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BIOREACTOR DIGITAL TWIN - AN ESSENTIAL MODELLING TOOL TO ESTIMATE LOCAL CELLULAR ENVIRONMENTAL CONDITIONS IN EXPERIMENTAL TISSUE ENGINEERING

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Summary: Recent meta-research in tissue engineering points out that a lack of control on cellular environmental conditions persists in mammalian cell cultures [1]. Cell local environmental parameters like dO2, dCO2, temperature or pH, are many times assumed to remain constant and left unsupervised without any control during the experiment. Regarding cell stimulation using electromagnetic or mechanic forces (fluid flow, ultrasound, hydrostatic pressure), in recent studies [2, 3], our group found huge variability in the different stimulation parameters involved, e.g. magnitude, frequency, waveform, duty-cycle. Some of these parameters, such as the electric field magnitude, spread a range of more than 6 orders of magnitude when comparing different experimental protocols or their numerical model predictions. Despite these differences, these studies report similar biological effects on the cell culture, which remains a drawback. To surpass difficulties in cell monitoring and to improve the prediction of the cellular environment, we propose a numerical framework involving a digital twin model of a bioreactor to better guide researchers, when choosing the environmental conditions, and adjusting their hypothesis to the real bioreactor system. This framework will also contribute to avoiding protocol mistakes during the in vitro experiments and may help with the definition of the design, setting construction parameters (component sizes, channel dimensions, or input variables magnitude) allowing to reach the desired environment surrounding the region of interest for a particular type of cell. Future multi-scale models may fuse the current bioreactor and scaffold models with different cellular models. Integrating cellular dynamics like movement, growth, secretome, and eventually, tissue-like interactions or cell relations may open new doors for tissue engineering strategies. Additionally, with the currently existing models, just by continuously predicting and adapting the culture conditions to the cellular differentiation phase and cell population needs, it will be possible to accommodate cell development in an environment that closely mimics the in vivo conditions.

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