# Study of the mixing time evolution during the scale-up of an animal cells culture in a stirred tank bioreactor

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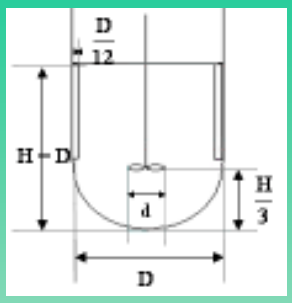
## THE BIOTECHNOLOGY ASPECT OF RESEARCH

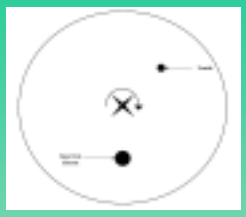
- This research is a collaboration between the company GlaxoSmithKline Biologicals and Laboratory of Chemical Engineering of Liege University.
- GSK BIO develops an industrial scale culture of animals cells in stirred tank, in which cells are adsorbed on microcarriers (non-porous beads made of reticulated dextran, mean size = 250 µm, density=1.03)
- Injection of alkali or nutrients are needed to regulate the pH and feed the cells respectively. These injections create concentration gradients which could be penalizing for the cells development.
- In laboratory scale, these concentrations gradients are rapidly eliminated by the turbulence created by impeller motion. But these concentration gradients could stay a longer time when the size of the bioreactor increases. Thus, the mixing time, which characterizes the time needed to reach concentration homogeneity, can become an important criterion in the scale-up strategy.
- The aim of this study is to measure the mixing time by conductometry in three bioreactors with increasing size in order to fit a correlation on these experimental data. This correlation will be, on later on, useful for the scale-up strategy.

## APPARATUS

**Bioreactor design:**

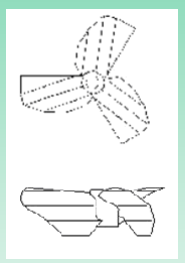



**Conductometry**



$C(t_M)-C_0 = 0.95\ (C_\infty-C_0)$

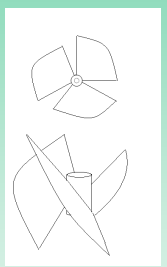
**Impeller design**



TTP (Mixel)

D/T=0.4

D/T=0.5



EE (Applikon)

D/T=0.5

**Operating conditions**

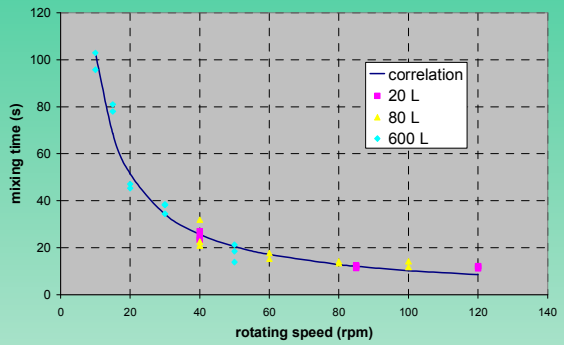
| | | | | | |
|---|---|---|---|---|---|
| **EE** | **20 L** | 20 rpm | 50 rpm | 85 rpm | 120 rpm |
| **(D/T=0.5)** | **80 L** | 20 rpm | 40 rpm | 51 rpm | |
| | **600 L** | 10 rpm | 15 rpm | 20 rpm | |
| **TTP** | **20 L** | 60 rpm | 120 rpm | 170 rpm | |
| **(D/T=0.4)** | **80 L** | 60 rpm | 90 rpm | 120 rpm | |
| **TTP** | **20 L** | 40 rpm | 85 rpm | 120 rpm | |
| **(D/T=0.5)** | **80 L** | 40 rpm | 60 rpm | 80 rpm | 100 rpm |
| | **600L** | 10 rpm | 15 rpm | 20 rpm | 30 rpm |

## RESULTS

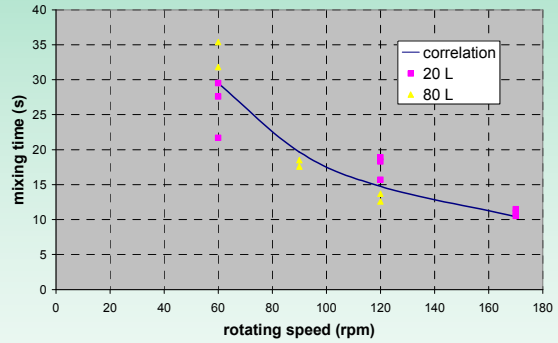
**Grenville et Al Correlation**(Greenville,R.K, Ruszkowski,S. and Garred, E. (1995), 15th NAMF Mixing conference, Banff, Canada )**:**

$$\theta_{95\%} = A\left(\frac{1}{N}\right)\left(\frac{1}{N_p}\right)^{\frac{1}{3}}\left(\frac{T}{D}\right)^{2}$$

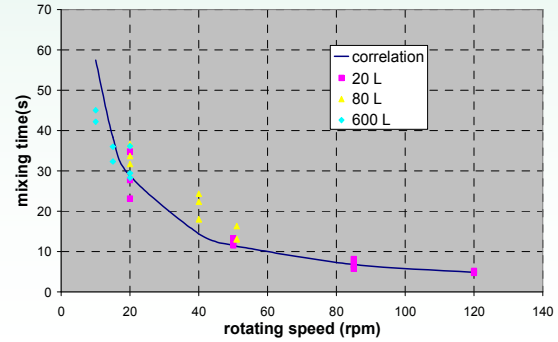
**TTP, D/T=0.5, Np=0.4, A=3.1**




**TTP, D/T=0.4, Np=0.4, A=3.48**




**EE, D/T=0.5, Np=2.12, A=3.08**




## CONCLUSIONS

The agreement between experimental values and those predicted can be considered good for all impellers in view of the fluctuations of the experimental mixing time in the same experimental conditions. This correlation will therefore be used with some confidence in the scale-up process

## ACKNOWLEDGEMENT

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