Integrated Engineering Systems

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***Abstract*—In this paper characterization of the biochemical parameters, physiological parameters, diffusion and rheological parameters were performed. Rheological parameters of microbial broth were studied. Mathematical description of DNA product was derived. The cell's metabolism and respiratory quotation were considered. The biochemical rate and diffusion rate were examined. The obtained results shows integrated effects of the biochemical reaction and diffusion as well as rheological behavior. The main contribution of this paper is developing integrated bioengineering system.**

Keywords—Biochemical transformation, diffusion rate, rheological state, physiological parameter, metabolism.

I. INTRODUCTION

The fermentation processes are highly nonlinear and nonstationary, hence their dynamical characteristics, change with time and consequently the model parameters vary during the cultivation. A common way to scope with this problem is to use less detailed models and parameter adaptive techniques to periodically fit these models to the actual process data. The efficiency of a specific implementation of measuring and control systems depend on the way by which these problems are treated. In order to cover the whole fermentation process, models are chosen in an overlapping way. Thus for a particular situation more than one model may be used to describe the process of that time instant.

The dynamic, structure and function of the biochemical reactions were studied in numerous literature. Synthetic analogous of naturally occurring enzymes find application in food industry, cosmetics, and pharmaceutical industry. There are many catalysts which catalyzed the biosynthesis. Some biokinetic models of the enzymatic transformation were derived and energy activation and frequency factor were determined.

Diffusional substance transfer rate has been investigated by many authors [1]-[6]. In the recent years, the subject of simultaneous diffusion and chemical reaction has received considerable attention from chemists and chemical engineers [7]-[17]. In this work biochemical reaction and diffusion are considered.

In cases where lack accurate information about a system or a system is complex to a point where a deterministic model is out of the question, resort is made to experimentation and statistics. In such cases, the system in question is treated as a black box or gray box, and its input-output relationships are studied through an experiment, which may be passive or active [12].

All of these contribute in biochemical, diffusion and rheological parameters transformation, that was the subject of this paper.

II. DNA TRANSFORMATION

DNA is a complex biopolymer that is organized as a double helix. The fundamental organizational element is the sequence of adenine A or guanine G with cytosine C and thymine T.

Recombinant DNA technology is used to diagnose existing diseases and predict the risk of developing a given disease.

$$DNA \rightarrow\Rightarrow\Rightarrow mRNA \rightarrow\Rightarrow\Rightarrow protein$$
$$transcription \qquad translation \qquad (1)$$

$$\frac{dc_{mRNA}}{dt} = k_P c_{gene} - k_d c_{mRNA} - \mu c_{mRNA} \quad (2)$$

(Synthesis) (Degradation) (Dilution by growth)

$$\frac{dc_P}{dt} = k_q c_{mRNA} - k_e c_P - \mu c_P \quad (3)$$

(Translation) (Degradation) (Dilution by growth)

where k_P is the specific biochemical constant of gene synthesis, k_d is the specific biochemical constant of oligonucleotides degradation, k_q is

oligonuleotides translation, k_e is the specific constant of protein degradation, and μ is specific growth constant.

III. BIOCHEMICAL PARAMETERS

Biochemical transformation can be described by the following scheme

$$S + E \Leftrightarrow^{k_1}_{k_{-1}} [SE] \Rightarrow^{k_2} P + E \quad (4)$$

where S is substrate, E is enzyme, SE is complex and P is product.

$$\frac{dc_{ES}}{dt} = k_1 \cdot c_E \cdot c_S - k_{-1} \cdot c_{ES} - k_2 \cdot c_{ES} \quad (5)$$

and product rate formation is:

$$r_P = \frac{dc_P}{dt} = k_2 \cdot c_{ES} \quad (6)$$

IV. METABOLISM

The grammar based model is much more computationally efficient than metabolism based models before. Recent studies in molecular biology provides us evidence, which insists these structures are formed by diffusive components of gene products. In some case, the reaction diffusion system, which creates the turning wave may play important role.

Organism's metabolism is considered as a system or a path of the system or some application results by substrate conversion in other substances and/or heat. Whole operations in the system is process transformation (Fig.1).

In these processes atomic species is conserved and saved in the process, in regard to, that micro-organisms can not carried out fission process.

For example, in typical aerobic process reactant can be sugar as source of the carbon, oxygen or nitrogen which converted in metabolites (H_2O, CO_2), cell's mass and bioproducts (enzymes, ethanol, penicillin, amino acids).

