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Application of the intercriteria analysis for selection of growth rate models for cultivation of strain *Kluyveromyces marxianus var. lactis* MC 5

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Abstract: In this study we have applied a new method named Intercriteria Analysis (ICrA) to evaluation and selection of growth rate models for a batch cultivation of the strain *Kluyweromyces marxianus var. lactis* MC 5. Different unstructured models (*Monod*, *Mink*, *Tessier*, *Aiba*, *Andrews*, *Haldane*, *Luong*, *Edward* and *Han-Levenspiel*) have been considered in order to explain the cell growth kinetics from the *lactose* and *oxygen*. The application of the ICrA for the growth rate from *lactose* and *oxygen* has shown that there are many strong correlation connections between the investigation models. the models have been reduced At growth rate from *lactose* only into two – *Monod* and *Mink*, and at growth rate from *oxygen* – into three – *Mink*, *Tessier*, and *Haldane*. In this way the application of the ICrA has permitted us to investigate only the combination of groups of models – *Monod* for *lactose* and *Mink*, *Tessier*, and *Haldane* for *oxygen*, as well as *Mink* with the same models for *oxygen*.

Keywords: Intercriteria analysis, Consonance, Growth rate models, Intuitionistic fuzzy sets, Index matrix, Intuitionistic fuzzy pairs.

AMS Classification: 03E72, 93A30, 92C45.

1 Introduction

The cultivation of the lactose oxidation from a natural substratum in the fermentation of *Kluyweromyces marxianus var. lactis* MC 5 uses non-conventional ways for receiving unicellular proteins. But the modeling of the process is not well studied. Therefore, a general mathematical model of the microbial synthesis does not exist because of the extreme complexity and great variety of living activity of microorganisms, although various models of the biotechnological process as well as of different parts of whey fermentation exist [1, 2].

The Intercriteria Analysis (ICrA) method [3] is based on the apparatus of the index matrices (IMs) and the intuitionistic fuzzy sets (IFs). The approach employs the concept of IMs, making particular use of some of the operations introduced over them the fuzziness concept of intuitionistic fuzzy sets, is also applied giving us the tools to construct the IMs of intuitionistic fuzzy pairs (IFPs). Thus we are able to define the presence or absence of dependency/correlation between any pair of criteria within the set [4-7].

Atanassova and co-authors [8, 9] have applied ICrA for the EU member states competitiveness analysis, temporal and threshold analysis. lkova and Petrov [10, 11] have employed the ICrA to the Mesta River pollution modelling and identification of *Escherichia coli* fed-batch process.

In this paper we will apply the ICrA method for selection of growth rate models from basic energetic substrates – *lactose* and *oxygen* of a batch cultivations of the strain *Kluyweromyces marxianus var. lactic* MC 5.

2 Kinetic model of the batch processes

The batch model of the processes includes the dependence between concentrations of the basic energetic substrates: *lactose* and *oxygen*, and the cell. The model is described as perfectly mixed in the bioreactor [12]:

$$\begin{aligned} \frac{dX}{dt} &= \rho(S,C)\,X \\ \frac{dS}{dt} &= -\frac{\rho(S,C)}{Y_{X/S}}X \\ \frac{dC}{dt} &= OTR - \frac{\rho(S,C)}{Y_{X/C}}X \end{aligned} \quad , \tag{1}$$

where: t is the process time, h; X – biomass concentration, kg·m^{-3}; S – *lactose* concentration, kg·m^{-3}; $\rho(S,C) = \rho(S)\rho(C)$ – specific growth rate of the cell from *lactose* and *oxygen*, h^{-1}; C – oxygen concentration, kg·m^{-3}; OTR – oxygen transfer rate, kg·m^{-3}·h^{-1}; $Y_{X/S}$, $Y_{X/C}$ – yield coefficients of biomass formation from *lactose* and *oxygen*.

Oxygen transfer rate can be calculated from:

$$OTR = \frac{k_l a}{(1-\varphi_G)}\,(C^* - C)$$

where: $k_l a$ is the mass-transfer coefficient, h^{-1}; φ_G – gas hold-up; C^* –*oxygen* concentration, kg·m^{-3}.

