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OPTIMIZING *Saccharomyces cerevisiae* PRODUCTION YIELD USING RESPONSE SURFACE METHODOLOGY ACCORDING TO pH, INITIAL BIOMASS AND AERATION RATE IN A BATCH BIOREACTOR

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Abstract:
The main objective of this work is to optimize the yield production of the industrial yeast *Saccharomyces cerevisiae*, applying Response Surface Methodology (RSM) to study the effect of pH, aeration rate and initial biomass charge. The optimized parameters were used to study the growth kinetic of the yeast in a batch airlift bioreactor.
According to our results, the yeast has a weak growth at pH 4.5 and 5.5 and a significant growth at pH 6.5. The low biomass charge of 100 mg/L gives high duplication rate in opposite of a charge of 400 or 700 mg/L. Aeration rate of 0.875 L/min allows the best duplication rate than 2.187 or 3.5 L/min.
Key words: *Saccharomyces cerevisiae* production yield, Response Surface Methodology, Batch airlift bioreactor.

I- Introduction :

A batch airlift bioreactor is a suitable type of bioreactor for the cultivation of *S. cerevisiae*. In an airlift bioreactor, the mixing of the culture is achieved by the introduction of gas bubbles at the bottom of the reactor, which creates a circulation of liquid and air.

To optimize the production yield of *S. cerevisiae,* response surface methodology (RSM) involves designing experiments to explore the effects of several experimental variables (including the initial glucose concentration, temperature, pH, aeration, and agitation rate) on the yield of *S. cerevisiae* production (response variable), and then using statistical models to identify the optimal values of these variables that maximize the response**.**

II- Material and Methods :

II.1. Batch culture bioprocess and Response Surface Methodology: The batch culture bioprocess consist of an air lift bioreactor equipped with a valve of in-out flux, then, the aeration pump play the role of culture oxygenation and agitation. In this work, the RSM consist of 17 experiments of a Full Factorial Design applied to the experimental field of 3 factors as shown in table 1.

Table 1.Experimental field for the Full Factorial Design

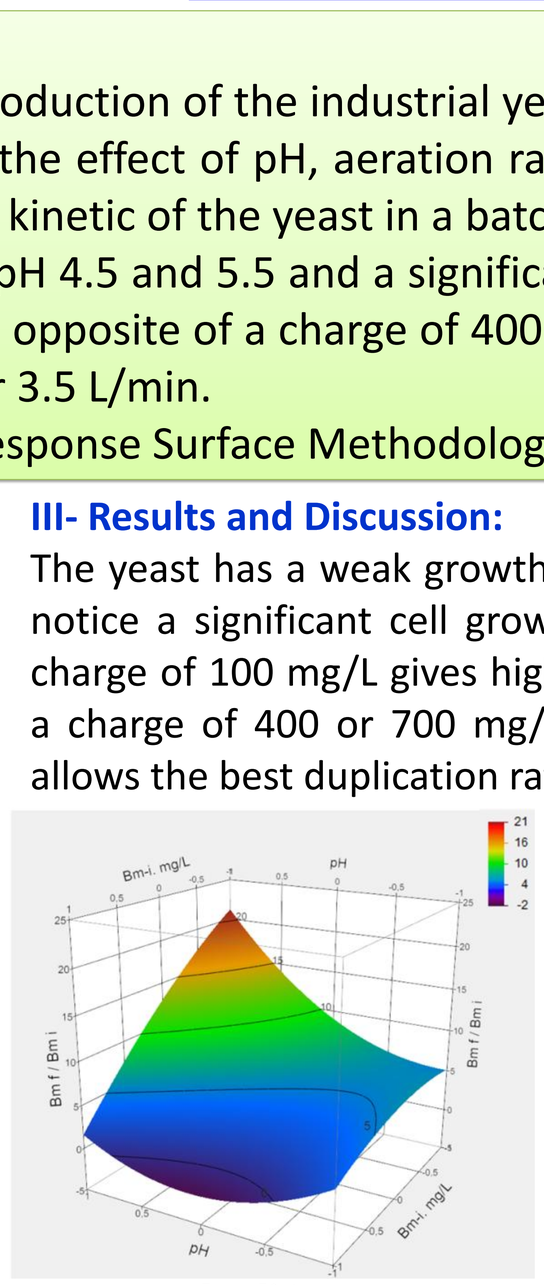
Factor (*Xi*)	min	mean	max	Studied response (*Yi*)
X_1: **pH**	4,5	5,5	6,5	Biomass production yield expressed by the *biomass growth rate* $Yi = BG_R = [Bm]_f / [Bm]_i$
X_2: **[*Bm*]*i* (mg/L)**	100	400	700	
X_3: **Aeration (L/min)**	0,875	2,18	3,5	

II.2. Study of the growth kinetic: A batch of optimized conditions was prepared and followed for 24 hours. Cell growth is monitored after several time intervals allowing determining the growth phases and studying the growth kinetic parameters: μ_{max} (*maximum growth rate*), θ (*Generation time*) and G_R (*Horary Growth Rate*) according to the following equations:

