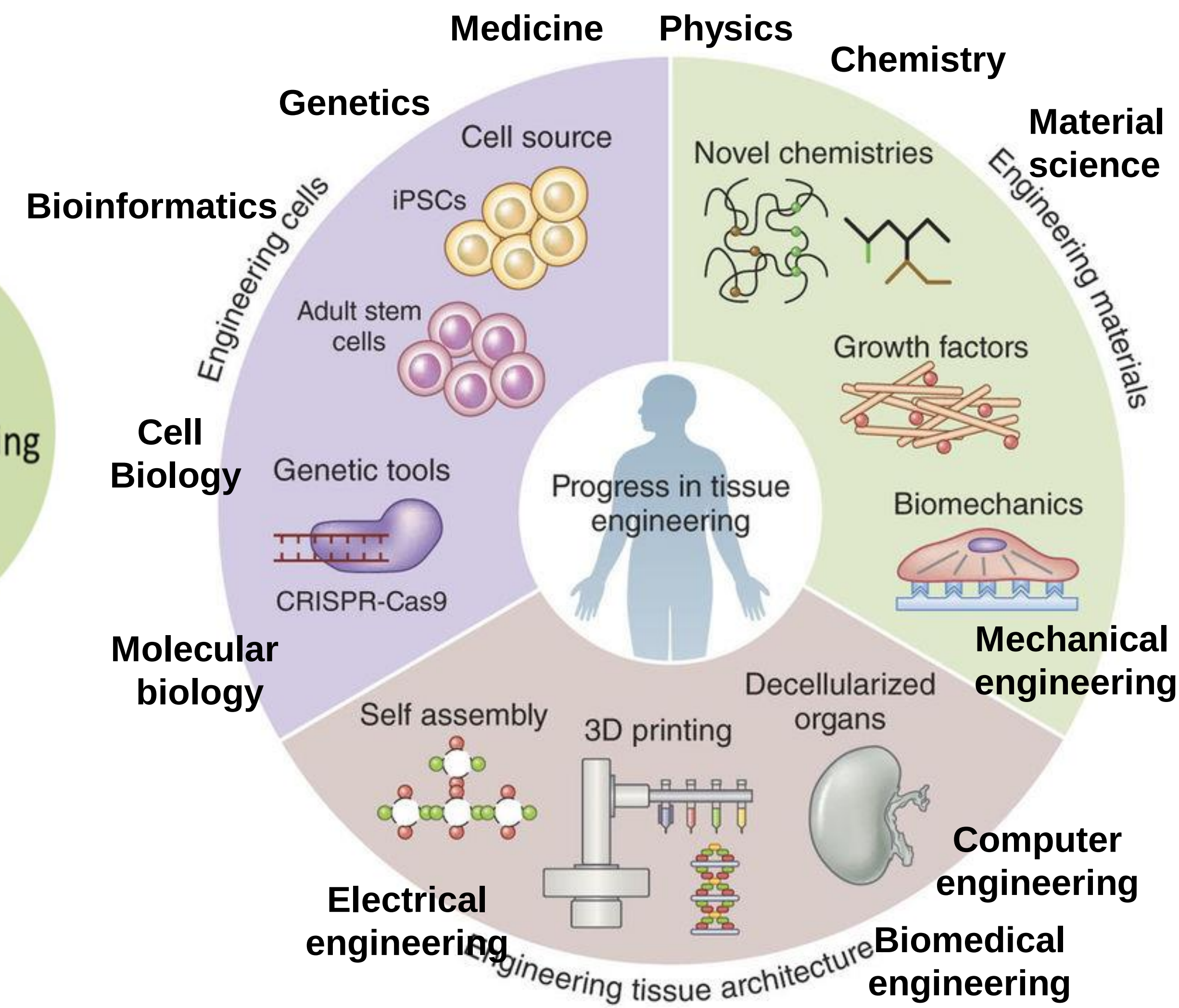


Interrelation between areas

Bioprinting is a multidisciplinary integration technology

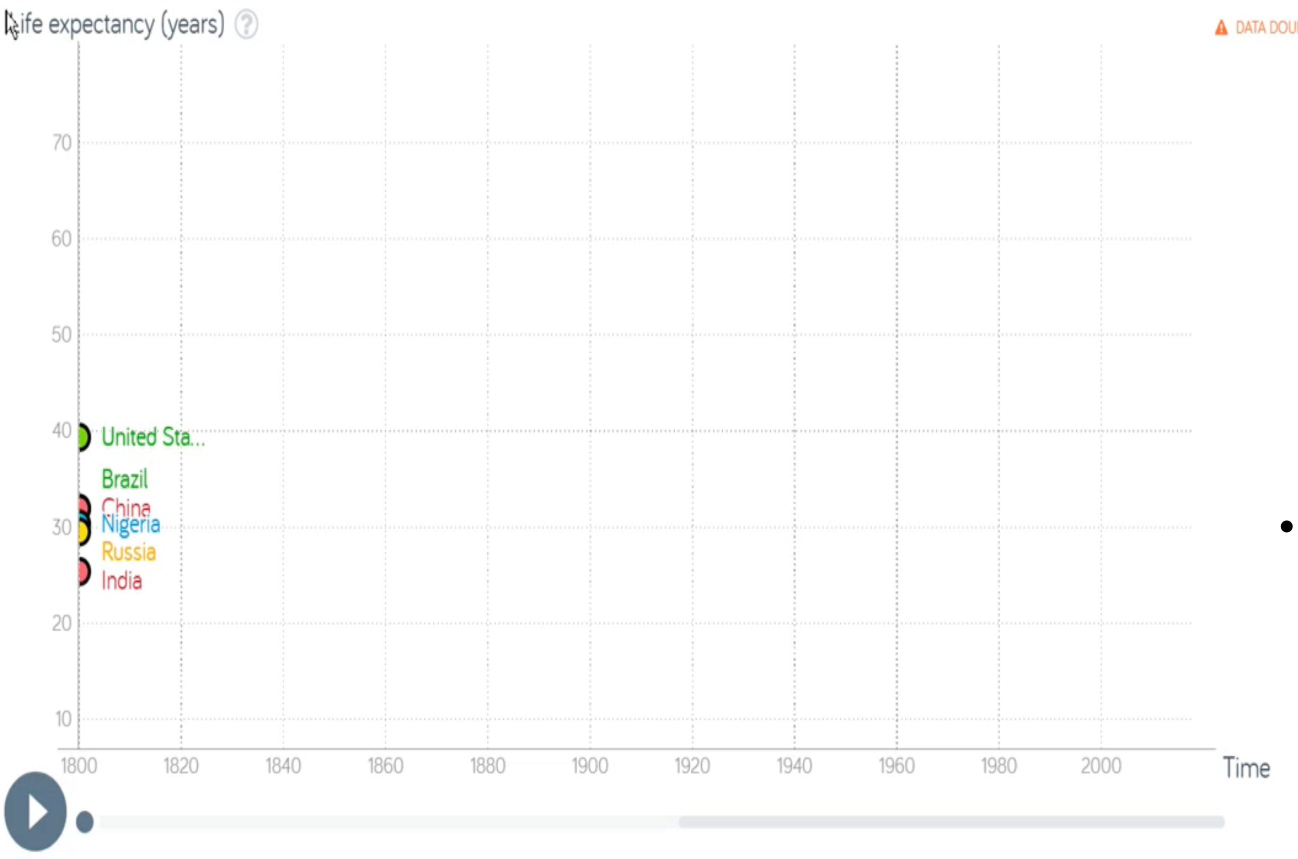


J Grollet al, *Biofabrication*, 2016



Motivation

Life expectancy is increasing globally

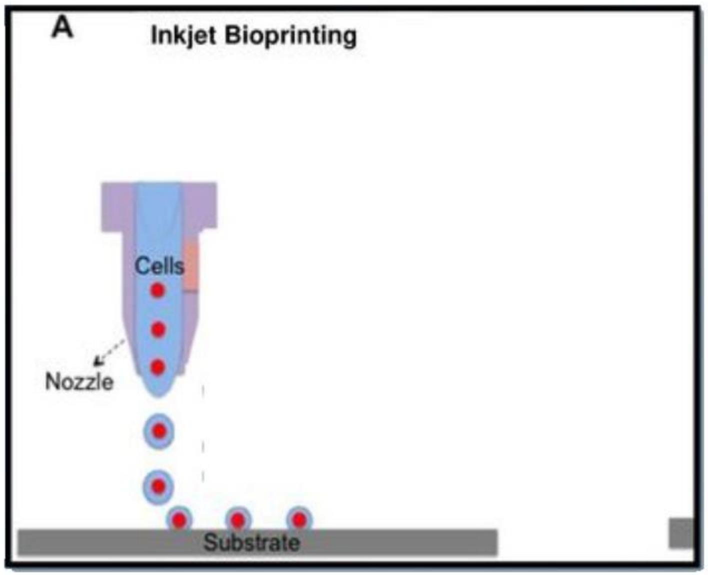


- **Health**
  - Aging
  - Disease
  - Accidents

- **Needs**
