OPTIMIZATION OF A DYNAMIC PERFUSION PROCESS USING A COMBINATION OF HIGH THROUGHPUT EXPERIMENTATION AND HYBRID MODELING APPROACHES

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BiosanaPharma is a biotechnology company leveraging end-to-end continuous biomanufacturing in single use equipment to produce biosimilars at low cost-of-goods and allowing to maximize productivity out of very small facility footprints. In parallel to their product development, a continuous manufacturing platform, the 3C platform, has been established which is based on an upstream process combining a dual perfusion bioreactor and expanded-bed centrifuge set-up, allowing multiple modes of operation depending on the needs of the specific expression / production system. One mode of operation involves dynamic perfusion cultures that are performed alternatingly in each bioreactor from a rolling seed train, thereby creating a continuous supply of clarified harvest for subsequent continuous DSP.

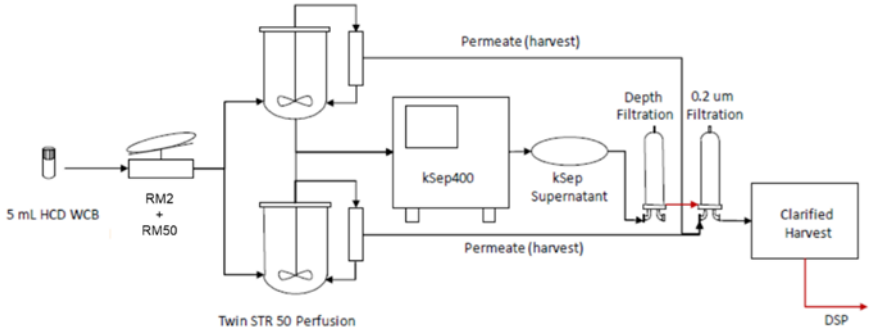

Figure 1 – 3C Process layout

Several key process parameters can affect the productivity, longevity, viability and product quality of the dynamic perfusion cell culture processes. For the expression system presented in this study, (partial) cell cycle arrest followed by cell size increase plays a key role in cell culture performance. A set of 5L benchtop and 250 mL Ambr HT perfusion bioreactor runs were performed to generate baseline scaled-down cell culture data, providing insight in the impact of cell culture conditions on the dynamic perfusion performance.
Based on the limited dataset, hybrid models are used to fit the data and subsequently, using process simulation, are used to predict optimal parameter settings.

During the experimental approach, several lessons were learnt in fine-tuning and optimizing Ambr HT perfusion performance, which will be shared.