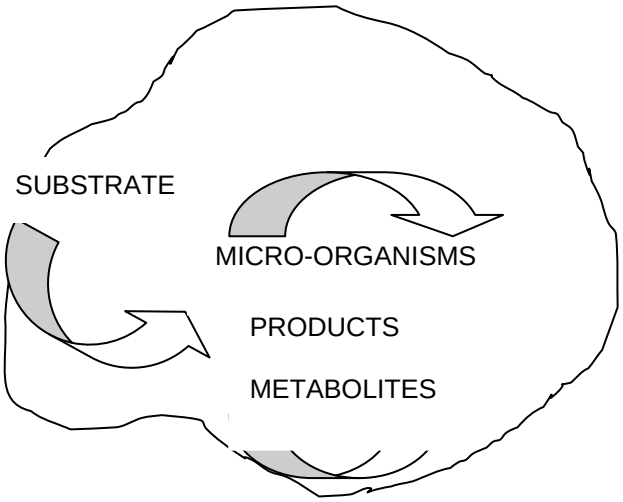

Fig.1 *Metabolism*

For instance,

$$sugar \xrightarrow{yeast\ \ cells} 2(ethanol) + 2CO_2 \quad (7)$$

In general case basic equation of the process is defined as::

$$IU+HM+O_2 \xrightarrow{microorganisms} PF+PM+ Q_F \quad (8)$$

where *IU* is carbon source, *HM* is nutrition materials, O_2 oxygen, *PF* is fermentation product, *PM* is product of metabolism, and Q_F is fermentation heat.

Products of metabolism are very often CO_2, hydrocarbons, and biomass.

Process in Fig. 1 use substrate such as carbon hydrates, oxygen, nitrogen sources etc., and converted them in cell mass, product, and metabolites (H_2O, CO_2, etc.), From the principal of the atomic species conversion the general stoichiometric equation can be derived:

$$C_nH_mO_kN_p + \sum_j \alpha_j A_j' \rightarrow \beta C_nH_aO_bN_c \quad (9)$$

Where

$C_nH_mO_kN_p$ -Formulae of the substrate for basic energy

$\sum_j A_j'$ - other substrate metabolites and products (O_2, CO_2, nitrogen sources)

$\sum_j \alpha_j, \beta$ -stoichiometric coefficients

and

$C_n H_a O_b N_C$ -microorganisms formulae

.

In the aim transition state modelling characteristic equations system for typical biochemical conversion can write as:

$$A(C_a H_b O_c) + B(O_2) + M(NH_3) \rightarrow$$
$$C_d H_e O_f N_q + L(H_2O) + E(CO_2) + F(C_h H_i O_j N_k) \quad (10)$$

Assuming the constant coefficients the following balances can be derived:

Carbon (C)
A a =d + E + hF (10.1)

Hydrogen
A b + 3M = e+ 2L + iF (10.2)

Oxygen
A c + 2B =f+ L + jF (10.3)

Nitrogen
M = q + kF (10.4)

Under corresponding conditions can derive still relation for respiratory quotation RQ, and consumption rate of nitrogen.:

Respiratory quotation RQ is defined as:

$$RQ = E / B = \frac{c_{CO_2}}{c_{O_2}} \quad (11)$$

Nitrogen consumption rate is:

$$q = M / B \quad (12)$$

V. DIFFUSION IN BIOSYSTEMS

Many aspects of passive diffusion in the environment were considered [14]. Passive diffusion is defined to be diffusion objects that are not capable of performing random motion the help of environment turbulence. Likewise active diffusion is defined to be the diffusion of objects, which perform motion by themselfs.

The smaller organism is, the more subject it is to the effect of environmental turbulence. Thus, the diffusion of smaller animals should be considered as partially passive and partly active. For instance, bacteria and pollen in the air and phytoplanktion in water diffuse almost passively, while many inserts in flight undergo varying proportions of passive and active diffusion, according to the degree of movement of the environmental fluid.

A. Diffusion of the substrate consumption

Taking into account diffusion, microscopic description in of a biochemical reaction, shown in Fig.1 can be described by equation (13)[13].

Sugar diffusion can be consider as passive:

$$\frac{\partial c_S}{\partial t} + v_x \frac{\partial c_S}{\partial x} + v_y \frac{\partial c_S}{\partial y} + v_z \frac{\partial c_S}{\partial z} = D_S \left(\frac{\partial^2 c_S}{\partial x^2} + \frac{\partial^2 c_S}{\partial y^2} + \frac{\partial^2 c_S}{\partial z^2}\right) + r_{S.} \quad (13)$$

where D_S is substrate diffusion parameters, c_S is substrate concentration, *x,y,z* dimension space, t is time, v is velocity, and r_S is biochemical conversion rate of substrate.

