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*Abstract*

# Cell Culture Bioreactor Manufacturing, from Material Selection to Numerical Models †

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Cell culture bioreactors play a paramount role in obtaining successful cell cultures that mature into tissue-like structures. Cellular growth is accomplished by supplying the seeded cells with sufficient nutrients while performing an adequate removal of cellular metabolic waste products [1]. At the same time, it is necessary for the cellular environment to maintain adequate biological levels of pH, temperature, gas concentration ($O_2$, $CO_2$), and hydrostatic pressure.

The current work presents a new methodology to create a shareable and easily reproducible cell culture bioreactor based on open source technologies, accessible materials, and ubiquitous construction techniques. Our bioreactor designs are continuously supported by corresponding digital twin numerical models to optimize their operation in current tissue engineering processes [2]. Numerical models also play a key role in understanding the local conditions imposed and consequent cellular effects, especially when cellular environmental conditions become unfavorable or are very difficult to measure and control. Specifically, our research is focused on modeling the delivery of external stimulation modalities, such as electromagnetic, fluid flow, wall shear stress, and hydrostatic pressure. Our overall goal is for our predictions to ultimately help to obtain critical insights into the environmental cues that lead cells to differentiate, proliferate, grow, and, finally, mature into tissues of interest.

As part of this project, we will present the developed bioreactor designs that will allow the validation of the digital twin models proposed. We will also present a detailed analysis of new developments and opportunities for numerical models and bioreactor in tissue engineering applications.

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