The dependences for determining the gas hold-up (φ_G), mass-transfer coefficient ($k_l a$), and basic indexes of the mass transfer as well as those for the mixing of the process are shown in [12].

The initial conditions are given as follows: $X(0)$ = 0.2 kg·m^{-3}, $S(0)$ = 44 kg·m^{-3}, $C(0)$ = $6.65\cdot10^{-3}$ kg·m^{-3}, and $C^*(0) = C(0)$.

2.1 Growth rate models

Petrov and Ilkova [12] have studied the following models for growth rate from *lactose* and *oxygen*: M_1 – *Monod*, M_2 – *Mink*, M_3 – *Tessier*, M_4 – *Aiba*, M_5 – *Andrews*, M_6 – *Haldane*, M_7 – *Luong*, M_8 – *Edward*, and M_9 – *Han-Levenspiel* (Table 1).

Mod.	$\rho(S)$	$\rho(C)$
M_1	$\rho_1(S)=\frac{\rho_m^S S}{K_S+S}$	$\rho_1(C)=\frac{\rho_m^C C}{K_C+C}$
M_2	$\rho_2(S)=\frac{\rho_m^S S^2}{K_S+S^2}$	$\rho_2(C)=\frac{\rho_m^C C^2}{K_C+C^2}$
M_3	$\rho_3(S)=\rho_m^S\left(1-\exp\left(-\frac{S}{K_{SI}}\right)\right)$	$\rho_3(C)=\rho_m^C\left(1-\exp\left(-\frac{C}{K_{CI}}\right)\right)$
M_4	$\rho_4(S)=\frac{\rho_m^S S}{K_S+S}\exp\left(-\frac{S}{K_{SI}}\right)$	$\rho_4(C)=\frac{\rho_m^C C}{K_C+C}\exp\left(-\frac{C}{K_{CI}}\right)$
M_5	$\rho_5(S)=\frac{\rho_m^S S}{(K_S+S)\left(1+\frac{S}{K_{SI}}\right)}$	$\rho_5(C)=\frac{\rho_m^C C}{(K_C+C)\left(1+\frac{C}{K_{CI}}\right)}$
M_6	$\rho_6(S)=\frac{\rho_m^S S}{K_S+S+\frac{S^2}{K_{SI}}}$	$\rho_6(C)=\frac{\rho_m^C C}{K_C+C+\frac{C^2}{K_{CI}}}$
M_7	$\rho_7(S)=\frac{\rho_m^S S}{K_S+S}R_S^n$	$\rho_7(C)=\frac{\rho_m^C C}{K_S+C}R_C^n$
M_8	$\rho_8(S)=\frac{\rho_m^S S}{K_S+S+\left(1+\frac{S}{K_{SI}}\right)\left(\frac{S^2}{K_S}\right)}$	$\rho_8(C)=\frac{\rho_m^C C}{K_C+C+\left(1+\frac{C}{K_{CI}}\right)\left(\frac{C^2}{K_C}\right)}$
M_9	$\rho_9(S)=\frac{\rho_m^S S R_S^n}{S+K_S R_S^m}$	$\rho_9(C)=\frac{\rho_m^C C R_C^n}{C+K_C R_C^m}$

Table 1. Structure of the models tested

In Table 1: $R_S=(1-S/S_m)$; $R_C=(1-C/C_m)$; ρ_m^S and ρ_m^C is the maximum specific growth rate from *lactose* and *oxygen*, h^{-1}; K_S, K_C – the saturation constants, $kg\cdot m^{-3}$; K_{SI}, K_{CI} – the inhibition constants in different models, $kg\cdot m^{-3}$; K_{SI} and K_{CI} – the constant in the *Edward* model; S_m, C_m – the critical inhibitor concentration above which the reactions stop, $kg\cdot m^{-3}$; m – the constant in the *Han-Levenspiel* model; n – the constant in the *Luong* and the *Han-Levenspiel* models.

