

INTERCRITERIA ANALYSIS FOR MODELLING OF PROCESS FOR THE UNICELLULAR PROTEIN PRODUCTION FOR TRAINING PEOPLE

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Abstract

This paper presents an application of a method for multicriteria decision making, namely InterCriteria Analysis (ICrA). The ICrA method gives possibility to compare some criteria or estimated by them objects. There we have applied this method to create a structural identification of a mathematical model of a whey fermentation process. The process is for production of unicellular protein by whey by the strain Kluyweromyces marxianus var. lactis MC 5. We have established the relation between the basic criteria (kinetic variable and coefficients): biomass, lactose, oxygen, flow rate, specific growth rate from lactose and oxygen, specific consumption rate for lactose, specific consumption rate for oxygen, yield coefficient for formation of biomass from lactose and yield coefficient for formation of biomass from oxygen with ICrA. With the founded relations between them, obtained with ICrA, and the biochemical kinetic laws we have developed a mathematical model of the process.

Key words: InterCriteria analysis, *Kluyweromyces marxianus var. Lactis MC 5*, fed-batch process, intuitionistic fuzzy sets, index matrices

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. The producing of lactose with using of cheese whey, which is a waste product at the production of white brine cheese leads to the receiving one of close cycle (Petrov, Ilkova & Vanags 2015). 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 (Petrov, Ilkova & Tzonkov 2005).

Atanassov, Mavrov & Atanassova 2014 introduced a new approach for multicriteria decision making, namely ICrA. This is a method for decision making, that is based on the apparatus of index matrices (IMs) (Atanassov 1987, 2010a, 2010b) and intuitionistic fuzzy sets (IFs) (Atanassov 2012, Atanassov, Szmidt & Kacprzyk 2013) and can be applied for decision making in different areas of science and practice. The new approach for multicriteria decision making makes it possible to compare certain criteria or objects estimated by them. At this moment, for two years, ICrA has applied in several areas of the science and different scientific and practical problems have been decided. For an example Atanassova et al. (2014a, b, 2015) applied ICrA approach in an EU member states competitiveness analysis. They carried out a temporal and threshold analysis.

So, also in Pencheva et al. 2015 ICrA has been applied for the first time in the field of parameter identification of fermentation processes (FP) models. The ICA implementation allowed to authors to establish relations and dependencies between two of the main genetic algorithms (GA) parameters - *numbers of individuals* and *number of generations*, on the one hand, and *convergence time*, *model accuracy* and *model parameters* on the other hand.

In Roeva et al. 2015a ICrA is applied to establish relations and dependencies between different *model parameters*. FP of bacteria *E. coli* and yeast *S. cerevisiae* are examined and six different GA are applied for the parameter identification. Further, ICA is applied to explore the existing relations and dependencies of defined *model parameters* and GA outcomes – *execution time* and *objective function*

value - in case of *S. cerevisiae* FP (Angelova, Roeva & Pencheva 2015) and *E. coli* FP (Roeva et al. 2015b). Moreover, ICA is applied for establishing the relations and dependencies between GAs parameter *generation gap* on the one hand, and *convergence time*, *model accuracy* and *model parameters* on the other hand in case of *E. coli* FP (Roeva & Vassilev 2016) and *S. cerevisiae* FP (Pencheva et al. 2016).

Finally, ICA is applied to establish the relations and dependencies of considered parameters based on different criteria referred to various metaheuristic algorithms, namely hybrid schemes using GA and Ant Colony Optimization (ACO) (Roeva, Fidanova & Paprzycki 2016).

The aim of this paper is an application of ICRA for determination of the relations between the basic kinetic variables (*biomass*, *lactose* and *oxygen*) also some important characteristics as the specific growth rate of the *biomass*, specific consumption rate for *lactose* and *oxygen*, yield coefficient for formation of *biomass* from *lactose* and *oxygen* in fed-batch process of the *Kluyweromyces marxianus* var. *lactis* MC 5 cultivation for aim of mathematical modeling. With these relations the model of the process will be synthesized.

