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Abstract

Study of Spheroids Fusion via Multiphysics Simulations: Feasibility of Applying Permanent Magnetic Field Gradients †

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Abstract: Cell spheroids represent a scaffold-free route to form cell aggregates through maximizing cell-cell interactions. Spheroids have gained significant attention for the engineering of multilayer tissues as they offer a closer resemblance of physiological conditions observed in vivo, compared with traditional 2D models where cells are grown on flat surfaces. Multilayered tissues are formed by allowing spheroids to interact with themselves within relevant matrices mimicking native conditions of extracellular matrices. However, such conventional fusion methods provide little control over spheroid–spheroid interactions, making their reproducibility very limited. Additionally, such methods are lengthy, which is undesirable from the scalability and economic viewpoints. We propose a methodology to accelerate spheroid fusion by applying magnetic forces externally on spheroids previously magnetized by the internalization of iron oxide nanoparticles. A base mathematical model of spheroids assembly was implemented in COMSOL Multiphysics and involved a laminar two-phase field approach, which was validated by employing a novel segmentation algorithm. The magnetic effect was introduced by an applied volumetric magnetic force, which was generated by the action of two neodymium permanent magnets positioned perpendicular to the computational domain. Our simulations showed that magnetized spheroids fusion can be accelerated by about 55% after applying a magnetic force. In addition, we successfully tested a new modeling approach that allowed taking into account interactions between spheroids and the medium, as evidenced by a standard error of only 13% with respect to the experimental results shown in the literature. Importantly, these simulations also showed that the time required to fuse the spheroids is reduced by about 55%. We are currently validating the model experimentally on extracellular-matrix-derived hydrogels embedded with magnetized spheroids. Future work will be dedicated to calibrating the model with the collected experimental data.

Keywords: spheroids fusion; cell spheroids; magnetic fields; COMSOL software; phase field

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