2.2 Criteria for evaluation of the model parameters

The mathematical estimation of the model parameters is based on the minimization of some quantities that can be calculated and the estimation of a function of parameters. The least-squares error is commonly employed as a criterion to inspect how close the computed profiles of the state variables come to the experimental observations. In this study, we have considered the time weighted least-squares error as a criterion for each experiment. The criterion is expressed in the form [13]:

$$\min_{\mathbf{u}} Q = \frac{1}{N_E}\sum_{j=1}^{N_E} t_j \left(\frac{(X_e(t_j) - X_m(t_j))^2}{X_{e\max}^2(t_j)} + \frac{(S_e(t_j) - S_m(t_j))^2}{S_{e\max}^2(t_j)} + \frac{(C_e(t_j) - C_m(t_j))^2}{C_{e\max}^2(t_j)} \right), \qquad (2)$$

where **u** is a vector of the estimated parameters, N_E is the number of experiments, t_j – time partitions.

2.3 Criteria for validation

The best dependences are defined by the statistical criteria: statistic λ, experimental correlation coefficient R_E^2, and experimental Fisher coefficient $F_E(j)$ for all kinetics variables j=1, …, 3. The coefficients R_E^2 and $F_E(j)$ are very popular statistical criteria for validation of models. Its formulas are well known and they are found in researches [14].

The statistic λ has $F(M, N_E - M)$ distribution. Statistic λ is defined by [15]:

$$\lambda = \frac{(N_E - M)}{(N_E - 1)} \frac{N_E}{M} \sum_{j=1}^{M} \frac{\Delta_j^2}{S_j}, \qquad (2)$$

where:

$$\Delta_{i,j}^2 = [X_e(i) - X_m(i)]^2 + [S_e(i) - S_m(i)]^2 + [C_e(i) - C_m(i)]^2$$

$$S_j = \frac{1}{N_E - 1}\sum_{i=1}^{N_E} (-\Delta_{ij})^2 \Delta_j \; ; \; \Delta_j = \frac{1}{N_E}\sum_{i=1}^{N_E} \sqrt{\Delta_{ij}} \; .$$

We have developed algorithm and program on Compaq Visual FORTRAN 90 to determine the parameters in the model (1), computing criteria (2)–(3), $R_E^2(j)$, and $F_E(j)$.

3 Intercriteria analysis method

Here, we will briefly repeat the theoretical framework of the approach proposed, [3], by slightly improving the notation from [4]. The approach employs an index matrix **M** of m rows $\{O_1,...,O_m\}$ and n columns $\{C_1,...,C_n\}$, where for every p, q ($1 \le p \le m$, $1 \le q \le n$), O_p is an evaluated object, C_q is an evaluation criterion, and $e_{O_p C_q}$ is the evaluation of the p-th object against the q-th criterion. It is defined as a real number or another object that is comparable according to relation R with all the rest elements of the index matrix **M**.

$$\mathbf{M} = \begin{array}{c|ccccccc} & C_1 & \dots & C_k & \dots & C_l & \dots & C_n \\ \hline O_1 & e_{O_1,C_1} & \dots & e_{O_1,C_k} & \dots & e_{O_1,C_l} & \dots & e_{O_1,C_n} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\ O_i & e_{O_i,C_1} & \dots & e_{O_i,C_k} & \vdots & e_{O_i,C_l} & \vdots & e_{O_i,C_n} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\ O_j & e_{O_j,C_1} & \dots & e_{O_j,C_k} & \dots & e_{O_j,C_l} & \dots & e_{O_j,C_n} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\ O_m & e_{O_m,C_1} & \dots & e_{O_m,C_k} & \dots & e_{O_m,C_l} & \dots & e_{O_m,C_n} \end{array}$$

Considering the requirement for comparability above, the relation $R(e_{O_iC_k}, e_{O_jC_k})$ for each *i*, *j*, *k is achieved*. The relation *R* has dual relation $\overline{R}$, which is true in the cases when relation *R* is false, and vice versa. Let $\overline{R}$ be the dual relation of *R* in the sense that if *R* is satisfied, then $\overline{R}$ is not satisfied and vice versa. For example, if "*R*" is the relation "<", then $\overline{R}$ is the relation ">", and vice versa. For the needs of our decision making method, pair-wise comparisons between every two different criteria are made along all evaluated objects. During the comparison, it is maintained one counter of the number of times when the relation *R* holds, and another counter for the dual relation.

