SUMMARY

↳Baker's yeast fed-batch process: 2 partial metabolic based models

↳Experiment design for the yield coefficients identification

↳Computation of optimal glucose feeding rate

↳Fed-batch experiments with the optimized glucose feeding rate

Baker's Yeast Metabolic Pathways

- <u>Oxidative growth on Glucose</u> (*respiration*):

  Glucose + Oxygen ⟶ Biomass + CO_2 + water

  $$k_1 S + k_5 O \xrightarrow{\mu_s^o} X + k_7 C$$

and

- <u>Reductive growth on Glucose</u> (*fermentation*):

  Glucose ⟶ Biomass + Ethanol + CO_2 + water

  $$k_2 S \xrightarrow{\mu_s^r} X + k_8 C + k_3 E$$

or

- <u>Oxidative growth on Ethanol</u> (*respiration*):

  Ethanol + Oxygen ⟶ Biomass + CO_2 + water

  $$k_4 E + k_6 O \xrightarrow{\mu_e^o} X + k_9 C$$

Baker's Yeast Partial State Model

Model RF: Respiro-fermentative state
(glucose oxidation + glucose fermentation)

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ E \\ O \\ C \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & -k_2 \\ 0 & k_3 \\ -k_5 & 0 \\ k_7 & k_8 \end{bmatrix} \begin{bmatrix} \mu_s^o \\ \mu_s^r \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ E \\ O \\ C \end{bmatrix} + \begin{bmatrix} 0 \\ DS_e \\ 0 \\ OTR \\ 0 \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ CTR \end{bmatrix}$$

Model R: Respirative state
(glucose oxidation + ethanol oxidation)

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ E \\ O \\ C \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & 0 \\ 0 & -k_4 \\ -k_5 & -k_6 \\ k_7 & k_9 \end{bmatrix} \begin{bmatrix} \mu_s^o \\ \mu_e^o \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ E \\ O \\ C \end{bmatrix} + \begin{bmatrix} 0 \\ DS_e \\ 0 \\ OTR \\ 0 \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ CTR \end{bmatrix}$$

General Dynamical Model

$$\frac{d\xi}{dy} = K\varphi - D\xi + F - Q$$

Model Identification
Yield Coefficients

$$\frac{d\xi}{dt} = K\varphi(\xi, t) - D\xi + U$$

⟹ 2 state partitions:
ξ_a (p elements)
ξ_b (n-p elements)

$Z = A\xi_a + \xi_b$ with $AK_a + K_b = 0$

$$\frac{dZ}{dt} = -DZ + AU_a + U_b$$

$Z = AZ_a + Z_b$

Auxiliary Model

$$\frac{dZ_a}{dt} = -DZ_a + U_a$$
$$\frac{dZ_b}{dt} = -DZ_b + U_b$$

$$Z_b - \xi_b = A(\xi_a - Z_a)$$

Yield Coefficients Identification

$Z_b - \xi_b = A(\xi_a - Z_a)$ ⟹ $y(t) = A\phi(t)$

$$\begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_{n-p} \end{bmatrix} = \begin{bmatrix} \theta_1 & \theta_2 & \cdots & \theta_p \\ \theta_{p+1} & \theta_{p+2} & \cdots & \theta_{2p} \\ \vdots & \vdots & \vdots & \vdots \\ \theta_{n-p+1} & \theta_{n-p+2} & \cdots & \theta_{(n-p)\times p} \end{bmatrix} \begin{bmatrix} \phi_1 \\ \phi_2 \\ \vdots \\ \phi_p \end{bmatrix}$$

⟹ $y_l(t) = \phi^T(t)\theta_l$

Experimental Planning

$$F_I = \sum_{i=1}^{n_T} \left(\frac{\partial y(t_i)}{\partial \theta}\right)^T \left(\frac{\partial y(t_i)}{\partial \theta}\right) \qquad F_I = \sum_{i=1}^{n_T} \phi^T(t_i)\,\phi(t_i)$$