2. MATERIAL AND METHODS

A laboratory bioreactor ABR 02M with maximum capacity 2 L has been used. Three fermentations were carried out in six aerobic batch cultivation of *Kluyweromyces marxianus* var. *lactis* MC5 strain. The strain was cultivated under the following condition (Petrov, Ilkova & Vanags 2015):

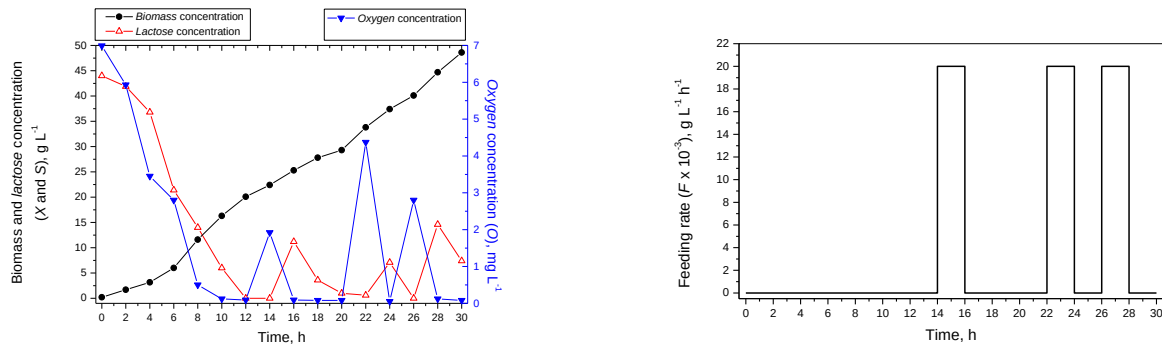
1. The nutrient medium with basic component – whey ultra filtrate with lactose concentration $44 \text{ kg}\cdot\text{m}^{-3}$. The ultra filtrate is derived from whey separated in production of white cheese and deproteinisation by ultra filtration on LAB 38 DDS with membrane of the type GR 61 PP under the following condition:
 - Temperature, $T_1 = 40 - 43 \text{ }^{\circ}\text{C}$
 - Input pressure, $P_{in} = 0.65 \text{ MPa}$
 - Output pressure, $P_{out} = 0.60 \text{ MPa}$
2. The ultra filtrate is used in native condition with lactose concentration 44 kg m^{-3} . The nutrient medium consist of:
 - (NH)HPO $- 0.6\%$
 - Yeast's autolysate $- 5.0\%$
 - Yeast's extract $- 1.0\%$
 - pH=5.0 – 5.2
3. The gas flow rate (Q_G) is $60 \text{ m}\cdot\text{m}^{-3}\cdot\text{h}^{-1}$ up to the 4th hour and $120 \text{ m}\cdot\text{m}^{-3}\cdot\text{h}^{-1}$ up to the end of the process under continuous mixing $N=800 \text{ rpm}$.
4. Temperature is $T_2 = 29 \text{ }^{\circ}\text{C}$.
5. The duration of the fed-batch fermentations is $t_f = 30 \text{ hours}$.

The changes of the micro biological process (lactose conversion in yeast's cells to protein) are studied during the strain growth (Petrov, Ilkova & Vanags 2012):

- a) the lactose concentration in the fermentation medium in the oxidation and assimilation of lactose by *Kluyweromyces marxianus* var. *lactis* MC5 is determined by enzyme methods by UV tests;
- b) the concentration of the cell mass and protein contents are determined on the basis of the nitrogenous contents;

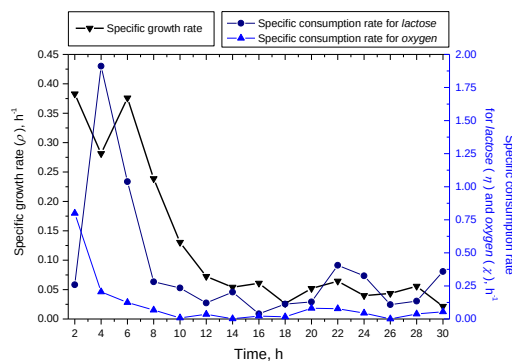
- c) the concentration of the dissolved oxygen in the fermentation medium in the process of oxidation and assimilation of lactose is determined by oxygen sensor.

