Bioreactor Design: Combining Direct Digital Manufacturing and Numerical Models

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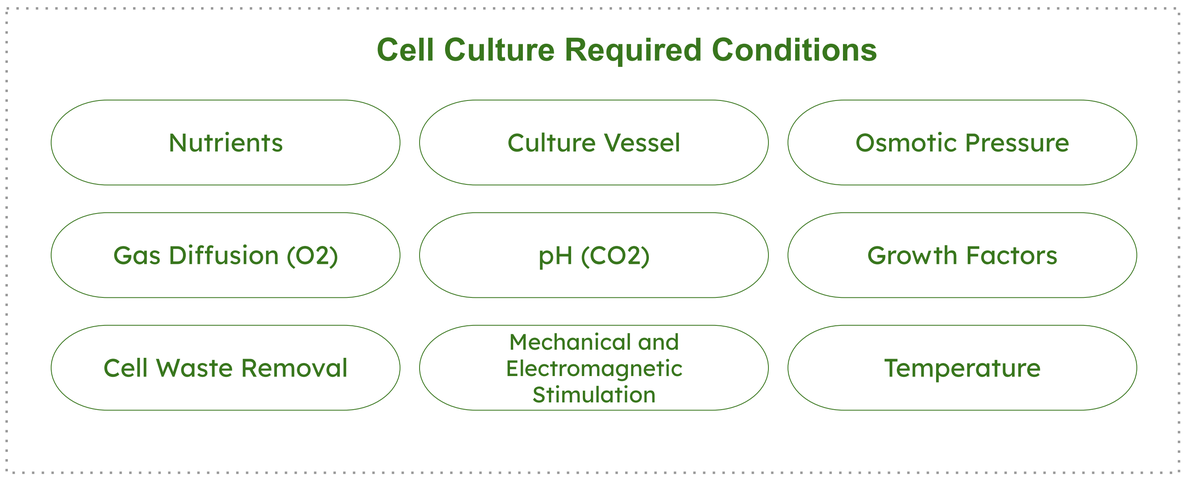
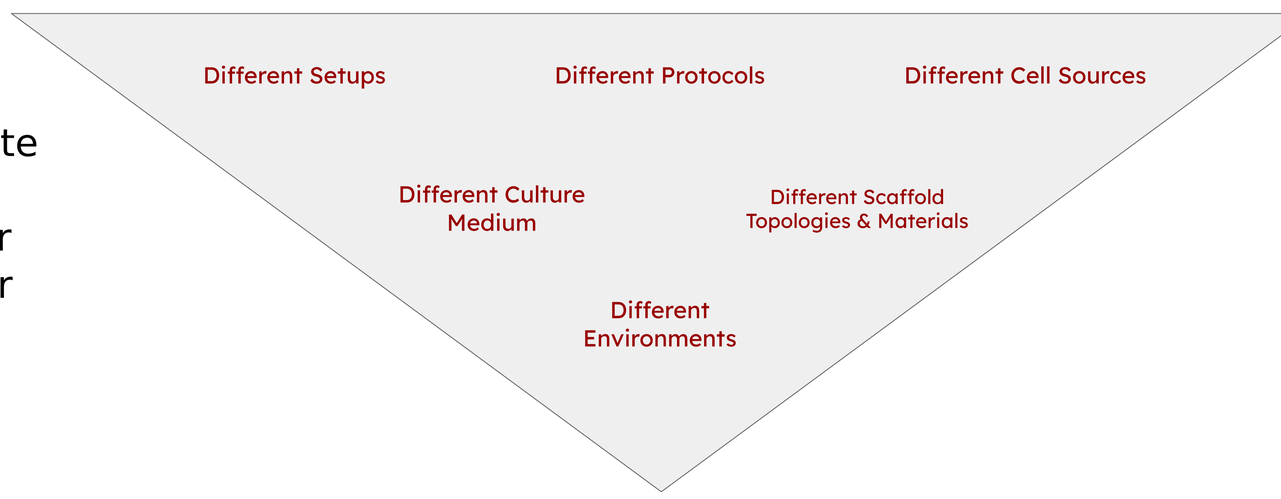
Motivation.
Bioreactor technology is of paramount importance in Tissue Engineering (TE), as it allows to establish the environmental conditions adequate for cellular growth, proliferation, differentiation and ultimately maturation into organ tissue. Injuries with growing prevalence among the Portuguese and European population, like bone fracture due to osteoporosis, will greatly benefit from autologous implants, but first, it is required to improve bioreactor technology to a new level of control and automation.

