Centro de Tecnologia da Informação Renato Archer

Presente e Futuro da Biofabricação de Órgãos

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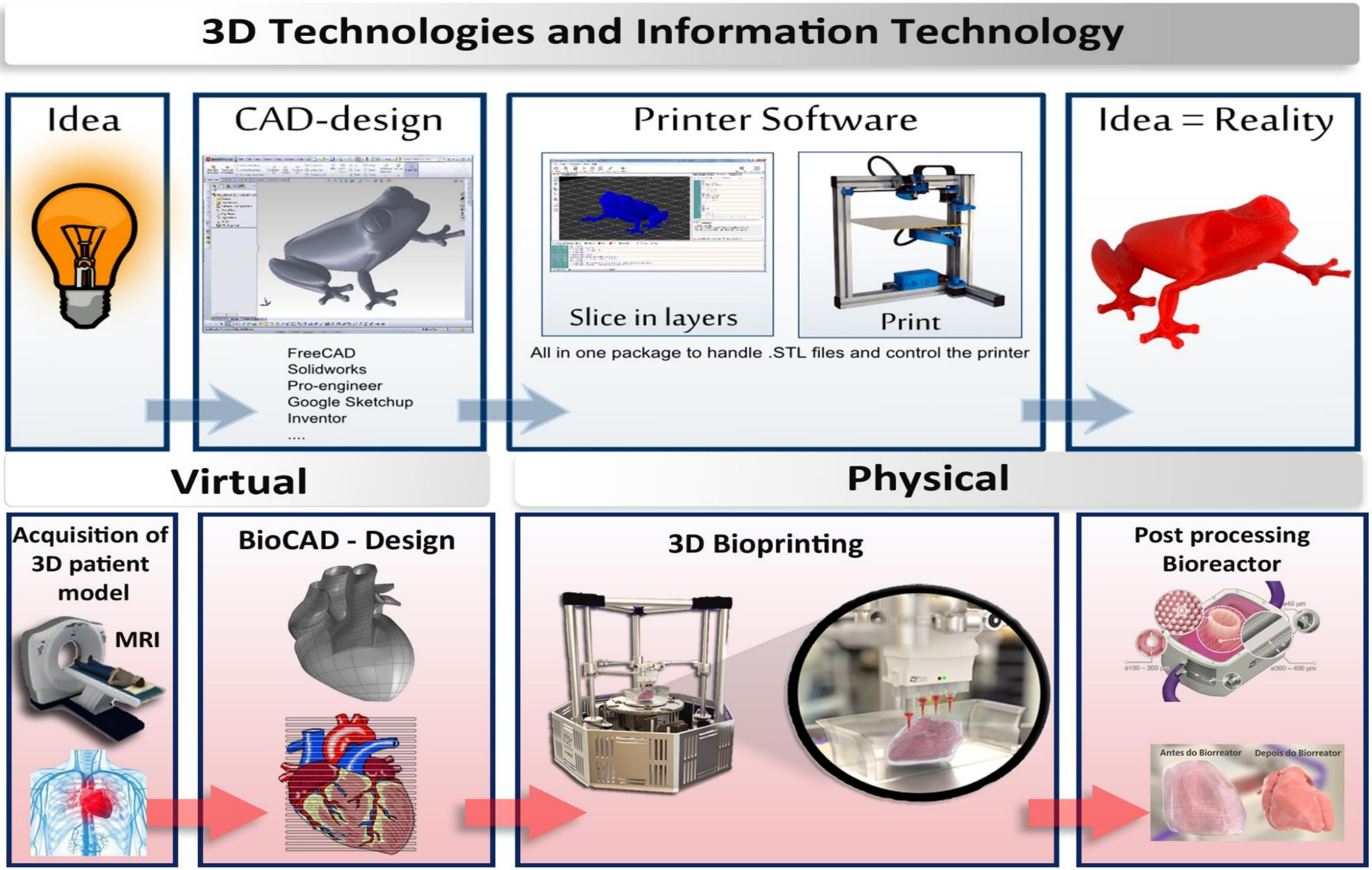
Fatec Sorocaba

VII Jornada de Sistemas Biomédicos Fatec Sorocaba

3D Technologies



Tissue Engineering - Timeline

1938

Published by Alexis Carrel (doctor) and Lindbergh (aviator) o *The Culture of Organs*

1950

Studies with stem cells in dogs exposed to high doses of radiation (regenerative medicine)

1967

Dr. Christiaan Barnard First heart transplantion

1988

Determinant contributions of the Vacanti Brothers

Dr. Skalak defines "Tissue Engineering" corroborated later by the ITRI report and NSF

1997

Joseph Vacanti and collaborators publish in *Plastic and Reconstructive Surgery*

2002

Tissue Engineering Report published by International Technology Research Institute – ITRI

National Science Foundation workshop on TE

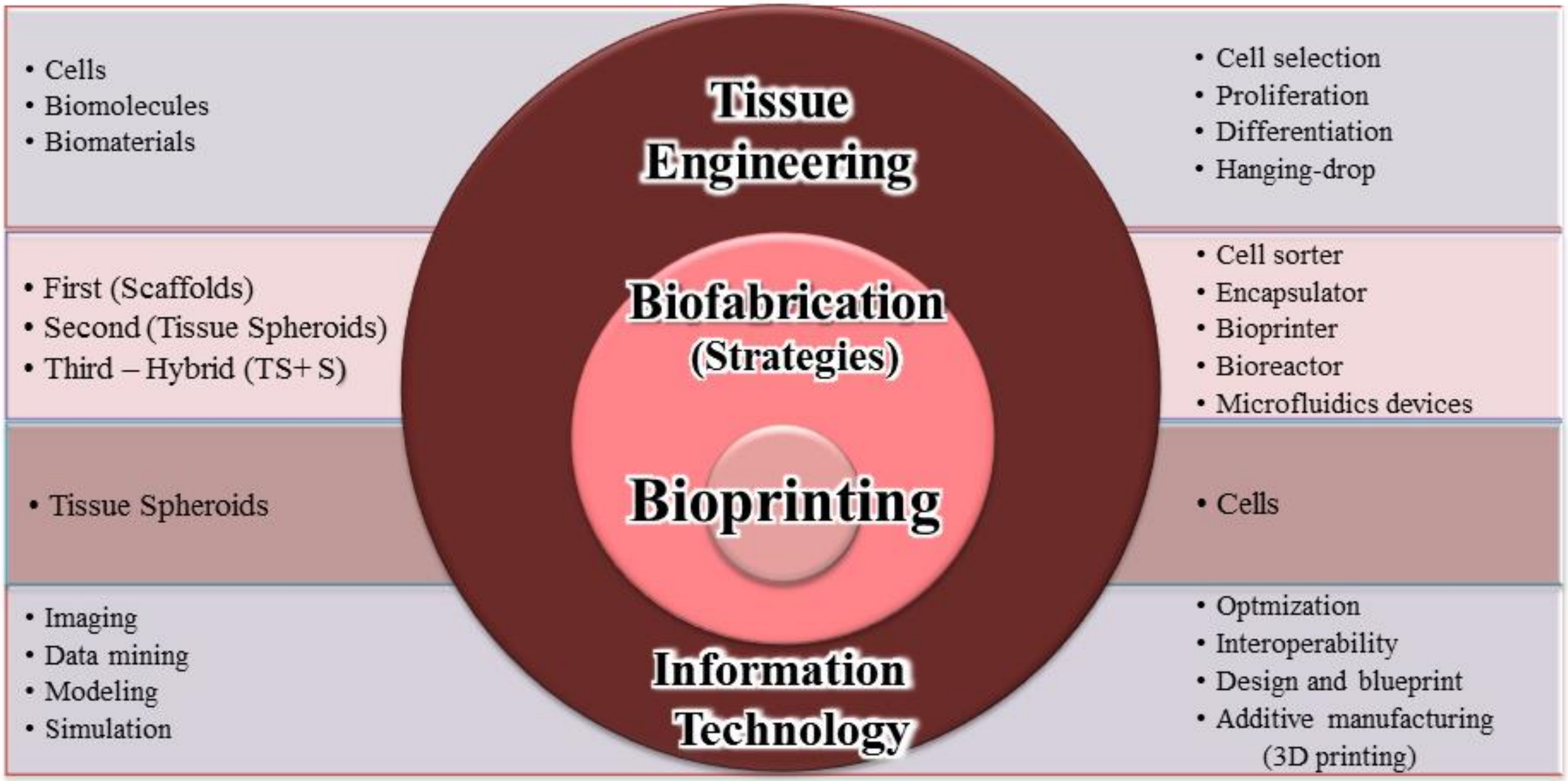
Consolidation of TE as a multidisciplinary domain

Definition of Tissue Engineering by NSF

"the application of principles and methods of engineering and life sciences to obtain a fundamental understanding of structure-function relationships in novel and pathological mammalian tissues and the development of biological substitutes to restore, maintain, or improve [tissue] function"

biodegradable polymer (polyglycolic acid) seeded with bovine chondrocytes implanted on back of athymic mice

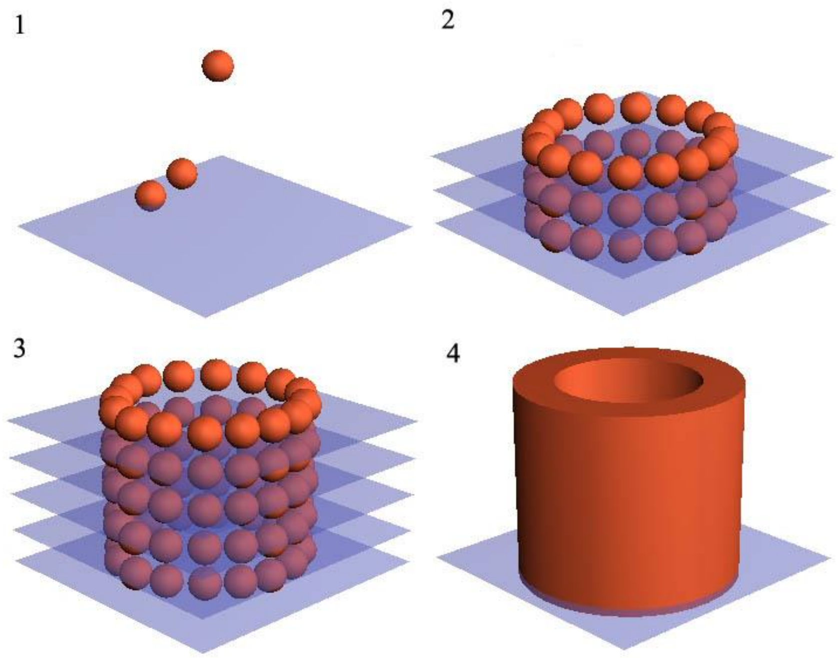
Tissue engineering, Biofabrication, Bioprinting and Information Technology



Dernowsek *et al.*, 2017

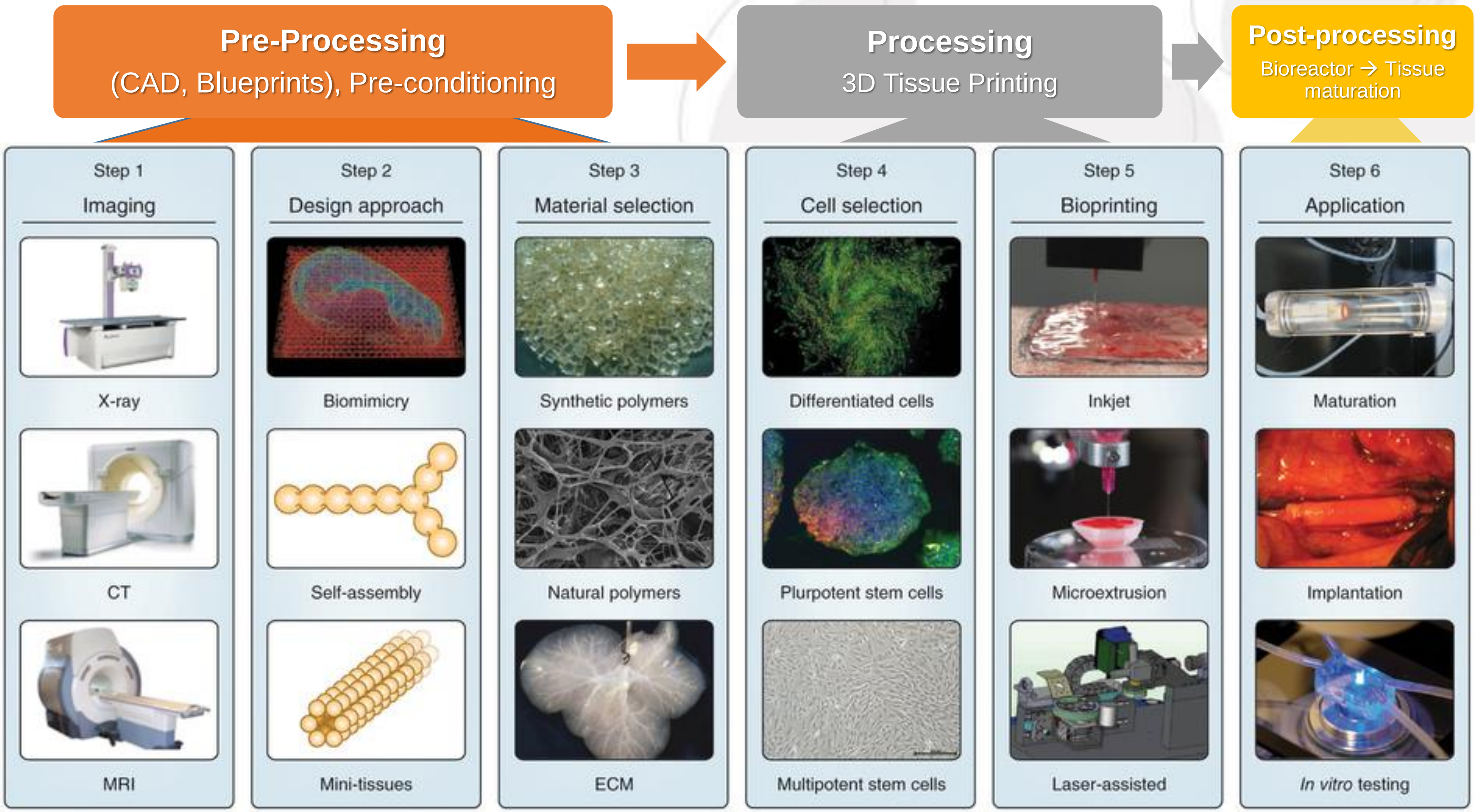
Bioprinting

Bioprinting is a computer-aided robotic layer by layer additive biofabrication of functional living human organ constructs



