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Lagrangian modeling of hydrodynamic–kinetic interactions in (bio) chemical reactors: Practical implementation and setup guidelines

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HIGHLIGHTS

- We apply Lagrangian CFD in reactors to allow dynamic study of the catalyst phase.
- The required number of tracked particles is predicted from physical parameters.
- Reaction models have been coupled to massless particle tracking in ANSYS FLUENT.
- Particle tracking has successfully been combined with the MRF impeller method.
- Guidelines for the practical setup of Lagrangian reactor simulation are presented.

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ABSTRACT

Large substrate concentration gradients can exist in chemical or biochemical reactions, resulting from a large circulation time compared to the turnover time of substrates. The influence of such gradients on the microbial metabolism can significantly compromise optimal bioreactor performance. Lapin et al. (2004) proposed an Euler–Lagrange CFD method to study the impact of such gradients from the microbial point of view. The discrete representation of the biomass phase yields an advantageous perspective for studying the impact of extra-cellular variations on the metabolism, but at significant computational cost. In particular, the tracked number of particles, as well as the applied time resolution, have a large impact on both the accuracy of the simulation and the runtime of the simulation. In this work we study the influence of these parameters on both the simulation results and computation time, and provide guidelines for accurate Euler–Lagrange bioreactor simulations at minimal computational cost.

1. Introduction

In many (bio)chemical reactors, reaction takes place inside a discrete phase such as micro-organisms or catalysts particles, with transport occurring in the bulk phase. If the timescale of bulk mixing is in the range of or longer than the reaction timescale, the competition between reaction and bulk mixing will result in spatial substrate heterogeneity. When the discrete phase is mobile, such as in a slurry reactor or fermentor, micro-organisms/particles will see continuous changes in their environment as they move around. The spatial substrate gradients inside the reactor, translate to temporal substrate variations from the organism or catalyst's reference frame.

Focusing now on a bioreactor, the biomass specific production rate q_p of the desired component is typically governed by a complex metabolic reaction network, with the reaction rates depending both on the availability of extra-cellular substrates (such as sugar and oxygen) and intra-cellular components (such as amino acids and ATP). The adaptation of organisms to their surroundings does not occur instantaneously (Heijnen, 2010), meaning that the intra-cellular and extra-cellular conditions will typically not be in equilibrium. Consequently, q_p may vary in time, being a function of the organism's trajectory through space. As a result, the observed production rate of the entire population may differ considerably from an ideal mixing situation (Larsson et al.,

Abbreviations: **RD**, Reaction dynamics; **EL**, Euler–Lagrange; **MRF**, Multiple Reference Frame; **SM**, Sliding Mesh

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Nomenclature

T	Tank diameter, m
A	Area, m^2
C_s	Substrate concentration, mol/m^3
C_X	Biomass concentration, kg/m^3
D_t	Turbulent diffusion coeff., m^2/s
D_m	Molecular diffusion coeff., m^2/s
ΔC	Off-bottom clearance, m
D	Impeller diameter, m
H	Tank height, m
K_s	Affinity constant for s, mol/m^3
k	Turbulent kinetic energy, m^2/s^2
$k_{s,max}$	Max. reaction rate of s
M	Impeller moment, N m
N_c	Total no. grid cells
N_p	Total no. parcels
$N_{p,c}$	No parcels in cell c
N_s	Impeller revolutions, 1/s
n	Radial divisions
q_s	biomass specific glucose uptake rate, mol/g/h
q_p	biomass specific production rate, mol/g/h
$R_{s,c}$	Vol. reaction of s, $mol/m^3/s$
$R_{s,p}$	Parcel-coupled reaction of s, $mol/m^3/s$
r	Radius, m
$S_{s,c}$	Source of s in cell c, mol/m^3
t	Time, s
V	Volume, m^3
Re	Reynolds number
St	Stokes number
Sc_t	Turbulent Schmidt no.
Po	Power number

