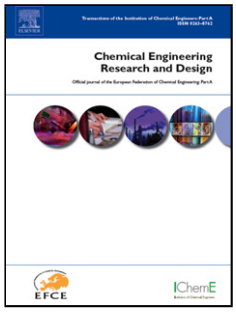

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Author: V. Quedeville H. Ouazaite B. Polizzi R.O. Fox P. Villedieu P. Fede F. Létisse J. Morchain

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A two-dimensional population balance model for cell growth including multiple uptake systems

V. Quedeville[2, 1], H. Ouazaite[1], B. Polizzi[2], R. O. Fox[3], P. Villedieu[4, 1], P. Fede[2], F. Létisse[1], and J. Morchain[1, *]

[1]Laboratoire d'Ingénierie des Systèmes biologiques et des Procédés, INSA de Toulouse, 135 Avenue de Rangueil, 31400 Toulouse, France
[2]Institut de Mécanique des Fluides de Toulouse, 2 Allée du professeur Camille Soula, 31000 Toulouse, France
[3]Department of Chemical and Biological Engineering, Iowa State University, 618 Bissell Road, Ames, Iowa 50011-1098
[4]ONERA de Toulouse, 2 Avenue Edouard Belin, 31055 Toulouse, France
[*]Corresponding author at INSA, LISBP, 135 Avenue de Rangueil, 31400 Toulouse, France.
Email address: morchain@insa-toulouse.fr

Abstract

Cell growth in a chemostat is a well-documented research topic. How cells uptake the available substrate to gain weight and engage cell division is not generally taken into account in the modelling bioreactors. In fact, the growth rate is related to a population doubling time whereas the microorganisms' growth in mass is due to the mass transfer of substrates from the liquid phase to the biotic phase. Clearly, growth in mass precedes growth in number. Similarly, the transport of substrates down to the cell scale precedes the mass transfer. This article's main feature is a two-dimensional population balance model that allows to uncouple growth in mass and growth in number when the equilibrium between a cell population and its environment is disrupted. The cell length and the rate of anabolism are chosen as internal variables. It is proved that the hypothesis "growth in number = growth in mass" is valid at steady-state or in exponential growth only. The glucose uptake is assumed driven by two transport systems with a different affinity constant for the substrate. This combination of two regulated uptake systems operating in parallel explains a 3-fold increase in the uptake following a glucose pulse, but can also predict substrate uptake rates higher than the maximal batch value as observed in some experiments. These features are obtained by considering carbon fluxes in the formulation of regulation principles for uptake dynamics. The population balance's implementation in a multi-compartment reactor is a natural prospective work and allows extensions to industrial processes.

keywords : Cell growth, population balance model, uptake rate, bioreactor, dynamic simulation