The bio-ink:
cell aggregates
The cartridge:
TS container
The bio-paper:
gel
The printer:
bio-printer

Bioprinting process workflow



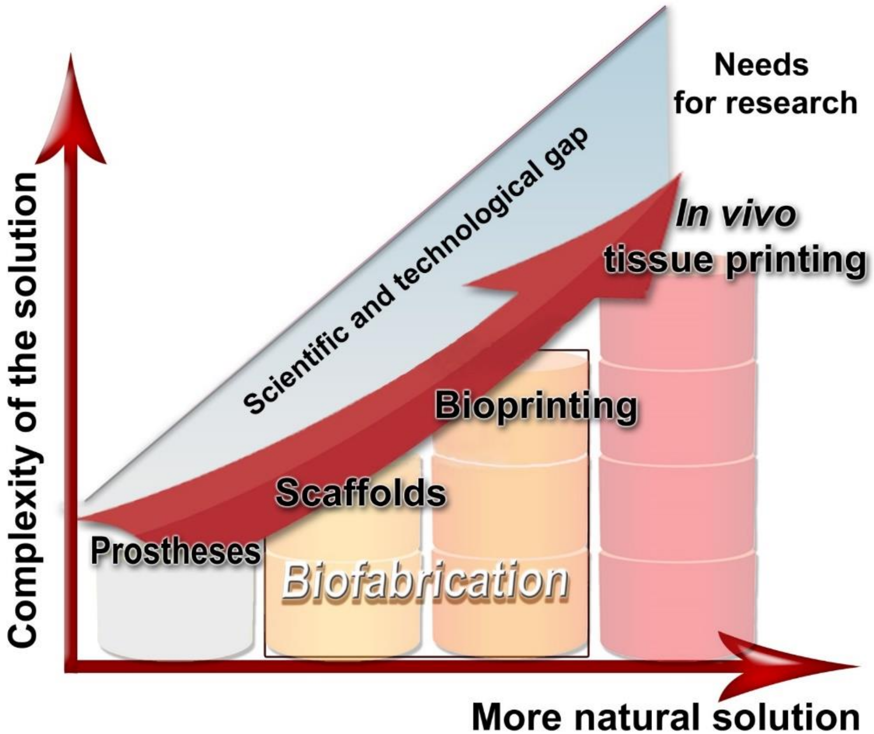
Murphy & Atala, 2014

Pre-Processing
Spheroid formation process →Hanging drop

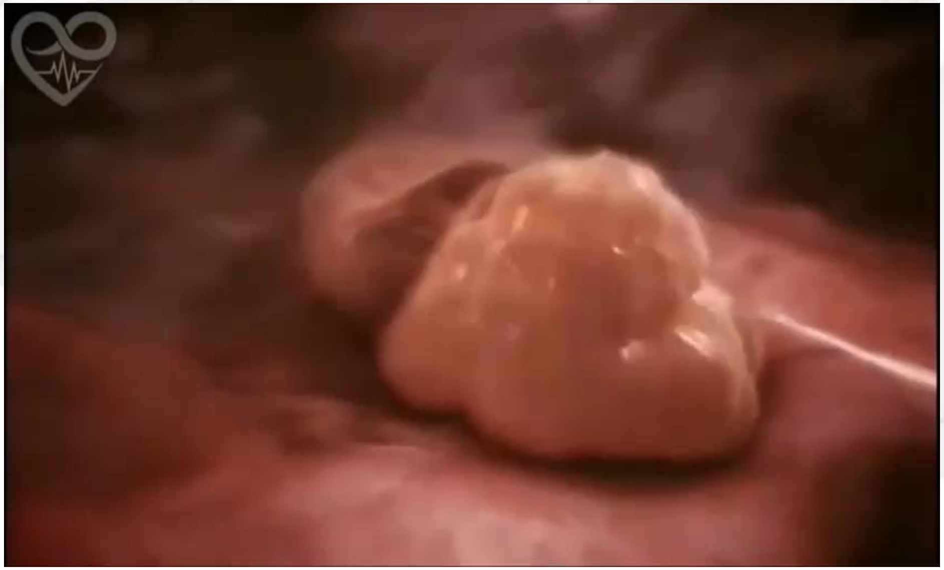
Bioprinting

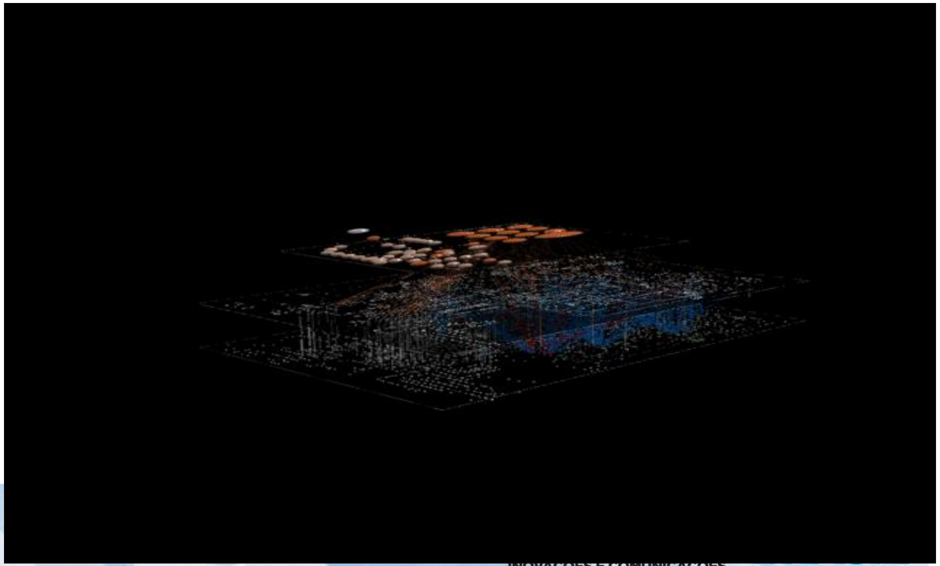
Bioreactor → Tissue maturation

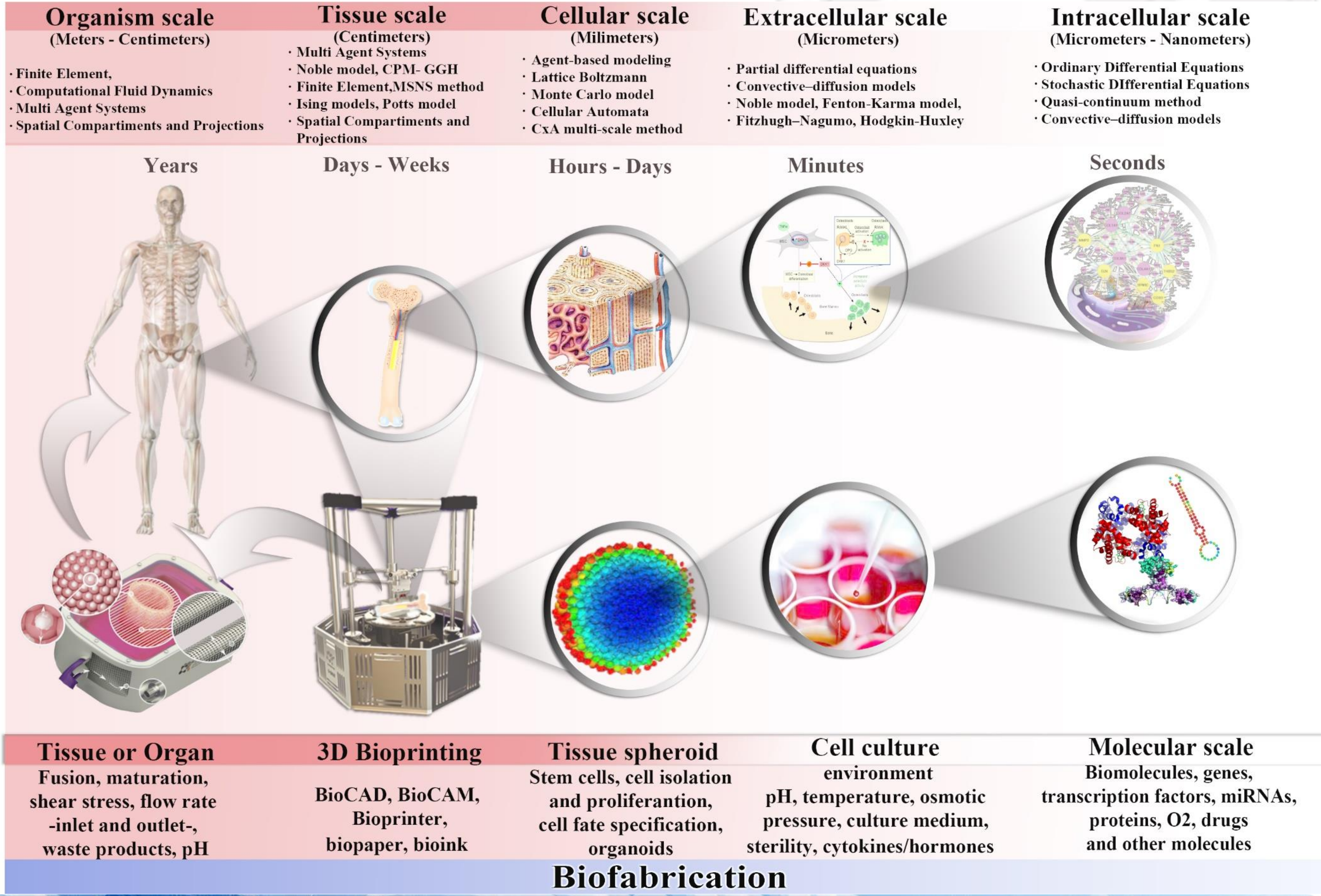
Biofabrication and the relationship between complexity and nature of the solution