  - New treatments
  - New drugs
  - New methods of analysis and diagnosis

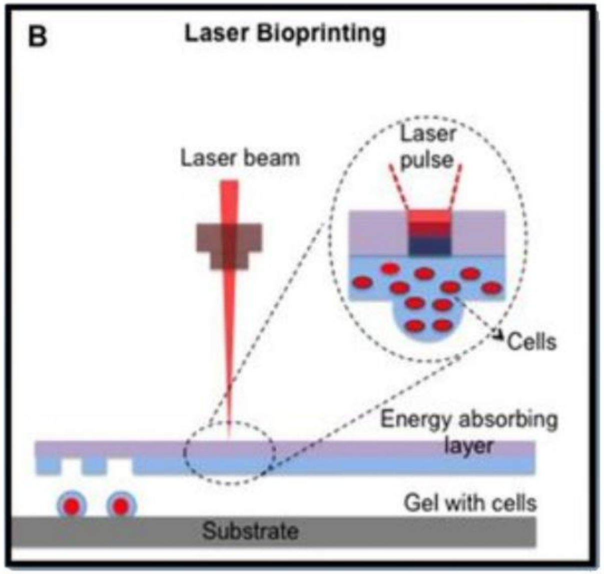
Types of Bioprinters

inkjet



Analogy: inkjet printer
Limitations:
- low viscosity
- bio-ink must solidify
- cell densities

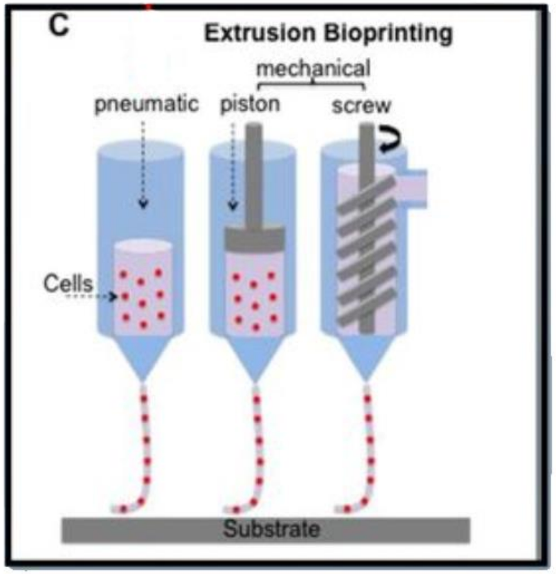
laser



Limitations:
- low printing speed
- Cannot print multiple layers easily
- wastefull