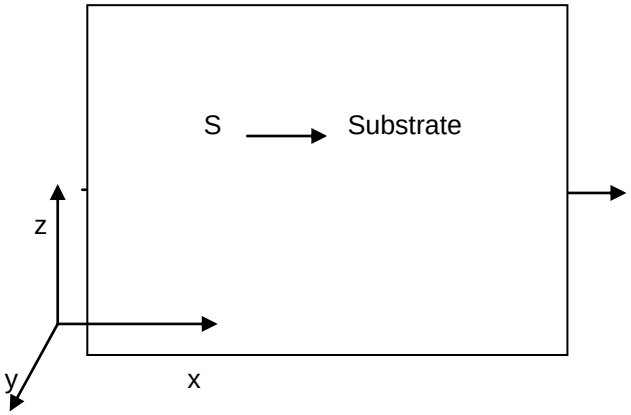

Fig.2 *The biochemical reaction with substrate diffusion*

B. Product diffusion

Product diffusion rate can be defined as:

$$\frac{\partial c_P}{\partial t} + v_x \frac{\partial c_P}{\partial x} + v_y \frac{\partial c_P}{\partial y} + v_z \frac{\partial c_P}{\partial z} = D_P \left(\frac{\partial^2 c_P}{\partial x^2} + \frac{\partial^2 c_P}{\partial y^2} + \frac{\partial^2 c_P}{\partial z^2}\right) + r_{.P} \quad (14)$$

where D_P is product diffusion parameters, c_P is product concentration, and r_P is biochemical product formation rate.

C. Biomass diffusion parameter

Biomass diffusion parameters determines rate of biomass formation, and biomass state can be described as:

$$\frac{\partial c_X}{\partial t}+v_x\frac{\partial c_X}{\partial x}+v_y\frac{\partial c_X}{\partial y}+v_z\frac{\partial c_X}{\partial z}=D_X\left(\frac{\partial^2 c_X}{\partial x^2}+\frac{\partial^2 c_X}{\partial y^2}+\frac{\partial^2 c_X}{\partial z^2}\right)+r_{X.} \quad (15)$$

where D_X means biomass diffusion coefficient, and r_X is reaction rate for biomass formation.

If mixing effects can be neglected equation (15) can be transformed:

$$\frac{\partial c_X}{\partial t}+v_x\frac{\partial c_X}{\partial x}+(-r_X)=D_{LX}\left(\frac{\partial^2 c_X}{\partial x^2}+\frac{\partial^2 c_X}{\partial y^2}+\frac{\partial^2 c_X}{\partial z^2}\right) \quad (16)$$

If diffusion can be neglected in y and z direction equation (16) can be restarted in the form:

$$\frac{\partial c_X}{\partial t}+v_x\frac{\partial c_X}{\partial x}+(-r_X)=D_{LX}\left(\frac{\partial^2 c}{\partial x^2}\right) \quad (17)$$

The distribution in one direction and time comes directly from the solution to the unsteady state diffusion in an infinite solid having a source at *x=0*, when t=0.

For the steady state condition and when velocity in the x direction can be neglected, equation (17) becomes:

$$D_{LX}\left(\frac{\partial^2 c_X}{\partial z^2}\right)=(-r_X) \quad (18)$$

Now, this partial differential equation becomes,

ordinary differential equation:

$$D_{LX}\left(\frac{d^2 c_X}{dx^2}\right)=(-r_X) \quad (19)$$

VI. RHEOLOGICAL PARAMETERS OF BIOMASS

Biomass viscosity changes during time making mycelium. If changes in *x* and *y* direction neglected, description of the microbilogical culture viscosity changing, in z direction can be defined as (Fig.3):

$$\frac{\partial \tau_z}{\partial t}+\rho\left(\frac{\partial v_z}{\partial t}+v_x\frac{\partial v_z}{\partial x}+v_y\frac{\partial v_z}{\partial y}+v_z\frac{\partial v_z}{\partial z}\right)= -\frac{\partial P_r}{\partial z}+\left[\frac{\partial}{\partial x}\left(\mu_{zx}\frac{\partial v_z}{\partial x}\right)+\frac{\partial}{\partial y}\left(\mu_{zy}\frac{\partial v_z}{\partial y}\right)+\frac{\partial}{\partial z}\left(\mu_{zz}\frac{\partial v_z}{\partial z}\right)\right]+\rho g_z \quad (20)$$

where ρ is microbial broth density, P_r is pressure, μ_d is dynamic viscosity, and g is gravity.

