Centro de Tecnologia da Informação Renato Archer

MODELING AND SIMULATION OF COMPLEX SYSTEMS FOR DESIGN OF TISSUES AND ORGANS TOWARD BIOFABRICATION

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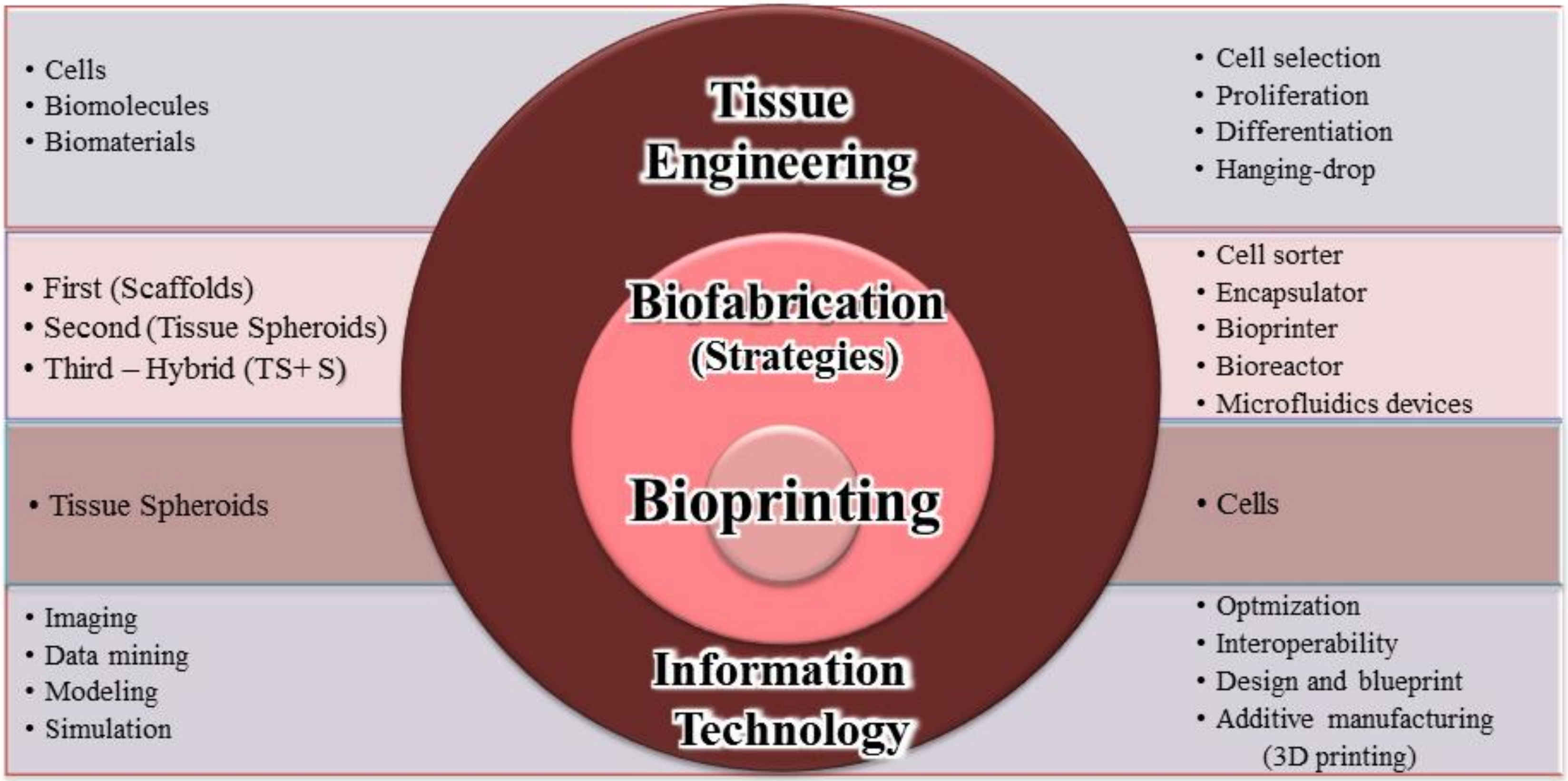
Tissue engineering, Biofabrication, Bioprinting and Information Technology



