Simulation of Lagrangian Sensor Particles as Resolved Particles in an Industrial Bioreactor through Lattice-Boltzmann Large Eddy Simulations

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Highlights

- Lagrangian Sensor Particles (LSP) to mimic lifelines [1] of CHO cells during fermentation
- Lattice Boltzmann Large Eddy Simulations of resolved particles to mimic LSPs
- Characterization of mixing heterogeneities and compartments in an industrial STR

1. Introduction

In the landscape of bio-pharmaceutical production, the quest for optimal process efficiency and product quality remains paramount. The essential factor of mixing and dispersion of reactants, production cells, and further media related to the fermentation process in a stirred tank reactor (STR) are insufficiently quantifiable on an industrial scale. To this end, as is the case in previous studies on a smaller scale [2], Lagrangian Sensor Particles (LSP) [3, 4] are studied as a tool for the characterization of mixing and the representation of lifelines [1] of cells during the cultivation and fermentation process. To date, several Lagrangian regime analyses and studies regarding the determination of compartments based on particles have been undertaken. However, most studies make use of random walk models on a set velocity grid yielded from sliding mesh models limiting possible particle size, to particles or massless tracers which do not violate the set grid spacing [5, 6]. The simulative study is conducted in a 15,000 L STR with a Rushton Turbine and a Pitched Blade impeller configuration for varying turbulent Reynolds numbers. Simulating the LSPs as resolved particles, in order to reconstruct their respective lifelines ultimately allowing for the analysis and quantification of mixing heterogeneities through compartmentalization of industrial-scale STR. The characterization of compartments through LSP lifelines is aimed at quantifying the further development of a scale-down model in which the free compartments of the large STR are reconstructed as forced compartments in an existing single multicompartment bioreactor [6].

2. Methods

The LSPs inspiring the simulative study are developed by Buntkiel et al. (d_p = 40 mm) [4], with which experimental studies for the characterization of compartments in STRs have been undertaken [3]. To generate representative and physically reliable LSP lifelines for further analysis, simulations are carried out using the Lattice Boltzmann Large Eddy Simulation (LB-LES) solver by M-Star Simulations, LLC. Due to the substantial LSP size, sufficient points across the diameter of the LSP are available, allowing for the physics behind the LSP lifelines to be quantified directly from the solver as resolved particles, without applying various modelling such as virtual mass. The solver harnesses the computational advantage of Graphical Processing Units (GPU), allowing for the use of a high-performance cluster consisting of two AMD Epyc 9334 64 core processors and two Nvidia Tesla H100 GPU cards. Subsequently, the extensive simulation is reduced to a computation time of around 14 days per operating point in the present study. As no such application of LB-LES is presently available in literature, a substantial grid independency study yielded a grid spacing with a total of 266 million lattice points across the STR. The STR is filled with water (ρ_f = 998.2 kg·m^{-3}) and is not aerated. At the air liquid interface, a free surface condition is simulated allowing for 3D spaciotemporal resolution of the surface. A total of 60 particles simulated as resolved particles (ρ_p = 999.7 kg·m^{-3}), are dumped at a specific location adjacent to the top pitched blade impeller after one second of simulation time. A simulation time of 635 s is set, with results being recorded from 35 s on. This allows for a sufficiently established steady state of the STR and dispersion of LSPs throughout the STR and a total of 10 min of simulated

LSP lifelines, amounting to a total of 10 h of simulated LSP trajectories. The reactor has a total volume of 15 m³ with the studied working volume being 12.5 m³. The impeller configuration studied is that of a Rushton and Pitched blade, with three wall-mounted baffles set at 120° to each other. Three distinct industrially relevant operating points are studied with Reynolds numbers ranging from $Re = 2.94 \cdot 10^5$, over $Re = 4.05 \cdot 10^5$, to $Re = 4.64 \cdot 10^5$ (40 rpm, 55 rpm and 63 rpm, respectively).

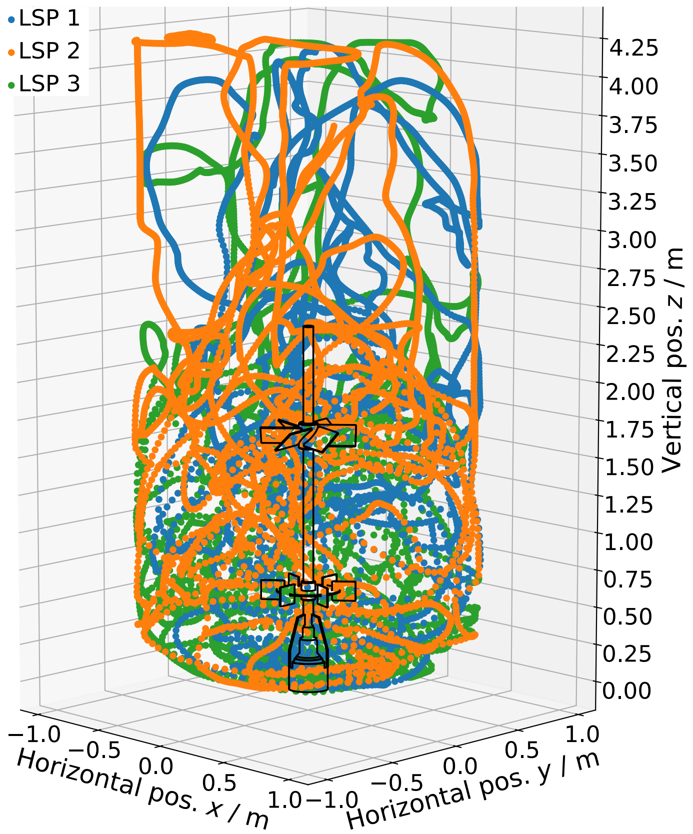

Figure 1. Exemplary lifelines of three LSPs visualized as a scatter plot, with the respective Rushton and Pitched Blade impellers superimposed.

3. Results and discussion

The simulated lifelines of the LSPs indicate the possibility for the characterization of axially and radially distributed compartments. Quantification and characterization rely on the analysis of the probability of presence, circulation times, local mixing times and residency times per hydrodynamic Lagrangian regime of the LSPs. Hereby, the hydrodynamic Lagrangian regime sets itself aside from the Eulerian perspective, as the individual LSP lifelines are accounted for rather than spatially fixed positions within the STRs. Initial results show the ability of accurately simulating the lifelines of LSPs, as shown in Figure 1. Subsequently, with further numerical simulations and analysis the characterization and quantification of compartments in industrial STRs based on experimentally available LSPs is attainable.

4. Conclusions

The use of numerical simulations to replicate the lifelines of LSPs for the characterization of compartments and mixing heterogeneities is possible. Leading to the quantification of local mixing time, circulation time, residence times per hydrodynamic Lagrangian regime and probability of presence of the LSPs. Validation through experimental data is to follow.

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Keywords

Lagrangian Sensor Particle (LSP), Lattice Boltzmann Simulation (LSP), Large Eddy Simulation (LES), stirred tank reactor (STR)

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