Placing cells precisely

extrusion

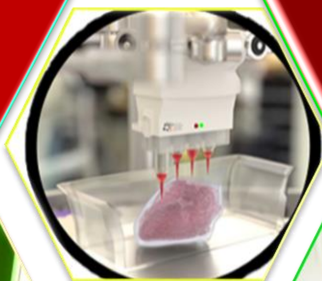


Limitations:
- Lower cellular viability
- Low resolution
- Slow print speed

Applications of Bioprinting

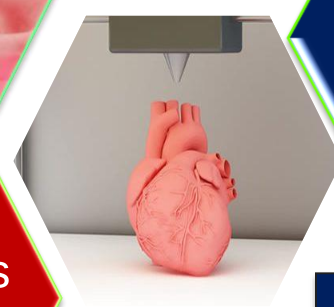
Today | Tomorrow | In the future

Bioprinting of tissues for Education



Bioprinting of tissues for Medicine

Bioprinting of organs for transplantation



To replace organs and tissues that suffered damages

Drug testing

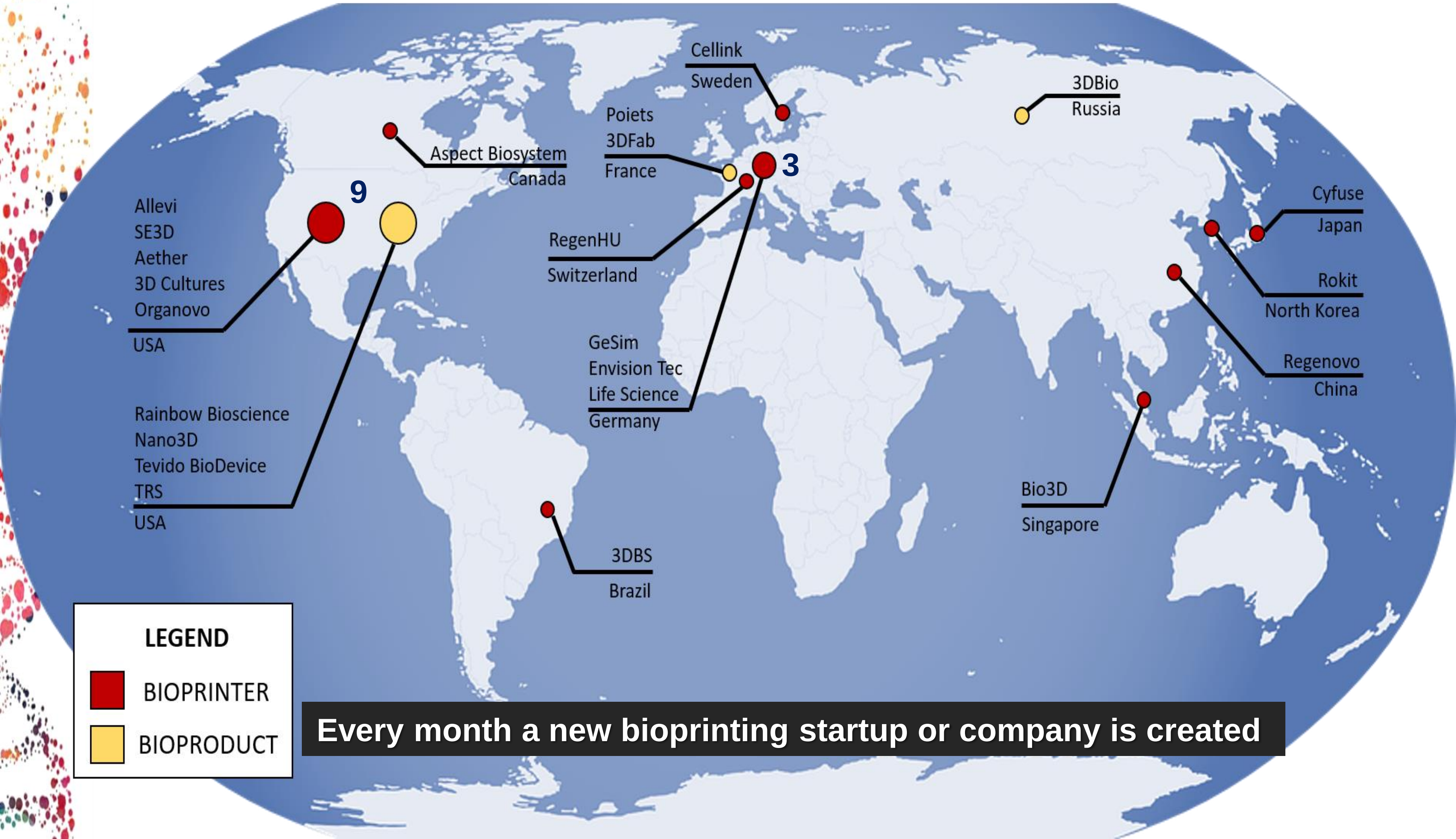
to minimize the use of animals

Cosmetics testing

Medicine 4.0