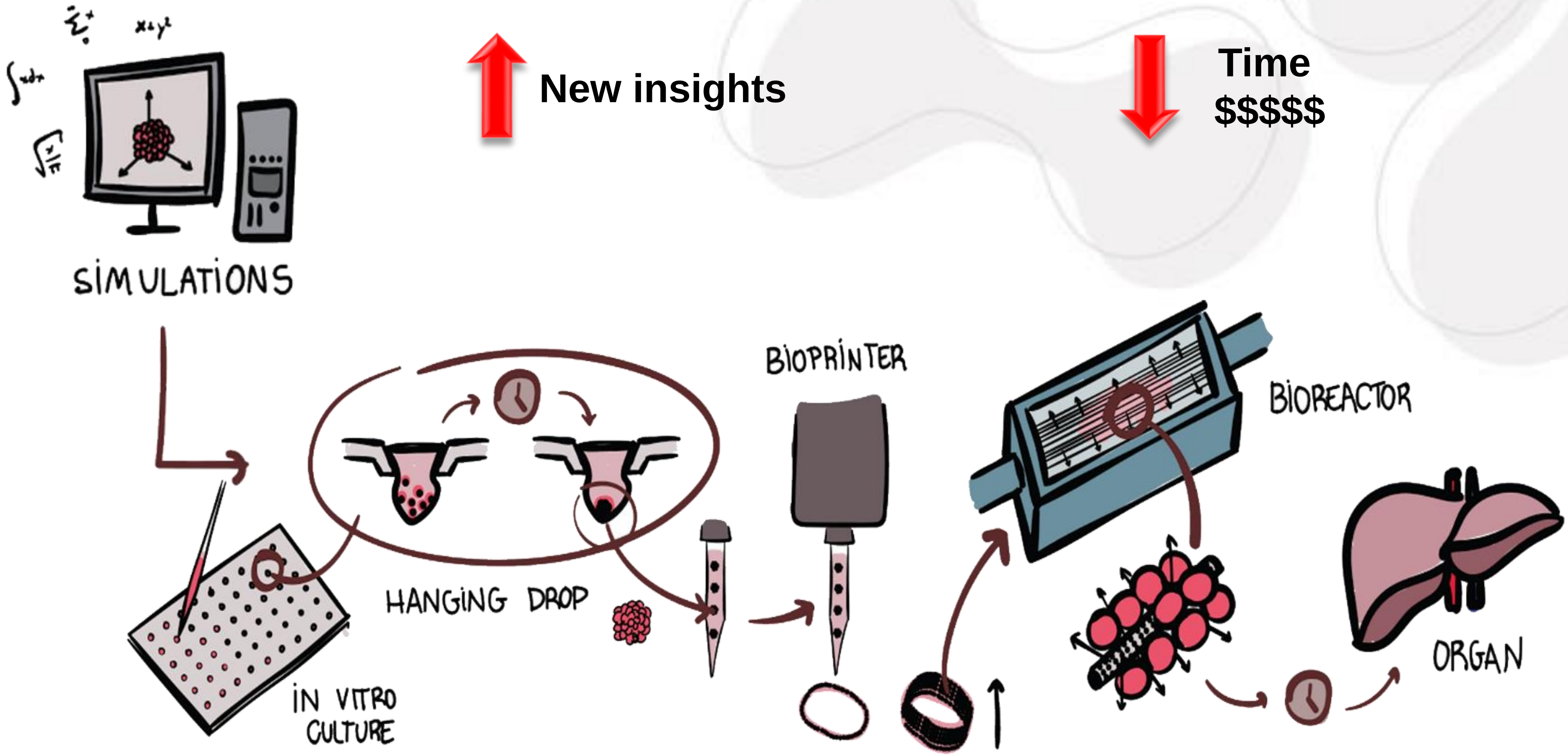
Dernowsek *et al.*, 2017

Biofabrication

Why do we need to simulate in the Biofabrication of tissue and organ?

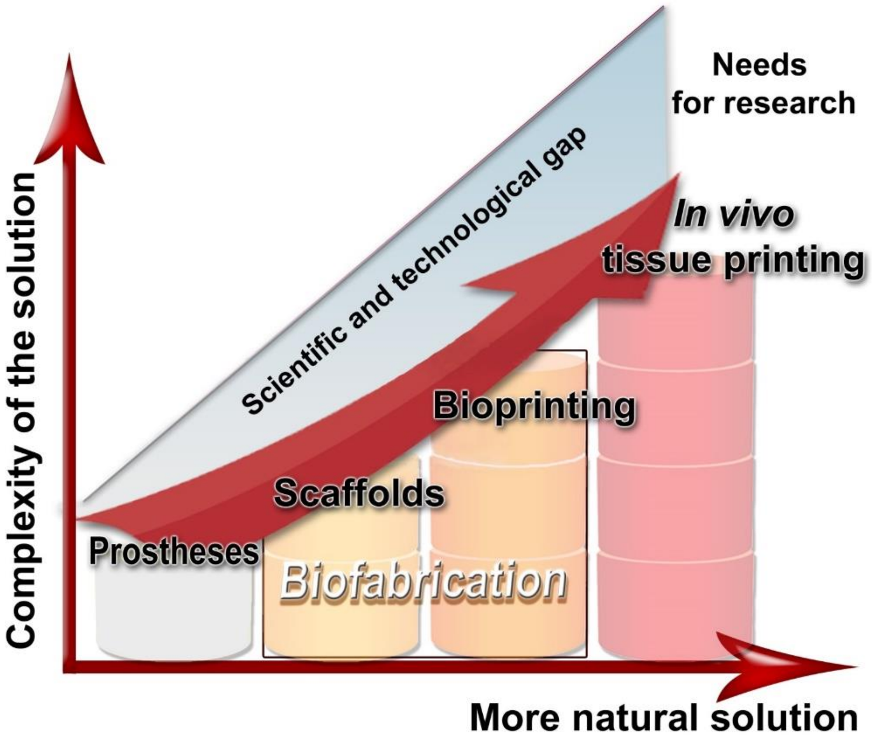
New insights

Time
$$$$$



When to use computer Simulation?