The experimental data for the fed-batch cultivation for *biomass*, *lactose* and *oxygen* mass concentration, specific growth rate, specific consumption rate for *lactose*, yield coefficients for formation of *biomass* from *lactose* and from *oxygen* of *Kluyweromyces marxianus* var. *lactis* MC5 strain are shown in Figure 1.

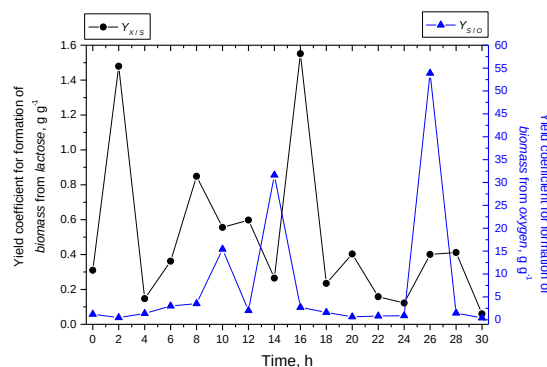


a) experimental data for fed-batch processes

b) feed flow rate



c) specific growth rate(ρ), specific consumption rate for *lactose* (η) and *oxygen* (χ)



d) yield coefficients for formation of *biomass* from *lactose* ($Y_{X/S}$) and from *oxygen* ($Y_{X/O}$)

Figure. 1. Basic kinetics variables and characteristics of *Kluyweromyces marxianus*

The specific growth rate (ρ), specific consumption rate for *lactose* (η) and *oxygen* (χ), and yield coefficients ($Y_{X/S}$, $Y_{X/O}$) for the formation of *biomass* from *lactose* is calculated by the equations:

$$\rho = \dot{X}/X, \eta = \dot{S}/X, \chi = \dot{O}/X, Y_{X/S} = \dot{X}/\dot{S}, Y_{X/O} = \dot{X}/\dot{O}$$

For the derivatives $\dot{X}$, $\dot{S}$, $\chi = \dot{O}/X$ and $\dot{O}$ the cubic spline procedure was used.

2. INTERCRITERIA ANALYSIS METHOD

Here, we will briefly repeat the theoretical framework of the approach proposed in Atanassov, Mavrov & Atanassova 2014, by slightly improving the notation from Atanassova et. al. 2014. The approach employs an index matrix $\mathbf{M}$ of m rows $\{O_1, \dots, O_m\}$ and n columns $\{C_1, \dots, C_n\}$, where for every p, q ($1 \leq p \leq m, 1 \leq q \leq n$), 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 $\mathbf{M}$.

		C_1	...	C_k	...	C_l	...	C_n
$\mathbf{M} =$	O_1	e_{O_1, C_1}	...	e_{O_1, C_k}	...	e_{O_1, C_l}	...	e_{O_1, C_n}
	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\ddots$	$\vdots$	$\ddots$	$\vdots$
	O_i	e_{O_i, C_1}	...	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}	...	e_{O_j, C_k}	...	e_{O_j, C_l}	...	e_{O_j, C_n}
	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\ddots$	$\vdots$	$\ddots$	$\vdots$
	O_m	e_{O_m, C_1}	...	e_{O_m, C_k}	...	e_{O_m, C_l}	...	e_{O_m, C_n}

Considering the requirement for comparability above, the relation $R(e_{O_i, C_k}, e_{O_j, C_l})$ for each i, j, k is achieved. The relation R has dual relation $\bar{R}$, which is true in the cases when relation R is false, and vice versa. Let $\bar{R}$ be the dual relation of R in the sense that if R is satisfied, then $\bar{R}$ is not satisfied and vice versa. For example, if “ R ” is the relation “ $<$ ”, then $\bar{R}$ 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 $S_{k,l}^\mu$ be the number of cases in which $R(e_{O_i, C_k}, e_{O_j, C_k})$ and $R(e_{O_i, C_l}, e_{O_j, C_l})$ are simultaneously satisfied. Let $S_{k,l}^\nu$ be the number of cases in which $R(e_{O_i, C_k}, e_{O_j, C_k})$ and its dual $\bar{R}(e_{O_i, C_l}, e_{O_j, C_l})$ 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:

$$0 \leq S_{k,l}^\mu + S_{k,l}^\nu \leq \frac{m(m-1)}{2}$$

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

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

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 with 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 $\mathbf{M}$ 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:

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

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:

$$\begin{aligned} (\alpha, \beta) & - \text{positive consonance, if } (\mu_{C_k, C_l} > \alpha) \text{ and } (\nu_{C_k, C_l} < \beta); \\ (\alpha, \beta) & - \text{negative consonance, if } (\mu_{C_k, C_l} < \beta) \text{ and } (\nu_{C_k, C_l} > \alpha); \\ (\alpha, \beta) & - \text{dissonance, otherwise.} \end{aligned}$$

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 $m \times m$.

2.1. Rules for determining the degrees of consonance and dissonance

Atanassov, Atanassova and Gluhchev 2015 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:

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

The triangular zone for *positive* consonance (PC) from Figure 2 corresponds to where the pairs of criteria which exhibit PC will be located. Formally, this area can be expressed as:

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

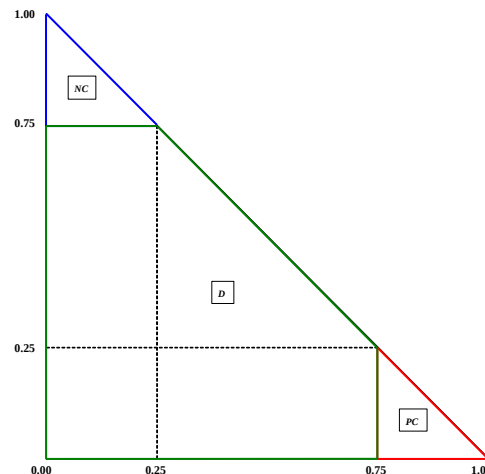


Figure 2. The triangle of positive, negative consonance and dissonance

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:

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

3. APPLICATION OF INTERCRITERIA METHOD TO MODELLING TO A FED-BATCH PROCESSES

We have experimental data for the examined process. This is a fed-batch with the following means: C_1 –*biomass* concentration, $\text{g}\cdot\text{L}^{-1}$; C_2 –*lactose* concentration, $\text{g}\cdot\text{L}^{-1}$; C_3 –*oxygen* concentration, $\text{mg}\cdot\text{L}^{-1}$; C_4 –feeding rate, $\text{g}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$; C_5 –specific growth rate, h^{-1} ; C_6 –specific consumption rate for *lactose*, h^{-1} ; C_7 –specific consumption rate for *oxygen*, h^{-1} ; C_8 –Yield coefficient for formation of *biomass* from *lactose*, g g^{-1} ; C_9 –Yield coefficient for formation of *biomass* from *oxygen*, g g^{-1} .

The index matrix $\mathbf{M}^*$ has the type shown in **Table 1**. Our colleagues have developed a program for the purpose of applying the method. The results are shown in **Tables 2**. In Figure 3 we present the dependencies between μ and ν .

