Multiscale Modelling of bioreactors for growing bone tissue

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Failure to grow thick (3D) implantable bone tissue is partly due to the lack of tissue vascularisation resulting from a fall in nutrient supply to the cells as the distance between the cells and nutrient sources increases. Previous attempts that used porous scaffold without hollow fibre (HF) produced tissues of less than 0.5mm thickness which are of limited clinical use. Recent studies suggest that HF membrane bioreactor (HFMB) may be used to grow bone tissues for implanting into patients with skeletal defects [1,2]. The HFMBs (Figure 1) mimic the capillary network that exists in bones and are effective in supplying nutrients to cells (to maintain cell metabolism) and removing waste products (e.g., excreta from micro-organisms, etc). In order to guide the design of HFMBs for bone tissue engineering, it is important to determine the quantitative relationships between the cell environment and tissue behaviour in HFMBs and their relationship with nutrient supply. However, the nutrient transport processes in these bioreactors depend on several scales: from the scale of the individual cell to the scale of the bioreactors (laboratory scale). Further, the significance of the mass transfer processes is different from one scale to another. At the sub-cellular scale (i.e., within individual cell), the transport processes are dominated by diffusive-reaction mechanisms. At the extracellular matrix, these processes are primarily diffusion dominated. The transport of nutrients in the capillary network is convection dominated. At the scale of the laboratory device, the transport behaviour is governed by non-linear coupled convection–diffusion and reaction processes. Therefore, to characterise the mass transfer processes, one needs an understanding of the processes at smaller scale (e.g., sub-cellular scale) and their manifestation at larger scale, such as the bioreactor (HFMB, in this case).

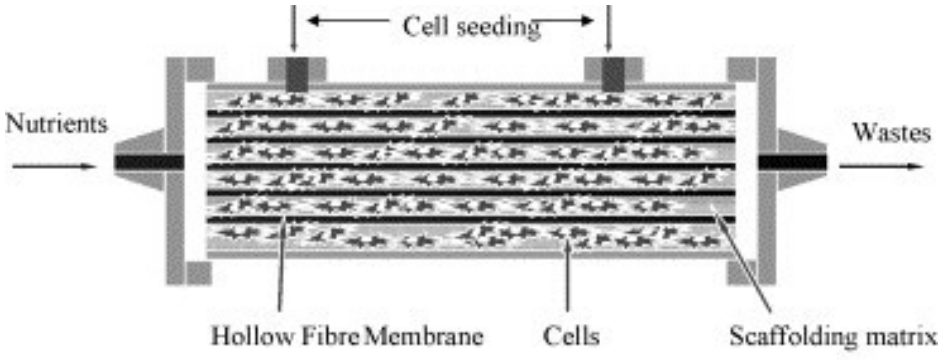

Figure 1. A schematic diagram of hollow fibre membrane bioreactor (HFMB)

The problem proposed involves developing further existing models [3,4] or developing new mathematical models (e.g. using homogenisation theory) to describe the important mass transport, flow dynamics and the key kinetics of a HFMB bioreactor. Another aim is to produce an accurate model that will be considerably less computationally expensive than existing approaches (e.g. CFD simulations in 3D). Such modelling could significantly assist in the acceleration and optimisation of the bioreactor design process. So the main purpose of this study group is to determine how to address the above issues.

References

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