Let $S^{\mu}_{k,l}$ be the number of cases in which $R(e_{O_i,C_k}, e_{O_j,C_k})$ and $R(e_{O_i,C_l}, a_{O_j,C_l})$ are simultaneously satisfied. Let $S^{\nu}_{k,l}$ be the number of cases in which $R(e_{O_i,C_k}, e_{O_j,C_k})$ and its dual $\overline{R}(e_{O_i,C_l}, e_{O_j,C_l})$ are simultaneously satisfied. Since the total number of pair-wise comparisons between the object is $m(m-1)/2$, it is seen that three of them have the inequalities:

$$0 \le S^{\mu}_{k,l} + S^{\nu}_{k,l} \le \frac{m(m-1)}{2}$$

Now, for every *k*, *l* such that $1 \le k < l \le m$, and for $m \ge 2$ the following two numbers are defined:

$$\mu_{C_k,C_l} = \frac{2S^{\mu}_{k,l}}{m(m-1)}, \qquad \nu_{C_k,C_l} = \frac{2S^{\nu}_{k,l}}{m(m-1)}$$

Obviously, both $\mu_{C_k,C_l}, \nu_{C_k,C_l}$ are numbers in the [0, 1]-interval, and their sum is also a number in this interval. What is complement to their sum 1 is the number π_{C_k,C_l}, which corresponds to the degree of uncertainty.

The pair which is constructed from these two numbers plays the role of the intuitionistic fuzzy evaluation of the relations that can be established between any two criteria C_k and C_l. In this way the index matrix **M** that relates to the evaluated objects with evaluating criteria can be transformed into another index matrix $\mathbf{M}^*$ that gives the relations among the criteria:

$$\mathbf{M}^* = \begin{array}{c|ccc} & C_1 & \dots & C_n \\ \hline C_1 & \langle \mu_{C_1,C_1}, \nu_{C_1,C_1} \rangle & \dots & \langle \mu_{C_1,C_n}, \nu_{C_1,C_n} \rangle \\ \vdots & \vdots & \ddots & \vdots \\ C_n & \langle \mu_{C_nC_1}, \nu_{C_n,C_1} \rangle & \dots & \langle \mu_{C_nC_n}, \nu_{C_n,C_n} \rangle \end{array}$$

Considering practice, it has been more flexible to work with two index matrices $\mathbf{M}^{\mu}$ and $\mathbf{M}^{\nu}$, rather than with the index matrix $\mathbf{M}^{*}$ of IFPs.

The final step of the algorithm is to determine the degrees of correlation between the criteria, depending on the user's choice μ and ν.These correlations between the criteria are called '*positive consonance*', '*negative consonance*' or '*dissonance*'. Let $\alpha,\beta \in [0;1]$ be the threshold values, and compare the values of μ_{C_k,C_l} and ν_{C_k,C_l} against them. We consider that criteria C_k and C_l are in:

- (α,β) – *positive consonance*, if $(\mu_{C_k,C_l} > \alpha)$ and $(\nu_{C_k,C_l} < \beta)$;
- (α,β) – *negative consonance*, if $(\mu_{C_k,C_l} < \beta)$ and $(\nu_{C_k,C_l} > \alpha)$;
- (α,β) – *dissonance*, *otherwise*.

In a completely identical way, it is possible (though not always meaningful) to build a matrix giving the correlations between the objects. The only difference is that the input index matrix $\mathbf{M}$ has to be transposed, and the resultant matrix, say $\mathbf{M}^{**}$, is with dimensions $m \times m$.