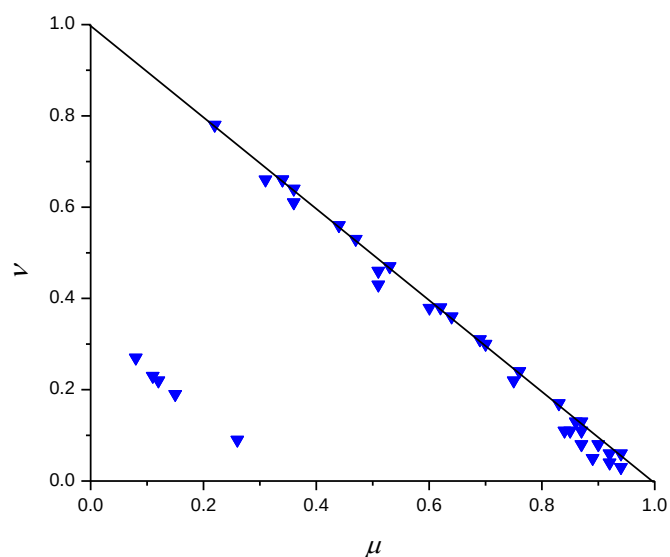


Figure 3. Relations between μ and ν for the different criteria

Table 1. Index matrix **M**

M=	t_2	t_4	t_6	t_8	t_{10}	t_{12}	t_{14}	t_{16}
C_1	1.70	3.15	6.00	11.6	16.3	20.1	22.4	25.3
C_2	41.9	36.8	21.4	14.0	6.00	0.00	0.00	11.2
C_3	5.93	3.45	2.80	0.50	0.12	0.09	1.92	0.09
C_4	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00
C_5	0.38	0.28	0.38	0.24	0.13	0.07	0.05	0.06
C_6	0.26	1.91	1.04	0.28	0.24	0.12	0.20	0.04
C_7	0.80	0.21	0.12	0.07	0.01	0.04	0.01	0.02
C_8	1.48	0.15	0.36	0.85	0.56	0.60	0.27	1.55
C_9	0.48	1.37	3.01	3.53	15.4	2.02	31.6	2.72
M=	t_{18}	t_{20}	t_{22}	t_{24}	t_{26}	t_{28}	t_{30}	
C_1	27.80	29.30	33.800	37.40	40.1	44.70	48.60	
C_2	3.60	1.00	0.600	7.10	0.00	14.60	7.40	
C_3	0.08	0.08	4.370	0.05	2.80	0.12	0.08	
C_4	0.00	0.00	0.020	0.00	0.02	0.00	0.00	
C_5	0.03	0.05	0.060	0.04	0.04	0.06	0.02	
C_6	0.11	0.13	0.410	0.33	0.11	0.14	0.36	
C_7	0.02	0.08	0.080	0.04	0.01	0.03	0.06	
C_8	0.23	0.40	0.160	0.12	0.40	0.41	0.06	
C_9	1.61	0.64	0.830	0.89	53.9	1.47	0.39	

Table 2. Index matrix $\mathbf{M}^*$ with pairs $\langle \mu_{C_k C_l}, \nu_{C_k, C_l} \rangle$

$\mathbf{M}^{*=}$	C_1	C_2	C_3	C_4	C_5
C_1	$\langle 1.00, 0.00 \rangle$	$\langle 0.31, 0.66 \rangle$	$\langle 0.85, 0.11 \rangle$	$\langle 0.94, 0.03 \rangle$	$\langle 0.94, 0.06 \rangle$
C_2	$\langle 0.31, 0.66 \rangle$	$\langle 1.00, 0.00 \rangle$	$\langle 0.87, 0.08 \rangle$	$\langle 0.92, 0.04 \rangle$	$\langle 0.87, 0.13 \rangle$
C_3	$\langle 0.85, 0.11 \rangle$	$\langle 0.87, 0.08 \rangle$	$\langle 1.00, 0.00 \rangle$	$\langle 0.92, 0.06 \rangle$	$\langle 0.83, 0.17 \rangle$
C_4	$\langle 0.94, 0.03 \rangle$	$\langle 0.92, 0.04 \rangle$	$\langle 0.92, 0.06 \rangle$	$\langle 1.00, 0.00 \rangle$	$\langle 0.12, 0.22 \rangle$
C_5	$\langle 0.94, 0.06 \rangle$	$\langle 0.87, 0.13 \rangle$	$\langle 0.83, 0.17 \rangle$	$\langle 0.12, 0.22 \rangle$	$\langle 1.00, 0.00 \rangle$
C_6	$\langle 0.89, 0.05 \rangle$	$\langle 0.86, 0.13 \rangle$	$\langle 0.90, 0.08 \rangle$	$\langle 0.15, 0.19 \rangle$	$\langle 0.64, 0.36 \rangle$
C_7	$\langle 0.84, 0.69 \rangle$	$\langle 0.75, 0.22 \rangle$	$\langle 0.87, 0.11 \rangle$	$\langle 0.08, 0.27 \rangle$	$\langle 0.69, 0.31 \rangle$
C_8	$\langle 0.34, 0.66 \rangle$	$\langle 0.51, 0.46 \rangle$	$\langle 0.51, 0.43 \rangle$	$\langle 0.11, 0.23 \rangle$	$\langle 0.70, 0.30 \rangle$
C_9	$\langle 0.44, 0.56 \rangle$	$\langle 0.36, 0.61 \rangle$	$\langle 0.84, 0.11 \rangle$	$\langle 0.26, 0.09 \rangle$	$\langle 0.53, 0.47 \rangle$
$\mathbf{M}^{*=}$	C_6		C_7		C_9
C_1	$\langle 0.89, 0.05 \rangle$		$\langle 0.84, 0.69 \rangle$		$\langle 0.34, 0.66 \rangle$
C_2	$\langle 0.86, 0.13 \rangle$		$\langle 0.75, 0.22 \rangle$		$\langle 0.51, 0.46 \rangle$
C_3	$\langle 0.90, 0.08 \rangle$		$\langle 0.87, 0.11 \rangle$		$\langle 0.51, 0.43 \rangle$
C_4	$\langle 0.15, 0.19 \rangle$		$\langle 0.08, 0.27 \rangle$		$\langle 0.11, 0.23 \rangle$
C_5	$\langle 0.64, 0.36 \rangle$		$\langle 0.69, 0.31 \rangle$		$\langle 0.70, 0.30 \rangle$
C_6	$\langle 1.00, 0.00 \rangle$		$\langle 0.76, 0.24 \rangle$		$\langle 0.34, 0.66 \rangle$
C_7	$\langle 0.76, 0.24 \rangle$		$\langle 1.00, 0.00 \rangle$		$\langle 0.47, 0.53 \rangle$
C_8	$\langle 0.34, 0.66 \rangle$		$\langle 0.47, 0.53 \rangle$		$\langle 1.00, 0.00 \rangle$
C_9	$\langle 0.36, 0.64 \rangle$		$\langle 0.22, 0.78 \rangle$		$\langle 0.62, 0.38 \rangle$

