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Computational studies of a novel magnetically driven single-use-technology bioreactor: A comparison of mass transfer models

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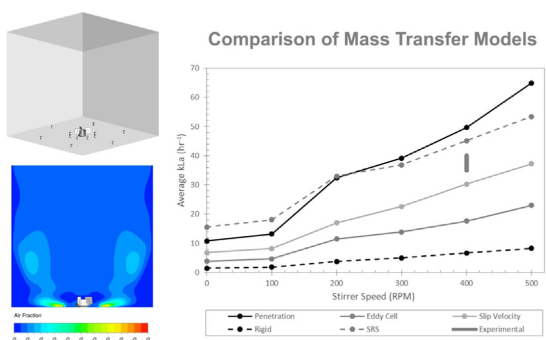
HIGHLIGHTS

- Computational analysis of a large-scale single-use-technology bioreactor.
- Slip velocity model is recommended for magnetically stirred reactors.
- Specific interfacial area is dominant in driving changes in mass transfer.
- Immersed solids method can be applied for modelling magnetic impeller motion.

GRAPHICAL ABSTRACT



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ABSTRACT

This work applies computational fluid dynamics (CFD) modelling to a novel 1000 L design of single-use-technology (SUT) bioreactor, with a magnetically driven floor-mounted impeller and spargers distributed across the tank floor. A two-phase Euler-Euler model using the k-ε turbulence model and population balance is presented alongside the use of immersed solid method for modelling the impeller motion. This work also provides the first CFD analysis of a large-scale SUT bioreactor, identifying key flow characteristics of the non-standard design at different operating conditions. Five models for the mass transfer coefficient, k_L, are compared, with k_La values compared to experimental measurements. The slip velocity model is found to be the best prediction of the mass transfer coefficient for this SUT system. Separating the influence of the mass transfer coefficient and specific area,a shows that the latter is the dominant driving force behind changes in k_La that occur at different operating conditions. Comparing the present work to previous studies for traditional stirred tanks highlights the need for understanding the hydrodynamics of non-standard reactor designs when identifying suitable mass transfer models in gas–liquid flow systems.

1. Introduction

Single-Use-Technology (SUT) reactors are a class of disposable bioprocessing equipment used mainly in the biopharmaceutical industry, where pre-sterilised plastic components are disposed of and replaced after use. The popularity and range of available SUT processes and equipment has increased in recent years, primarily in the biopharmaceuticals industry (Lopes, 2015). SUT bioreactors provide a viable alternative to traditional stainless steel bioreactors, and can be categorised by agitation mechanism as rocking (up to 500 L scale) or stirred type (up to 2000 L scale) (Brecht, 2009). Benefits of the adoption of SUT concepts in production processes

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Nomenclature

a	specific are (m^{-1})
C_D	drag coefficient (–)
C_{O_2}	dissolved oxygen concentration ($mol\ m^{-3}$)
$C^*_{O_2}$	saturation oxygen concentration ($mol\ m^{-3}$)
$C_{\varepsilon 1}$	k-ε equation constant (–)
$C_{\varepsilon 2}$	k-ε equation constant (–)
C_μ	k-ε equation constant (–)
d_b	bubble diameter (m)
d_i	mean MUSIG group diameter (m)
d_{max}	maximum bubble diameter (m)
d_{min}	minimum bubble diameter (m)
$D_{g,l}$	interphase drag force ($N\ m^{-3}$)
D_L	mass diffusivity ($m^2\ s^{-1}$)
F^{TD}	turbulent dispersion force ($N\ m^{-3}$)
$\mathbf{g}$	gravitational vector
$g(m;\varepsilon)$	specific breakup rate (s^{-1})
i	MUSIG group number (–)
k	turbulent kinetic energy ($m^2\ s^{-2}$)
k_l	volumetric mass transfer coefficient ($m\ s^{-1}$)
K	proportionality constant (–)
N	number of MUSIG groups (–)
N_{O_2}	oxygen transfer rate ($mol\ m^{-3}\ s^{-1}$)
$n(m,t)$	number density (m^{-3})
P	pressure (Pa)
P'	modified pressure (Pa)
$Q(m;\varepsilon)$	specific coalescence rate ($m^3\ s^{-1}$)
Re	Reynolds number (–)
Re_m	mean Reynolds number (–)
S_k	momentum source term ($N\ m^{-3}$)
Sc	Schmidt number (–)
Sh	Sherwood number (–)
$\mathbf{u}$	velocity vector (ms^{-1})
ν	kinematic viscosity ($m^2\ s^{-1}$)
V_G	superficial gas velocity ($m\ s^{-1}$)
ν_b	slip velocity ($m\ s^{-1}$)
α	volume fraction (–)
ε	turbulence dissipation ($m^2\ s^{-3}$)
μ	dynamic viscosity (Pa s)
μ_{eff}	effective viscosity (Pa s)
μ_T	turbulent viscosity (Pa s)
ρ	mass density ($kg\ m^{-3}$)
σ_k	k-ε equation constant (–)
σ_ε	k-ε equation constant (–)