3.1 Rules for determining the degrees of consonance and dissonance

Atanassov and co-authors [16] have discussed an important aspect of the ICrA approach related to the possibilities for defining the intuitionistic fuzzy threshold values that help discriminate between the *positive* consonance, the *negative* consonance and the *dissonance* between the criteria (Figure 1). The triangular zone for the *negative* consonance (*NC*) from Figure 1 corresponds to where the pairs of the criteria which exhibit *NC* will be located. Formally, this area can be expressed as:

$$NC = \{\langle \mu,\nu\rangle \,|\, \mu \in [0.00,0.25] \,\&\, \nu \in [0.75,1.00] \,\&\, \mu+\nu \le 1\}$$

The triangular zone for *positive* consonance (*PC*) from Figure 1 corresponds to where the pairs of criteria which exhibit *PC* will be located. Formally, this area can be expressed as:

$$PC = \{\langle \mu,\nu\rangle \,|\, \mu \in [0.75,1.00] \,\&\, \nu \in [0.00,0.25] \,\&\, \mu+\nu \le 1\}$$

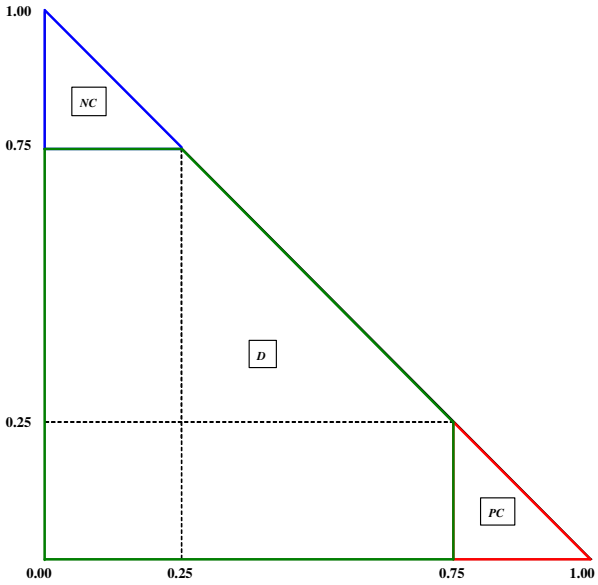

Figure 1. The triangle of positive, negative consonance and dissonance

The pentagonal zone for *dissonance* (*D*) corresponds to the place where the pairs of criteria which are in *D* will be located. Formally, this area can be expressed as:

$$D = \{\langle \mu, \nu \rangle \,|\, \mu \in [0.00, 0.75] \,\&\, \nu \in [0.00, 0.75] \,\&\, \mu + \nu \le 1\}$$

The following levels of positive consonance apply to the following membership functions (μ): *Weak* ($0.75 \le \mu \le 0.85$), *Good* ($0.85 < \mu \le 0.90$), *Very good* ($0.90 < \mu \le 0.95$), *Strong* ($0.90 < \mu \le 0.95$), *Strict* ($\mu = 1.00$).

For selecting growth rate models we have to have many high values of the *membership* function because we have accepted $\alpha = 0.95$ and $\beta = 0.05$ in this study.

4 Application of the ICrA for selection of growth rate models

In this paper we have used the ICrA method for selection of growth rate models from *lactose* and *oxygen*. The criterions (2), (3), coefficients R_E^2, and F_E were used to determine correlations between models with ICrA, i.e. $C_1 = Q \times 10^{-3}$ (eq.2); $C_2 = \lambda$ (eq.3), and $C_k = R_E^2(j)$, k = 3, 4, 5, $C_k \equiv F_E(j)$, k = 6, 7, 8, for j = 1, 2, 3.

Now, we can construct the IMs of growth rate dependent on *lactose* (**A1**) and *oxygen* (**A2**). The elements $e_{M_p C_q}$ of the IMs **A1** and **A2** for every criterion (C_q), q = 1, …, 8 and model (M_p), p = 1, …, 9 are shown below:

A1 =

	C_1	C_2	C_4	C_4	C_5	C_6	C_7	C_8
M_1	111.208	0.804	0.986	0.950	0.902	1.234	1.115	1.053
M_2	67.545	13.587	0.996	0.962	0.958	1.015	1.312	1.013
M_3	45.219	17.575	0.996	0.964	0.962	1.000	1.124	1.039
M_4	151.296	0.434	0.980	0.933	0.869	1.230	1.106	1.146
M_5	76.871	1.780	0.993	0.950	0.923	1.108	1.041	1.117
M_6	148.070	0.446	0.981	0.936	0.848	1.102	1.113	1.213
M_7	71.548	1.373	0.954	0.988	0.934	1.030	1.263	1.087
M_8	80.477	1.014	0.952	0.985	0.921	1.055	1.270	1.156
M_9	68.998	1.538	0.955	0.989	0.939	1.027	1.259	1.063

A2 =

	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8
M_1	9.564	201.665	0.995	0.989	0.995	1.014	1.016	1.000
M_2	10.345	509.302	0.998	0.984	0.995	1.018	1.000	1.013
M_3	10.326	117.469	0.998	0.986	0.987	1.019	1.021	1.070
M_4	14.246	127.104	0.993	0.988	0.995	1.010	1.046	1.047
M_5	9.892	150.430	0.998	0.985	0.990	1.017	1.021	1.053
M_6	9.934	184.094	0.993	0.990	0.994	1.036	1.041	1.019
M_7	9.892	167.171	0.993	0.990	0.994	1.031	1.038	1.017
M_8	10.047	243.714	0.997	0.986	0.994	1.007	1.005	1.006
M_9	20.185	32.037	0.996	0.987	0.968	1.035	1.023	1.201

The values of membership function (μ) and non-membership function (ν) have been calculated with the help of the software developed by our colleagues for the realization of the method.

4.1 ICrA for growth rate from lactose

The index matrix $\mathbf{A}_1^{\mu}$ *for* $\rho(S)$ has the following form:

$\mathbf{A}_1^{\mu}$ =	M_1	M_2	M_3	M_4	M_5	M_6	M_7	M_8	M_9
M_1		0.75	0.71	**0.96**	0.71	0.89	0.68	0.79	0.68
M_2	0.75		**0.96**	0.71	0.89	0.71	0.93	0.82	0.93
M_3	0.71	**0.96**		0.68	0.93	0.75	**0.96**	0.86	**0.96**
M_4	**0.96**	0.71	0.68		0.75	0.93	0.64	0.75	0.64
M_5	0.71	0.89	0.93	0.75		0.75	0.89	0.79	0.89
M_6	0.89	0.71	0.75	0.93	0.75		0.71	0.82	0.71
M_7	0.68	0.93	**0.96**	0.64	0.89	0.71		0.89	**1.00**
M_8	0.79	0.82	0.85	0.75	0.79	0.82	0.89		0.89
M_9	0.68	0.93	**0.96**	0.64	0.89	0.71	**1.00**	0.89	

The triangle of IFs for growth rate from *lactose* only in the real borders of μ and ν are shown in Figure 2.

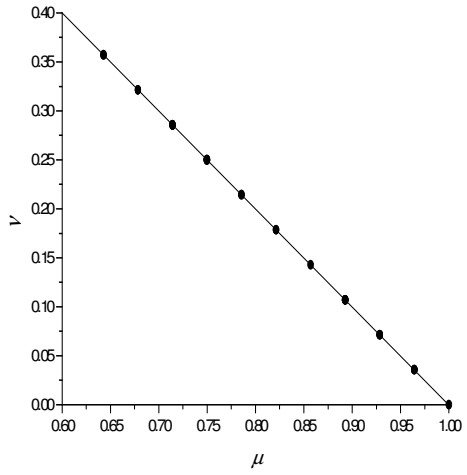

Figure 2. Intutionistic fuzzy triangle for growth rate dependent on *lactose*

The comparatively high value of the membership function $\mu \in [0.64, 1.00]$, the low value of nonmembership function $\nu \in [0.00, 0.36]$, and the *zero* uncertainty $\pi = 0$ (matrix $\mathbf{A}_1^{\mu}$ in Fig. 2) show that the models investigated which depend on *lactose* are dependent on each other, as well The index matrix $\mathbf{A}_1^{\mu}$ in Figure 2 shows there is a *strict* positive consonance, with μ=1.0, ν=0.0, and π=0.0 for the pair M_7 – M_9. There is also a *strong* positive consonance with membership function μ=0.96, non membership function ν=0.04, and uncertainly π=0.00 for the following pair and four models: M_1 – M_4, M_2 – M_3 – M_7 – M_9.