Non-linear behavior



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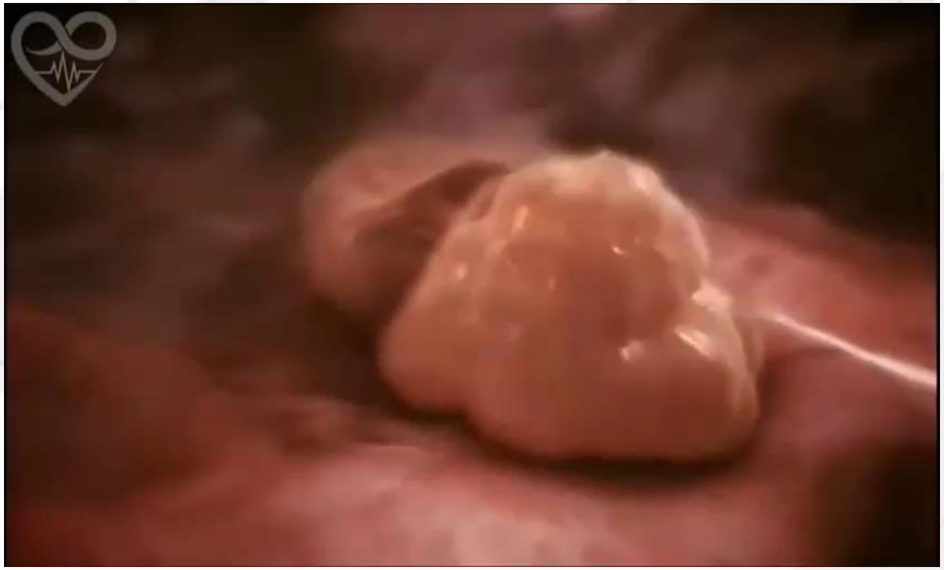
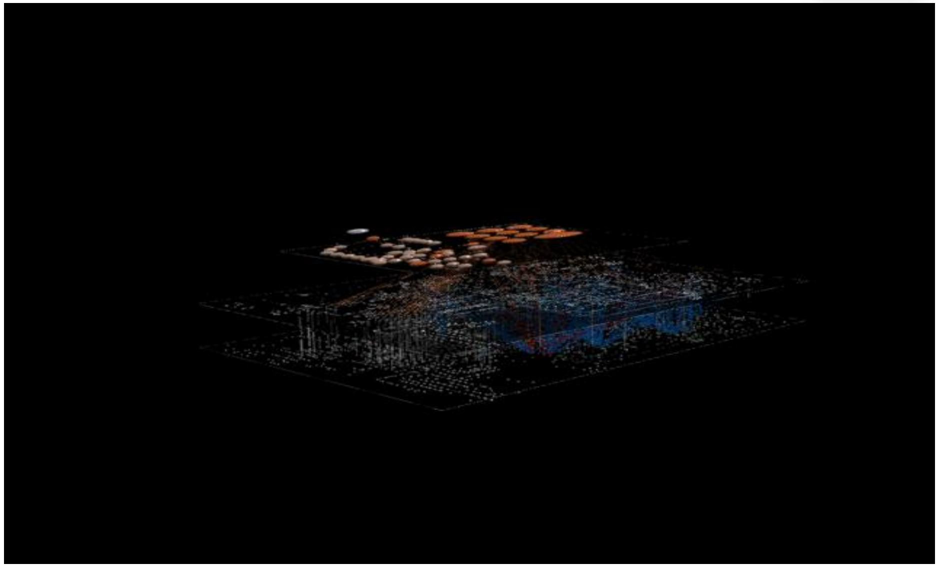
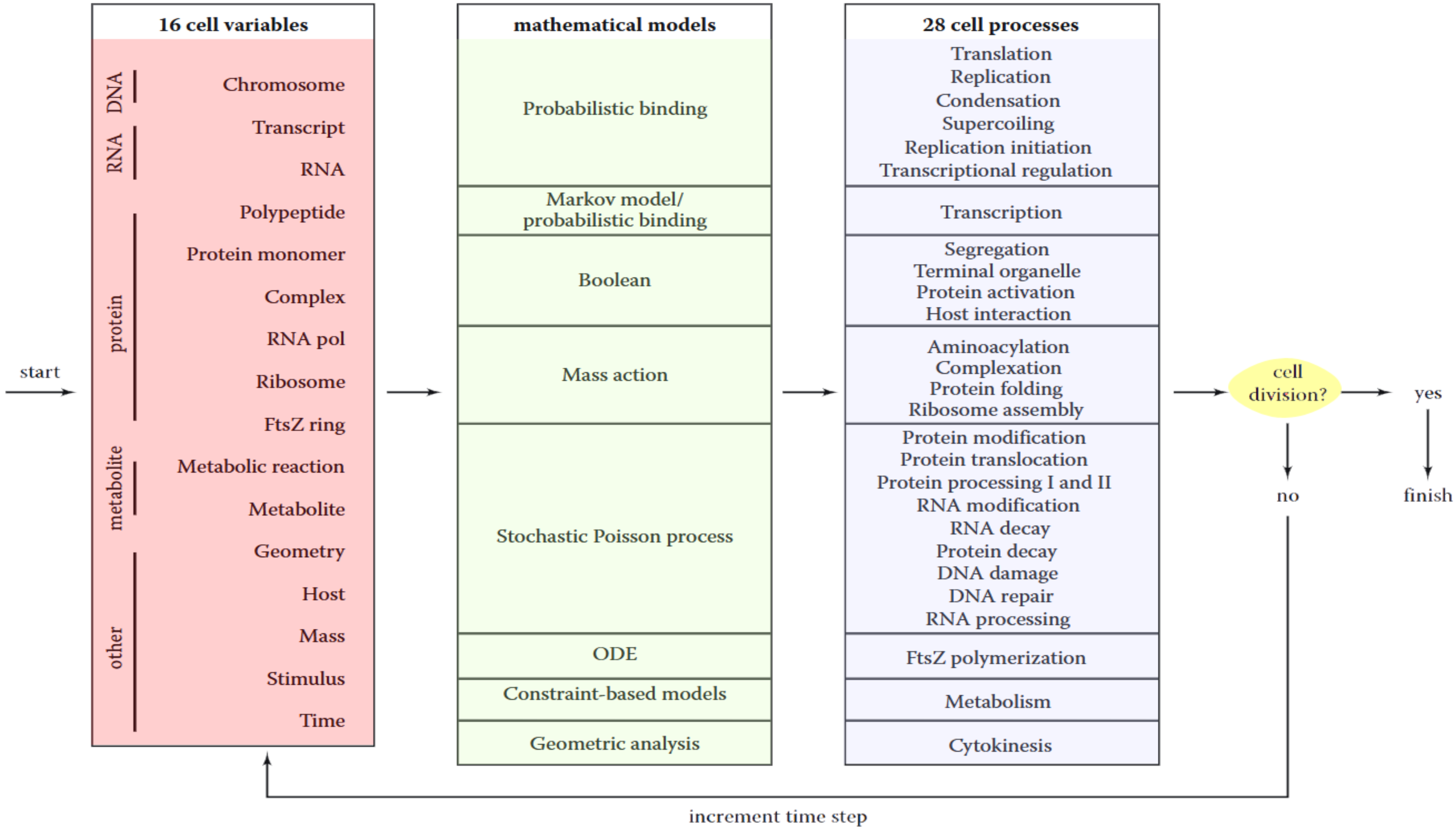


