Optimal feed control for maximization of lipid production from dilute acetic acid by an engineered oleaginous yeast *Yarrowia lipolytica*

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Acetic acid can be generated in syngas fermentation, lignocellulosic biomass degradation, and anaerobic digestion of organic wastes. Compared to sugar-based lipid production, microbial conversion of acetate into triacylglycerols for biofuel production can be economically more affordable due to low- or negative-cost feedstocks. The main issue is the dilute nature of acetate produced in such systems, a problem we tackled with cell recycle. To this end, we established an efficient process for converting dilute acetate into lipids by the oleaginous yeast, *Yarrowia lipolytica* engineered for lipid overproduction. The process design utilized low-strength acetic acid as substrate with dual feed of acetic acid and acetate, as well as nitrogen for cell growth with a cross filtration module for cell recycle. Various types of feed control were deployed including one based on a fermentation model and on-line measurement of the Respiratory Quotient. The optimized process was able to utilize 3% acetic acid for high density cell culture and achieved a lipid titer of 115 g/L, lipid conversion yield of 0.16g/g and an overall productivity of 0.8 g L⁻¹ h⁻¹.