Experimental validation of solid-liquid simulations of microcarrier suspension in a stirred-tank bioreactor

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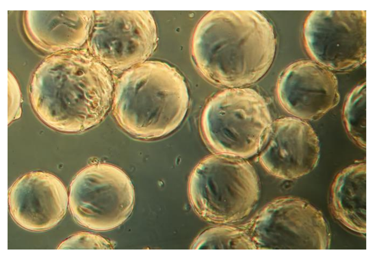
Introduction

Context

Expansion of **stem cells** adhered on **microcarriers** in stirred tank bioreactors



Constraints on agitation rate:

- No motionless microcarrier at the tank bottom to avoid microcarrier aggregation
- Low agitation to avoid **hydromechanical** stresses
- Compromise: $N = N_{js}$ (complete suspension)

Objectives

Development of a **CFD mulitphase flow** modelling approach for **microcarrier suspension** in stirred tank bioreactor for predicting:

- the just-suspended agitation rate (N_{js})
- the spatial distribution of the solid fraction
- the hydromechanical stresses

Challenges

Extensive literature on glass/sand particles ($\rho_S / \rho_L = 2.5$) but scarce on microcarriers ($\rho_S / \rho_L \cong 1$)

Small volume (≈ 1 L) and small agitation rate:

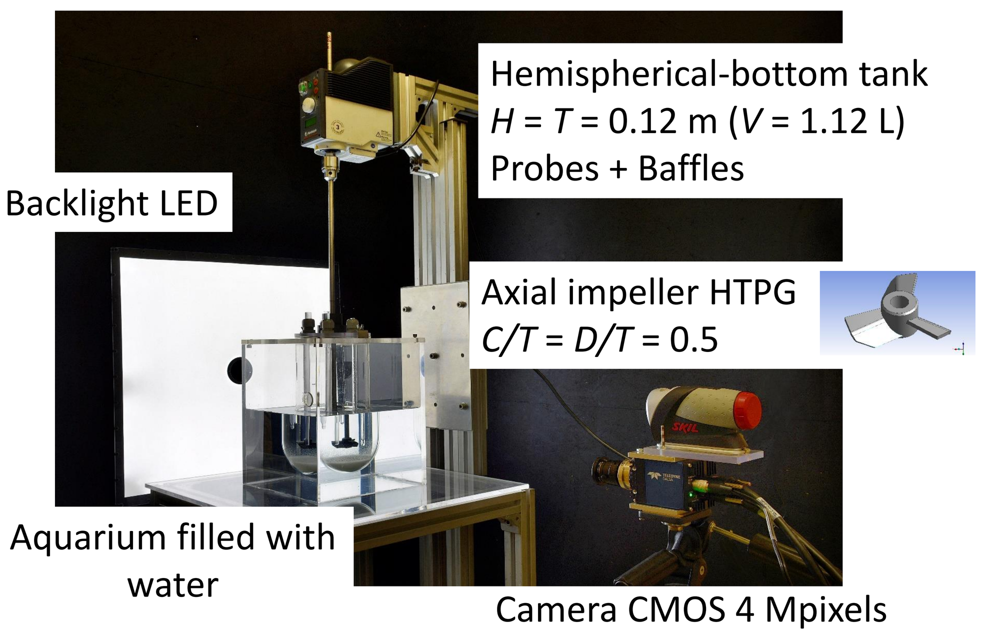
⇒ Low Reynolds number (< 10 000) = Not fully turbulent

⇒ Small Wall-y^+ at the tank bottom: Near-wall modelling ?

Validation step needed = Based on the measurements of solid spatial distribution by a light attenuation technique

Experimental approach

Light attenuation technique



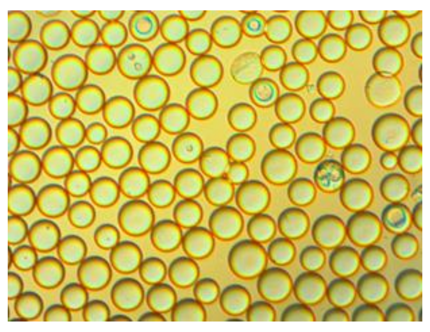
Material

Liquid : Phosphate Buffer Saline (PBS) 0.01 M (similar to water)

