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Simulation of mixing processes for the manufacture of pharmaceutical products

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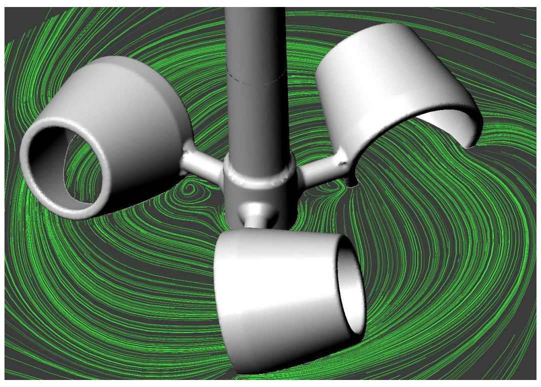
Introduction

In the pharmaceutical industry mixing and dissolution processes of highly viscous media are still an area of ongoing research. The effects of impeller and tank geometries on the mixing quality is hard to be deeply understood due to the wide range of physiochemical properties of the mixed fluids.

In case of bulk solid suspensions the definition of the powder feeding system also represents a critical issue in the development of a mixing device. Therefore, the definition of process parameters is often based on experience and trial-and-error practices.



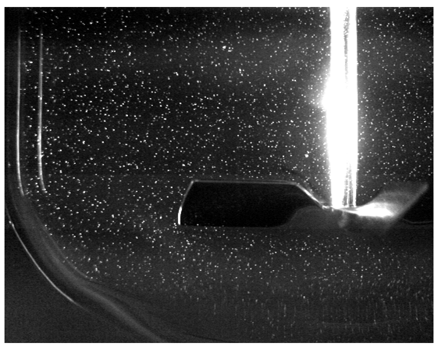
Goals

- Development of a broad understanding of fluid/solid pharmaceutical mixing based on detailed CFD, Computational Fluid Dynamics, methods (CFD-Code: “AVL Fire”).
- Experimental validation of the simulated flow field by means of PIV (Particle Image Velocimetry) technique.
- Characterization of the rheology of the mixed solutions.
- Investigation and optimization of an industry-scale process under consideration of CFD as an optimization tool.

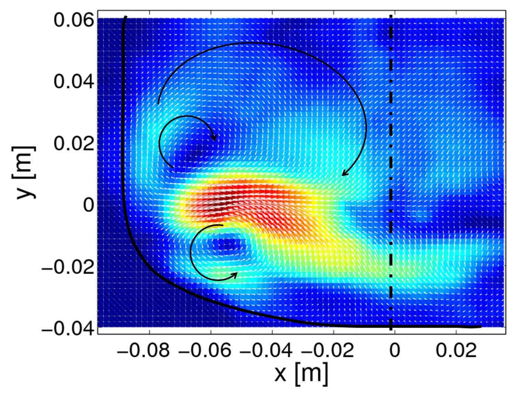
Numerical Method

- Simulation of the liquid flow with the κ–ζ–f turbulence model.
- MRF (Multiple Reference Frame) and Sliding Mesh (SD) methods for the steady and unsteady description of the rotating impeller.
- Bulk particles motion with Euler-Lagrange approach and dissolution with Frössling’s equation.
- Transport of liquid species and variable viscosity of the mixed fluid.

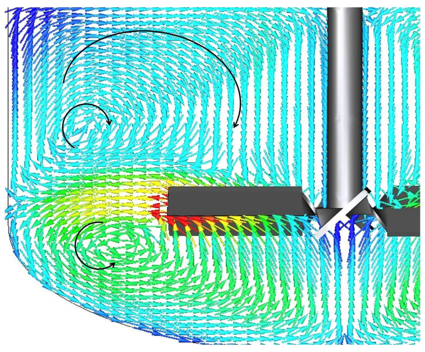
Validation



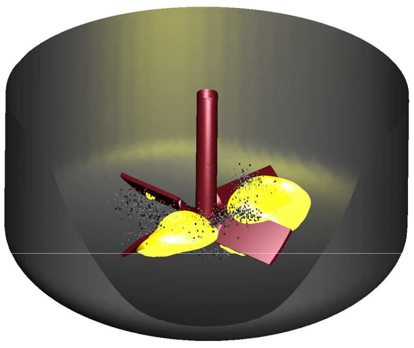
High-speed camera images of the flow field



PIV averaged velocity profiles

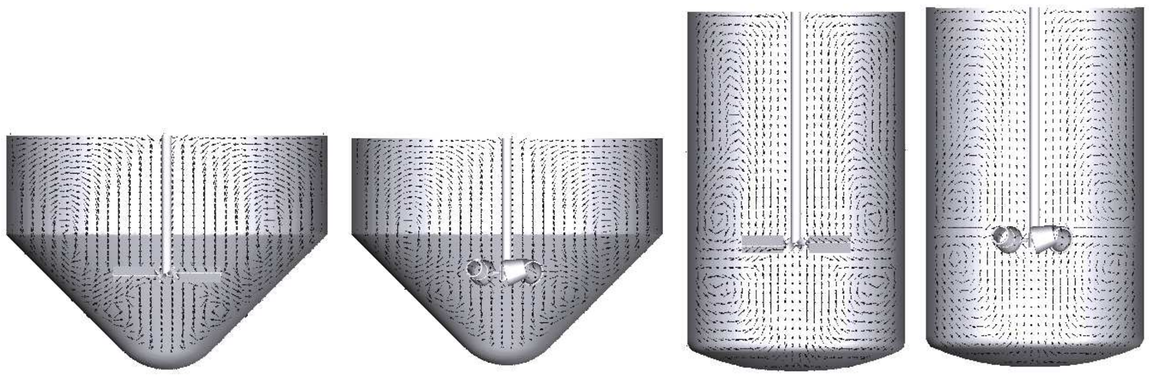


Velocity vectors in the CFD Simulation



Simulation with bulk particles (isosurface of dissolved species)

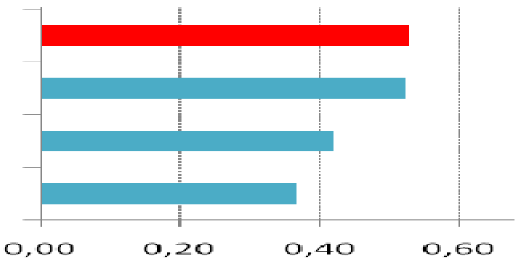
Optimization



Comparison of different tank and impeller geometries

$$I_H = \sum_j \frac{V_j}{V_{TOT}} \left| \frac{v_j - v_{mean}}{v_{mean}} \right|$$

j = cell index
V = cell volume
V_{TOT} = total mesh volume
v = flow velocity



Homogeneity indexes I_H for different test cases

Conclusions

- The simulated flow field inside a stirred tank has been validated for different impeller geometries.
- The mixing quality in an industry-scale device has been assessed with respect to parametrical variations.
- Models for bulk powder transport and dissolution have been successfully developed.

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