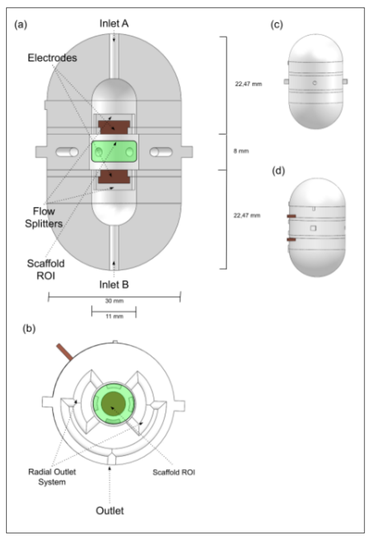


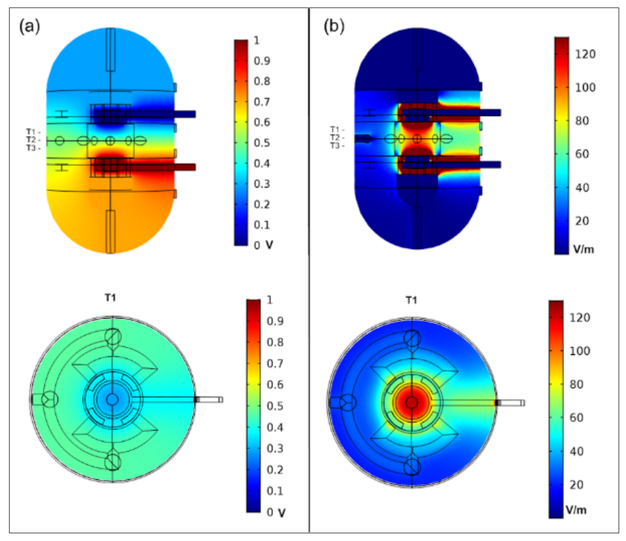
Challenges.
(1) Cell cultures for Tissue Engineering require a complex multiparameter control process capable of delivering an adequate cellular environment to promote cell growth and differentiation into the desired tissue. Besides choosing the appropriate cellular line and cell culture medium to reach the proposed goals, proper aseptic and subculture/passages techniques must be applied;
(2) 3D Cell Culture challenges come mostly from optimization of culture conditions when going from 2D cultures to 3D cultures;
(3) Tissue engineering research presents a high experimental variability. This makes comparisons of results nearly impossible and generates strong replication problems;



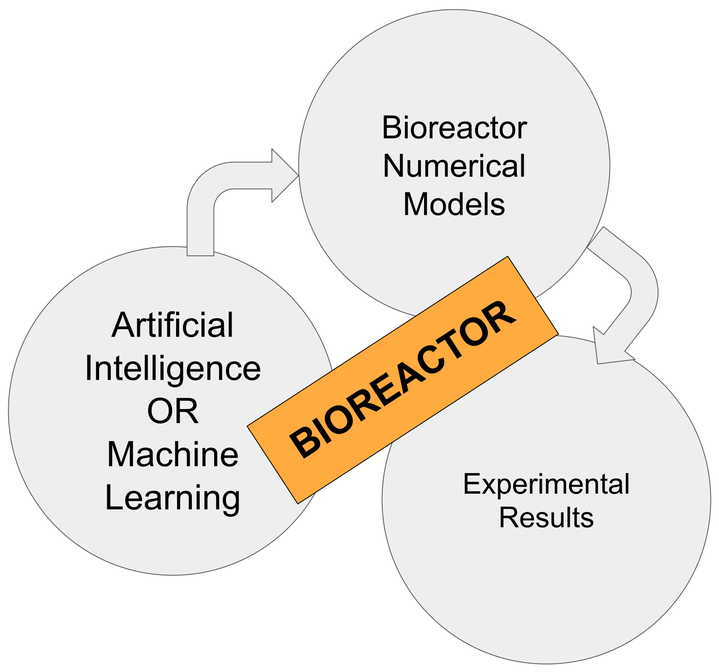
3DP Physical Bioreactor + Digital Twin Models

Opportunities.
Due to strong variability in experimental setups and protocols, Tissue Engineering offers an opportunity for progressive standardization;





Our Strategy.
A new bioreactor concept composed of a physical part and a digital twin model can contribute to improve the replication and comparison between different works. On one hand, this comprises opensource Direct Digital Manufacturing 3D printer ready bioreactor parts that can be shared and easily reproduced in low-cost 3D printers. On the other hand, its numerical digital twin model that solves physics conditions generated by the bioreactor for each group of input conditions is also shared. Therefore the knowledge of the environmental conditions involved in the cell culture region is further understood and shared between different research works;



Future Path.
The bioreactor may be seen as a big data problem, where many sensors outputs, system inputs and cellular reactions come into play. Progressively, the physical system and its digital twin counterpart will integrate further information from controllers/ sensors networks and ultimately integrate data and models from cellular responses/effects, becoming capable of understanding and generating the required environment for adequate cell growth, proliferation and maturation.

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