With the help of these tables, we will investigate the dependencies between the basic kinetic variables of the process and other important factors. The basic kinetic variables include biomass concentration, substrate concentration, oxygen concentration. Other are the flow rate, specific growth rate from *lactose* and *oxygen*, specific consumption rate for *lactose*, Specific consumption rate for *oxygen*, yield coefficient, formation of *biomass* from *lactose* and yield coefficient, formation of *biomass* from *oxygen*.

Biomass

- Dependencies of the biomass to substrate – the pair $\langle \mu, \nu \rangle$ is $\langle 0.31, 0.66 \rangle$ it seems that the biomass is not dependence from substrate. However, there is too large uncertainty $\pi=0.32$. In this case, we use the biochemical laws in who the biomass strong dependences form substrate.
- Biomass to oxygen – the pair $\langle \mu, \nu \rangle$ is $\langle 0.85, 0.11 \rangle$ and the uncertainty is $\pi=0.04$, because of that the oxygen will be present in the equation of the biomass. Probably the oxygen will be in the specific growth rate.
- Biomass to the flow rate – the pair $\langle \mu, \nu \rangle$ is $\langle 0.94, 0.03 \rangle$, $\pi=0.03$, because of that the flow rate will be in the equation of the biomass.

- Biomass to the specific growth rate from *lactose* and *oxygen* - the pair $\langle \mu, v \rangle$ is $\langle 0.94, 0.06 \rangle$, and there we do not have any uncertainty. Because of that, the specific growth rate from *lactose* and *oxygen* strong will be in the equation of the biomass.
- Biomass to the specific growth rate from *lactose* – the pair $\langle \mu, v \rangle$ is $\langle 0.89, 0.05 \rangle$ and there is small uncertainty and we can say that the specific growth rate from *lactose* will take a place in the equation for the biomass.
- Biomass to the specific growth rate from *oxygen* – the pair is $\langle \mu, v \rangle \langle 0.84, 0.69 \rangle$. We have high μ and little uncertainty. We can conclude that the specific growth rate from *oxygen* will be concluded in the equation for the biomass.
- Biomass to yield coefficient, formation of *biomass* from *lactose* and yield coefficient, formation of *biomass* from *oxygen*. Two pair $\langle \mu, v \rangle$ are $\langle 0.34, 0.66 \rangle$ and $\langle 0.44, 0.56 \rangle$. This shows that μ in two dependences is small and we have a little uncertainty. Because of that yield coefficient, formation of *biomass* from *lactose* and yield coefficient, formation of *biomass* from *oxygen* will be eliminated from the biomass equation.

