

110b Automated Flow Cytometry for Identification of Population Balance Models

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Population balance models are the most accurate descriptions of cell culture behavior as the models account for the single cell heterogeneities inherently present in culture. The implementation of population balance models as a predictive or a control device has been limited to date since the necessary parameters of growth rate and partitioning of cellular material at the single cell level are largely unknown. While it is in principle possible to identify the parameters under specific situations such as balanced growth conditions, it is completely unclear how the functions change during transient substrate conditions. Through the use of automated flow cytometry and high frequency sampling, it is possible to extract this desirable information. The transient of the growth rate function in response to changes in glucose concentration, specifically glucose upshifts, are of particular interest. A glucose upshift was performed for a strain of *Saccharomyces cerevisiae* resulting in cessation of cell division for a period of time. During this time, the single cell growth rate function can be extracted. It was determined that larger cells adjust more quickly to the higher specific growth rate than smaller cells after a glucose upshift. This effect is likely due to the fact that larger cells already are committed to growth whereas small cells may be in a resting state. Consequently the capability to model cultures accurately is greatly expanded through the inclusion of experimentally determined transient responses.