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

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Introduction: Nowadays, 3D bioprinting processes can be used to produce biocompatible products in a variety of formats, structural complexities, based on different properties and materials, cell types, growth factors, and differentiation stage. Moreover, the extracellular matrix composition, mechanical properties, macro and microvasculature, and the technical challenges associated with the creation of biomodels that mimic vascularized organs are also required for the biomanufacturing steps. BioCAD model is potentially designed by an association among software for the treatment of imaging, computer-aided design (CAD) and computer-aided engineering (CAE). However, the specific and detailed understanding of the structural and vascular organization as well as the cellular composition, the extracellular matrix, biomolecules diffusion and biophysical factors becomes a challenge for the successful development of the tissue, requiring an integrative and interdisciplinary approach.
Methods: The emergence of integrated platforms to understand complex systems in multiscale levels will enable the prediction and creation of biological structures [1]. This platform for estimating biological process has been named as BioCAE, which will become the key for important steps of the biofabrication processes. Biological Computational Aided Engineering (BioCAE) is a new computational approach to understanding and bioengineer complex tissues (biofabrication) using a combination of different methods as multi-scale modeling, computer simulations, data mining, and systems biology. This work will have a computer character aiming the use and integration of engineering techniques, biological databases and graphical tool, able to design a biological tissue to bioprinting.
Results and Discussion: To implement our model we use a program with the graphical user interface called CompuCell3D (CC3D). The CC3D program allows simulating a series of complicated biological processes, including microtissues in a 3D environment, using the Monte Carlo method known as cellular Potts model. Details from figure 1 show some results obtained by computer simulations of angiogenesis and cell proliferation of tissue spheroids. The angiogenesis assay *in silico* was compared with *in vitro* experiments as demonstrated by Heiss and collaborators [1] using endothelial cell spheroids. Interestingly, the *in silico* assays show us that sprouting and elongation of cells were similar to the *in vitro* experiment. Simulations of microtissues were done to understand the behavior of angiogenesis during cell proliferation on tissue spheroids.

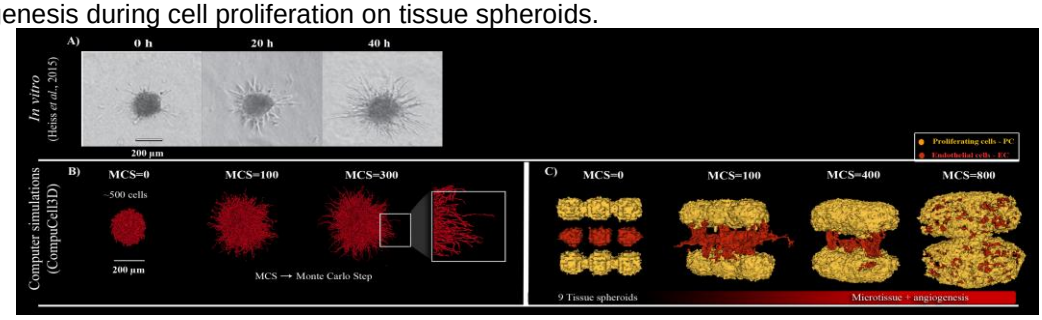

Figure 1. In vitro experiments (A) and computer simulations on tissue spheroids (C-B).

Conclusion: The data generated will facilitate the understanding of tissue functioning in multiscale levels and the development of 3D hybrid tissue design, because of an integrated solution among biology, physics, chemistry, mathematics, and engineering.
References:
[1] Heiss, et al. Endothelial cell spheroids as a versatile tool to study. FASEB J., 29:3076-3084, 2015.