531b Investigation of Shear Stress- and Hypoxia-Induced Mammalian Cell Damage in Aerated Bioreactors

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Aerated bioreactors are often used for the cultivation of mammalian cell cultures, necessary for the production of viral vaccines, hormones, lymphokines and monoclonal antibodies, among others. In these reactors, the cells are suspended in viscous broths, through which oxygen-supplying bubbles are sparged. Despite the simplicity of their construction, special care must be exercised during the operation of such reactors, in order to minimize damage to the shear-sensitive cellular cultures. As the hydrodynamics of bubbly flows (and therefore the associated shear stresses) change considerably as a function of system parameters and operating conditions (such as viscosity, bubble size, etc.), in-depth understanding of these correlations is necessary for optimal reactor design and operation.

In our work, we performed high resolution Direct Numerical Simulations of oxygen providing, deformable bubble swarms rising through viscous cellular suspensions. Cell damage, caused by shear has been modeled, allowing the monitoring of the health of cells exposed to different bubbly flows over long periods of time. More than 500,000 individual cells have been tracked in order to develop statistical correlations, relating cell damage to the fluid dynamics, which are obtained from first-principle simulations.

Since the simulations describe a system, in which no external stirring is provided, the only source of continuous-phase mixing is the motion of the bubbles themselves. Effective transport in the liquid phase is crucial for the timely delivery of dissolved oxygen to all suspended cells and the poor mixing associated with some bubbly flows can lead to the formation of oxygen-deprived stagnation zones. In such zones, hypoxia can cause cell injury and, over extended periods of time, even death. These indirect consequences of the bubble motion are accounted for through the inclusion of a model describing the gas-liquid interfacial mass transfer from first principles as well as the subsequent transport of the dissolved oxygen and its consumption by the cells.