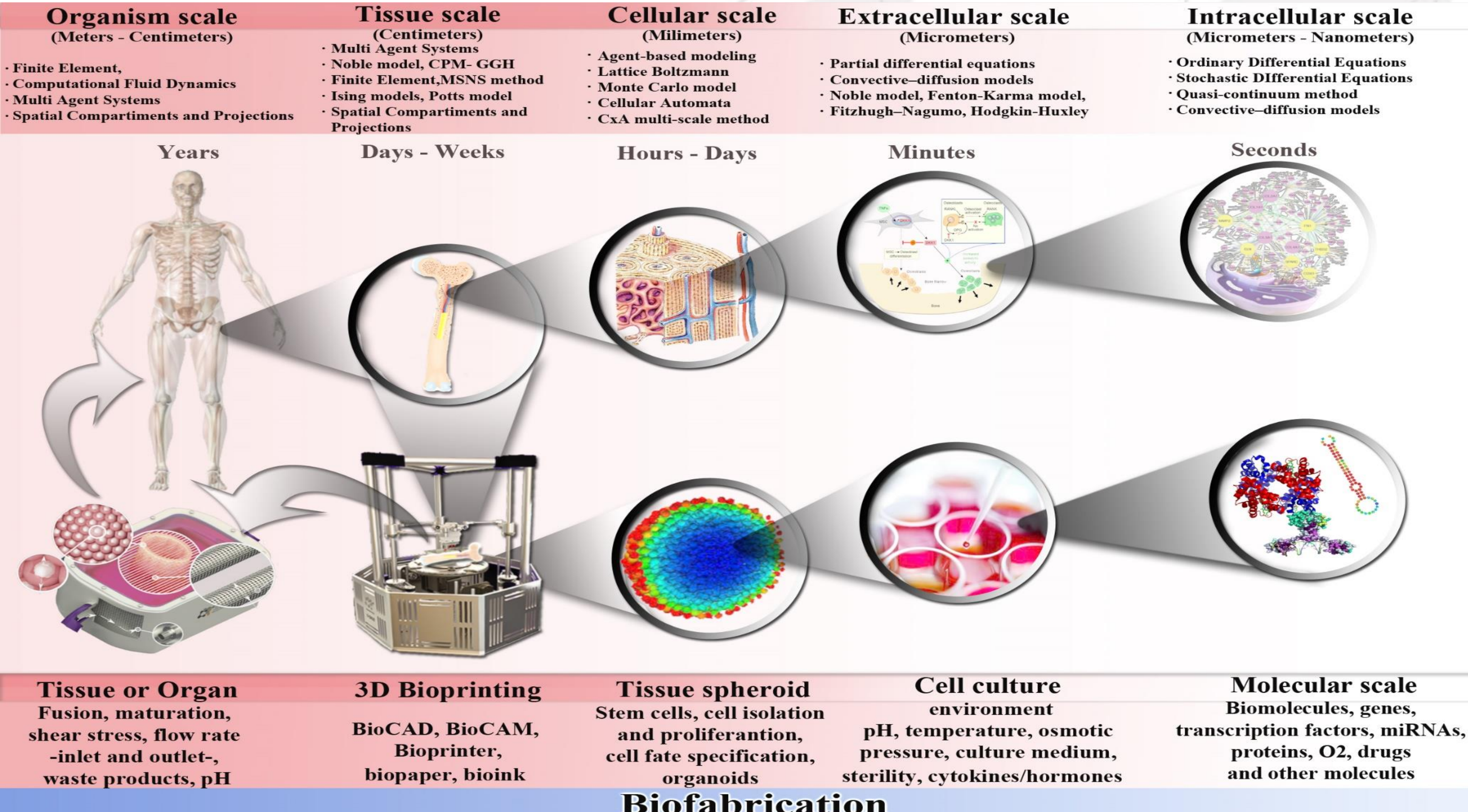


When to use computer simulation?

Large number of variables, methods and processes



Computational and mathematical methods to study complex models at several levels of biological organization



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Methods

SBML

python

CC3D

ParaView

ANSYS Structural Mechanics

ANSYS

ANSYS

CFX

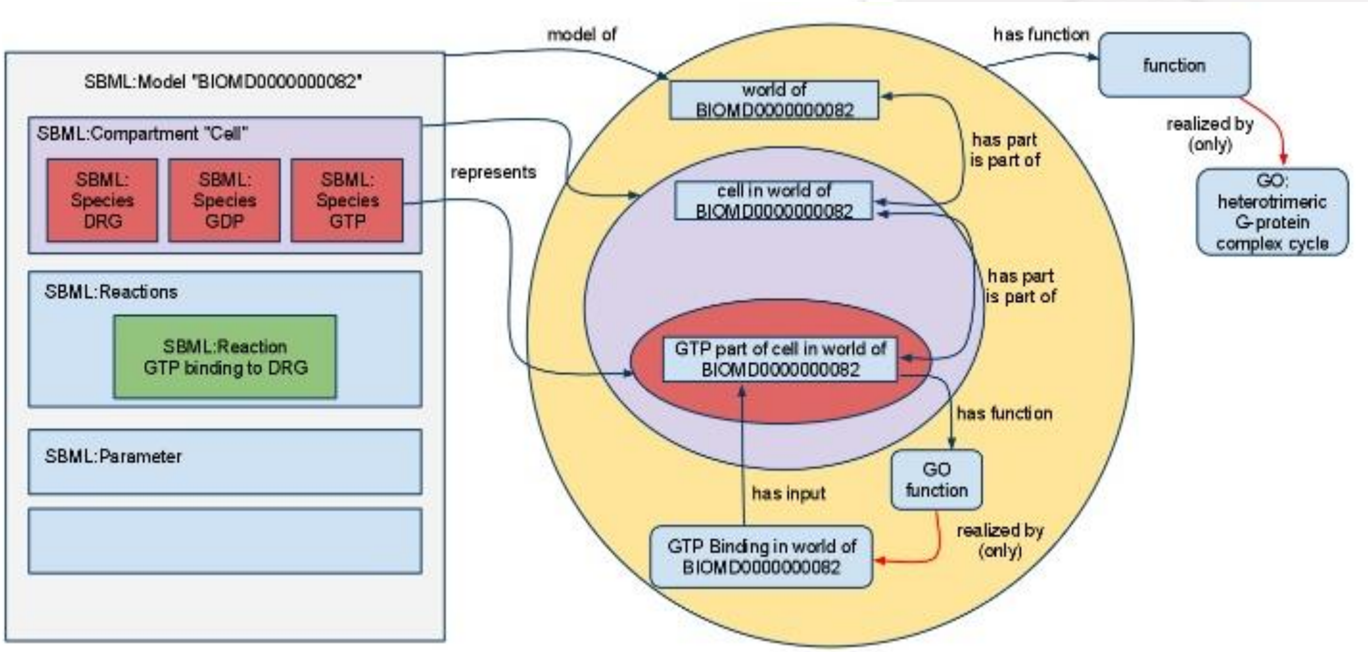
Cellular Potts Model (CPM) implemented in CompuCell3D (CC3D)

