Preventing overflow metabolism in Crabtree-positive microorganisms using the PAT approach: progress and challenges

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At growth rates above a particular critical value, Crabtree-positive microorganisms exceed their respiratory capacity and enter diauxic growth metabolism. Excess substrate is converted to an overflow metabolite, resulting in decreased biomass yield and productivity. To prevent this scenario, the cells can be cultivated in a fed-batch mode at a growth rate maintained below the critical value, μ_{crit}. This approach entails by two major difficulties: accurately estimating the current specific growth rate and controlling it successfully over the course of the fermentation. In this presentation, the results obtained with *S. cerevisiae* and *E. coli* fermentations will be reported with a focus on the specific challenges that were encountered.