Experimental methods and modeling techniques for description of cell population heterogeneity

With the continuous development, in the last decades, of analytical techniques providing complex information at single cell level, the study of cell heterogeneity has been the focus of several research projects within analytical biotechnology. Nonetheless, the complex interplay between environmental changes and cellular responses is yet not fully understood, and the integration of this new knowledge into the strategies for design, operation and control of bioprocesses is far from being an established reality. Indeed, the impact of cell heterogeneity on productivity of large scale cultivations is acknowledged but seldom accounted for. In order to include population heterogeneity mechanisms in the development of novel bioprocess control strategies, a reliable mathematical description of such phenomena has to be developed. With this review, we search to summarize the potential of currently available methods for monitoring cell population heterogeneity as well as model frameworks suitable for describing dynamic heterogeneous cell populations. We will furthermore underline the highly important coordination between experimental and modeling efforts necessary to attain a reliable quantitative description of cell heterogeneity, which is a necessity if such models are to contribute to the development of improved control of bioprocesses.

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