204d Computational Approach to Characterization of Cell-Culture Bioreactors

Kumar Dhanasekharan, John Strauss, Atul Gupta, Kenneth Hamilton, Sanjeev Ahuja, Basav Ghosh, David Keller, and Alex Fotopoulos

Cell-culture is a critical process to produce large-molecule, protein-based therapeutics. A rise in the demand for these products has prompted a need to develop processes for large-scale bioreactors. A good scale up is imperative due to high costs associated with construction of bioreactors and their subsequent evaluation at large scale.

Computational approaches such as CFD, used to understand the fundamental fluid mechanics and mixing characteristics of bioreactors, can be highly valuable in developing the scaling protocol of bioreactors. In this work, CFD is used to predict the flow field that governs the performance of liquid – liquid mixing. The flow field includes detailed maps of the velocity profiles, turbulence and shear profiles in the reactor, as well as power requirements and bulk liquid mixing pattern.

A systematic, staged approach using CFD to simulate Biogen Idec's bioreactors is described and the results of power number, liquid mixing times, and flow field are verified against experimental data. The methodology development, and subsequent comparison with experimental data, discussed in this work shows the need to ensure that the correct simulation techniques are used. A case study identifies the practical implications of the simulation results and an estimate is made of the cost/benefit of the CFD based approach. A comparison of the predicted performance of proposed bioreactor designs is performed to aid in the selection process.

The above approach allows a fundamental framework to understand bioreactor performance and a systematic approach to process scale-up. When complemented with alternative techniques such as experimentation and empiricism, CFD can increase accuracy and understanding of the bioreactor mixing process, reduce time lines, and potentially save significant development and equipment costs.