Dernowsek et al. 2017

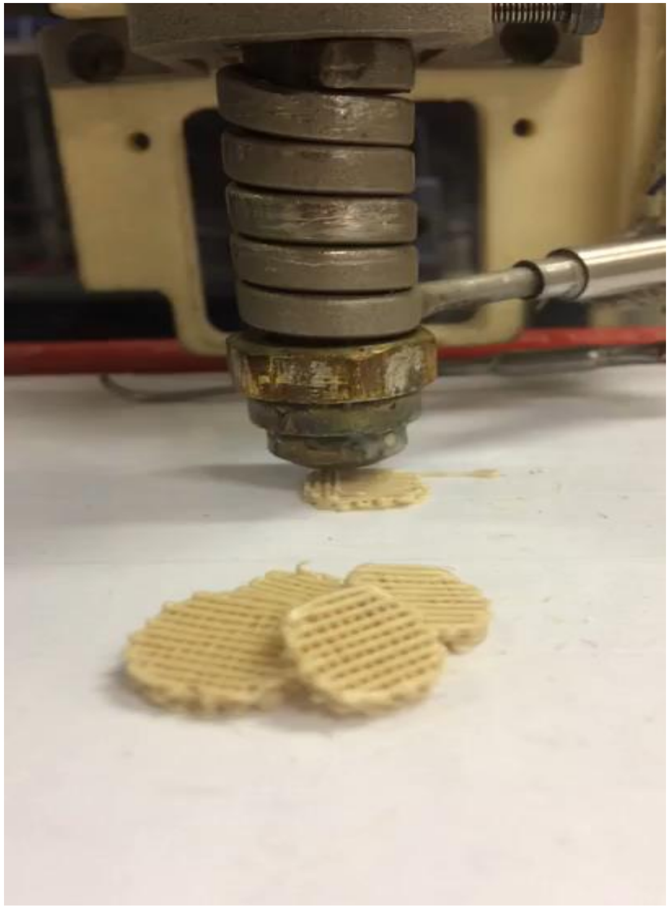


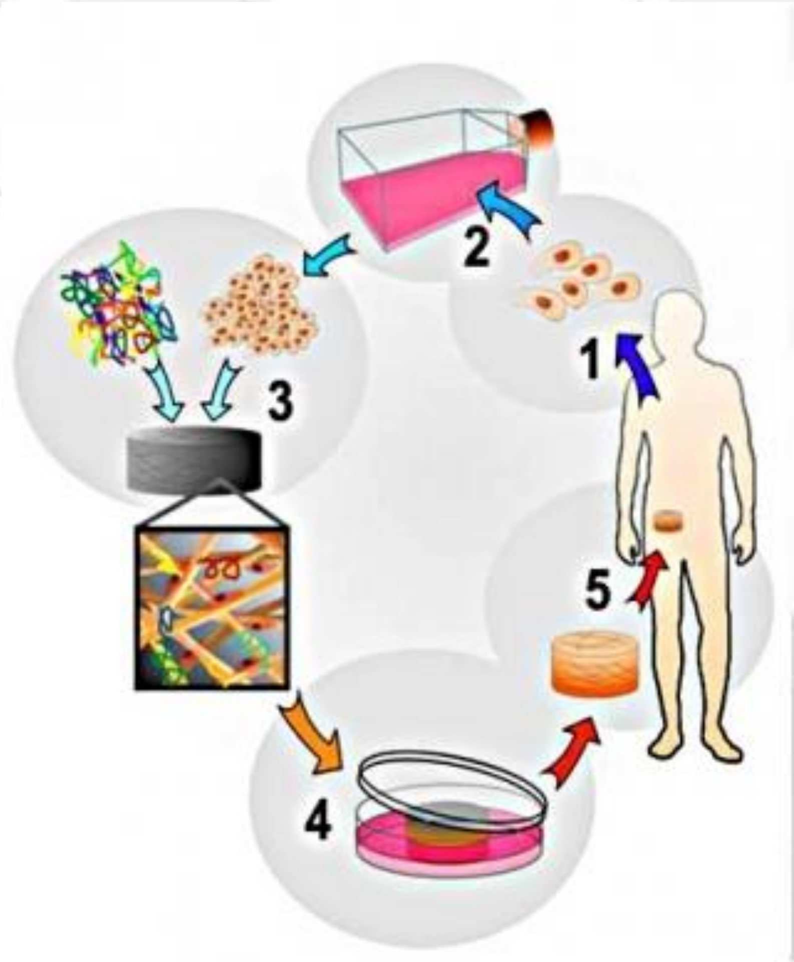




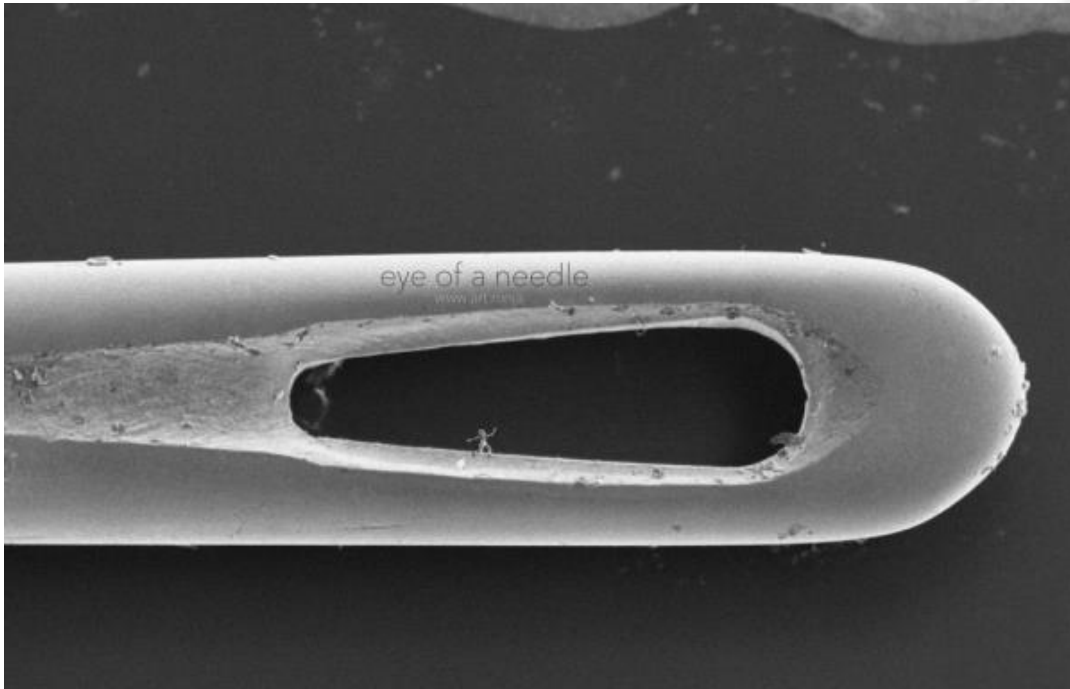
Dernowsek *et al*., 2016

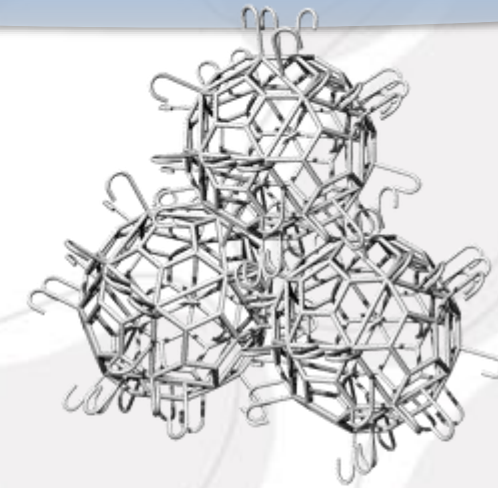
Techniques for Manufacturing Polymer Scaffolds with Potential Applications in Tissue Engineering

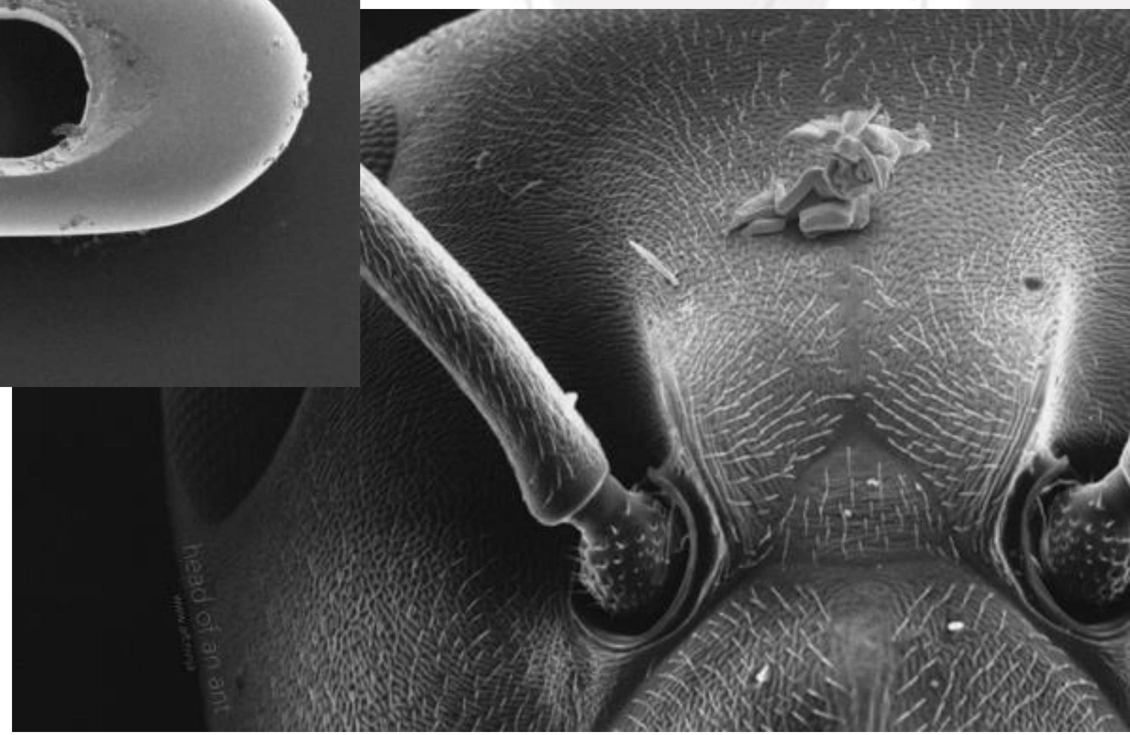


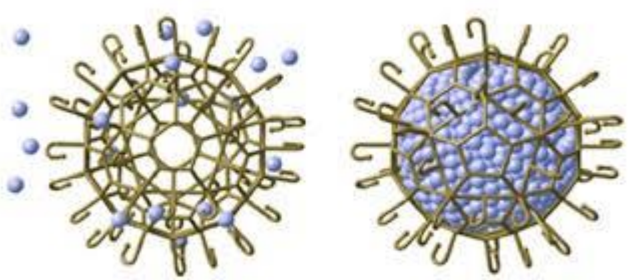


Two Photon Polymerization – 2PP









Source: http://www.3ders.org/articles/20141115-jonty-hurwitz-3d-printed-nano-sculptures-at-the-same-scale-as-a-human-sperm.html

Two-Photon Polymerization

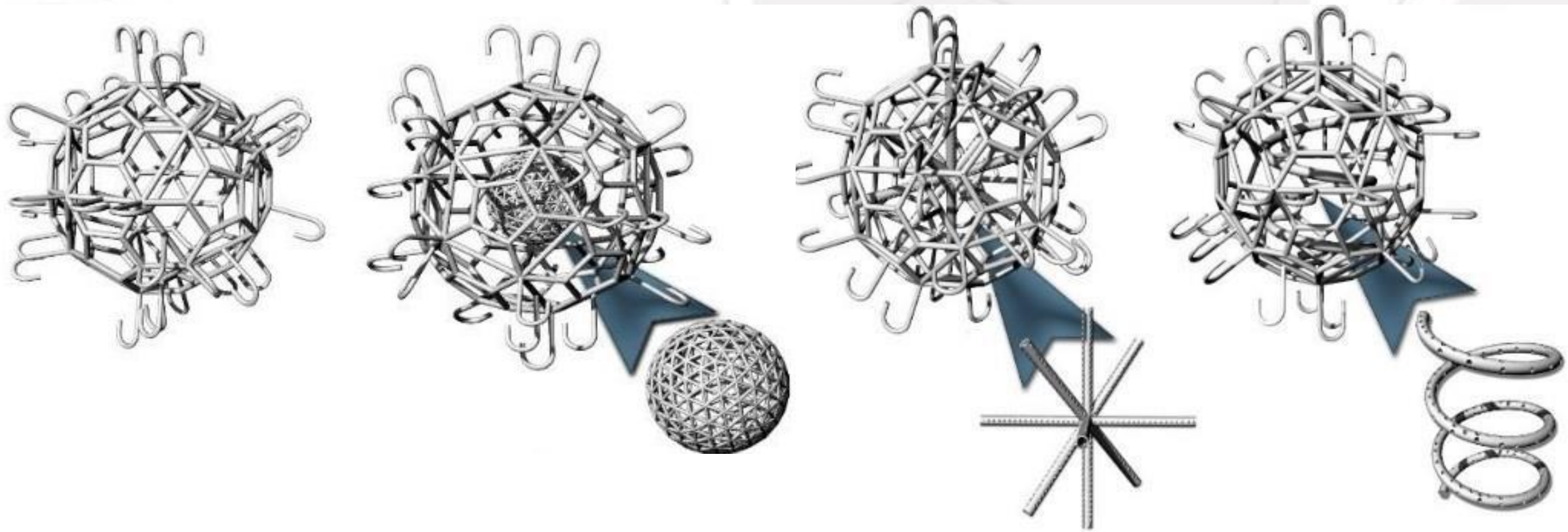
FINEP 8 Mi Grant

nanoscribe

True 3D Laser Lithography

Application Video: 3D µ-Printing

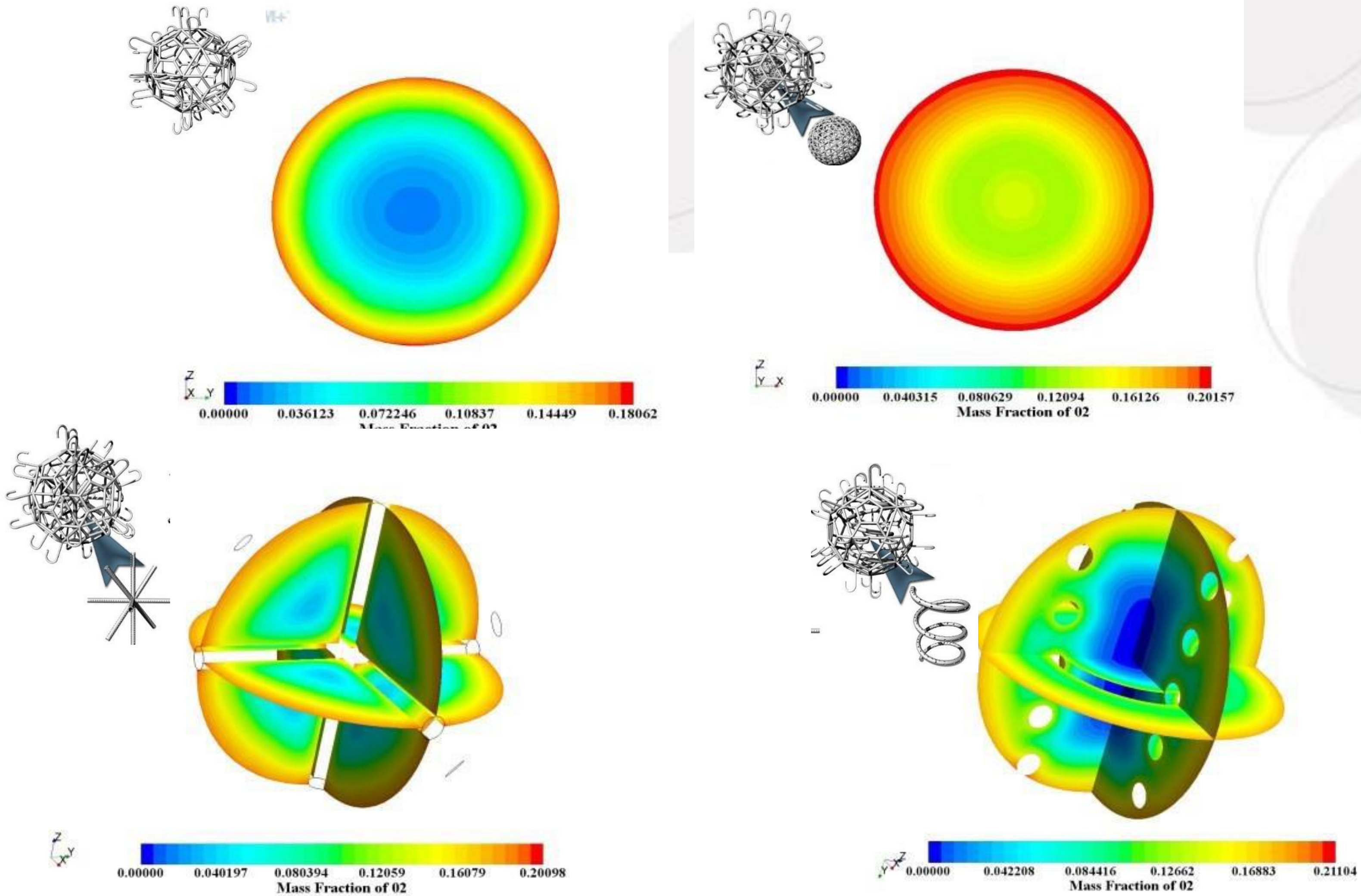
Modeling and Simulation of Diffusion Process in Tissue Spheroids Encaged into Microscaffolds



