DESCRIPTION FOR THE GENERAL PUBLIC

The demand for macromolecular biopharmaceuticals, such as monoclonal antibodies, protein conjugates, virus like particles (VLP) etc., in modern biotechnology and pharmaceutical industry is constantly rising. The production of bioactive proteins for therapeutic use generally starts in a cell culture tank, which is the upstream part of the process. Cell cultures that are the most widely applied for production biopharmaceuticals are: Chinese Hamster Ovary (CHO) and Escherichia coli. The key product, which is a protein produced by the cells, has to be isolated from the fermentation medium, which due to the complexity of post-fermentation mixtures, requires efficient and also predicable purification techniques. The downstream processing usually includes three purification stages, i.e.: the protein capture from a multicomponent mixture, intermediate separation and polishing step, which provide a product with desired purity. In all purification stages chromatography is used as one of the crucial separation technique. Because of large doses expected in future therapeutic uses of biopharmaceuticals and a high cost of stationary phases needed for their recovery and purification, chromatographic processes are expected to be a significant portion of the total cost as well as a critical step in the path to rapidly develop and bring to market new drugs. Therefore, efficient design of large scale chromatographic operation is a factor of major importance. However, because of complex retention behavior of proteins in chromatographic columns, scaling up of chromatographic processes is a challenging task. Very often, the process conditions appropriate for separation in a small-laboratory scale do not apply for large-scale columns, which operate under different hydrodynamic conditions. Thus, scaling up of protein chromatography is often performed by a trial and error method, which is cost and time consuming. An attractive alternative is to describe protein retention by a mechanistic model, which includes the most important paths of the mechanism of protein interactions with functional groups on the adsorbent surface. The goal of the project is to contribute in solving the scale-up problem by developing an efficient mathematical tool. The mathematical model will be used to predict the effectiveness of protein separations using various chromatographic techniques based on different adsorption mechanisms involving electrostatic, hydrophobic and affinity interactions, dedicated to protein capture, intermediate and polishing step of the purification process. The models will be formulated based on experimental chromatographic runs for at least two model recombinant proteins obtained from CHO and E.coli cell cultures. The purification performance will be predicted for various operating conditions moving from a small scale up to a large scale, depending on the volume of chromatographic columns used in the purification process.