- **Cross-platform**, **open-source** environment for building and running **multi-cell multi-scale simulations of tissues and organs**
- A library of **Python/C++** modules that implement the **CPM**;
- **Describes models** using combination of **XML** and/or **Python;**
- Simulation-wizards, simulation editors, graphical interfaces, visualization tools, **SBML** solvers, and FE solvers (experimental support) included;
- Ability to import, control and run **SBML models.**

Systems Biology Markup Language

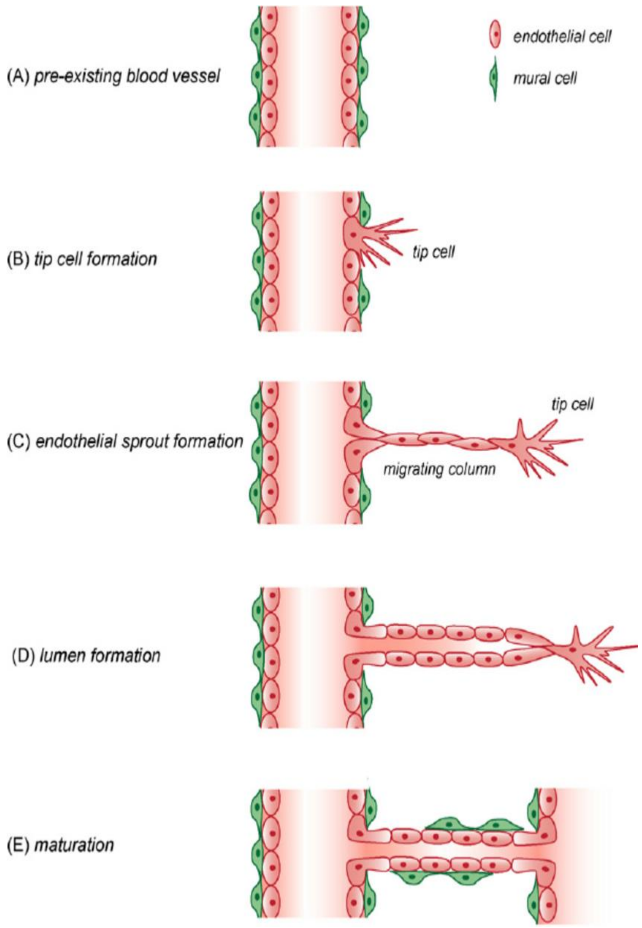
Mathematical models are key in studying the behavior of biological systems

Systems Biology Markup Language



XML-based representation of biochemical models, their components (compartments, species, reactions, events), descriptors (rules, constraints, functions, units)

Biological phenomenon → Angiogenesis

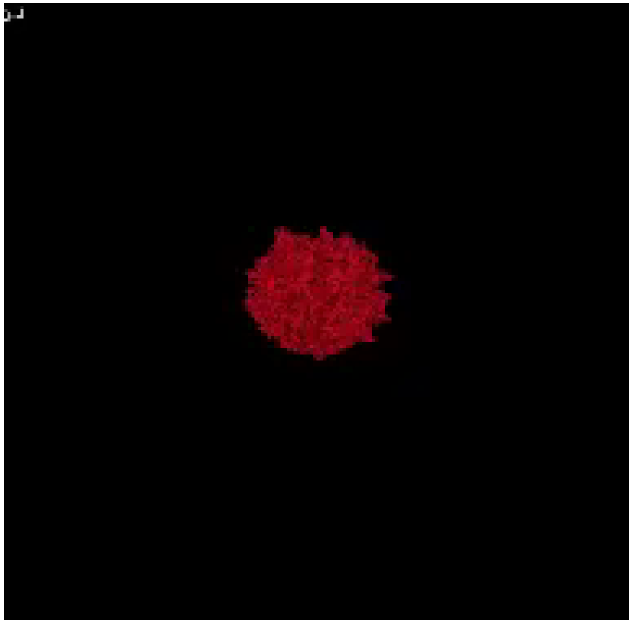


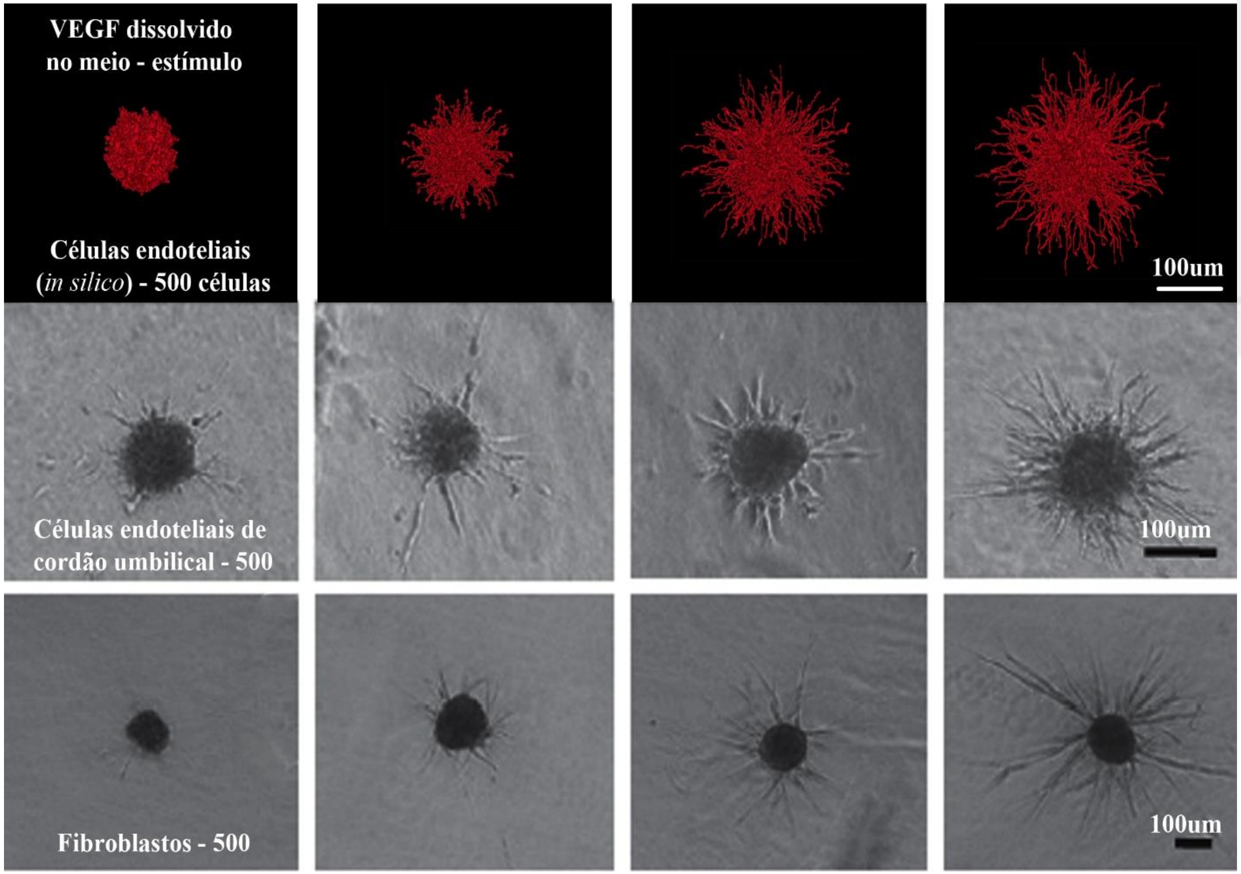
- The *in silico* study focuses on the biological process of the angiogenesis of an aggregate of endothelial cells (EC).