Solid : Cytodex-1 microcarrier

Diameter depends on the salt concentration

Translucent

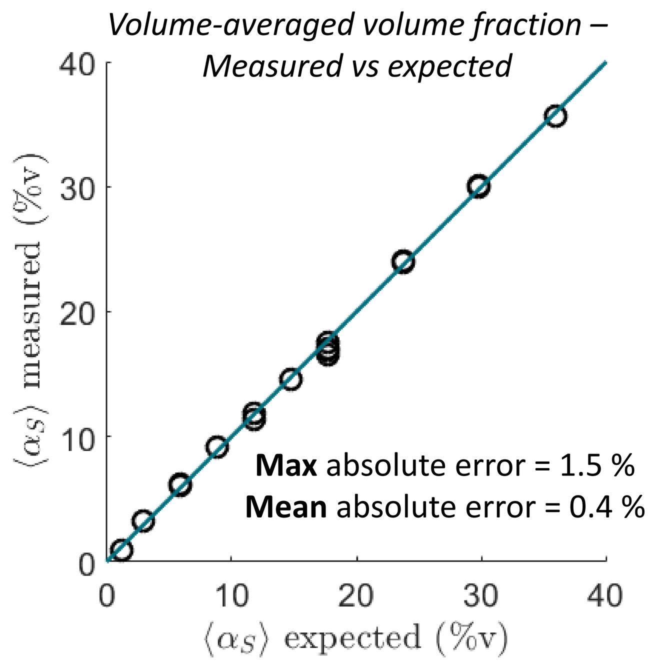


ρ_S (kg m^{-3})	**1020**
$d_{P,mean}$ (µm)	**162**
$d_{P,50}$ (µm)	161
$d_{P,5}$ (µm)	133
$d_{P,95}$ (µm)	194

Calibration

Measurements at N **= 200 rpm** (uniform suspension) for **10 volume fractions** ($1 \leq \langle\alpha_S\rangle \leq 40$ %)

Calibration pixel by pixel using a **3rd degree polynomial**



Operating conditions

Averaged solid volume fraction: $\langle\alpha_S\rangle$ **= 10 %**

Impeller speed: $N = [20:5:100]$ rpm

Visual estimation of complete suspension: N_{js} **= 87 ± 2 rpm**

Numerical approach

Multiphase flow

CFD code: ANSYS Fuent 18.2

Mulitphase modelling: **Euler-Granular model**

Turbulence modelling: **'Mixture' standard *k-epsilon***

Near-wall modelling: Scalable Wall Function (**SWF**) or Enhanced Wall Treatment (**EWT**)