Four geometries were modelled to simulations. (A) Solid microscaffold without internal structure (original lockyball) (Danilevicius et al., 2015). (B, C, D) Solid microscaffolds with internal structures to improve the oxygenation cells

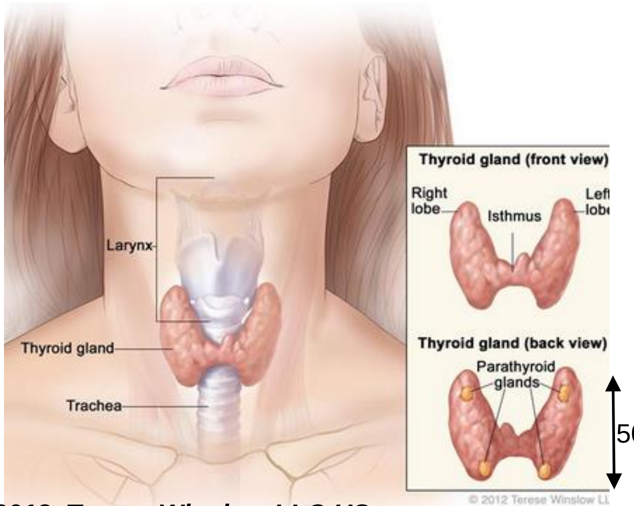
Dernowsek *et al*., 2016

Modeling and Simulation of Diffusion Process in Tissue Spheroids Encaged into Microscaffolds



Dernowsek et al., 2016

Near future organ bioprint - Thyroid gland



50 – 55mm

25 – 30mm

2013. Terese Winslow LLC US.

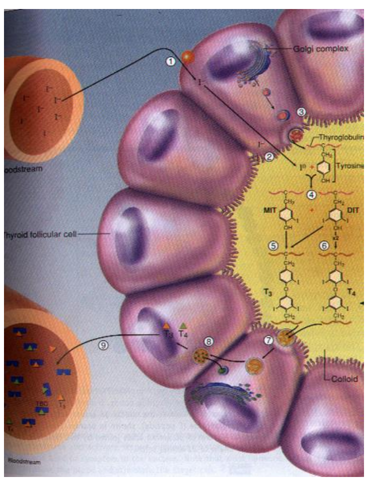
Hystology & Fisiology

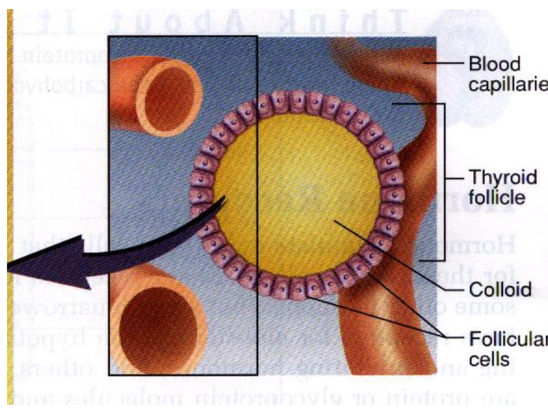
Comprised of aggregates or lobules of **spherical follicles** that are **filled with colloid**

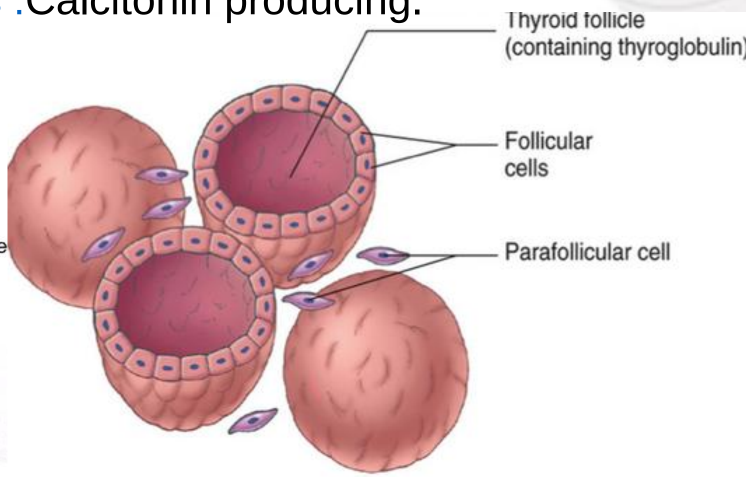
Functional units, hormone synthesis. Single layer of follicular cells. θ=500μm aprox

T3 + T4

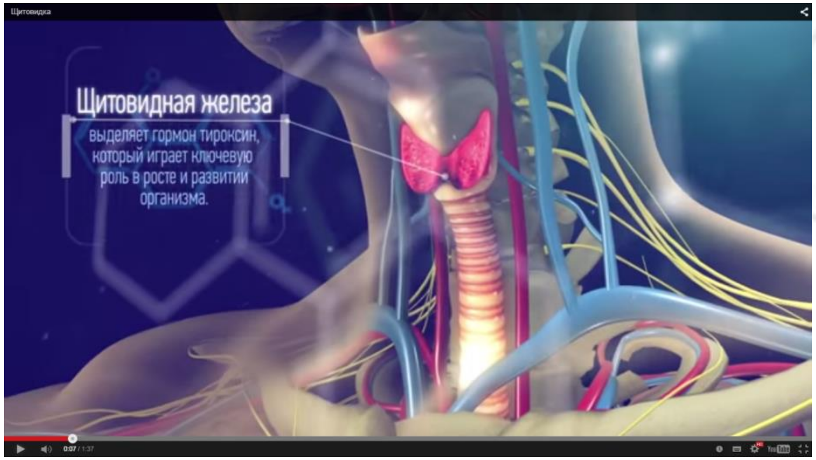
Parafollicular cells :Calcitonin producing.

