Computer-based simulation of multicolour bioprinting

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Even though building 3D vascularized organs is still a technological barrier to overcome, bioprinting has shed light on advancing the field of tissue engineering into a new era. Organ printing or bioprinting of tissues and organs can be defined as layer-by-layer additive robotic biofabrication of three-dimensional functional living macrotissues and organ constructs using tissue spheroids as building blocks. Closely placed tissue spheroids undergo tissue fusion, a process that resembles the 'self-assembly' principle of morphogenesis [1].

The detailed biophysical and biochemical mechanism of tissue fusion is not fully understood so far given the complexity of cell motility. Modern mathematical modelling and computer simulations can provide insight into the physical nature of tissue fusion process by predicting plausible outcomes that are essential for designing optimal bioprinting processes. Following the Differential Adhesion Hypothesis (DAH), the cellular aggregates and the surrounding hydrogels can be treated as highly viscous, incompressible fluids in the time scale comparable to cellular aggregate fusion. The phase field formulation is then a natural way to formulate the multiphase immiscible fluids model [2].

Most studies to date have focused on homogeneous 3D bioprinting with single material and and single cell type. However, 3D bioprinting has great potential to fabricate heterogeneous tissues with multiple cell types, biohybrid materials and/or different mechanical properties. For example, aortic heart valve function is heavily dependent on its geometry and material composition [3].

We therefore propose a multi-phase field model based on the Cahn-Hilliard equation to simulate multiple cell-type (multicolor) bioprinted tissues using isogeometric analysis. The governing equations include fourth-order spatial differential operators that we discretize using globally C^1 continuous basis functions in a variational formulation through the concept of isogeometric analysis [4].

Preliminary results show that the time for fusion of the multicellular systems depends on the initial packing of the cellular spheroids. Tight packing can result in shorter fusion time. Mathematical modeling and simulation can therefore provide guidance to the bioprinting process in precision.

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