Lactose

- Substrate to the oxygen. The pair $\langle \mu, v \rangle$ is $\langle 0.87, 0.08 \rangle$, and the uncertainty is 0.05. In this way, emphatically the oxygen will present in the equation for the substrate but in biochemical kinetic explanations it will be in some specific rate.
- Substrate to the flow rate. The pair $\langle \mu, v \rangle$ is $\langle 0.92, 0.06 \rangle$, the uncertainty is $\pi=0.04$. In this case we can assume that the flow rate will have place in the equation of the substrate.
- Substrate to the specific growth rate from *lactose* and *oxygen*. The pair $\langle \mu, v \rangle$ is $\langle 0.87, 0.12 \rangle$, the uncertainty is $\pi=0$. We can decide that the carbon dioxide specific growth rate from *lactose* and *oxygen* will be in the equation for lactose (substrate).
- Lactose to the specific growth rate from *oxygen*. The pair $\langle \mu, v \rangle$ is $\langle 0.75, 0.22 \rangle$ and there is small uncertainty and we can say that the specific growth rate from *lactose* will participate in the equation for the substrate.
- Lactose to the specific growth rate from *lactose*. The pair is $\langle \mu, v \rangle \langle 0.86, 0.13 \rangle$, and there is little uncertainty. We can say that the specific growth rate from *oxygen* will be concluded in the equation for the lactose.
- Lactose to yield coefficient, formation of *biomass* from *lactose*. The pair $\langle \mu, v \rangle$ are $\langle 0.91, 0.06 \rangle$ and $\langle 0.44, 0.56 \rangle$, μ in two dependences is high and we have a little uncertainty. Because of that yield coefficient for formation of *biomass* from *lactose* will be in the lactose equation.
- Substrate to yield coefficient, formation of *biomass* from *oxygen*. The pair $\langle \mu, v \rangle$ is $\langle 0.36, 0.61 \rangle$. This shows that yield coefficient for formation of *biomass* from *oxygen* will be eliminated from the biomass equation.

Oxygen

- Oxygen to the flow rate. The pair $\langle \mu, v \rangle$ is $\langle 0.92, 0.06 \rangle$, $\pi=0.02$. We can conclude that the oxygen depends from the flow rate.
- Oxygen to the specific growth rate from *lactose* and *oxygen*. The pair $\langle \mu, v \rangle$ is $\langle 0.83, 0.17 \rangle$, $\pi=0$. We can decide that the specific growth rate from *lactose* and *oxygen* will present in the equation of oxygen.
- Oxygen to the specific growth rate from *lactose*. The pair $\langle \mu, v \rangle$ is $\langle 0.90, 0.08 \rangle$ and we have a small uncertainty and we can accept that the specific growth rate from *lactose* will take a part in the equation for the biomass.

- Oxygen to the specific growth rate from *oxygen*. The pair is $\langle \mu, \nu \rangle \langle 0.87, 0.11 \rangle$. We have high μ and little uncertainty. We concluded that the specific growth rate from *oxygen* will be included in the equation for the biomass.
- Oxygen to yield coefficient for formation of *biomass* from *lactose*. The pair $\langle \mu, \nu \rangle$ is $\langle 0.51, 0.43 \rangle$. This shows that yield coefficient for formation of *biomass* from *lactose* will be not in the oxygen equation.
- Substrate to yield coefficient for formation of *biomass* from *oxygen*. The pair $\langle \mu, \nu \rangle$ is $\langle 0.84, 0.11 \rangle$. This gives us right to decide that the yield coefficient for formation of *biomass* from *oxygen* will be in the oxygen equation.

