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Multiscale Transport Modelling of Nutrient Transport in Bioreactor for Growing 3D Bone Tissues: Sub-Cellular to Laboratory scale

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Recent experimental studies suggest that hollow fibre membrane bioreactors (HFMBs) may be used to grow bone tissues, which may then be implanted into patients to repair various skeletal defects. The HFMBs mimic the capillary network that exists in bones and are very effective in supplying nutrients to cells (to maintain cell metabolism) and removing waste products (e.g., excreta from micro-organisms, dead cells, etc). In order to guide the design of effective bone tissue engineering protocols, we need to elucidate the quantitative relationships between the cell environment and tissue behaviour in HFMBs and their relationship with nutrients supply. This necessitates that the appropriate bioreactor conditions for generating neotissues, and the mass transfer and chemical reaction during cell growth and extracellular matrix formation, are studied thoroughly. One should also be aware that the mass transfer processes in growing bone tissues in bioreactors take place at several scales – from the scale of the individual cell to the scale of the laboratory device (Figure 1). However, the significance of the mass transfer processes may be very different from scale to scale. For example at the sub-cellular scale, the transport processes are dominated by diffusive-reaction mechanisms. At the extracellular matrix, these processes are primarily diffusion dominated. At the scale of the laboratory device, the transport processes are governed by convection-diffusion and reaction. Therefore, to characterize the 'overall' mass transfer processes, one also needs an understanding of the processes at smaller scale and their manifestation at larger scale, such as the laboratory device.

This paper will present our attempt at modelling and simulation of nutrients transport in HFMB for growing 3D bone tissues using a finite element model. In specific, a computational framework will be presented which has been used to upscale the mass transfer processes at sub-cellular scale to larger scale. The framework is then to carry out a systematic analysis of the influence of various process parameters of HFMB used in bone tissue engineering, e.g., cell density, cellular size, hydrodynamics behaviour, etc.

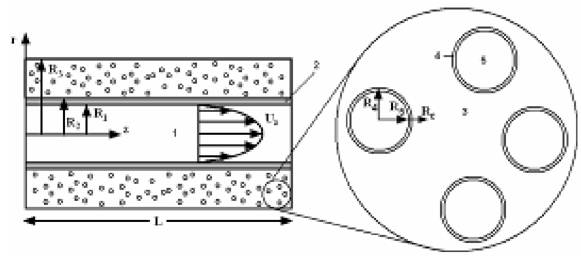

Fig 1: Cross Section of an individual hollow fibre

See, for example, Figure 2 our results for the effects of cell size on mass transfer behaviour. These simulations have been run with various radii of cells, i.e., $5x10^{-7}$ m, $10x10^{-7}$ m and $25x10^{-7}$ m, while the cell membrane thickness and cell density are kept the same. As expected, the figure shows that increasing cell size lead to decrease in nutrient concentration, glucose in this case. Figure 3 shows the distribution of glucose in the cells of HFMB.

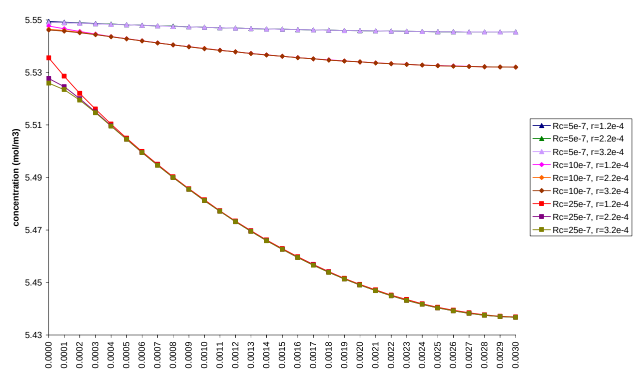

Fig 2: Axial glucose concentration profiles in cells of HFMB for various cells sizes

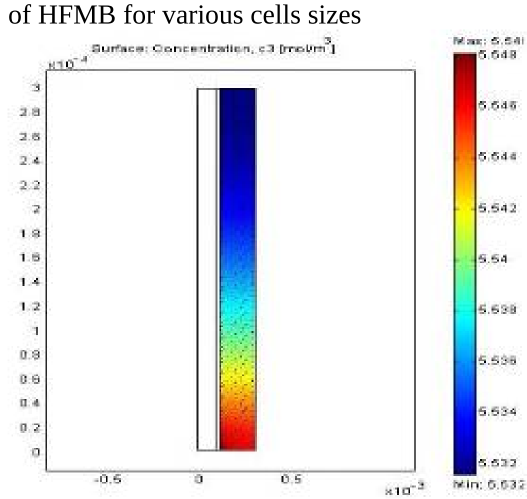

Fig 3: Distribution of glucose in the cells of HFMB