Towards personalized medicine

Bioprinters and Bioproducts Companies

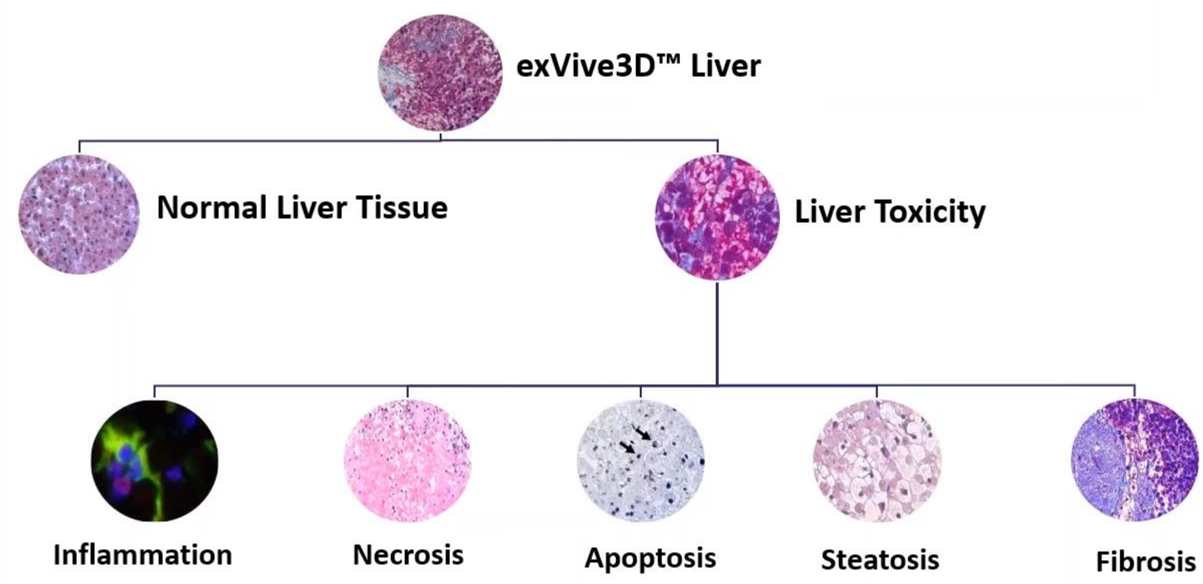


Every month a new bioprinting startup or company is created

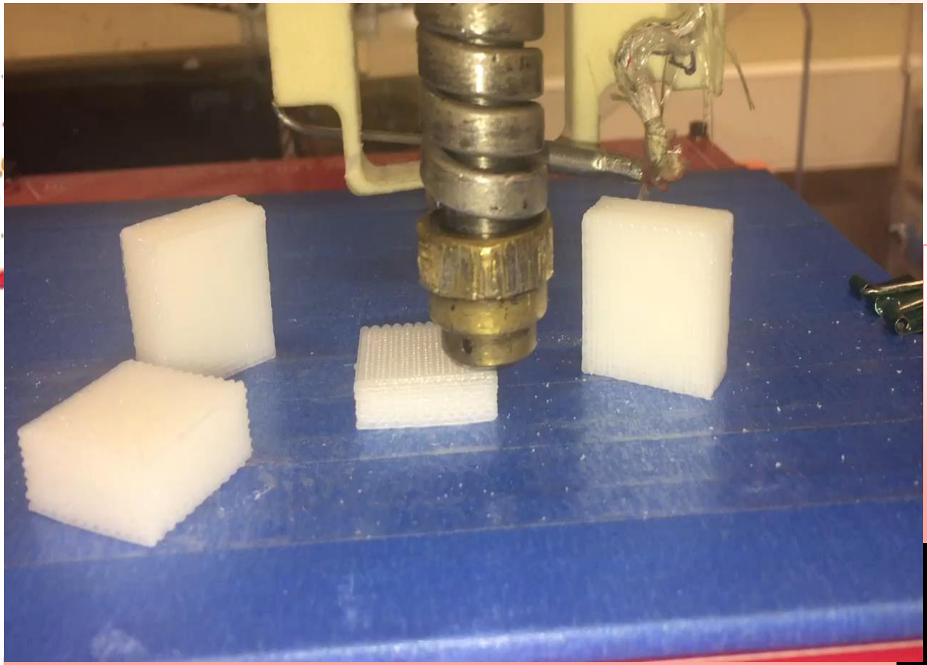
Bioprinters and Bioproducts Companies

organovo®

Organovo is a biotech company that has developed a leadership position with its revolutionary ability to bioprint tissues.



Projects at the CTI Renato Archer - Brazil

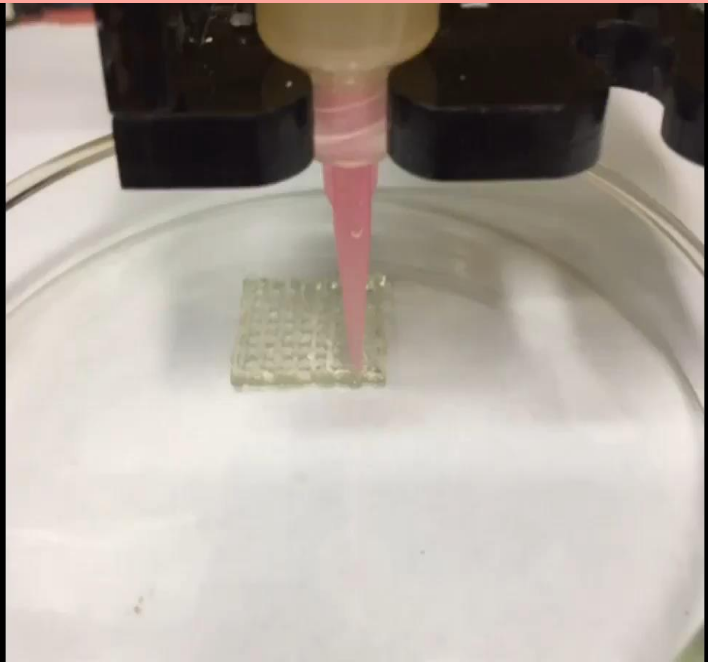


3D printing of rigid scaffolds for bone tissue engineering using synthetic or biomaterials