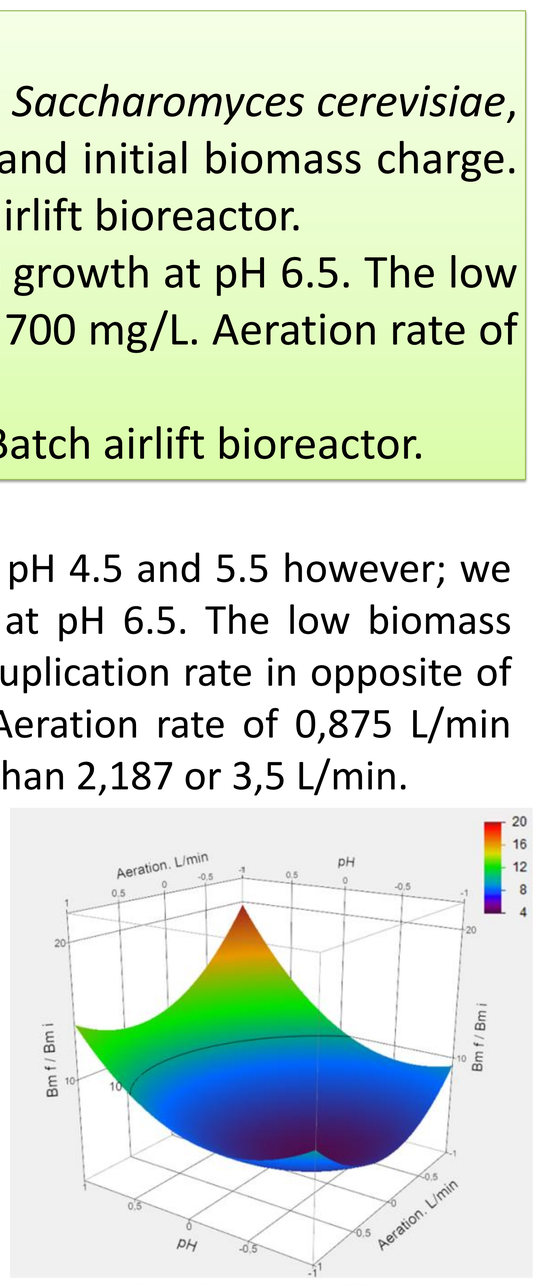
$$\mu = (\log_N Bm_2 - \log_N Bm_1) / (t_2 - t_1)$$
$$Q = (Bm_2 - Bm_1) / (t_2 - t_1)$$
$$\Theta = \log_N 2 / \mu = 0.693 / \mu$$
$$G_R = 1 / g$$

III- Results and Discussion:

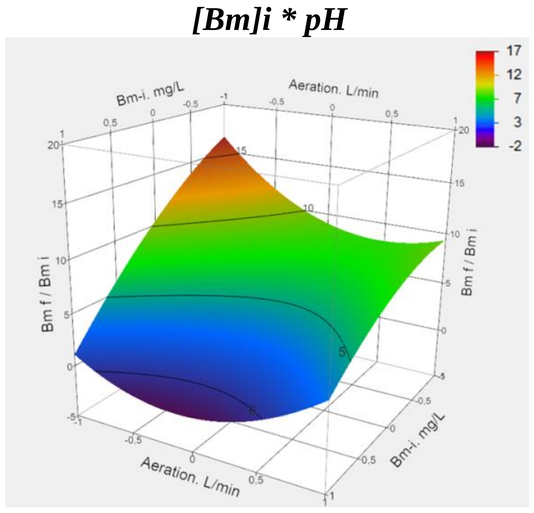
The yeast has a weak growth at pH 4.5 and 5.5 however; we notice a significant cell growth at pH 6.5. The low biomass charge of 100 mg/L gives high duplication rate in opposite of a charge of 400 or 700 mg/L. Aeration rate of 0,875 L/min allows the best duplication rate than 2,187 or 3,5 L/min.



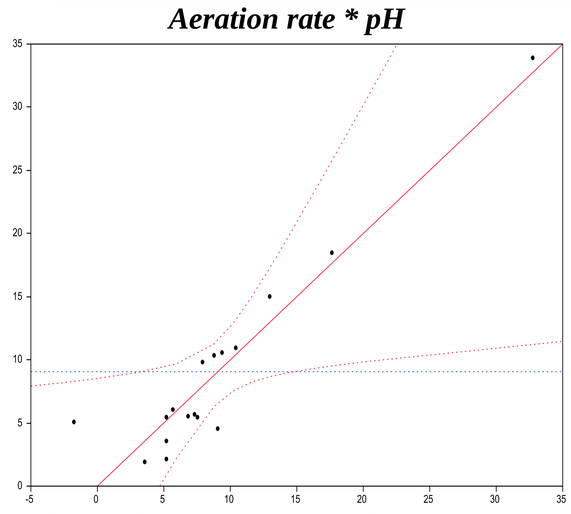
*[Bm]i * pH*



*Aeration rate * pH*



*Aeration rate * [Bm]i*



Observed Vs Provisional values; R^2 = 0.89

Figure 1: Response Surface of [Bm]f / [Bm]i following [Bm]i , pH and Aeration rate.

Conclusion:

According to our results, the yeast has an optimal growth at pH 6.5, biomass charge of 100 mg/L and an aeration rate of 0,875 L/min allows the best duplication rate of 33,878. The significant effect coefficients are those of biomass charge, the interaction between pH and biomass charge, and these of pH, than, the obtained polynomial model is the following:

[Bm]f / [Bm]i = 5.22+ 3.65 pH – 5.41 Bmi - 4.41 pH *Bmi

The growth kinetic is characterized by five phases (latency: 800 min, acceleration: 220 min, exponential: 150 min, deceleration/stationary: 200 min and decline: 200 min) with µmax of 0,0043 min-1, θmin of 234 min and a Horary Growth Rate of 0,8347 h^{-1}.