Greek

α	Proportionality parameter
β	Theoretical error
$\beta_{m,c}$	Max. β in cell c
$\beta^*_{m,c}$	$\beta_{m,c}/(4\pi^2/3)$
χ	Mean fluctuations ($\langle\overline{COV_x}\rangle$)
ϵ	Turbulent energy dissipation, m^3/s^2
$\tau_{r,c}$	Reaction time in cell c
$\tau_{m,p}$	Parcel-mixing time
σ_x	St. dev. of parameter x
ρ	Density, kg/m^3
μ_l	Molecular viscosity, Pa s
μ	Biomass specific growth rate, 1/s
λ	Interphase substrate imbalance, %
θ	Mean reaction time $\frac{\Delta t_c k_{s,max} X}{K_s}$

Subscripts

t	Turbulent
T	Total
p	Particle
c	Gridcell
s	Substrate

Other

$\overline{x}$	Time-average of x
$\langle x\rangle$	Volume-average of x
COV_x	Coeff. of variation of x, $\frac{\sigma_x}{\langle x\rangle}$

1996). Second, there may be considerable heterogeneity *within* the population (Delvigne and Goffin, 2014).

Substrate concentration gradients originate from the fact that the bulk circulation time equals or exceeds the turnover time of metabolites (Wang et al., 2015). Since the circulation time is dependent on the reactor scale, but turnover times are not, the extracellular conditions in a (typical ideally mixed) laboratory scale fermentor will not reflect the non-ideal industrial scale operation. This indicates that microorganisms are tested and selected under conditions that do not represent their future working environment (Noorman, 2011). For a reliable process design, effects of substrate concentration gradients on q_p should be taken into consideration during both process and organism development.

Scale-down simulators offer the possibility to study micro-organisms under industrially representative conditions by deliberately introducing spatial concentration gradients using multi-compartment systems, or temporal concentration gradients via a fluctuating feed. (Neubauer and Junne, 2010; Wang et al., 2015). A recurring problem in scale-down simulation is to select the proper setup to reasonably match the industrial environment. Detailed information about the industrial environment is often scarce, or unavailable. It has been proposed to use computational fluid dynamics (CFD) coupled with reaction dynamics (RD) to gain insight in the industrial environment (Noorman, 2011; Wang et al., 2014). In this way it is possible to study the magnitude of gradients and their effect on microorganisms (Lapin et al., 2004, 2006; Morchain et al., 2013), providing valuable input for the design of scale-down simulators. Although this communication focuses on bioreactor applications, the outlined methods are applicable to any system dealing with similar dynamics.

1.1. CFD-RD coupling

Due to computational constraints, early CFD-RD work related to bioreactors often remained limited to the application of unstructured kinetic models (i.e. Larsson et al., 1996), simulating only the uptake of substrate, or linking growth and production rate directly to the substrate uptake rate via a Herbert–Pirt equation. As such models assume an instantaneous adaptation of the metabolism to the extra-cellular conditions, such an approach is unsuitable to assess the effect of substrate concentration gradients.

More recently, the adaptation of the metabolism to environmental fluctuations has been included via two approaches: the population balance approach and Euler–Lagrange (EL) approach. In the population balance approach, micro-organisms are modeled as a component of the liquid phase. The biomass specific growth rate μ is typically applied to describe population heterogeneity (Morchain et al., 2013, 2014; Pigou and Morchain, 2015). This method is suitable for situations where all relevant processes are coupled to μ. However, metabolic fluctuations may take place on shorter timescales than growth rate fluctuations, and may have complex mutual interactions. To capture such processes, population balance approaches are unsuitable, as the biomass population heterogeneity is not described solely by μ.

In EL-approaches the biomass phase is represented by a large number of virtual particles carrying an internal parameter vector describing their state (Lapin et al., 2004, 2006). These virtual particles are further referred to as parcels to distinguish between computational and physical biomass particles. A large number of intra-cellular components and their mutual interactions can be tracked for each particle via a structured metabolic model. This