- The angiogenesis assay *in silico* was compared with *in vitro* experiments as demonstrated by Heiss and collaborators (2015) using endothelial cell spheroids.

Results

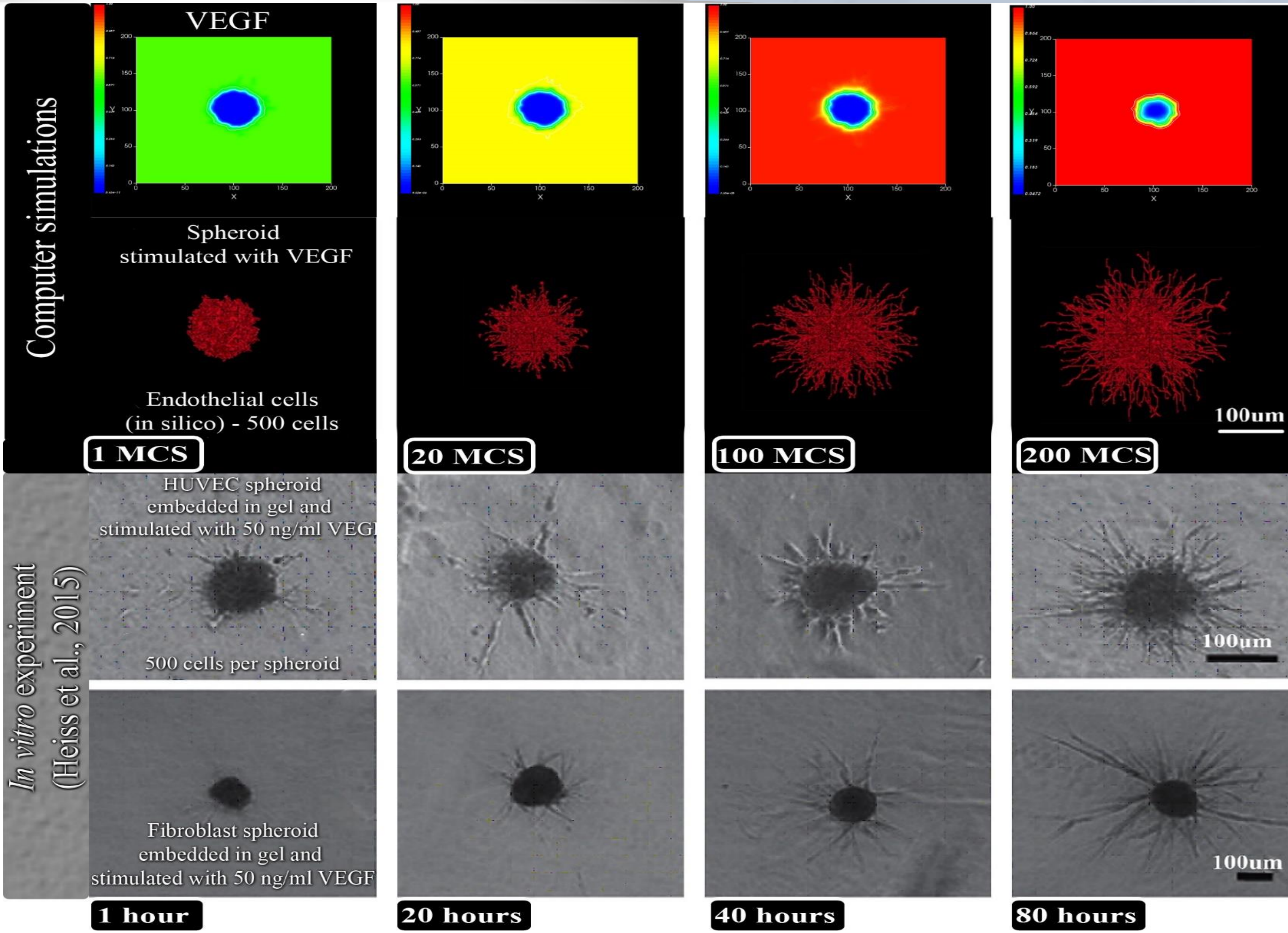
Endothelial cell spheroids as a versatile tool to study angiogenesis in vitro and in silico





