ADVANCED NUMERICAL CHARACTERIZATION OF A WAVE-MIXED BIOREACTOR USED IN THE BIOPHARMACEUTICAL INDUSTRY

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Single-use bioreactors have been established in the biopharmaceutical industry over the last 20 years. Typically, rigid or flexible bioreactor vessels are used to cultivate mammalian suspension cells, insect cells, plant cells, and microorganisms. To optimize such a bioprocess, a detailed understanding of the cultivation system must be available. In addition to classical, experimental process engineering characterization, a system can also be characterized digitally utilizing computational fluid dynamics (CFD). CFD is particularly well accepted for stirred systems, as CFD not only allows time- and spatially resolved parameters to be investigated, but also more sophisticated investigations. However, non-stirred and non-rigid systems, such as wave-mixed systems, pose two additional challenges for CFD investigations compared to classical stirred systems made of stainless steel or glass. First, the geometry of the bags is extremely complicated due to their buckling and wrinkling, and second, they involve more complex motions. The first problem is typically ignored in the literature due to oversimplifications.

Using the CELL-tainer single-use bioreactor (Fig. 1) as an example, it is demonstrated here, for the first time, how complex geometry can accurately be modeled and how the two degrees of freedom movement (rotation and translation) can be incorporated into the computer simulation. The complex geometry of the CELL-tainer bioreactor was digitized in several steps using 3D scanning. The complex bioreactor movement was recorded using motion-capturing techniques. In addition to standard process parameters such as power input, mixing time, and oxygen transfer, the hydrodynamic heterogeneity and the time-dependent Kolmogorov length scale distribution were also investigated (Fig. 2). This novel assessment allows the prediction of potential cell damage due to hydrodynamic stress in a transient system. In the case of the CELL-tainer, it was shown that oxygen transport is superior to that of classic wave-mixed bioreactors. Furthermore, it was shown that in the cell culture version of the CELL-tainer the critical Kolmogorov length is not exceeded in any simulation. This makes the system interesting for inoculum production as well as for the production of cell therapeutics, monoclonal antibodies, therapeutic hormones, and vaccines. The method described here for motion and geometry capture can also be used to characterize other single-use systems using CFD.

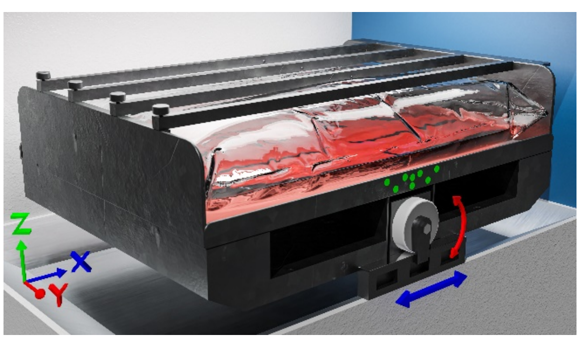

Figure 1 – Computer generated image of the investigated CELL-tainer bioreactor, indicating rotation (red arrow) and translation (blue arrow).

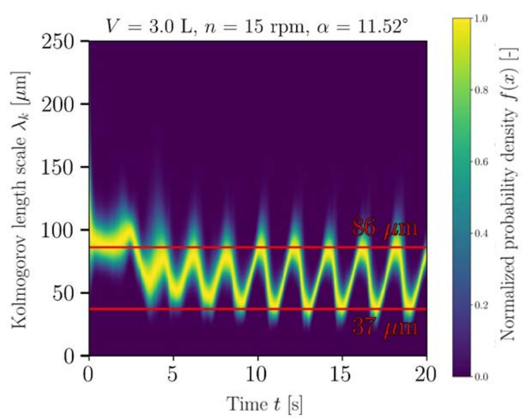

Figure 2 – Time resolved analysis of the hydrodynamic stress by means of the Kolmogorov length scale during a cultivation.