Drag modelling: Huilin-Gidaspow model

Turbulence dissipation, lift and virtual mass forces not included

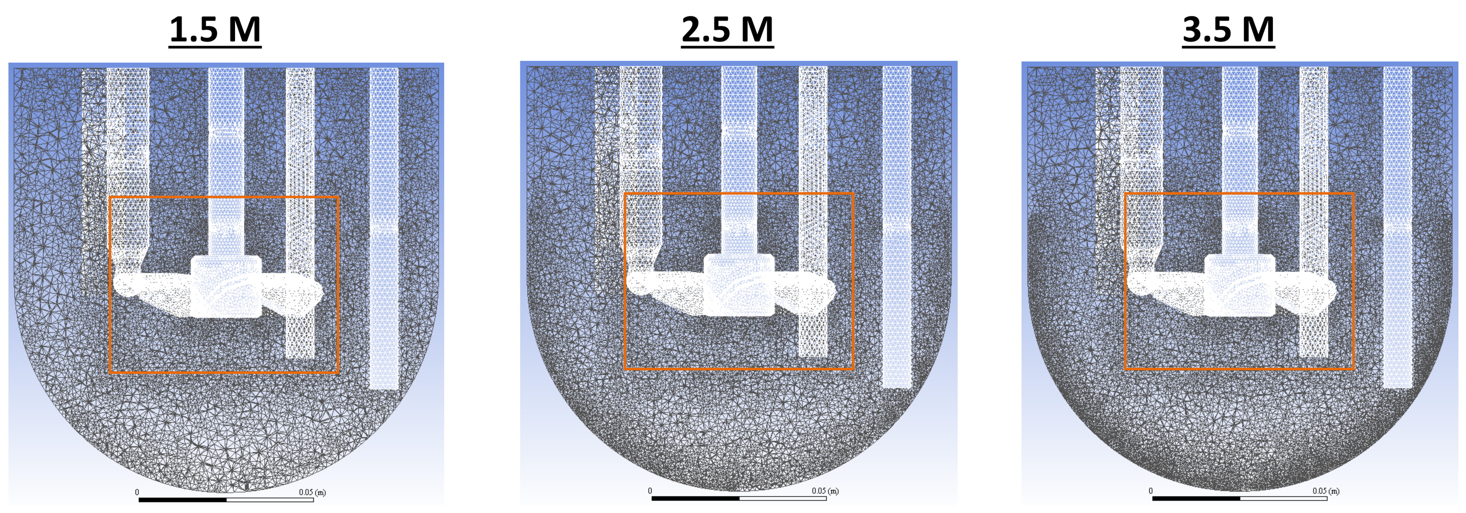
Solution strategy

Impeller motion: Moving Reference Frame

Initialization: Uniform solid fraction

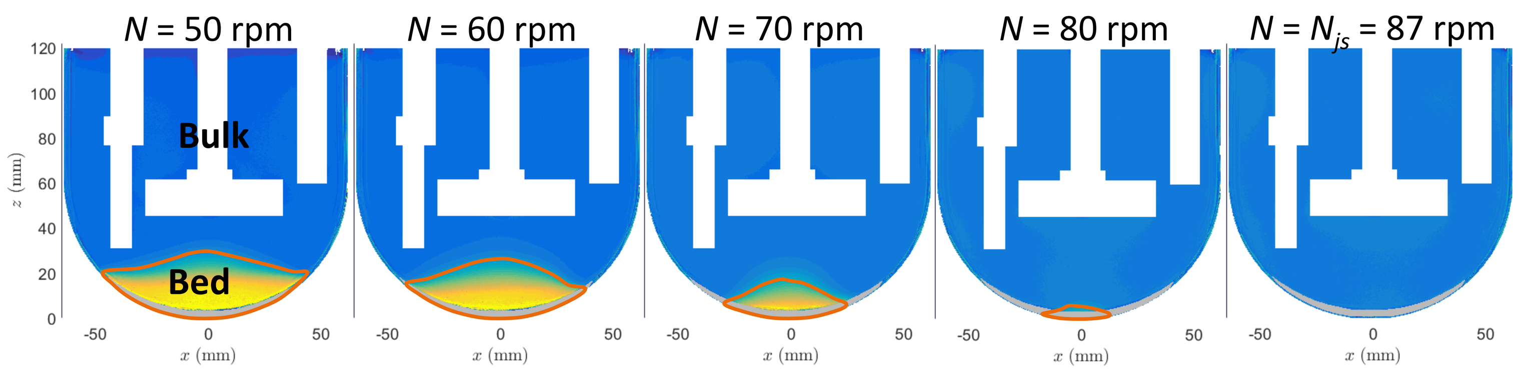
3 mesh sizes

Fixed number in the rotating zone around the impeller - Refined at the bioreactor bottom



Experimental results

Solid spatial distribution



Bulk: $\alpha_{S,bulk} \leq \langle\alpha_S\rangle$ Uniform solid fraction in the bulk at any N

Bed: $\alpha_{S,bed} = \alpha_{S,max}$ Bell-shape bed of motionless particles for $N < N_{js}$

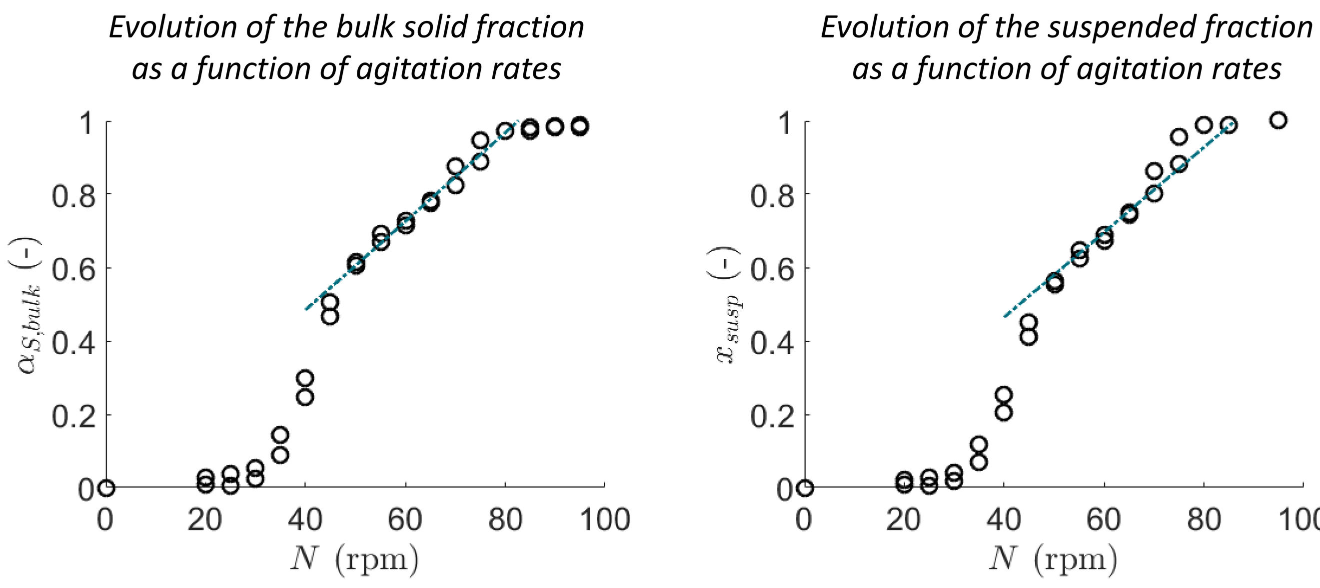
No visible layer without particles below the surface ($V_{layer} = 0$)

