An Individual-based Model to Study Growth Inhibitors of Yeast Cells in Batch Cultures.

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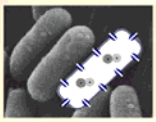

Research Group:
"Modelling and discrete simulation of biological systems"
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INDISIM

An Individual based Model (IbM) computer simulation program INDISIM (INDividual DIScrete SIMulation) was developed and designed to simulate the growth and behaviour of microbial cultures . INDISIM is discrete in space and time, and controls each cell of a culture, at each time step, using a set of random, time-dependent variables for each bacterium (1). "Eigen experiments" controlling all the elements of the system can be done. The strength of IbM lies in their ability to differentiate the relative importance of different mechanisms involved in a biological process

This work is concerned with the use of this simulator to compare the evolutions of yeast batch cultures from different initial medium conditions(2). The aim is to study the influence of the initial substrate and ethanol concentration on these yeast population evolutions (3-8) and on some stoichiometric and kinetic parameters.

CELL MODEL

1 MOTION
2 UPTAKE
3 VIABILITY?
4 ANABOLISM
5 REPRODUCTION?

1 Random motion

2 The cell takes up glucose from the medium

Glucose uptake — Constants — Random numbers from $Zi = N(0,\sigma_i)$

$$U = U_1 [\, 1 - k_1 s - (k_2 + z_2)\, v - (k_3 + z_3)\, \eta \,]$$

Depending on cellular surface — Number of bud scars of the cell — Glucose concentration — Ethanol concentration

3 A part of the glucose is used for the cellular maintenance. If there is not enough glucose the cell dies.

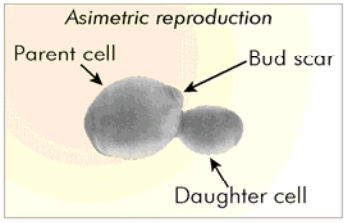
4 The remaining glucose allows the cell to synthesize new biomass.

5 The cell cycle has two phases: the unbudded phase and the budding phase.

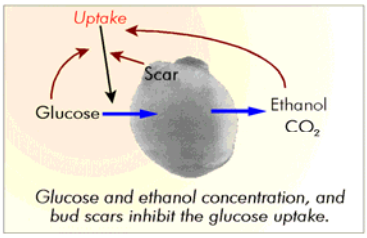
To be over the unbudded phase the cell needs:
- a minimum cellular mass.
- a minimum growth of biomass.

To be over the budding phase the cell needs:
- a minimum growth of biomass.
- a minimum time interval.

Asimetric reproduction

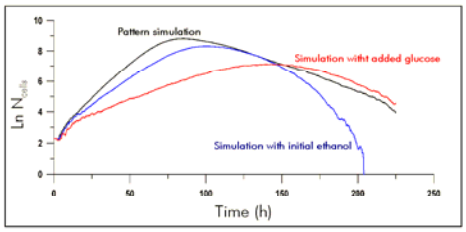


INHIBITORY FACTORS



Glucose and ethanol concentration, and bud scars inhibit the glucose uptake.

Three simulations have been done to evaluate the effects of the ethanol and glucose. The first one has been used as a pattern, while ethanol and glucose have been added to the culture medium in the second and the third simulation respectively. Both factors inhibit the growth of the yeast, but as a result of the metabolism they affect in a different way the phases of the culture growth.



The glucose affects specially the initial phases of the growth. The glucose concentration decreases as a result of the metabolic activity. In the final phases, the growth is very similar to the pattern simulation one.

As a result of the metabolism the ethanol concentration increases. The inhibiting effect of ethanol increases progressively.

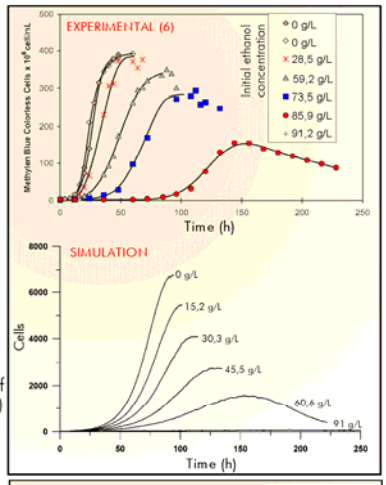
RESULTS

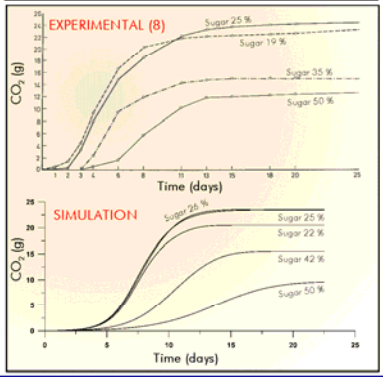
In a previous work (2), the behaviour of multiple experimental parameters has been correctly reproduced: glucose and ethanol concentrations, number of viable and nonviable cells, biomass, cell mass distributions, genealogical ages distributions, duration of the two cellular phases, etc.

The simulation results shown in the figures have been obtained with the same parameters and conditions of the simulations of the previous work (2), only the initial concentrations of glucose or ethanol have been changed.

In a first series of simulations, growth with different initial ethanol concentrations has been studied. Qualitatively, the experimental results of Medawar *et al.*, 2003 (6) have been reproduced.

Afterwords, simulated growths with different initial glucose concentrations have been done. Qualitatively, the experimental results of Xandri, 1977 (8) have been reproduced.





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