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## Physical and biological dynamic interactions in cell cultures in a bioreactor: on-line and off-line rheological characterizations

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### Abstract

Rheological behaviour of culture broth stands as a fundamental parameter in bioprocess performances because it affects simultaneously heat and mass transfer as well as flow pattern. It is then of first interest to get on-line characterization and to model the rheological behaviour of the fermentation broth relating to the microbial activity (specific kinetics, growth rate, physiology, morphology, cell concentration).

In this context, our scientific objectives deals with the identification of the impact of physical properties of complex three-phase broth on bioprocess performances with the development of an experimental platform enabling on-line rheometry measurements during cell cultures. In this way, a bioreactor was equipped with a derivation loop including a specific on-line rheometric device. In a first time, friction curves of calibrated ducts were achieved with Newtonian and non-Newtonian shear-thinning model fluids. In a second time, axenic cultures with two microorganisms of different size (*Escherichia coli* and *Yarrowia lipolytica*) were carried out in order to produce high biomass concentrations.

The uniqueness of friction curve is confirmed with model fluids, and validates our approach to investigate on-line rheometry of broths. The results obtained with *E. coli* and *Y. lipolytica* cultures respectively ranging between  $\sim 40\text{--}110\text{g}_{\text{CDW}}\cdot\text{l}^{-1}$  and  $\sim 75\text{--}105\text{g}_{\text{CDW}}\cdot\text{l}^{-1}$  are reported. For *Y. lipolytica*, off-line rheometry demonstrated a shear-thinning behaviour in relation with biomass concentration whereas on-line viscosity measurements established in laminar flow regime for higher shear rates highlighted a Newtonian plate. For *E. coli*, on-line and off-line viscosities exhibited the same tendency but strongly differed in term of magnitude. In this case, several assumptions could be formulated to explain this difference: (i) thermal dependency of apparent viscosity, (ii) biological activity, (iii) volume gas fraction (aeration and biological production) in broth ( $\sim 30\text{--}40\%$  v/v) and (iv) shear rates (correlated to flow regime).

Impact of different phases on apparent viscosity for high biomass concentration above  $110\text{g}_{\text{CDW}}\cdot\text{l}^{-1}$  will be investigated in close future.

**Key words :** cell culture, bioreactor, viscosity, on-line rheology.