Solid mass balance

$$\langle\alpha_S\rangle = \frac{\alpha_{S,bulk}V_{bulk} + \alpha_{S,bed}V_{bed}}{V} \qquad V = V_{bulk} + V_{bed} + V_{layer}$$

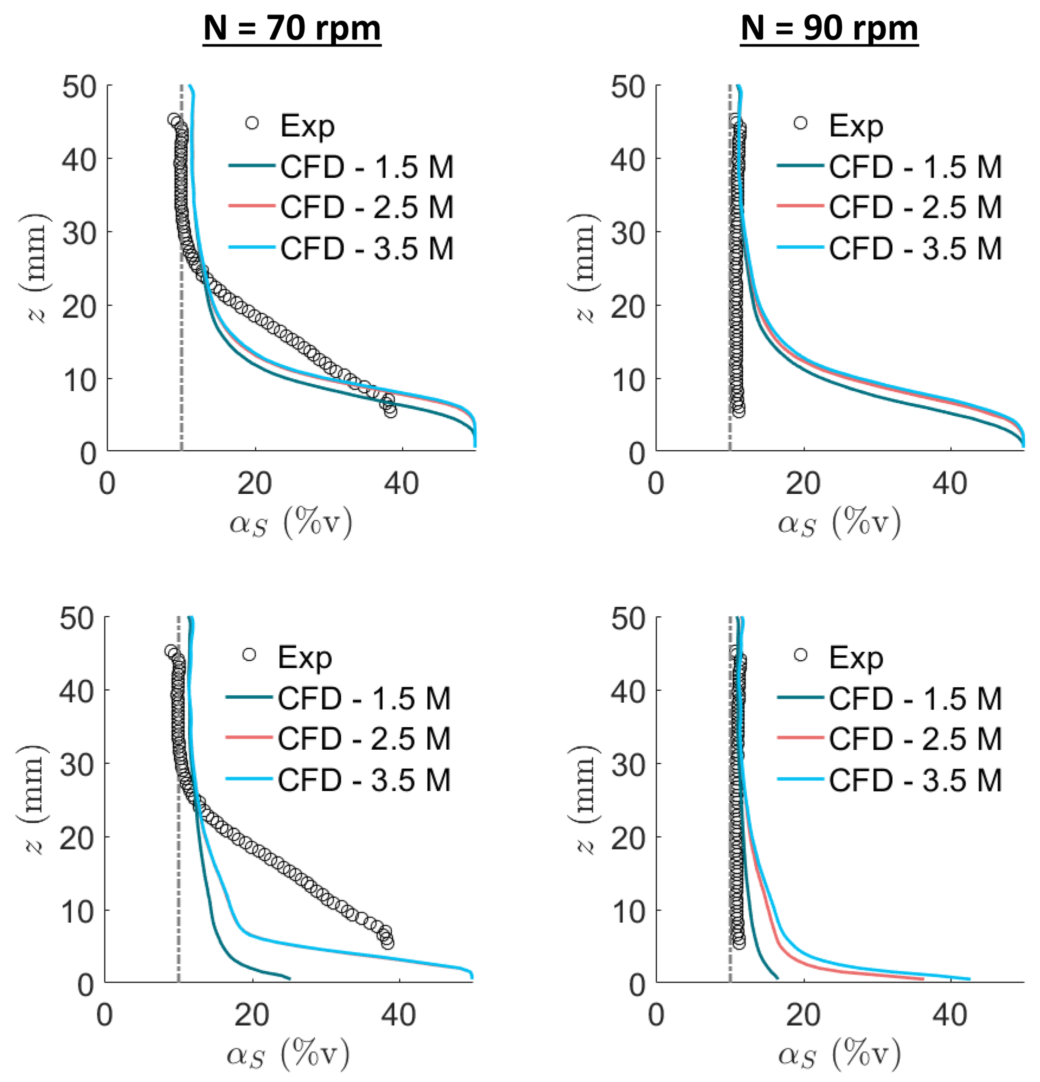
Volume fractions integrated over the tank thickness + Light distorsion at the tank bottom (masked in gray) ⇨ V_{bed} and V_{bulk} not known *a priori*