Flow rate

- The pair $\langle \mu, \nu \rangle$ for flow rate to the specific consumption rate for *lactose* and *oxygen*, specific consumption rate for *lactose*, specific consumption rate for *oxygen*, yield coefficient for formation of *biomass* from *lactose* ($Y_{X/S}$), yield coefficient for formation of *biomass* from *oxygen* ($Y_{X/O}$) are $\langle 0.12, 0.22 \rangle$, $\langle 0.15, 0.19 \rangle$, $\langle 0.15, 0.19 \rangle$, $\langle 0.08, 0.27 \rangle$, $\langle 0.11, 0.23 \rangle$ and $\langle 0.26, 0.09 \rangle$. We have small μ . They will not be included in the flow rate equation. The dependence for the flow rate will have

$$\frac{dV}{dt} = F$$

standard form biochemical kinetic explanations -

Specific consumption rate for *lactose* and *oxygen*

- Specific consumption rate for *lactose* and *oxygen* to specific consumption rate for *lactose*. The pair $\langle \mu, \nu \rangle$ is $\langle 1.00, 0.00 \rangle$. We concluded that the specific growth rate from *oxygen* will be included in the equation for the specific consumption rate for *lactose* and *oxygen*.
- Specific consumption rate for *lactose* and *oxygen* to the specific consumption rate for *oxygen*. The pair $\langle \mu, \nu \rangle$ is $\langle 1.00, 0.00 \rangle$. We concluded that the specific growth rate for *lactose* and *oxygen* strong dependences from specific consumption rate for *oxygen*. With biochemical kinetic explanation the dependence is $\rho(S, C) = \rho(S) \rho(C)$

Other criteria we will not discuss because they do not have relation from biochemical kinetics (Petrov & Ilkova 2014).

We can generalize all these results and interpret the basic kinetic dependencies. The results are shown in **Table 3**.

Table 3. Dependencies between the basic kinetic criteria

Criteria	Kinetics variables	Symbol	Depended on
C_1	Biomass	X	$S, O, F, \rho(S, C), \rho(S), \rho(C)$
C_2	Lactose	S	$X, O, F, \rho(S, C), \rho(S), \rho(C), Y_{X/S}$
C_3	Oxygen	O	$X, S, F, \rho(S, C), \rho(S), \rho(C), Y_{X/S}$
C_4	Flow rate	F	no one
C_5	Specific growth rate from S and O, h^{-1}	$\rho(S, C)$	$\rho(S), \rho(C)$
C_6	Specific consumption rate for <i>lactose</i> , h^{-1}	$\rho(S)$	no one
C_7	Specific consumption rate for <i>oxygen</i> , h^{-1}	$\rho(C)$	no one
C_8	Yield coefficient, formation of X from S	$Y_{X/S}$	no one
C_9	Yield coefficient, formation of X from O	$Y_{X/O}$	no one

Thus the fed-batch model of the processes includes the dependence between the concentrations of the basic energetic substrates: lactose and oxygen concentration, and cell concentration (Petrov, Ilkova & Vanags 2015). The model is described by a perfectly mixed in bioreactor:

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

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

The oxygen transfer rate can be calculated from:

$$OTR = \frac{k_L a}{(1 - \varphi_G)} (C^* - C) \quad (2)$$

where: $k_L a$ – mass-transfer coefficient, h^{-1} ; φ_G – gas hold-up; C^* – mean oxygen concentration, $\text{kg}\cdot\text{m}^{-3}$.

CONCLUSIONS

In this paper we have illustrated an application of ICRA. The application is modeling of a process for production the unicellular protein by strain *Kluyweromyces marxianus* var. *Lactis* MC 5. With ICRA we have searched the dependences between the basic kinetic variables of the process also we have searched relations between some parameter and coefficient of the process. When we have established positive consonance we have used it to say that there are relations of these criteria and they have included each other in their kinetic equation. Also we have based on the biochemical kinetic laws. In this way we have synthesized the model of the process with the basic equation for the biomass, lactose, oxygen and flow rate. It is different application of ICRA for modelling a such interesting process.

The process is useful and interesting because it uses a superfluous product from cheese production - rennet whey and strain *Kluyweromyces marxianus* var. *Lactis* MC 5 produces by it unicellular protein. In this way we have received one waste-free and highly economical process.

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