Dynamic partnership aims to reduce cell harvest time

Cell therapy products and recombinant therapeutic proteins that are produced in cellular systems need to be harvested at the end of the production process. Cell harvesting is often achieved using membrane-based systems, which separate intracellular product and cells from unwanted material in the culture medium or their secreted products from cells.

Business interaction voucher funding from BioProNET has enabled Yuhong Zhou from University College London to work with John Philip Gilchrist of BioPro Control Tech on a project that aimed to reduce the time taken to harvest cells. Reducing cell harvest time could result in a better quality of product and reduced costs. Their project initiated work on a computer-based system that could be used to optimally control the flow of cells and culture medium across a membrane-based separation unit.

"We would not have been able to carry out such a project without the collaborating company," says Yuhong. "The company developed software and hardware to implement the control method, and we did all the wet laboratory experiments at University College London," she explains.

Their work centred on a cross-flow filtration membrane system (which has two exit streams) in an ultra-scale down device – so that low volumes (tens of ml) of culture media could be used in the laboratory setting. They aimed to reduce cell harvest time by using the computer-based control system to balance the flux of the culture medium across the membrane against the fouling of the membrane with unwanted material (which could reduce the efficiency of the membrane).

As a simple preliminary test system, the collaborators used a suspension of Baker's yeast to generate data on the viscosity of the culture medium at several different cell concentrations, which was then used to develop a mathematical model to control flux. An open-source electronics platform was used as the control system hardware and software was written in house to drive the pressure sensor for online monitoring.

"Our results have provided evidence that the control method has the potential to achieve significant process efficiency", says Yuhong, noting that further studies will be needed to investigate results in industrially relevant feed systems, such as lysates from *E. coli* or mammalian cell culture broth. Their work also indicates that cost-savings are possible if the control system is integrated into the membrane separation processes.

There are plans to continue the work to further develop the control system and study the application in large scale cross-flow membrane filtration processes. "This work has provided us considerable preliminary data for a new bid for further development of the dynamic control system," says John Philip. "We would like to collaborate further to develop more sophisticated software for commercial application," he concludes.

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