Optimality Criteria

- ☐ **D** max *det*(F_I)
- ☐ **E** max λ_{min}
- ☐ **NC** min ($\lambda_{max}/\lambda_{min}$)

Yield Coefficients Identification
Baker's Yeast

Partial Models:

$$\begin{bmatrix} X - Z_{b1} \\ C - Z_{b2} \\ E - Z_{b3} \end{bmatrix} = \begin{bmatrix} \theta_1 & \theta_2 \\ \theta_3 & \theta_4 \\ \theta_5 & \theta_6 \end{bmatrix} \begin{bmatrix} Z_{a1} - S \\ Z_{a2} - O \end{bmatrix}$$

$dZ_{a1}/dt = -DZ_{a1} + DSe$
$dZ_{a2}/dt = -DZ_{a2} + OTR$
$dZ_{b1}/dt = -DZ_{b1}$
$dZ_{b2}/dt = -DZ_{b2} - CTR$
$dZ_{b3}/dt = -DZ_{b3}$

RF:

$$\frac{1}{k_2 k_5}\begin{bmatrix} k_5 & (k_2 - k_1) \\ k_5 k_8 & (k_2 k_7 - k_1 k_8) \\ k_5 k_3 & -k_1 k_3 \end{bmatrix}$$

R:

$$\frac{1}{k_1 k_6}\begin{bmatrix} (k_6 - k_5) & k_1 \\ (k_6 k_7 - k_5 k_9) & k_1 k_9 \\ k_4 k_5 & -k_1 k_4 \end{bmatrix}$$

Validation:

$$\hat{X}(t) = \hat{Z}_{b1}(t) + \theta_1\phi_1(t) + \theta_2\phi_2(t)$$
$$\hat{C}(t) = \hat{Z}_{b2}(t) + \theta_3\phi_1(t) + \theta_4\phi_2(t)$$
$$\hat{E}(t) = \hat{Z}_{b3}(t) + \theta_5\phi_1(t) + \theta_6\phi_2(t)$$

Optimization of the Feeding Rate

Fermentor

Initial volume: 2 L
Maximum volume: 5 L
Run time: 20 hr.

Initial values of state variables

Biomass: 0.7 g/l
Substrate: 1.7 g/l
Ethanol: 2.2 g/l
Dissolved O_2: 0.002 g/l
Dissolved CO_2:

Optimization strategy

- Optimality critirion:
  - max $(\det(F_{I1}) \cdot \det(F_{I2}))$
- F discretized into 10 node points
- Linear feeding profile between node points
- Optimization methods:
  - Simulated annealing
  - Adaptive Random

Dissolved oxygen mantained at a constant value
Total amount of glucose in fed-batch medium: 45g

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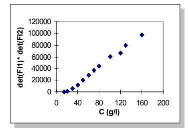
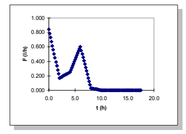
Optimization



Influence of substrate inlet concentration



Feed Rate Profile

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Baker's Yeast Fed-batch Experiment

Fermentor

Initial volume: 2 L
Final volume: 5 L

State variables

X - biomass
S - substrate (sugar)
E - Ethanol
O - dissolved Oxygen
C - dissolved

On-line measurements

- Ethanol in liquid phase
- Inlet and exit gas composition (CO_2, O_2, N_2)
- Air feed rate
- Sugar feed rate

Dissolved oxygen mantained at 2 mg/l
Glucose concentration in the feeding medium: 15 g/l

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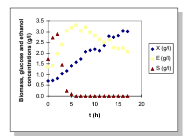
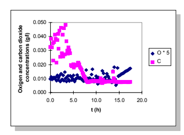
Experimental Profiles



Biomass, sugar and ethanol



Dissolved Oxygen (O) and carbon dioxide (C)

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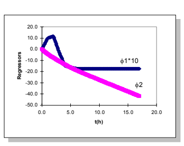
Regressors



Regressors for the identification experiment

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Conclusions

- Yield coefficients can be well identified using data from fed-batch experiments with an optimized feed flow pattern
- This iterative approach requires a priori knowledge on the yield coefficients

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