Changes in y- direction:

$$\frac{\partial \tau_y}{\partial t}+\rho\left(\frac{\partial v_y}{\partial t}+v_x\frac{\partial v_y}{\partial x}+v_y\frac{\partial v_y}{\partial y}+v_z\frac{\partial v_y}{\partial z}\right)= -\frac{\partial P_r}{\partial y}+\left[\frac{\partial}{\partial x}\left(\mu_{yx}\frac{\partial v_y}{\partial x}\right)+\frac{\partial}{\partial y}\left(\mu_{yy}\frac{\partial v_y}{\partial y}\right)+\frac{\partial}{\partial z}\left(\mu_{yz}\frac{\partial v_y}{\partial z}\right)\right]+\rho g_y \quad (21)$$

where v-rate, τ-shear stress, μ -dynamic viscosity , ρ-density и t-time. P_r is pressure, g_z is gravity and x,y,z-space coordinates.

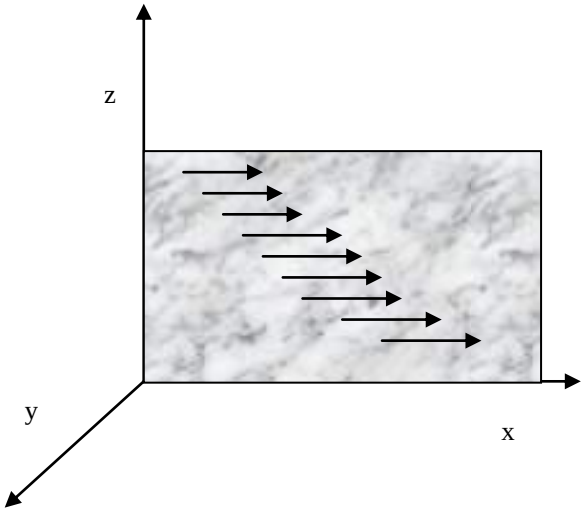

Fig.3 *Shear stress in microbial broth*

Viscosity changes in x-direction:

$$\frac{\partial \tau_x}{\partial t}+\rho(\frac{\partial v_x}{\partial t}+v_x\frac{\partial v_x}{\partial x}+v_y\frac{\partial v_x}{\partial y}+v_z\frac{\partial v_x}{\partial z})=$$
$$-\frac{\partial P_r}{\partial x}+[\frac{\partial}{\partial x}(\mu_{xx}\frac{\partial v_x}{\partial x})+\frac{\partial}{\partial y}(\mu_{xy}\frac{\partial v_x}{\partial y}) \quad (22)$$
$$+\frac{\partial}{\partial z}(\mu_{xz}\frac{\partial v_x}{\partial z})]+\rho g_x$$

where v-rate, τ-shear stress, μ -dynamic viscosity , ρ-density и t-time. P_r is pressure, g_z is gravity and x,y,z-space coordinates.

Shear stress functions equations (20)-(22)can be expressed as:

$$\frac{\partial \tau_z}{\partial t}+\rho(\frac{\partial v_z}{\partial t}+v_x\frac{\partial v_z}{\partial x}+v_y\frac{\partial v_z}{\partial y}+v_z\frac{\partial v_z}{\partial z})=$$
$$-\frac{\partial P_r}{\partial z}+(\frac{\partial \tau_{zx}}{\partial x}+\frac{\partial \tau_{zy}}{\partial y}+\frac{\partial \tau_{zz}}{\partial z})+\rho g_z \quad (23)$$

$$\frac{\partial \tau_y}{\partial t}+\rho(\frac{\partial v_y}{\partial t}+v_x\frac{\partial v_y}{\partial x}+v_y\frac{\partial v_y}{\partial y}+v_z\frac{\partial v_y}{\partial z})=$$
$$-\frac{\partial P_r}{\partial y}+(\frac{\partial \tau_{yx}}{\partial x}+\frac{\partial \tau_{yy}}{\partial y}+\frac{\partial \tau_{yz}}{\partial z})+\rho g_y \quad (24)$$

$$\frac{\partial \tau_x}{\partial t}+\rho(\frac{\partial v_x}{\partial t}+v_x\frac{\partial v_x}{\partial x}+v_y\frac{\partial v_x}{\partial y}+v_z\frac{\partial v_x}{\partial z})=$$
$$-\frac{\partial P_r}{\partial x}+(\frac{\partial \tau_{xx}}{\partial x}+\frac{\partial \tau_{xy}}{\partial y}+\frac{\tau_{xz}}{\partial z})+\rho g_x \quad (25)$$

There is more correlations for these equations solutions.