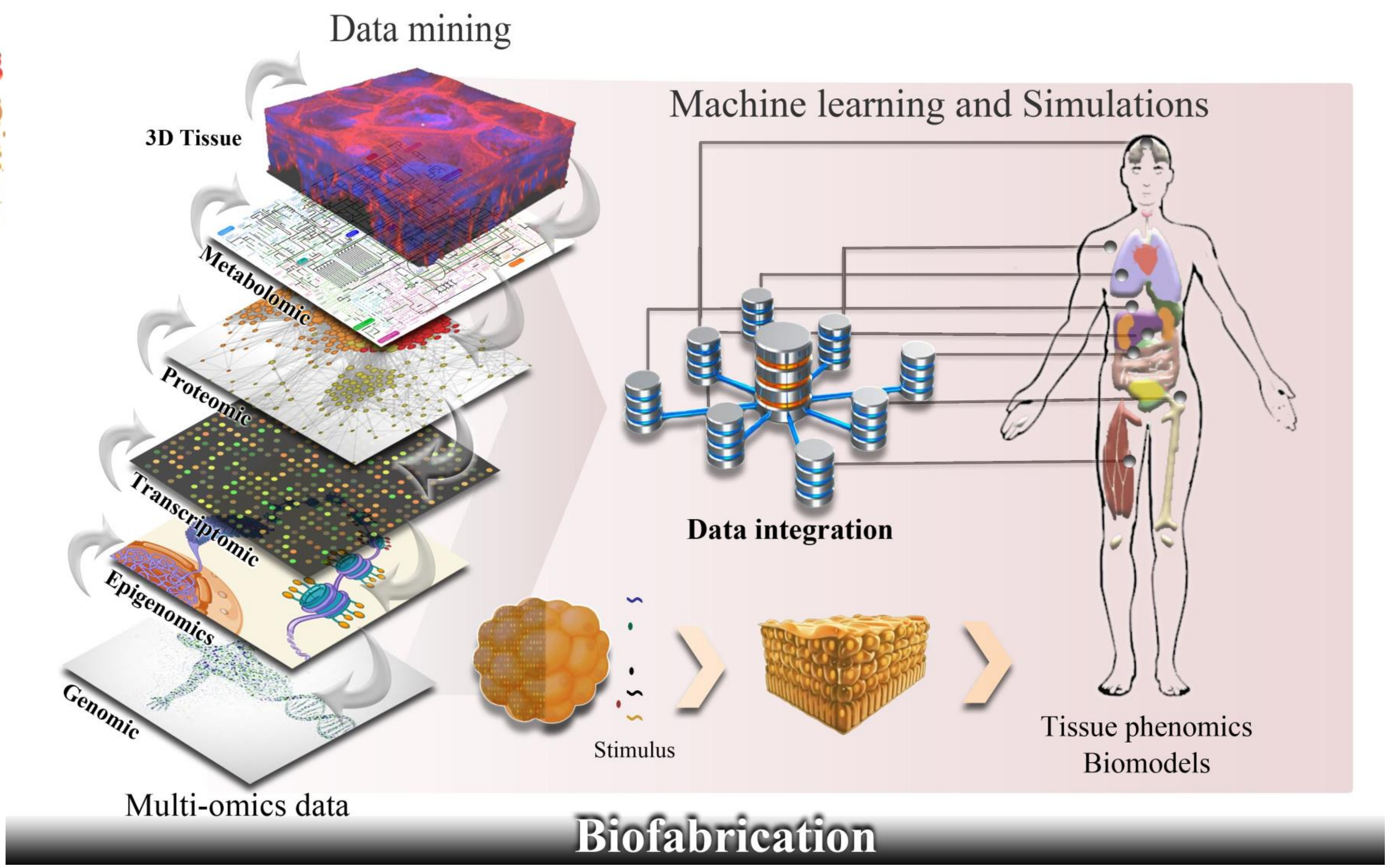
- PCL
- PLA
- PHB
- Bioglass
- B-TCP
- PCL + Bioglass
- PCL + Lycopene
- PHB + B-TCP

Bioprinting of hydrogel and plant cells to study the extrusion process and the shear stress on cells

- **Alginate + agarose**

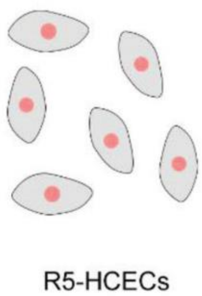


Projects at the CTI Renato Archer - Brazil



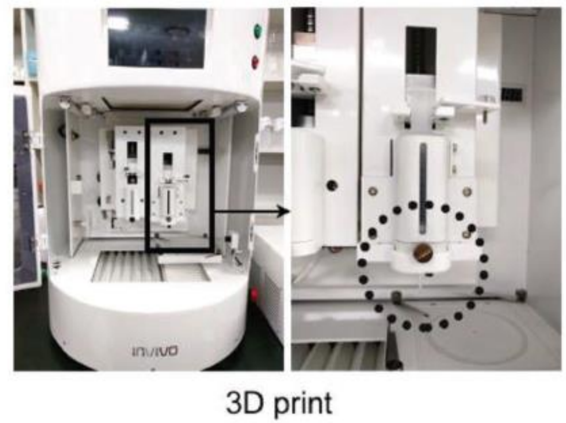
Bioprinting technology in ophthalmology

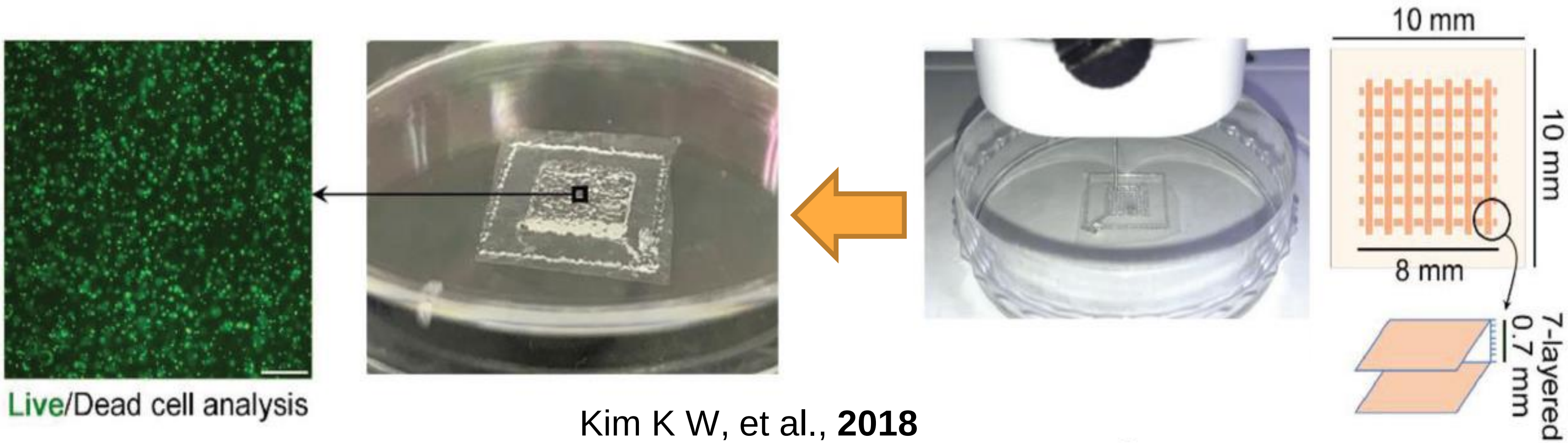
Bioprinting of corneal endothelium



Ribonuclease (RNase) 5 is a protein that is well known for promoting cell survival