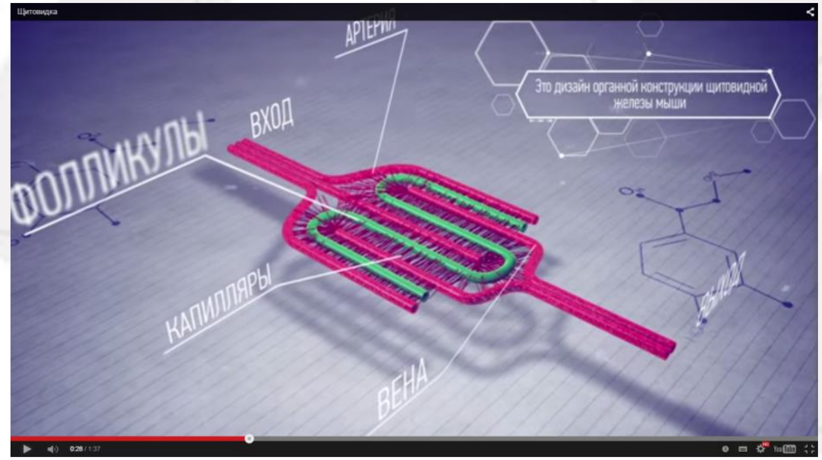


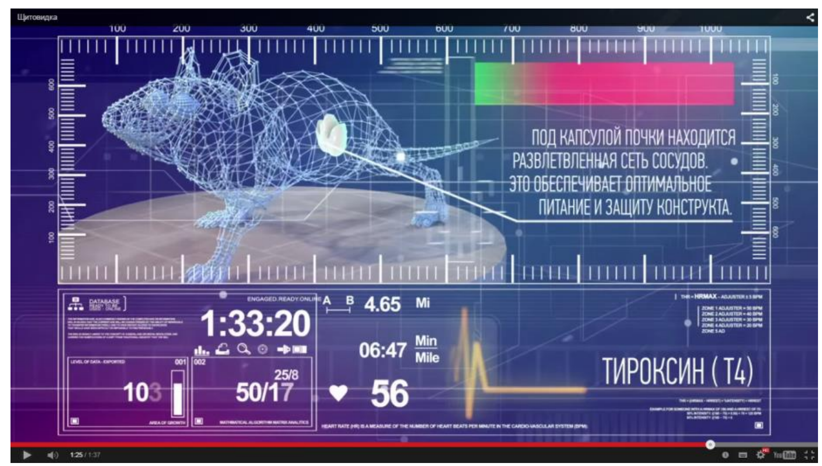




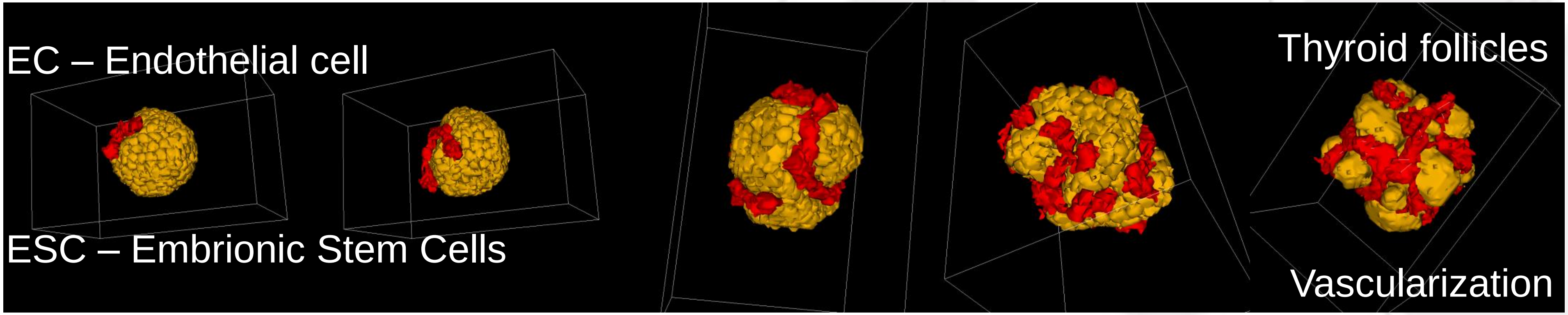
3D Bioprinted Thyroid Gland

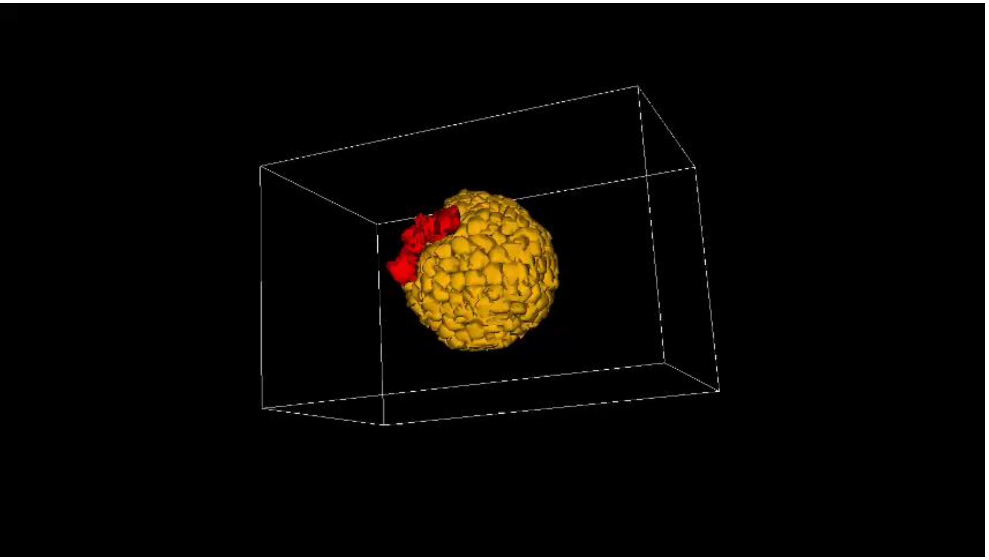






3D multicellular simulation during the self-formation of thyroid follicles

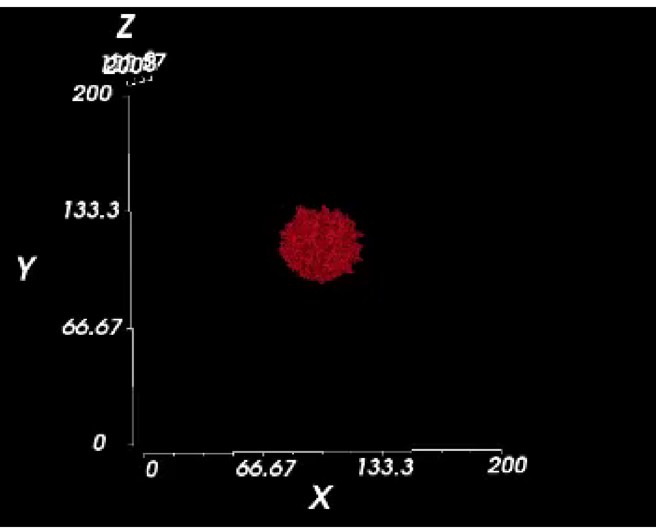


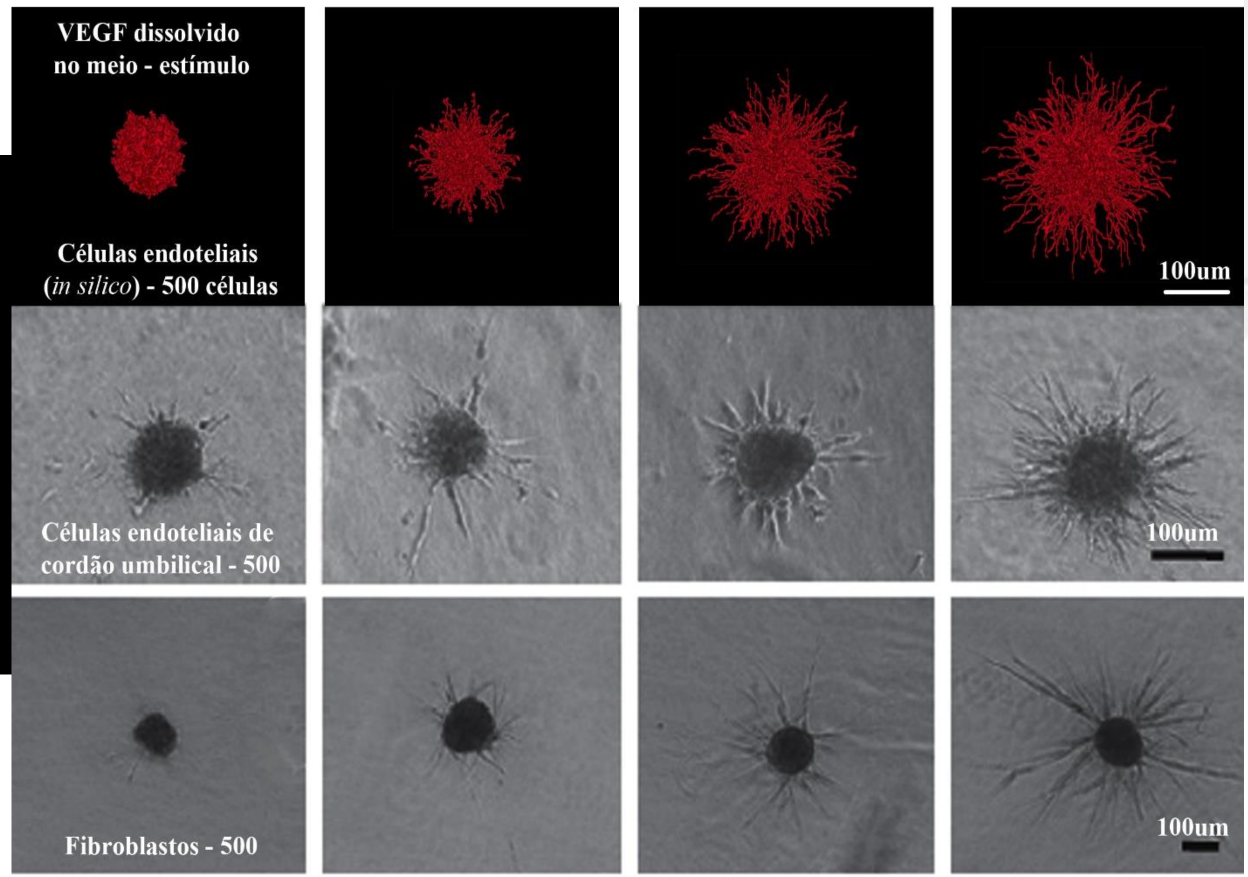


1. Simplified 3D multicell simulation of angiogenesis during the self-formation of thyroid follicles
2. It can be easily extended and adapted to describe other biological phenomena
3. This simulation allowed us to study how the cells interact each other and modulate the growth and morphology of the multicellular spheroids.

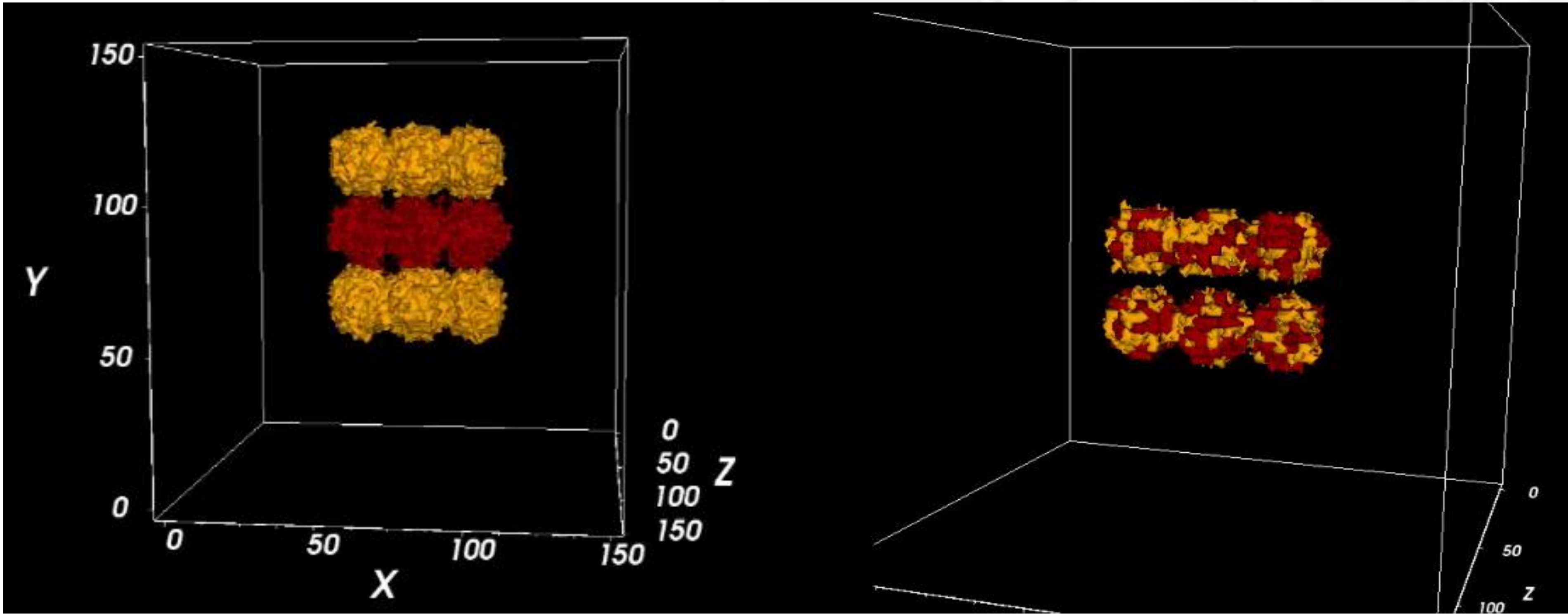
Computational approaches for biofabrication of Tissues → Angiogenesis

Endothelial cell spheroids as a versatile tool to study angiogenesis *in vitro* and in *silico*

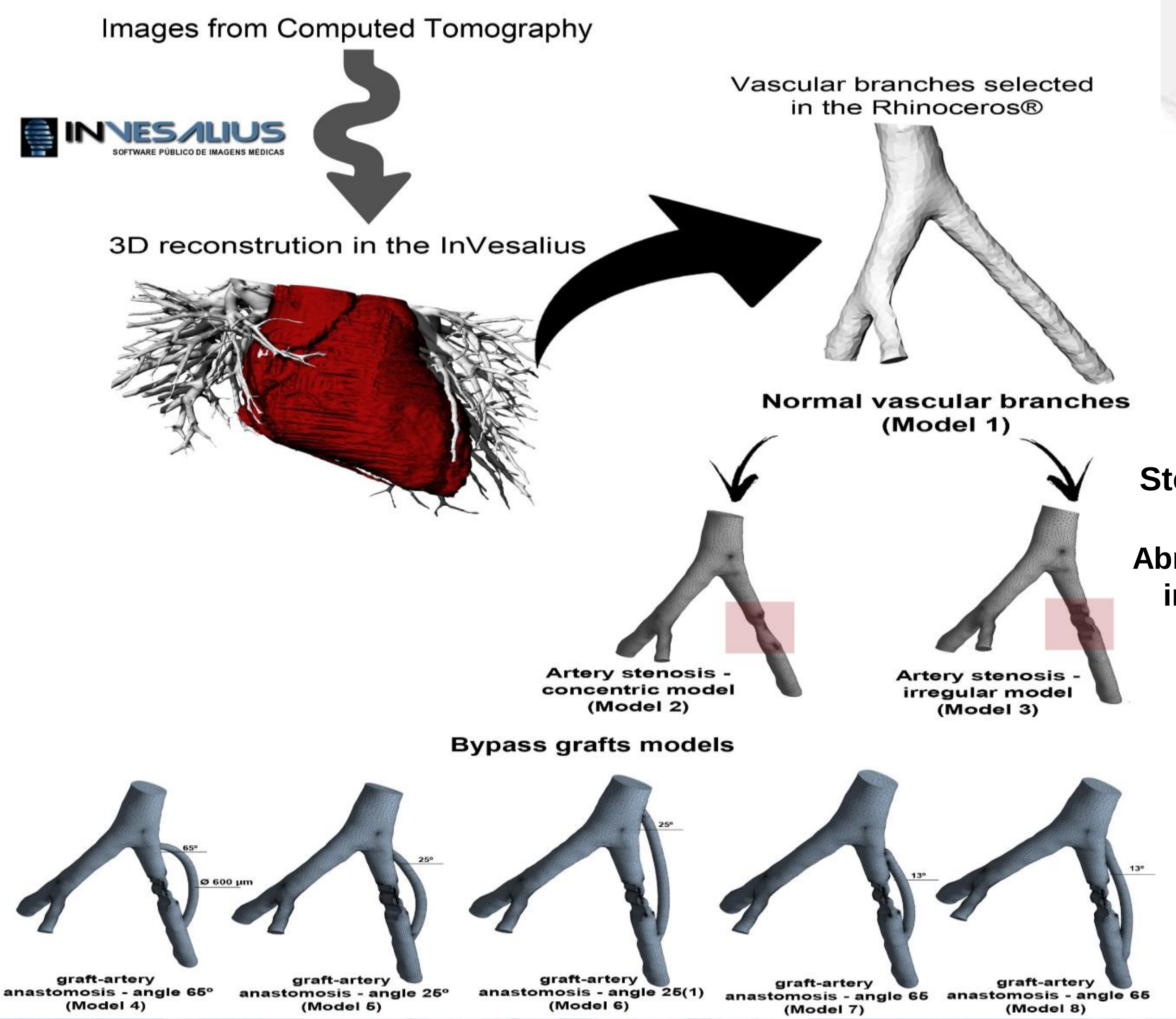




Computational approaches for biofabrication of tissues → Angiogenesis + Proliferating cells



Hemodynamics in artery bypass grafts models based on computational fluid dynamics simulations