VII. Conclusion

In this paper the biochemical reaction rate and diffusion rate for various dynamic and steady state conditions were examined. The analysis of the biochemical reaction progress and diffusion progress characterization were developed. The obtained expressions show dynamic behavior of the component during the biochemical reaction with reactants and products diffusion. Production requirements represent the knowledge consisting of reaction objectives, coupling constraints user's requirements and performance expectations.

Rheological behavior of microbial broth were examined. Rheological parameters were analyzed and defined.

The main contribution of this paper is advanced theory developing in biochemical systems.

Notation

D -diffusion, cm/s

c -concentration, g/cm^3

E -enzyme

g -gravity, cm/s^2

k_1 -substrate and enzyme complex formation constant, h^{-1}

k_{-1} -substrate and enzyme complex degradation constant, h^{-1}

k_2 -product formation constant, h^{-1}

k_d - *oligonucleotide's degradation constant,* h^{-1}

k_e - protein's degradation constant, h^{-1}

k_P -gene synthesis constant, h^{-1}

k_q -oligonucleotide's translation constant, h^{-1}

P -product

P_r - pressure, Pa

r – transformation rate, g/h

S -substrate

t -time, s

v -geometrical rate, cm/s

Greek symbols

μ -dynamic viscosity, Pas

ρ -density, g/cm^3

τ -shear stress, Pa

Index

P -product

S -substrate

X -biomass

REFERENCES

[1] J. Crank, Mathematcs of diffusion, Clarendon, Oxford,1975.

[2] M. Knudsen, Die Gesetze der Molecularstromung und der inneren Reibungsstromung der Gase durch Rohren, Ann. Physik.vol. 28,1909,pp.75.

[3] A. Einstein, Zur Thearie der Brownschen Bewegung, Ann. der Physik vol. 19,1906, 371.

[4] J. Savkovic-Stevanovic, Simultaneous diffusion and chemical reaction as a Monte Carlo process, 10th International Congress CHISA90, Praha, Czechoslovakia, p.A7.125, 25-29 August, 1990.

[5] J. Savkovic-Stevanovic, M.Misis-Vukovic, G. Boncic-Caricic, B.Trisovic,S.Jezdic, Reaction Distillation with ion exchangers, Sep. Sci. Technol., vol.27,1992, 613-630.

[6] J. Savkovic-Stevanovic, M. Ivanovic, Dynamic of three ethyl citrate formation, 3rd Inter.Conference of the Chem Soc.of the South-East European Countries,pp.256, Bucharest, 22-25 September,2002.

[7] J. Savkovic-Stevanovic, M.Misis-Vukovic, G. Boncic -Caricic, B.Trisovic, S. Jezdic, Distillation with esterification reaction in a column packed bed by ion exchangers, Proceedings of the 3rd World Congress of Chemical Engineering, Vol.II, pp.672-675, Tokyo, Japan, September 20-25,1986.

[8] G. Kabel, H.Mayer, and B.Seid, Reaktionen in Destillations Kolonnen, Chem. Ing. Techn., vol. 50, 586,1980.

[9] T. Mosorinac, M. M.Stevanovic-Huffman, Savkovic-Stevanovic J., Process system toxicity, CHISA2012-20th Inter. Congress on Process Engineering and Equipment Symposium on environment engineering, p.no.146, 25-29 August, Prague,2012.

[10] T. Mosorinac, Chemometrics and regression analysis of the chemical reaction systems, Comput. Ecol.Eng.vol. 6, 2010, 17-23.

[11] M. Ivanovic-Knezevic, J. Djurovic, Molecular modelling of the esterification reactions, Comput. Ecol. Eng., 6,2010, 10-16.

[12] M. Stevanovic-Huffman, J. Savkovic-Stevanovic, The chemical system dynamics, Proceedings of the 2nd Conference on Modelling and Simulation, pp. 52-57, Belgrade, 28-29 September, 2011, ISBN 978-86-911011-6-9.

[13] J. Savkovic-Stevanovic, Process modelling and simulation, University of Belgrade, Faculty of Technology and Metallurgy,Belgrade,1995.

[14] J. Savkovic-Stevanovic, M. Stevanovic-Huffman, Diffusional system, Proceedings of the 2nd Conference on Modelling and Simulation, pp.223-228, Belgrade 28-29 September, 2011, ISBN 978-86-911011-6-9.

[15] L. Wilhelmy, Pogg.Ann., 81, 1850,413-499.

[16] S .Arrhenius, Z.Physik Chem.vol. 4,1889, 226.

[17] H. Eyring and M. Polanyl, Z.Physik Chem.

B,vol.12, 279, 1931.