MASTER RESEARCH PROJECT

Mathematical Modelling of Mass Transfer in 3D Cell Cultures

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Background

The cell culture industry has applications in the production of biopharmaceuticals (biopharma), drug testing and cellular therapies. For all these applications the cells have been mostly cultured as planar, two dimensional sheets, which are far from the original cellular context /microenvironment. While in biopharma this flaw has been offset by high productivities drug testing and cellular therapy critically need to adopt three dimensional (3D) cell cultures in order to increase the biological relevance. One of the main limitations of such 3D cell cultures is the lack of knowledge of the microenvironment in these 3D cellular structures.

Objectives

In this project the aim is to model the gradients and phenotypes that are established in the interior of 3D cellular structures. The use of mathematical models to calculate theoretical gradients of nutrients (oxygen, glucose), metabolites (pH, lactate) and growth factors/cytokines (basic fibroblast growth factor, Wnt) has been described in the past 20 years' literature (ten Berge et al., 2008; Curcio et al., 2007; Langer and Vacanti, 1993). However, such theoretical insights have seldom been of practical use, mainly due to the lack of analytics to probe phenotypical gradients inside cellular aggregates. The long standing expertise in 3D cell culture and analytic methodologies of the Animal Cell Technology Unit of iBET (ACTU) (Estrada et al., 2016; Moreira et al., 1995; Serra et al., 2010), including several image-based analytical methods that generate spatially contextualized molecular information, will enable the application of mathematical models of mass transfer models to to several types of 3D human cell cultures being developed and characterized at the ACTU.
Overall, this project will deliver a rational approach for studying physiologically relevant 3D cell cultures, whether these are used as drug development tools or as a source for cellular therapies.

References

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