Cells + Biogel (gelatin)

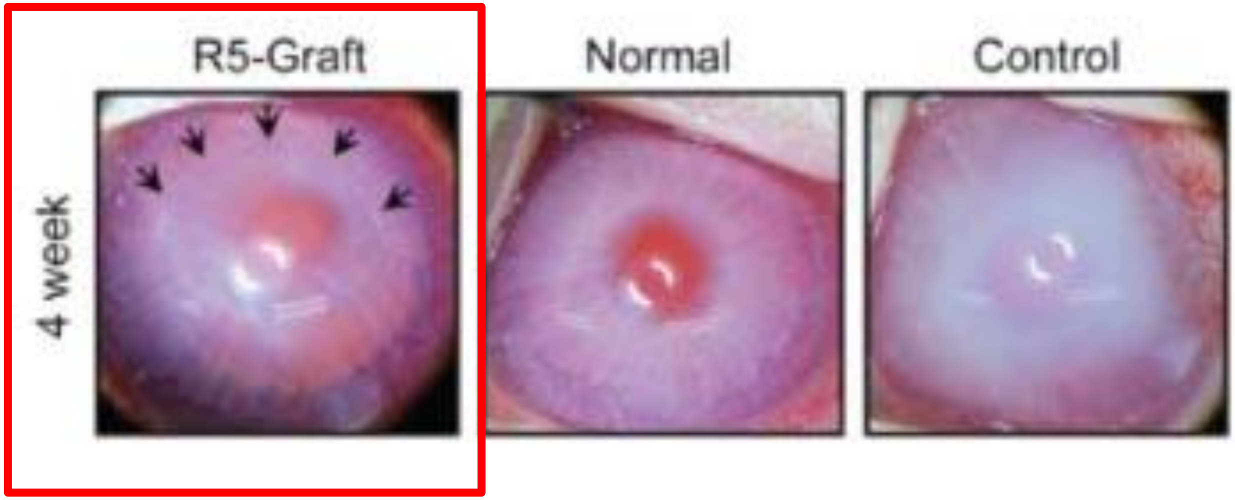




Kim K W, et al., **2018**

Bioprinting technology in ophthalmology

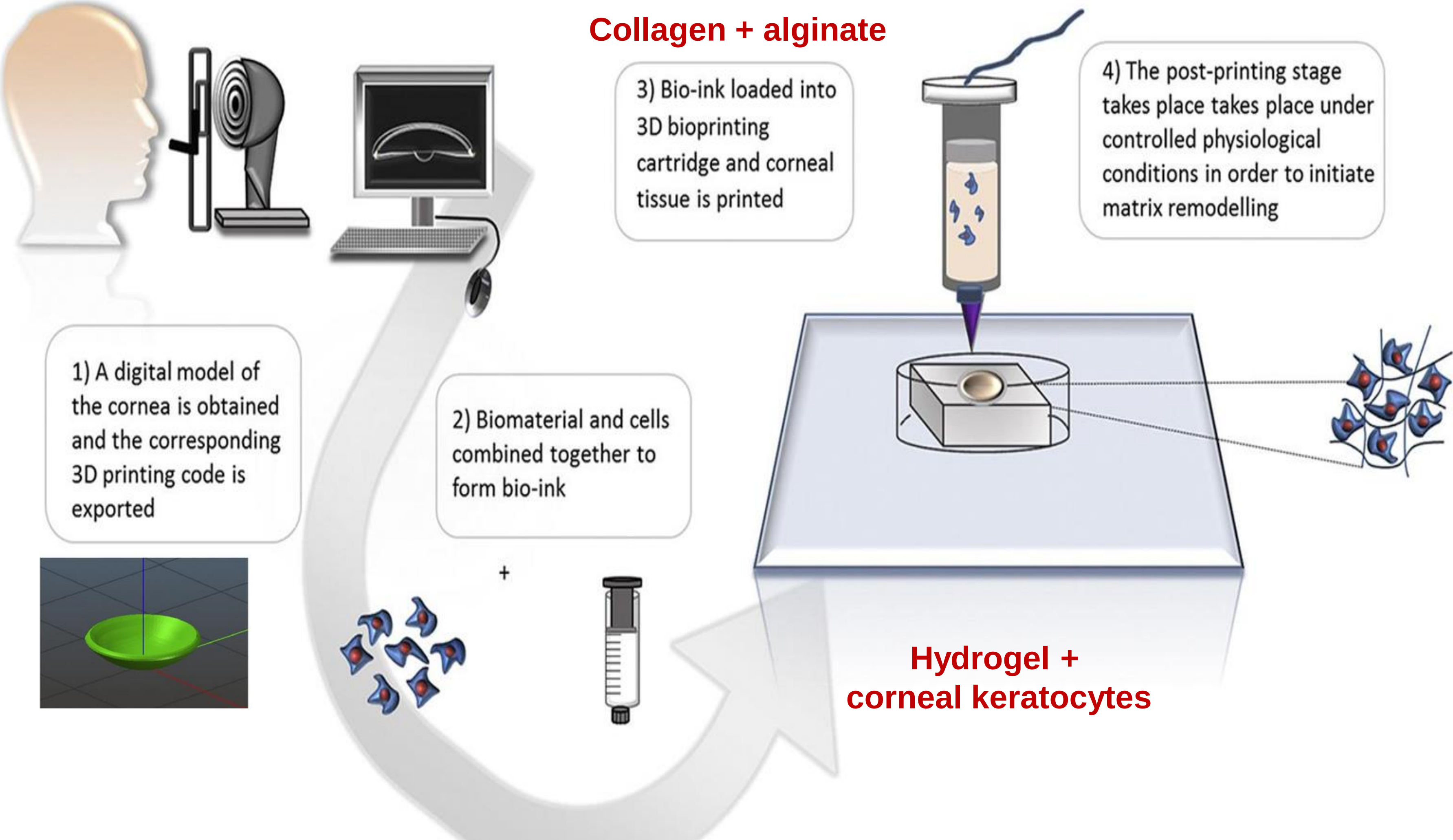
Kyoung Woo Kim - **Ex Vivo Functionality of 3D Bioprinted Corneal Endothelium Engineered with Ribonuclease 5-Overexpressing Human Corneal Endothelial Cells.** Adv. Healthcare Mater. **2018**, 1800398