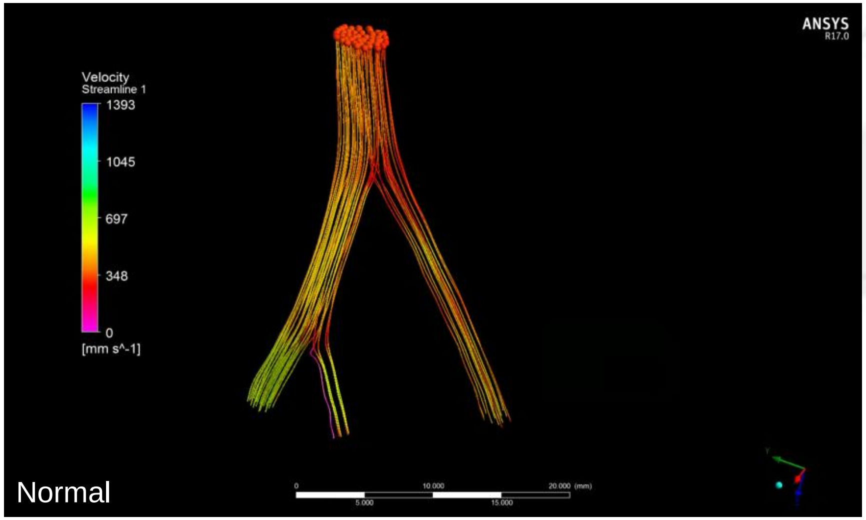


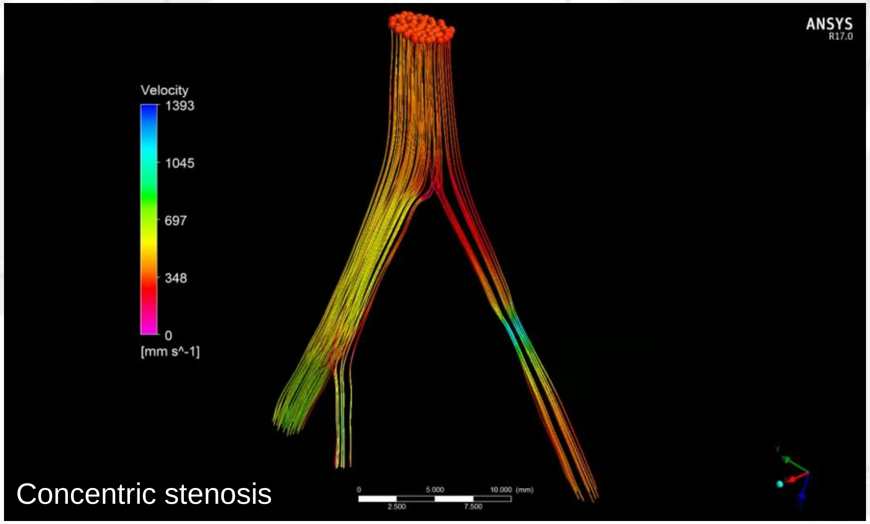
Stenosis models

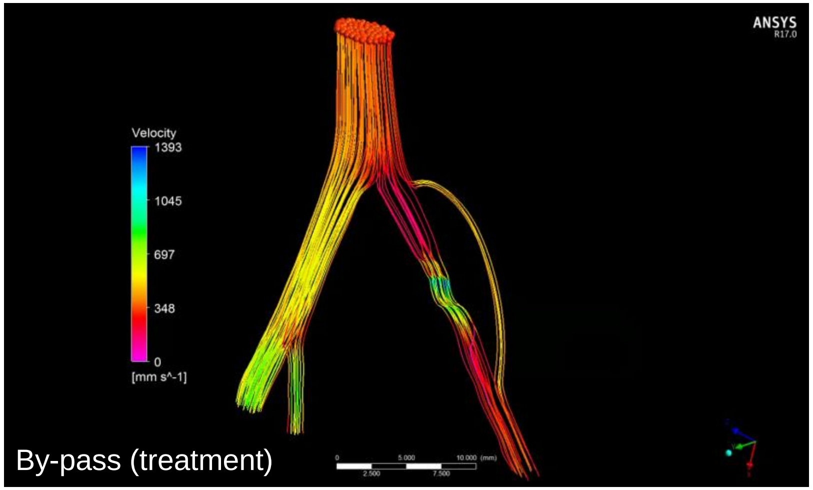
Abnormal narrowing in blood vessels

Bypass grafts models

Computer simulation – Stenosis and Bypass graft models

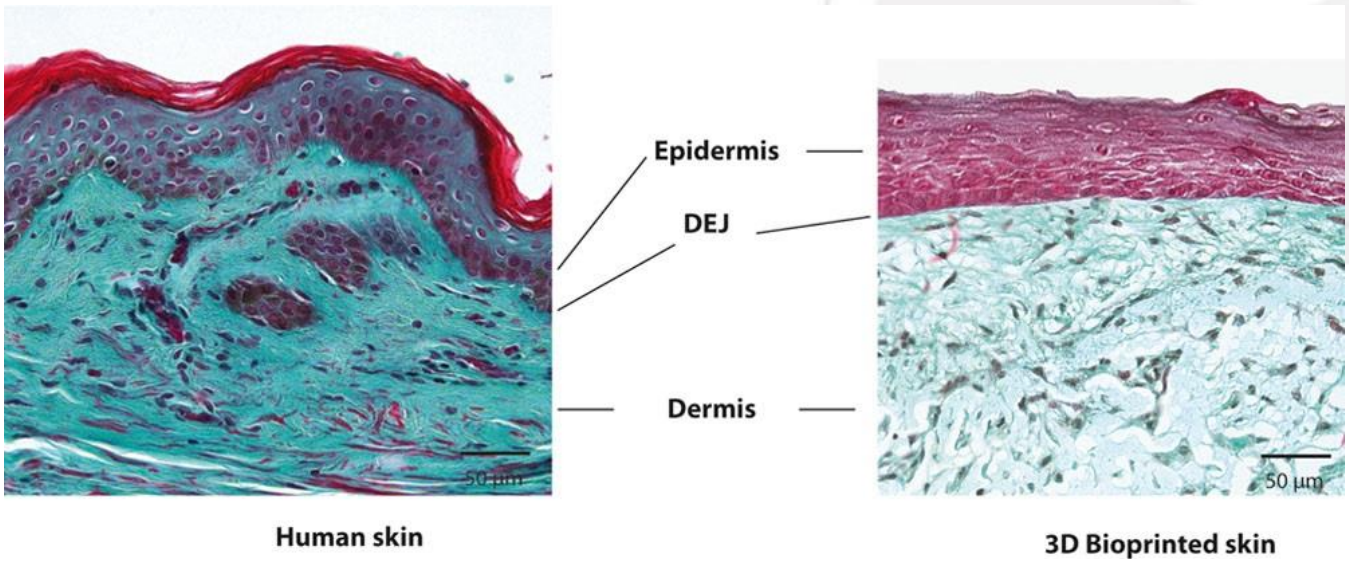






3D printing: Human skin is now being printed in labs

Today



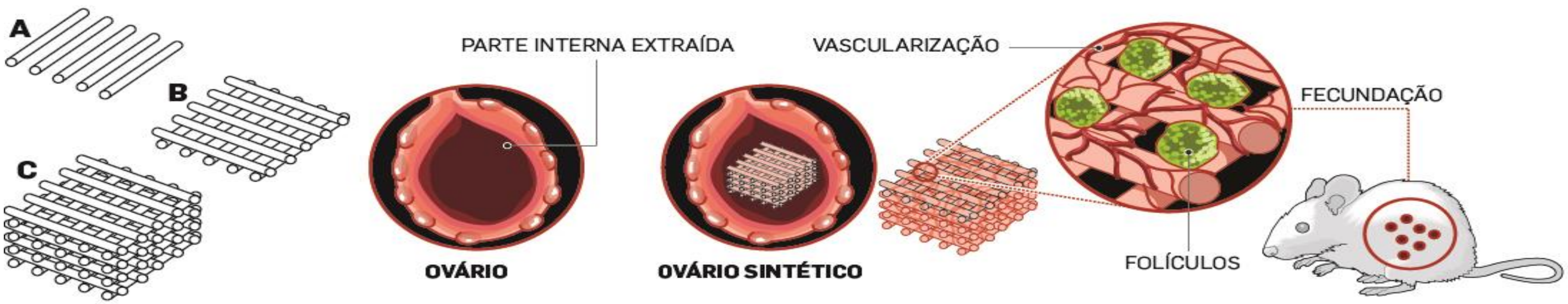
Comparison of optical microscopy images of equivalent slices of normal human skin and printed skin after 26 days of culture. The tissues were stained with Masson's trichrome. DEJ, dermoepidermal junction.

Ovary created using 3D printed scaffolds restores ovarian function

Today

OVÁRIO SINTÉTICO

- **Próteses de hidrogel feitas em impressora 3D substituíram os ovários de camundongos, [illegible] deram gerar filhotes; objetivo era testar se infertilidade causada por tratamentos contra o câncer pode ser revertida em mulheres**



1 A **prótese de hidrogel biológico** foi montada, camada a camada, em uma impressora 3D

2 A parte interna dos ovários dos camundongos foi extraída, tornando o **animal infértil**. A prótese feita em 3D foi implantada na cavidade, formando um **ovário sintético**

3 Em uma semana, o ovário sintético já estava **vascularizado**. A prótese recebe **folículos** - as pequenas bolsas com fluidos que contêm ovócitos (óvulos imaturos)

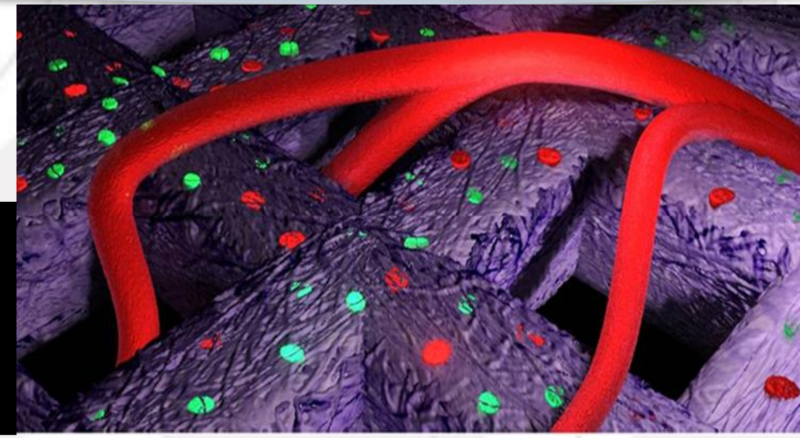
4 O folículo se desenvolveu e **gerou óvulos maduros**. Sete camundogos com ovários sintéticos foram fecundados naturalmente e deram à luz filhotes saudáveis

FONTE: NATURE COMMUNICATIONS

INFOGRÁFICO/ESTADÃO

3D Printed Human Cartilage Cells in Mice

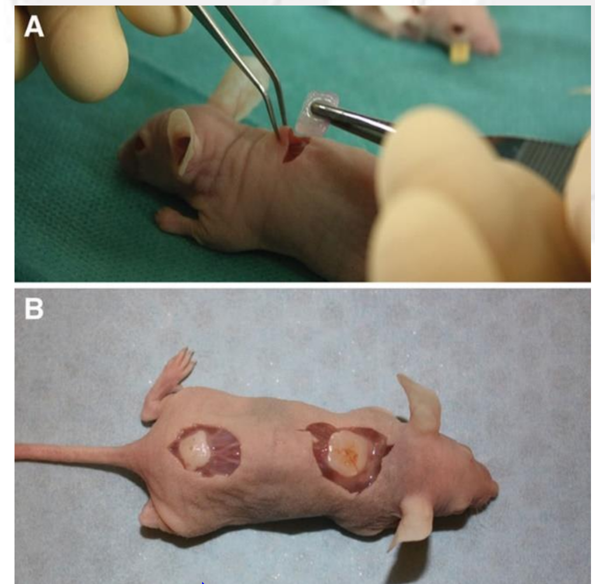
Swedish Researchers successfully Implant 3D Printed Human Cartilage Cells in Mice

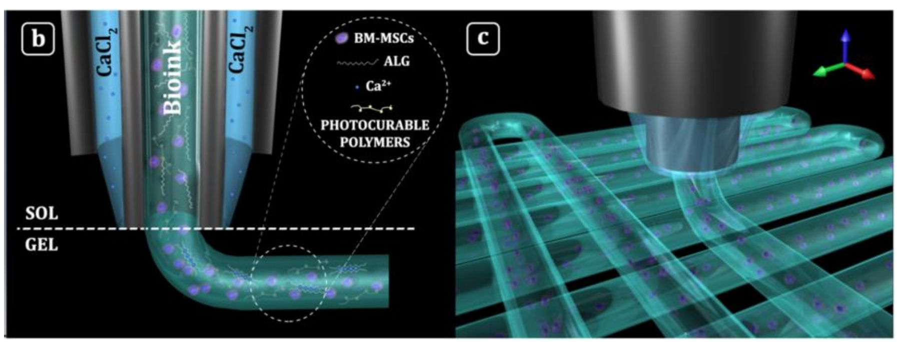


In Vivo Chondrogenesis in 3D Bioprinted Human Cell-laden Hydrogel Constructs

Thomas Möller, MSc*
Matteo Amoroso, MD†
Daniel Hägg, PhD*
Camilla Brantsing, MSc‡
Nicole Rotter, PhD§
Peter Apelgren, MD†
Anders Lindahl, PhD‡
Lars Kölby, PhD†
Paul Gatenholm, PhD*

Background: The three-dimensional (3D) bioprinting technology allows creation of 3D constructs in a layer-by-layer fashion utilizing biologically relevant materials such as biopolymers and cells. The aim of this study is to investigate the use of 3D bioprinting in a clinically relevant setting to evaluate the potential of this technique for in vivo chondrogenesis.
Methods: Thirty-six nude mice (Balb-C, female) received a 5- × 5- × 1-mm piece of bioprinted cell-laden nanofibrillated cellulose/alginate construct in a subcutaneous pocket. Four groups of printed constructs were used: (1) human (male) nasal chondrocytes (hNCs), (2) human (female) bone marrow–derived mesenchymal