include reduced cross-contamination and assured sterility, flexibility, financial, productivity and environmental considerations. The use of SUT bioreactors largely eliminates the need for sterilisation and cleaning between processes, with the manufacturer of a 100 L wave-type SUT bioreactor claiming a reduction in turnaround time from 8 to 10 h for a traditional stainless steel technologies to just 1–2 h (Kranjac, 2004). Furthermore, a similar turnaround time is claimed between different products, significantly increasing the flexibility of a process whilst simultaneously reducing downtime and labour requirements. It has also been reported that significant cost savings can be made by adopting SUT processes. This takes the form of reduced capital costs through reduced equipment purchase costs and shorter build times, and reduced operating costs, largely through reduced cleaning and labour requirements. A lifecycle analysis approach by Pietrzykowski et al. (2013) has shown that the overall environmental impact of an SUT facility can be significantly lower than comparable stainless steel processes, with the greatest improvements coming from water and energy use due to cleaning. However, using SUT components does lead to an increase in plastic waste generation of up to 455% for a fully SUT facility (Lopes, 2015), which will increase the consumables requirement and requires appropriate disposal.

There is a range of currently available stirred SUT bioreactors with varying production capacity (Lopes, 2015); however these have been largely limited to applications in the production of high-value products from mammalian (Eibl et al., 2010), and less commonly plant cells (Eibl et al., 2009). This leaves the wider industrial biotechnology sector largely untouched by SUT concepts, with only small-scale microbial investigations reported (Dreher et al., 2013). There is also a lack of industry standardisation, with the supply chain often tied to the fate of a single component supplier (Lopes, 2015), however this also gives the option to tailor the equipment and sparger design to a particular process need to a degree that is not generally possible with traditional stainless steel bioprocessing equipment.

The use of CFD modelling as a tool for assessing the flow in stirred tanks is a field which has been developing since the mid-1980s with the single-phase models of Harvey and Greaves (1982a, 1982b). Since then, the complexity of the models has increased alongside an increase in available computing power, with more complex impeller motion and turbulence models amongst the most significant developments. The modelling of two-phase gas-liquid systems first became feasible in 2D in the mid-1990s, with the development of Euler-Euler methods, with 3D simulations developing during the early 2000s using a range of different interfacial drag and population balance models applied. A thorough analysis of the development of single and two-phase modelling in stirred tanks is reported in the review series of Joshi et al. (2011a, 2011b). Within the published body of work surrounding stirred tank modelling, a wide range of different shaft-driven impeller and baffle geometries have been used. However, there is a lack of analysis of non-cylindrical reactor designs and magnetically stirred tanks.

Oxygen transfer in bioreactors and fermenters is a very important characteristic, as dissolved oxygen can become the limiting factor in processes with high oxygen demand such as some bacterial fermentations. It is routinely reported in terms of the combined value k_La, which can be easily measured experimentally from dissolved oxygen measurements using various techniques (Garcia-Ochoa et al., 2010; Doran, 1995), both with and without the presence of biomass. Separating the terms k_L and a is difficult experimentally, however it is an approach commonly used in CFD modelling to describe the mass transfer in two-phase systems. The two most commonly used models for the study of mass transfer in gas-liquid flows are the penetration and eddy cell models, which both take the form of Eq. (1). For the ease of comparison, models of this form will be referred to collectively as the eddy model. The penetration model is based on Higbie's penetration theory of interfacial transfer (Higbie, 1935), with the assumption that the contact time can be approximated by the Kolmogorov length scale due to the influence of small eddies on the mass transfer. In contrast, the eddy cell model was derived by Lamont and Scott (1970) by modelling the mass transfer into idealised eddies of sizes across the energy scale, giving a theoretically derived proportionality constant of 0.4.

$$k_L = K\sqrt{D_L\sqrt{\frac{\varepsilon}{\nu}}} \tag{1}$$