In conclusion, the biofabricated corneal endothelium with ECs modified easily survives and functions as corneal endothelium in vivo.

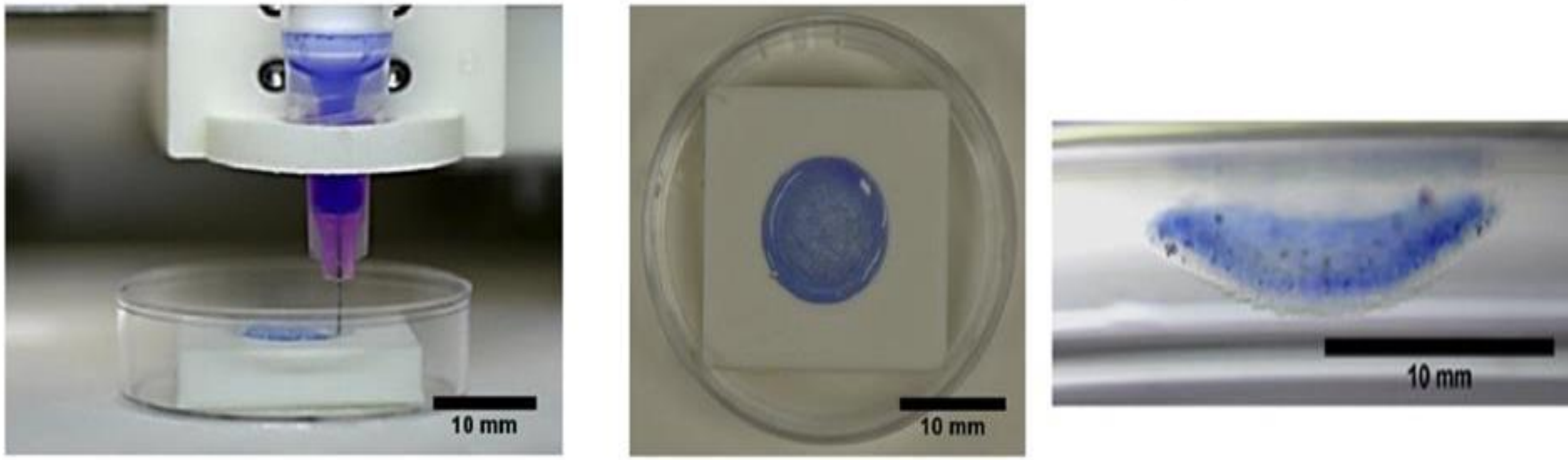
Bioprinting technology in ophthalmology

Bioprinting of corneal stroma equivalent



Isaacson A, Swioklo S, Connon CJ. **3D bioprinting of a corneal stroma equivalent**. Exp Eye Res. **2018** 30;173:188-193.

Bioprinting of corneal stroma equivalent



Keratocytes exhibited high cell viability both at day 1 post-printing (>90%) and at day 7 (83%)

One of the limitations of extrusion bioprinting is the generation of shear stress-induced cell deformation at the needle wall and which is diminished by the use of low viscosity bio-inks to which low air pressures can be applied.

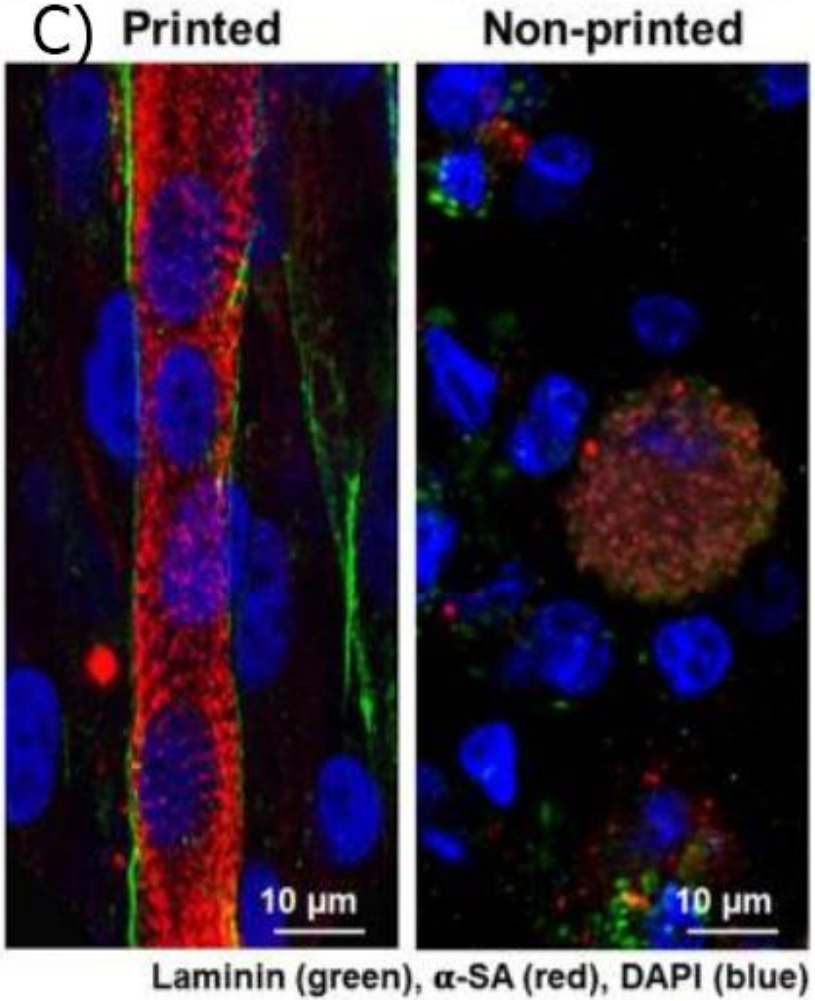
Isaacson A, Swioklo S, Connon CJ. **3D bioprinting of a corneal stroma equivalent**. Exp Eye Res. **2018** 30;173:188-193.