The pair M_7 – M_9 has *strict* and *strong* positive consonance with M_2 at the same time.

The equivalence models obtained show we can eliminate the models M_3 (*Tessier*), M_7 (*Luong*), and M_9 (*Han-Levenspiel*).They take part in a quadruple combination together with

strong positive consonance with M_2 (*Mink*). Furthermore, it (M_2) can also change them. We have another pair ($M_1 - M_4$) with *strong* positive consonance and we can eliminate the model M_4 (*Aiba*), too.

The application of ICrA for determination of the correlation connections between the growth rate models from *lactose* $\rho(S)$ gives us an opportunity to reduce the models investigated from 9 to 2 - $\mathbf{M}_1$ (*Monod*) and $\mathbf{M}_2$ (*Mink*). They will participate in a combination with the obtained models for $\rho(C)$ after application of the ICrA for growth rate from *oxygen*.

4.2 ICrA for growth rate from oxygen

The computing index matrix $\mathbf{A}_2^{\mu}$ *for* $\rho(C)$ has the following form:

$\mathbf{A}_2^{\mu} =$	M_1	M_2	M_3	M_4	M_5	M_6	M_7	M_8	M_9
M_1		0.89	0.89	0.89	0.89	**0.96**	**0.96**	0.89	0.82
M_2	0.89		0.93	0.89	0.93	0.89	0.89	**1.00**	0.93
M_3	0.89	0.93		**0.96**	**1.00**	0.89	0.89	0.92	0.93
M_4	0.89	0.89	**0.96**		**0.96**	0.93	0.92	0.89	0.89
M_5	0.89	0.93	**1.00**	**0.96**		0.89	0.89	0.93	0.93
M_6	**0.96**	0.89	0.89	0.93	0.89		**1.00**	0.89	0.82
M_7	**0.96**	0.89	0.89	0.93	0.89	**1.00**		0.89	0.82
M_8	0.89	**1.00**	0.93	0.89	0.93	0.89	0.89		0.93
M_9	0.82	0.93	0.93	0.89	0.93	0.82	0.82	0.93	

The triangle of IFs for growth rate from *oxygen* only in the real borders of μ and ν is shown in Figure 3.

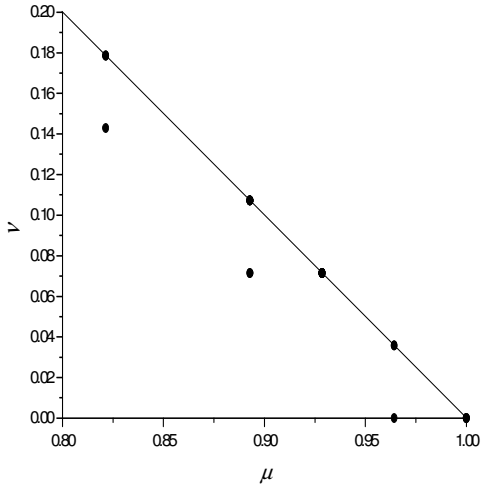

Figure 2. Intuitionistic fuzzy triangle for growth rate dependent on *oxygen*

The comparatively high value of membership function $\mu \in [0.82, 1.00]$, the low value of non-membership function $\nu \in [0.00, 0.18]$, and the small uncertainty $\pi \in [0.00, 0.04]$ (matrix $\mathbf{A}_2^{\mu}$ and Fig. 3) shows the investigated models that depend on *oxygen* are also dependent on each other. The index matrix $\mathbf{A}_2^{\mu}$ shows there is a *strict* (μ = 1.0, ν = 0.0, π = 0.0) positive consonance between the pairs $M_2 - M_8$; $M_3 - M_5$; $M_6 - M_7$, and *strong* positive consonance for

the following pair and triple models: $M_1 - M_6 - M_7$ ($\mu = 0.96$, $\nu = 0.00$, $\pi = 0.04$), $M_3 - M_4$ ($\mu = 0.96$, $\nu = 0.04$, $\pi = 0.00$).

