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Finite element modeling of physical processes in multilayer spheroids based on Functional Representations

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Motivation and Aim: The current study is motivated by the need to study biological objects that have heterogeneous structures. Such objects emerge in various fields of modern biotechnology, but the current study focuses on objects that come to existence via bioprinting and organoid cultivation. 3D bioprinting – a branch of 3D printing that uses cell-infused hydrogel instead of plastic – is based on tissue spheroids [1], three-dimensional cell cultures, fusing together following the tension forces. Tissue spheroid is similar to an organoid [2] – three-dimensional structure grown from stem cell culture in vitro. Viability of a tissue spheroid and an organoid depends on the same physical process – diffusion of oxygen, nutrients and other important chemicals. Studying the physical processes within a spheroid and an organoid requires non-trivial mathematical apparatus due to the complexity of spheroid/organoid shapes.
Methods and Algorithms: We use functional representations (FRep [3]) to provide the geometry of the multilayer spheroid – a three-dimensional cell culture that possesses a layered inner structure. A similar geometry is constructed for an organoid. The geometry is used as a mesh for the Finite Element Method computations (with the use of the Firedrake [4] framework).
Results: We propose an approach to model the diffusion processes within a spheroid and an organoid. The method unites numerical modeling with finite elements for solving time-dependent differential equations for diffusion and deformation and geometrical modeling with implicit functions within the Functional Representations (FRep) framework. We perform the simulations for two different kinds of chemicals that could be diffused within an object of interest – oxygen and a fluorescent dye (calcein).
Conclusion: The results of our study shows that the proposed method provides for accurate evaluation of the fluorescent calcein concentration field that complies with experimental results [5]. Our method also allows for analysis of cell viability and predictions for emergence of anoxic regions in case of analyzing oxygen diffusion.

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