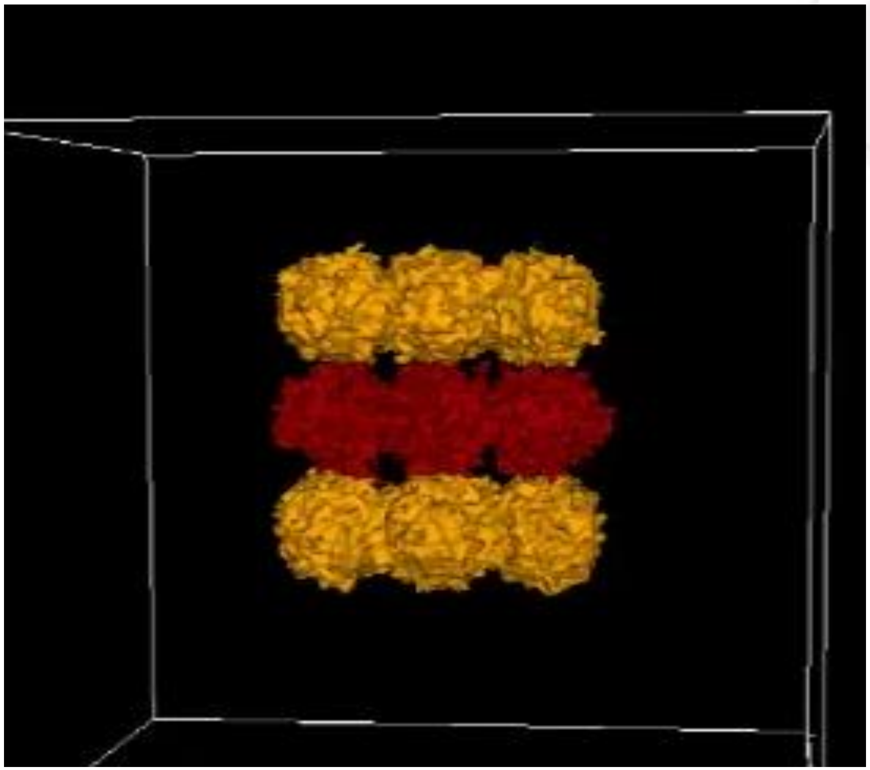
***In silico* assays** show us that sprouting and elongation of cells were similar to the ***in vitro* experiments.**

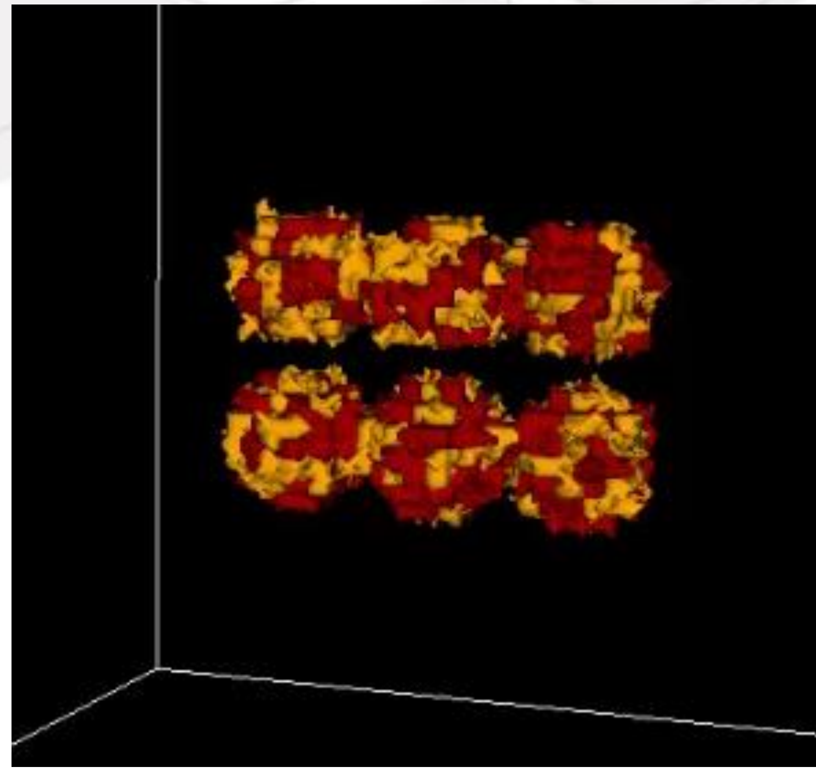
Heiss, *et al.*, FASEB J., 29:3076-3084, 2015.



Computer simulations
VEGF
Spheroid
stimulated with VEGF
Endothelial cells
(in silico) - 500 cells
1 MCS
20 MCS
100 MCS
200 MCS
100um
In vitro experiment
(Heiss et al., 2015)
HUVEC spheroid
embedded in gel and
stimulated with 50 ng/ml VEGF
500 cells per spheroid
100μm
Fibroblast spheroid
embedded in gel and
stimulated with 50 ng/ml VEGF
100um
1 hour
20 hours
40 hours
80 hours

Computational approaches for biofabrication of tissues → Angiogenesis + Proliferating cells