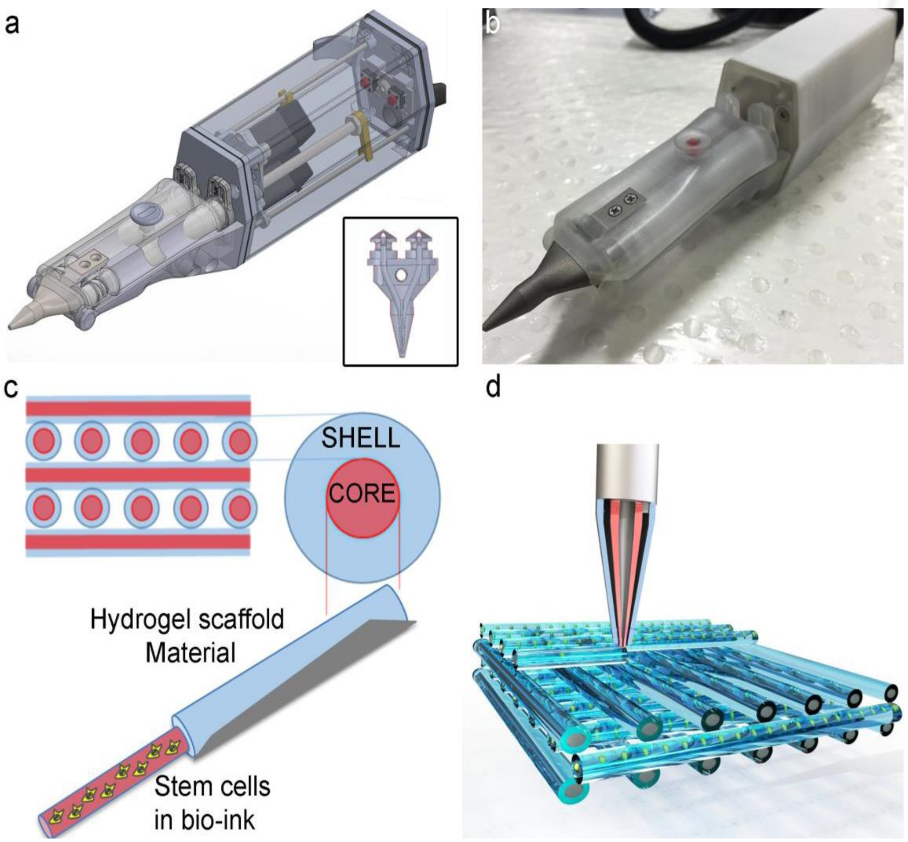


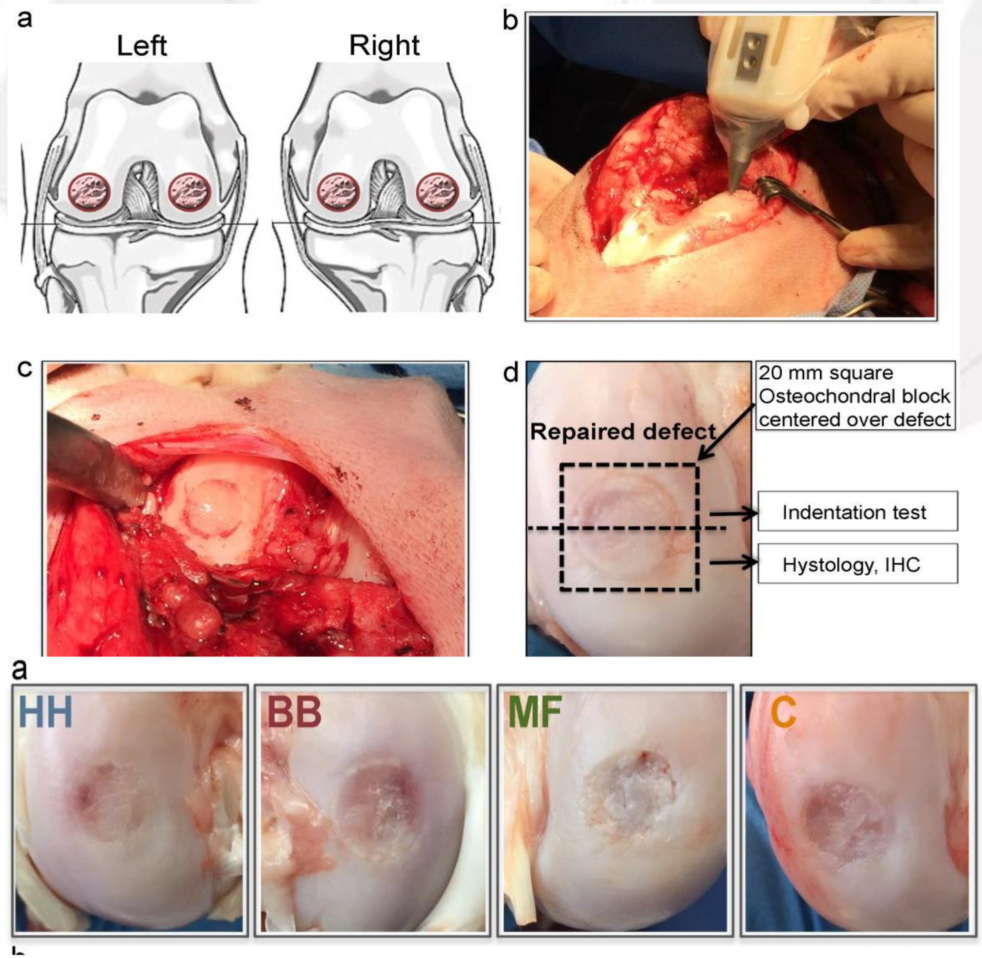


Today

In-situ handheld 3D Bioprinting for cartilage regeneration - May 2017

Journal of Tissue Engineering and Regenerative Medicine

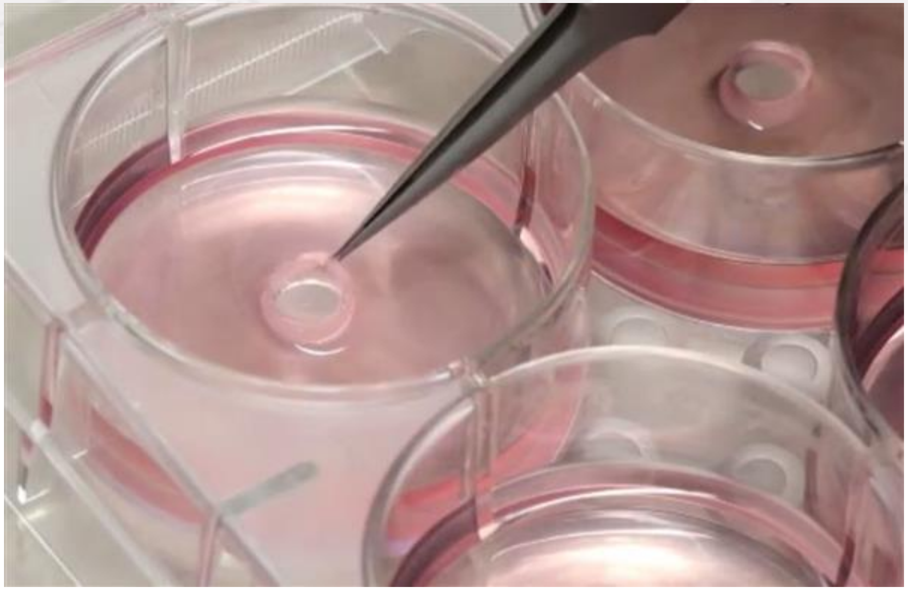




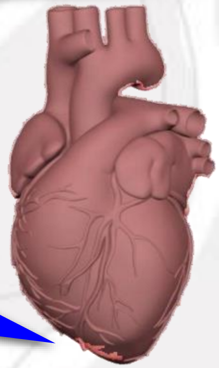
A Scientist Is 3D Printing Blood Vessels for Sick Children

Today

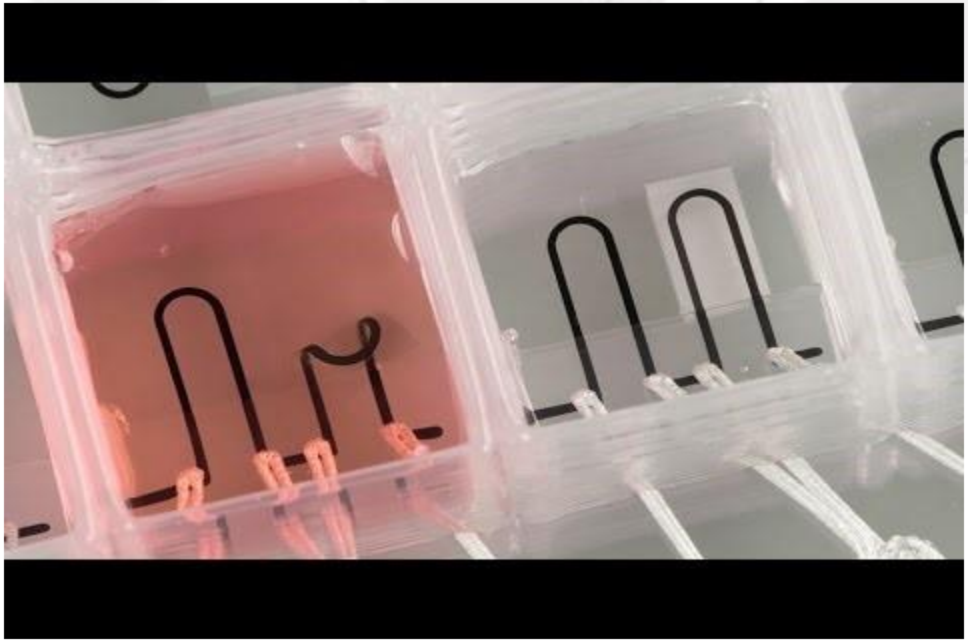
- Scientists are developing flexible materials to 3D print blood vessels
- **Arlington bioengineer awarded $211K NIH grant to develop 3D printed blood vessels for children**



3D-printed heart-on-a-chip with integrated sensors

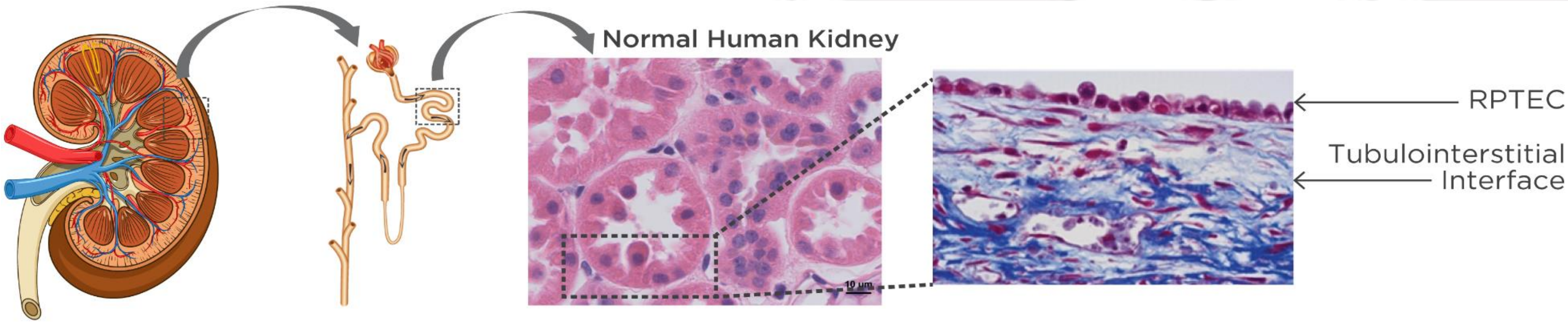


Harvard University researchers have made the first entirely 3D-printed organ-on-a-chip with integrated sensing. Built by a fully automated, digital manufacturing procedure, the 3D-printed heart-on-a-chip can be quickly fabricated and customized, allowing researchers to easily collect reliable data for short-term and long-term studies.

