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Investigating the interactions between physical and biological heterogeneities in bioreactors using compartment, population balance and metabolic models

Maxime Pigou, Jérôme Morchain



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A generic model for the description of biological population dynamics in industrial bioreactors is detailed. Hydrodynamics, mass transfer between the cell and the surrounding fluid, population heterogeneity, metabolism and biological adaptation have to be considered with equal interest and, if possible, simultaneously. This model couples a hydrodynamic model, a population balance model for the growth rate adaptation and a metabolic model predicting the reaction rates depending on the state of the individuals. This approach dissociates the growth rate from local concentrations leading to a good understanding of the effects of a changing environment on a microbial population. Our model is applied to *Escherichia coli* for which experimental data exist in literature for batch and fed-batch cultures. The considered strain is known for producing acetate when exposed to heterogeneities. When simulating a large bioreactor using a compartment model approach for hydrodynamics, our coupled model could predict that, under certain conditions, acetate is simultaneously produced and consumed in different areas of the reactor.

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