Moving from a bioreactor scale-up/scale-down approach to a more holistic operational design space view

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MOVING FROM A BIOREACTOR SCALE-UP/SCALE-DOWN APPROACH TO A
MORE HOLISTIC OPERATIONAL DESIGN SPACE VIEW

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Key words: bioreactor, scale-up, scale-down, reduced scale model, design space

Scale-up of bioreactor processes for biologic products has been an area of focus in the industry for over 50
years and the results have generally been successful through the application of a number of specific
correlations across scales for mass transfer, mixing, etc. However, the ability to visualize and understand
the bioreactor design space in terms of these parameters has generally been limited as has any general
understanding of how close a given process comes to certain sensitivity limits at various scales. As part of
a project which involved establishing scale-down models at two different sites with long-term objectives of
moving processes to multiple scales and sites, two-dimensional operational design space diagrams were
constructed using power per volume (P/V) and superficial sparge gas velocity (V_s) as the axes. The use of
such an operational design space to identify and visualize process sensitivity boundaries such as interfacial
or turbulent eddy shear limits as well as pCO₂ isobars will be presented for both small and large scale
operations. This visualization of the operational design space allows for a clearer assessment of time-
dependent process sensitivities over the duration of a bioreactor run. The use of process sensitivity
analysis will also be discussed in terms of fine tuning reduced scale models to lessen the impact of specific
sensitivities, especially when operating at the edge of a design space at certain times, and improvements
to the overall process robustness.