293g Prediction of Shear Damage in Industrial Scale Process Using an Ultrascale-down Device

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Many biomaterials, like fusion proteins and plasmid DNA, which have huge potential for the improvement of future health care, are complex macromolecules which may lose their integrated structure due to shear stress in downstream recovery, separation, and formulation operations. It is of vital importance to be able to assess the ease of the processing these materials during early stages of drug discovery and development. At such a point in time, only a small amount of biomaterials will typically available with which to test for process compatibility. In this context, an UltraScale-Down (USD) device with a working volume of 20mL has been developed to predict the shear damage in large-scale processes. The paper will demonstrate how such a USD device has been applied successfully for mimicking shear damage occurring in centrifuge and pump processes.

In the feed zone of a centrifuge, fragile biomaterials may be broken, and this results in a decrease in centrifuge separation efficiency and the possibility that small fine particles may affect the following separation steps, by virtue for example of fouling in chromatographic processes. In operation, the USD device is used to generate the equivalent energy dissipation rates to those prevailing in the feed zone of the centrifuge. The separation capacity was mimicked using a laboratory-scale centrifuge. Results are presented that show how the clarification of solids in the large-scale centrifuge process can be predicted using the combination of USD device and the lab-scale centrifuge.

Pumps are a common method for the transport of fluid within bioprocesses and to generate the required pressures for membrane or chromatographic processes. Computational Fluid Dynamics analysis shows that the volume of high shear region in a positive displacement rotary vane pump is tiny compared to the volume of processed materials. However, in the USD device, the ratio of the volume of high shear region to the working volume is much higher than that in the pump. This means that processing biomaterials at the USD device with a short time can be represented for that in the pump operation for a long process time. Experiments using mammalian cells support the theoretical analysis.

In conclusion, only a small amount of biomaterials are needed at the USD device and the process time is relatively short, but it can be used to predict the shear damage in large-scale operations.