Multiphase Modeling of Vascularized Tissues: An Integrated Experimental and Numerical Approach

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This thesis is a key component of the ANR MATISSe project, which aims to optimize the fabrication of artificial vascularized tissues using organoids, which is currently a frontier in regenerative medicine. The primary challenge in tissue engineering is the creation of a functional vascular network capable of perfusing and oxygenating the entire structure to prevent necrosis. Within the Institute of Mechanics and Engineering of Bordeaux (I2M), this work addresses the challenge by treating tissue as a multiphase porous medium, where cell growth, angiogenesis (vessel formation), and anastomosis (vessel connection) are governed by complex mechanical and fluid-dynamic interactions.

A major contribution of this research is the development of a sophisticated, 3D-printed experimental setup designed to provide high-quality, real-time biological data. While traditional models often overlook physical forces, this platform is specifically engineered to apply precise static mechanical pressure to 3D cell aggregates. Fabricated from gas-impermeable resin, the microfluidic chip features a dual-circuit system for nutrient renewal and pressure regulation. This ensures that the environmental conditions such as oxygen transport and mechanical stress remain physiologically relevant. Thus providing the empirical foundation necessary to validate the complex mathematical laws of mass conservation and endothelial cell migration.

In parallel, the research develops a high-fidelity Digital Twin based on the theory of reactive, deformable porous media. By integrating experimental data into poro-mechanical simulations, the digital twin models the evolution of the tissue, simulating the interaction between vascular cells and the extracellular matrix.

The ultimate objective of this thesis is to reach a level of predictive accuracy where the Digital Twin can pilot the experimental setup automatically. In this closed-loop configuration, the virtual model predicts the optimal conditions for angiogenesis and growth, then adjusts physical parameters such as pressure, flow rates, and biochemical gradients, without human intervention. This methodology enables the optimization of culture conditions in real-time, identifying the exact factors that promote successful vascularization.

The convergence of multiphase modeling and autonomous feedback loops represents a significant leap forward in computer-assisted tissue design. By combining advanced imaging (confocal and OCT) with predictive *in silico* tools, this research provides a robust framework for understanding vascular interactions across multiple scales. Ultimately, this integrated approach aims to accelerate the production of functional artificial tissues for regenerative medicine while significantly reducing the reliance on animal models.