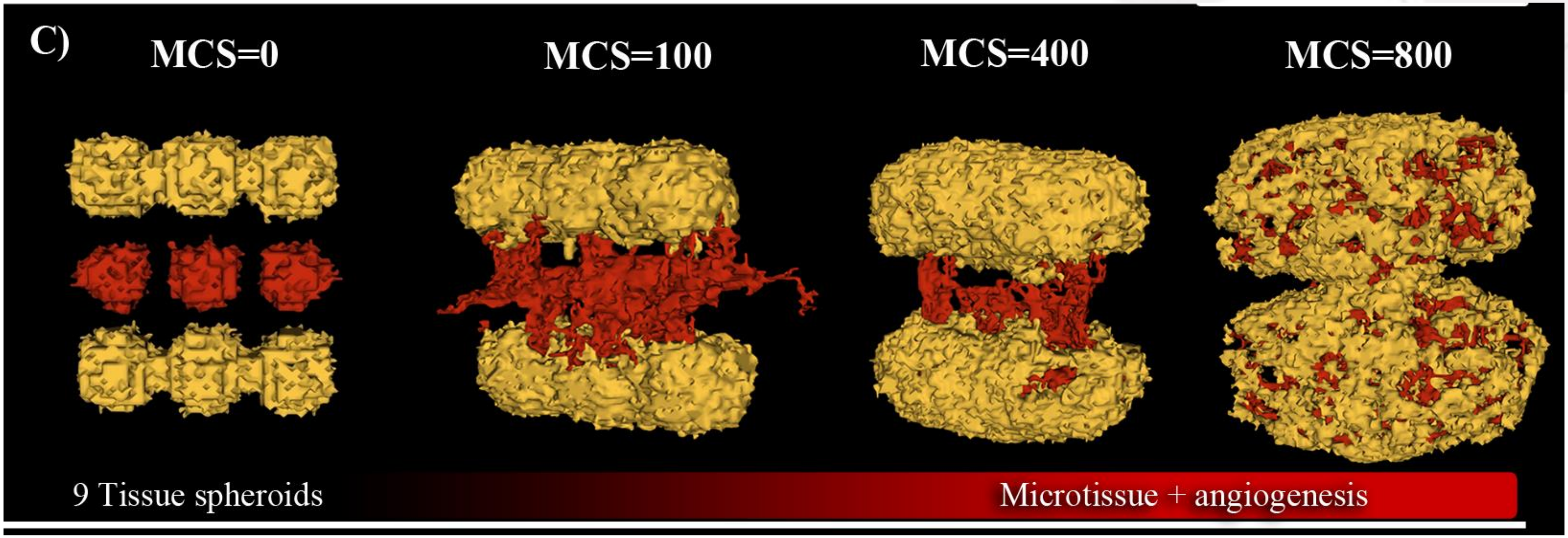


● Proliferating cells - PC

● Endothelial cells - EC

Conclusions

- The data generated will facilitate the understanding of tissue functioning in multiscale levels and the development of **3D tissue design**.

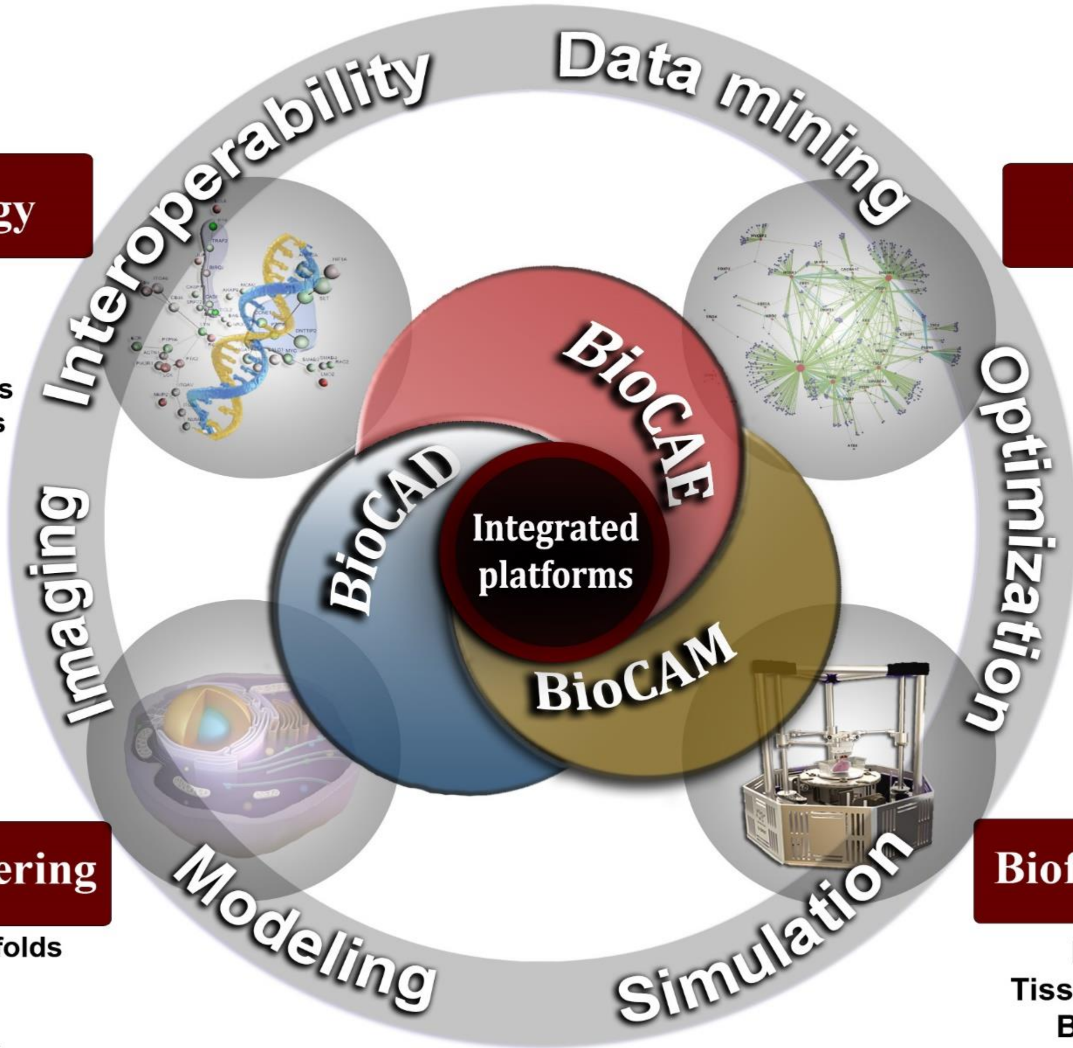


Systems Biology

Genomics
Transcriptomics
Proteomics
Interaction networks
Pathway databases

Information technology

Data mining
Network algotithms
Data integration
Multi-agent systems
Machine learning



Tissue engineering

Biomaterials scaffolds
Stem cells
Signaling
Biomolecules
Tissue microenvironments
Microfluidics

Biofabrication

Blueprint
Tissue spheroids
Bioprinting
Constructs
Microtissues
Bioreactor

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Challenges

- ✓ **Integration Engineering x Life Sciences;**
- ✓ **Development of new file function representation**
- ✓ **Development of scalable technology**
- ✓ **Development of integrated operational system integration of robotic bioprinters (special software);**
- ✓ **Development of new biomaterials and materials for tissue engineering;**
- ✓ **Laws and regulations → <u>* Safety + Security</u>**
- ✓ **A New Integrated Platform for Biofabrication of Tissue and Organs**

Thank you for your kind attention!