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COMPUTATIONALLY-GUIDED DESIGN OF CELL CULTURE BIOREACTORS

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MINI-SYMPOSIUM PROPOSAL

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1 MINI-SYMPOSIUM PROPOSAL

Cell culture bioreactors are a fundamental tool for research in regenerative medicine and drug screening. The configuration of such systems is becoming increasingly complex, for example in those cases where multi-functional tissue must be generated. In this context, computational analysis represents a powerful tool to guide the bioreactor design and validation process, in alternative to the trial and error approach.
We aim to gather researchers who have successfully adopted computational approaches to bioreactor design or optimization and those who are aiming at designing innovative bioreactors and seek the help of new computational methodologies to support their investigation.
The main goal is the study of the effect of forces and mass transport on cellular response in prolonged *ex vivo* culture. For example, the group led by Lacroix D. has successfully employed finite element simulations to optimize the shape of scaffolds in tissue engineering [1]. These optimization studies have also been applied to predict the fluid-dynamic stimulation and mass transfer of nutrients within advanced high throughput bioreactors, in the context of osteochondral tissue engineering and drug screening [2]. A recent application of computational analysis to bioreactor design concerns modeling the fluid-dynamics and oxygen consumption in a porous scaffold stimulated by cyclic squeeze pressure, in the context of cardiovascular tissue engineering [3].
Some frontier applications of computational bioreactor design address the millifluidic bioreactor scale, instead of the traditional macrofluidic scale, with the aim to explore cell function/disease/therapeutic strategies in prolonged culture within miniaturized scaffolds, optically-accessible to fluorescence diagnostics [4]. For example, some groups have tried to add complexity to the 3D cell culturing concept by using a microfluidic bioreactor, where cells are cultured for several days under a continuous flow of medium, thus mimicking the interstitial fluid movement that actually perfuses the body tissues, including the brain, to model neurodegeneration. Multiphysics 3D models are able predict tissue growth under interstitial perfusion in such miniaturized bioreactors [5].
Finally, bioreactors capable of hosting or generating different tissue types that are naturally adjacent to each other, such as cartilage and bone [6], are gathering more and more interest as they allow the studying of tissue-tissue interactions and can be used to predict drug interactions. In fact, while drugs are often targeted to a specific tissue, frequently the very same drug causes undesirable responses from other tissue (side effects). Advanced modelling has been used to determine the feasibility and predict the functionality of multiphasic tissues, such as osteochondral constructs that are aimed at high throughput drug screening [2] and that can be used to assess the natural cross-signaling between adjacent tissues.
Overall, computational approaches to bioreactor design or optimization are key in developing a more realistic understanding of cell and tissue functionality in health and disease, and the potential effect of

candidate treatments. In this context, this symposium aims at exploring the potential of a computational approach to effectively guide experimental implementation of cell and tissue culture bioreactors.

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