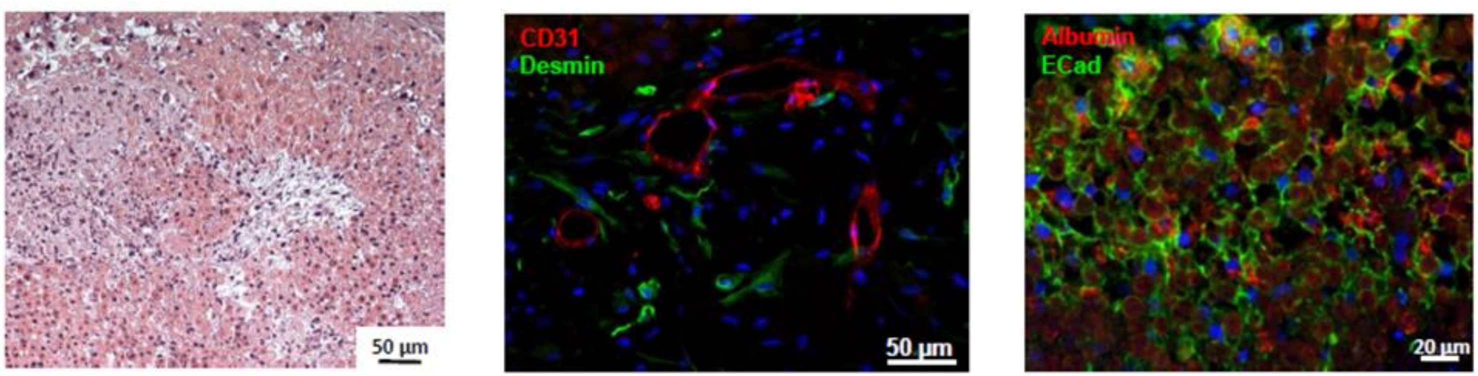


ExVive™ 3D Bioprinted Human Tissue Models

ExVive™ Human Kidney Tissue



ExVive™ Human Liver Tissue Performance



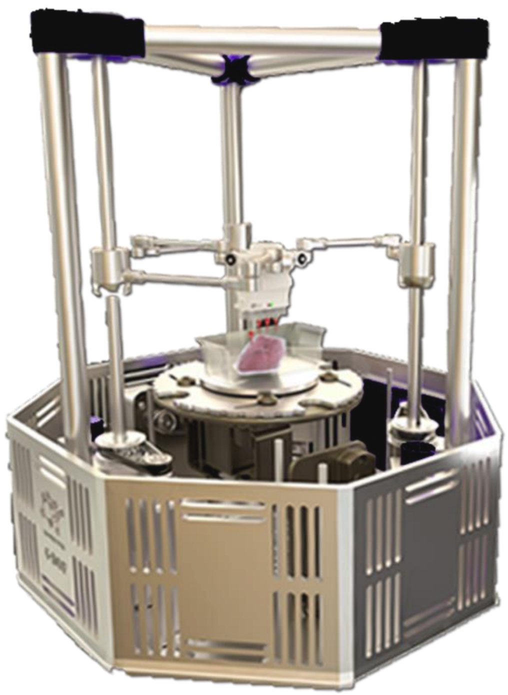
Outlook

Today
- Small scale tissues
- Drug Discovery
- Toxicity testing

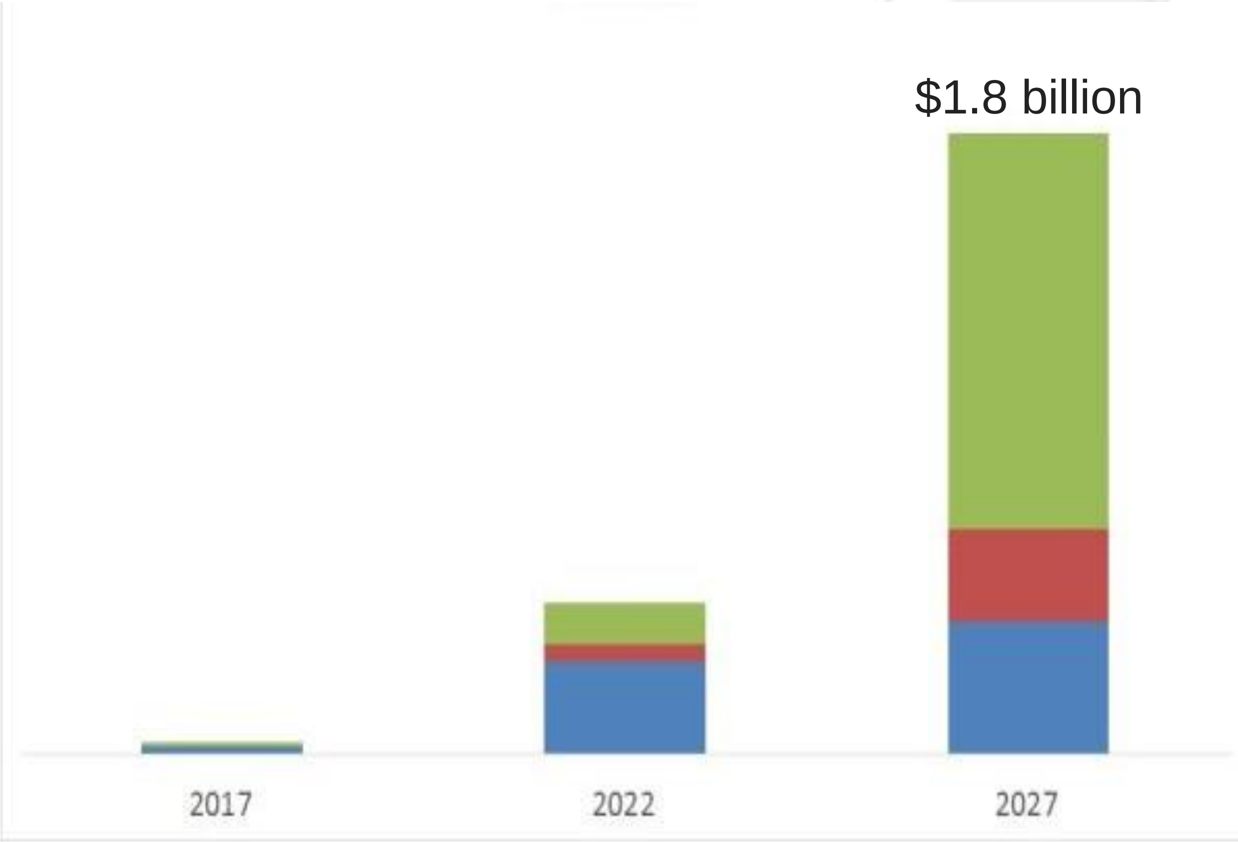
Tomorrow
- Microtissues
- Implants

Future
- Lobes
- Pieces of organs

Uncertain future
- Full organs



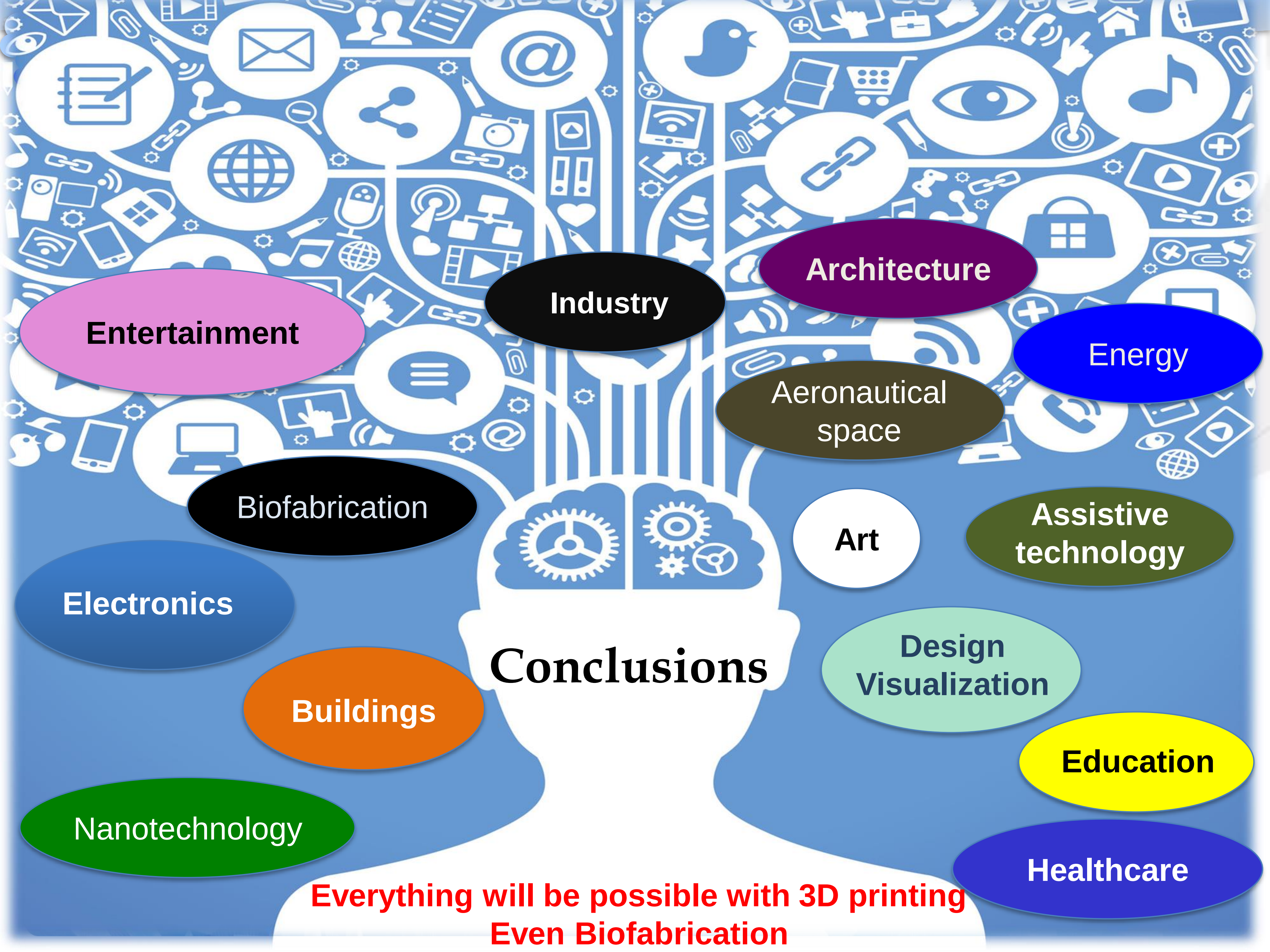
Market projections for 3D Bioprinting.



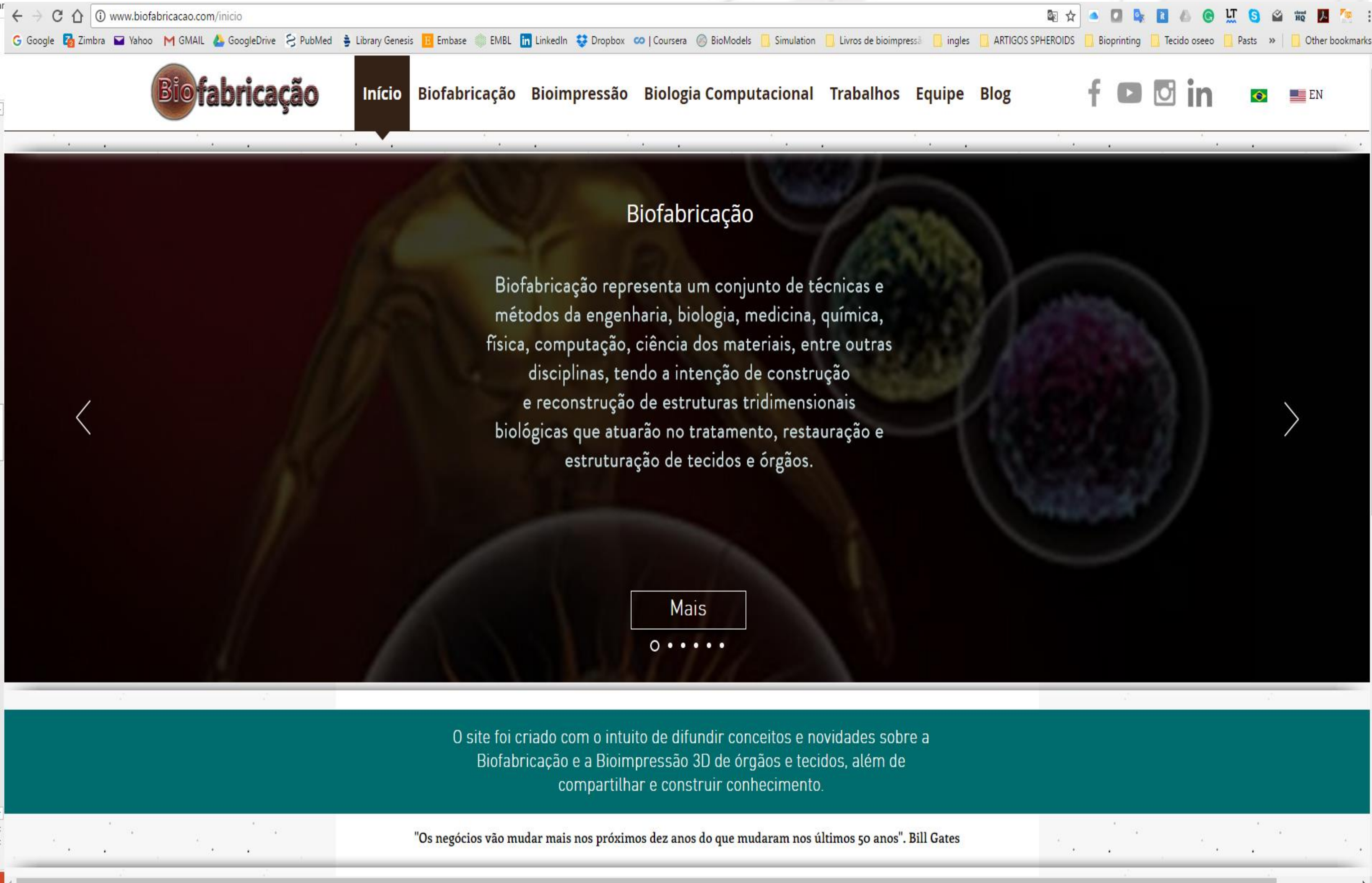
(Credit: IDTechEx)

Challenges

- √ Integration Engineering x Life Sciences;
- √ Development of "blueprint" for bioprinting of 3D human tissue and organs;
- √ Development of new STL file-free function representation based CAD software for digital bioprinting;
- √ Development of scalable technology for biofabrication millions uniform tissue spheroids (robotic tissue spheroids biofabricators);
- √ Development of integrated operational system integration of robotic bioprinters (special software);
- √ Increasing speed and printing resolution of robotic bioprinters;
- √ Development of new bioreactor for 3D bioprinted tissues;
- √ Development of *in situ* bioprinting technologies (*in vivo* bioprinting of skin,
- √ cartilage, bones);
- √ Development of bioprintable biomaterials;
- √ Laws and regulations → <u>* Safety + Security</u>


Conclusions
Entertainment
Industry
Architecture
Energy
Aeronautical space
Biofabrication
Art
Assistive technology
Electronics
Design Visualization
Buildings
Education
Nanotechnology
Healthcare
Everything will be possible with 3D printing
Even Biofabrication

http://www.biofabricacao.com



Thank you for your kind attention!