425c Modeling and Scale up a Fibrous Bed Bioreactor for Mammalian Cell Culture

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A fibrous bed bioreactor (FBB) was developed for mammalian cell cultures and tissue engineering applications. The fibrous matrix in the FBB provides 3-D environment to mimic in vivo culturing conditions for animal cells, and thus has been shown to have superior performance in both cell density and reactor productivity for culturing anchorage dependent and anchorage independent cells. The objective of this study was to develop a kinetic model for fluid flow, mass transfer, and cell growth in the FBB. Models for fluid flow in both ordered-disc packed bed and spirally-wound packed bed were tested and validated with the residence time distribution data. It was found that the axial dispersion model simulated mass transfer in the ordered-disc packed bed well. For the spirally-wound packed bed, both radial and axial convection and dispersion contributed significantly to the mass transfer, which is consistent with our previous finding that the spirally wound FBB was more efficient in mass transfer and had higher cell density and productivity as compared to conventional packed bed bioreactors. The model was then applied to the FBB culture of embryonic stem cells. With continuous perfusion, the FBB culture could reach a tissue-like density of 109 cells/ml in 22 days. Diffusion limitation in cell aggregates occurred when the aggregate size was greater than 270 ƒÝm, which could be partially controlled by reducing the fibrous matrix pore size. The maximum superficial velocity of fluid in the FBB without causing significant shear damage to cells was found to be 0.17 m/s. The model can simulate the profiles of fluid velocity, shear stress, pressure drop and concentration of the limiting nutrient (oxygen) in the FBB. The information from model simulation can be used to guide the design and scale up of the FBB to optimize the cell density and reactor productivity for industrial applications.