Bioprinted Human Skeletal Muscle Constructs

These results show that the

- **bioprinted organized muscle structure can accelerate the tissue maturation,**
- **while the microchannel structure can allow the diffusion of nutrient and oxygen to maintain the cell viability.**

- **Human muscle progenitor cells (hMPCs) + Gelatin bioink**
- **Polycaprolactone (PCL) for structuring the filaments of hydrogel.**



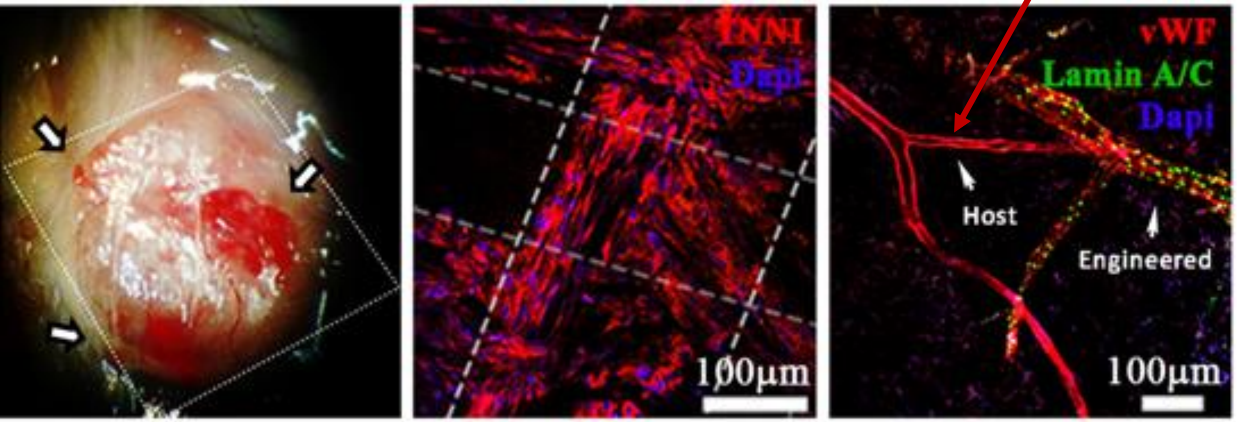
Kim Ji Hyun, et al., 3D Bioprinted Human Skeletal Muscle Constructs for Muscle Function Restoration, 2018.

Bioprinting and microfluidic for Cardiac Tissue Engineering

The constructs were made with this composition:

- Human Umbilical Vein Endothelial Cells (HUVECs)
- Induced pluripotent cell-derived cardiomyocytes (iPSC-CMs).
- Alginate and PEG-Fibrinogen (PF) and extruded through a custom microfluidic printing head (MPH)

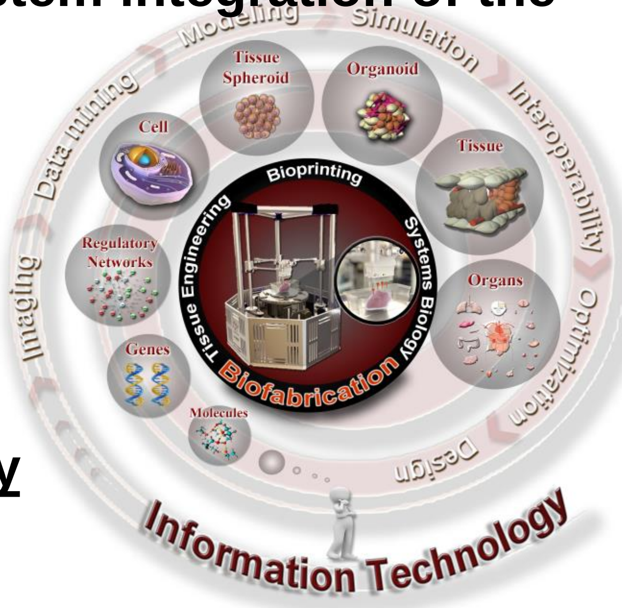
The group obtained a 3D cardiac tissue compose of iPSC-derived CMs with a high orientation index imposed by the different defined geometries and blood vessel-like shapes generated by HUVECs



Maiullari F. et al., A multi-cellular 3D bioprinting approach for vascularized heart tissue engineering based on HUVECs and iPSC-derived cardiomyocytes, ***Scientific Reports***, **8** 2018.

Challenges

- ✓ **Integration Engineering x Life Sciences;**
- ✓ **To understand the regulatory networks of cells and tissues;**
- ✓ **Development of new “Blueprint/BioCAD" for bioprinting;**
- ✓ **Development of scalable technology for biofabrication millions uniform tissue spheroids;**
- ✓ **Development of integrated operational system integration of the bioprinters (special software-hardware);**
- ✓ **Development of new bioreactor;**
- ✓ **Development of *in situ* bioprinting;**
- ✓ **Development of bioprintable biomaterials;**
- ✓ **Laws and regulations → <u>* Safety + Security</u>**



http://www.biofabricacao.com

Thank you!

obrigada

Janaina Dernowsek, PhD
Researcher at CTI Renato Archer

jadernowsek@gmail.com

Bio3Data
Founder
bio3data@gmail.com