Fraction of suspended particles x_{susp}: $x_{susp} = \frac{\alpha_{S,bulk}V_{bulk}}{\langle\alpha_S\rangle V} = 1 - \frac{\alpha_{S,bed}V_{bed}}{\langle\alpha_S\rangle V}$



Numerical results

Axial profile of solid fraction below the impeller (x = 0 mm)



Scalable Wall Function

No significant influence of the mesh refinement

$N < N_{js}$: Small understimation of the bed height

$N \geq N_{js}$: Significant overestimation of the solid fraction at the bottom

	1.5 M	2.5 M	3.5M
Bottom wall y^+ (N = 90rpm)	7.5	7	6.5

Enhanced wall treatment

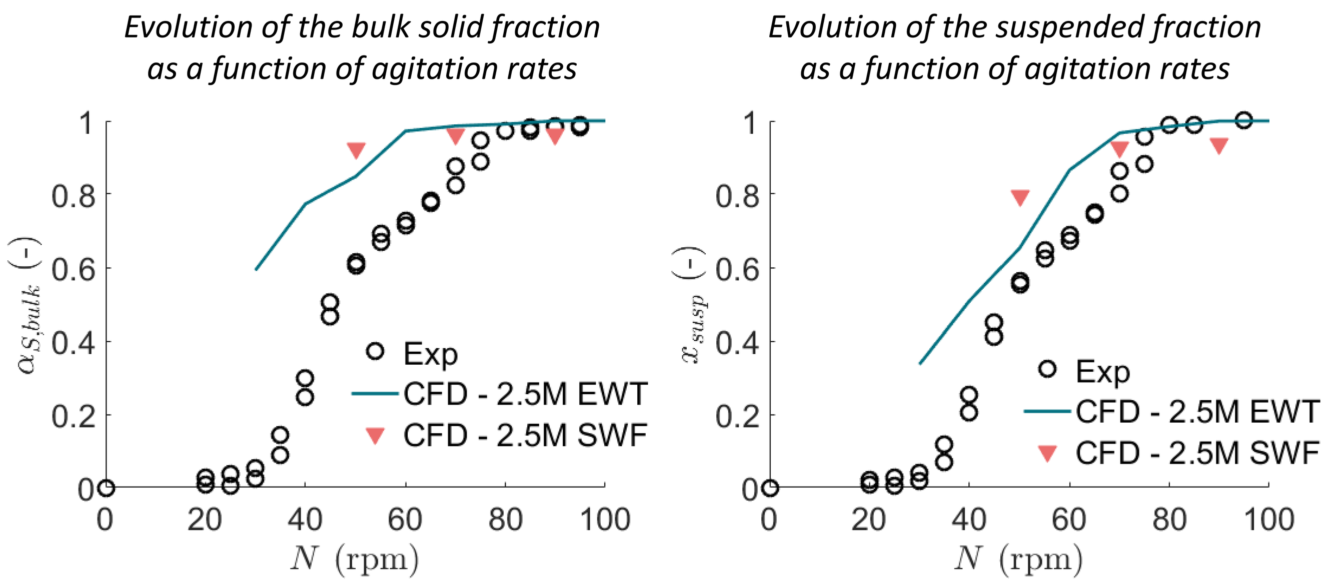
Strong influence of the mesh refinement up to 2.5 millions mesh elements

$N < N_{js}$: Understimation of the bed height

$N \geq N_{js}$: Sligh overestimation of the solid fraction at the bottom

	1.5 M	2.5 M	3.5M
Bottom wall y^+ (N = 90rpm)	3	1.2	1

Solid mass balance



Prediction of a layer without particles up to 90 rpm (not shown)

⇒ Overestimation of the solid fraction in the reactor bulk

⇒ Underestimation of the bed height at the bottom

Accurate estimation of N_{js} with EWT but overestimation with SWF

Conclusions/Perspectives

Strong influence of the near-wall modelling and mesh refinement at the tank bottom on the prediction of the just-suspended agitation rate N_{js} and the solid spatial distribution

Overall good agreement between experiments and CFD multiphase simulations using the **Enhanced Wall Treatment** and a **refined mesh** at the tank bottom but some discrepancies persist that may be related to:

- Validity of the *k-epsilon* closure model for not fully turbulent flow **BUT** Limited number of turbulence models available with the Euler-Granular approach
- Accuracy of the MRF approach to take into account the impeller motion **BUT** High computational cost with the Sliding Mesh (SM) approach

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