The pair $M_6 - M_7$ has *strict* and *strong* positive consonance at the same time, and the model M_3 once participates in the pair $M_3 - M_5$ with *strict* and once in the pair $M_3 - M_4$ with *strong* positive consonance. They can be united in the following triple combination: $M_3 - M_4 - M_5$.

We can eliminate M_1 (*Monod*), M_4 (*Aiba*), M_5 (*Andrews*), M_7 (*Luong*), M_8 (*Edward*) and M_9 (*Han-Levenspiel*), From the equivalence models obtained. The last one is in *dissonance* with the rest.

In our studies [17] we have used the model M_6 (*Haldane*)for modeling of the growth rate from *oxygen*. We can join the models M_2 (*Mink*) and M_3 (*Tessier*) to M_6. Thus instead of 9 models we have only 3. We have received the following two groups of models:

First group

1.1. $\mathbf{M}_1$ (*Monod*) for $\rho(S)$ – $\mathbf{M}_2$ (*Mink*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S}{(K_S + S)} \frac{C^2}{(K_C + C^2)}, \tag{4}$$

1.2. $\mathbf{M}_1$ (*Monod*) for $\rho(S)$ – $\mathbf{M}_3$ (*Tessier*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S}{(K_S + S)} \left(1 - \exp\left(-\frac{C}{K_{CI}}\right)\right), \tag{5}$$

1.3. $\mathbf{M}_1$ (*Monod*) for $\rho(S)$ – $\mathbf{M}_6$ (*Haldane*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S}{(K_S + S)} \frac{C}{\left(K_C + C + C^2 / K_{CI}\right)}, \tag{6}$$

Second group

2.1. $\mathbf{M}_2$ (*Mink*) for $\rho(S)$ – $\mathbf{M}_2$ (*Mink*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S^2}{(K_S + S^2)} \frac{C^2}{(K_C + C^2)}, \tag{7}$$

2.2. $\mathbf{M}_2$ (*Mink*) for $\rho(S)$ – $\mathbf{M}_3$ (*Tessier*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S^2}{(K_S + S^2)} \left(1 - \exp\left(-\frac{C}{K_{CI}}\right)\right), \tag{8}$$

2.3. $\mathbf{M}_2$ (*Mink*) for $\rho(S)$ – $\mathbf{M}_6$ (*Haldane*) for $\rho(C)$

$$\rho(S,C) = \frac{\rho_m S^2}{(K_S + S^2)} \frac{C}{\left(K_C + C + C^2 / K_{CI}\right)}, \tag{9}$$

The final choice will be made after repeated identification and application of the ICrA for the model (4)-(9). This will be done in the next studies.

5 Conclusions

The application of the ICrA for determination of the correlation connections between the growth rate models from *lactose* has shown that 7 models can be eliminated from all 9 initial models. Only the models of *Monod* and *Mink* have remained. The investigation of the correlation connections at the growth rate models from *oxygen* has shown that we can eliminate 6 models (models of *Mink*, *Tessier*, and *Haldane remain*) that have been included in the general model.

The ICrA has allowed us to determinate the combination of models for describing the growth rate kinetics of the process which gives a more complete notion for the existing correlation relations between the separate models. The application of the method for establishment of the correlation connections between different models for the growth rate for modeling of this processes is very useful not only to assess and eliminate the equivalence model, but also to determine (by *dissonance*) how much each of the patterns is closer to the actual experimental data. In establishing of correlations between these types of models using ICrA we cannot talk about negative consonance. If we did his would mean that the models would not reflect the real situation about the process and the purpose would have a completely different description of the growth kinetics.

In our next work on parametric identification we will determine the obtained models which are most appropriate for the specific growth rate, by using the ICrA.

The full picture of the model of the process will be clear when we carry out the identification and fed-batch processes and make a simultaneous identification of batch and fed-batch processes.

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