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The Modified Complex Method as Applied to an Optimization of Aeration and Agitation in Fermentation

Mitsuyasu Okabe*, Shuichi Aiba, and Mitsumasa Okada**

Institute of Applied Microbiology, University of Tokyo, Tokyo

Abstract

After reviewing briefly the complex method exploited by Box, some modification of the original method has been discussed to establish an algorithm for an optimization of aeration and agitation in fermentation. Supposing that annual production rate of a fermentation product is given, the optimization here is to determine the conditions required of aeration and agitation such that the annual expenditures of the process are minimized. The applicability of the modified complex method to a penicillin fermentation has been demonstrated by using a correlation between penicillin yield and volumetric coefficient of oxygen transfer. In this demonstration, the volumetric coefficient of oxygen transfer, $K_V \cdot p$ and aeration rate, QAF have been employed as independent variables. The optimal solution to this exemplified problem has been obtained quite rapidly within 60 sec, using HITAC 8700/8800, Computer Center, University of Tokyo.

Introduction

One of the interesting problems remaining to be studied in the fermentation industry is in determining aeration rate and agitation intensity of fermenters such that sum total of annual expenditures of equipment and utilities can be minimized.

It has been claimed by many workers that aeration and agitation occupy a considerable fraction of the expenditures required for running the process. Here, the process signifies the fermentation *per se*, excluding the separation and purification of product. An experience has pointed out tacitly that the aeration must be kept decreased in view of high aeration cost, while the agitation intensity increased to keep up with the value of $K_V \cdot p$ required for a specific fermentation. Herein lies the necessity of delineating the above-mentioned experience from the standpoint of minimizing the cost of aeration and agitation.

However, it must be mentioned of the fact that specific conditions to have a fermentation product concentration in the broth maximized are not necessarily compatible with those to have the cost of aeration and agitation minimized. Conversely, the optimization of aeration and agitation to be studied here is tantamount to a "sub-optimization" in the sense that the optimal solution to the aeration and agitation in this paper remains to be further studied from the viewpoint of the fermentation pattern, i.e., product accumulation vs. fermentation time, auxiliary operations such as sterilization of fermentation media and air, and in addition, a sequence of operations to separate and purify the product to have an optimization of the fermentation process as a whole.

Present address:
* Central Research Lab., Sanraku-Ocean Co., Ltd., Fujisawa
** Hitachi Works, Ltd., Tokyo

The purpose of this paper is in establishing an appropriate algorithm to have a "sub-optimization" of aeration and agitation, and in demonstrating the usefulness of the algorithm, provided:

(1) annual production rate of a fermentation product is given,

(2) correlation between product yield and volumetric coefficient of oxygen transfer is given.

Optimization Algorithm

Generally, an optimization problem of a chemical process can be defined mathematically as follows :

Minimize

$$\phi=\phi(\boldsymbol{x}, \boldsymbol{u})^{*} \tag{1}$$

Subject to

$$\boldsymbol{x}=f(\boldsymbol{u}) \tag{2}$$

$$g(\boldsymbol{x}, \boldsymbol{u})\geqslant 0 \tag{3}$$

$$\boldsymbol{u}\in U \tag{4}$$

$$\boldsymbol{x}\in X \tag{5}$$

where

$\boldsymbol{u}$ =decision vector

$\boldsymbol{x}$ =state vector

f, g =vector-valued functions

U =admissible set of decision vectors

X =admissible set of state vectors

ϕ =objective function

The problem is to find the value of $\boldsymbol{u}$ which minimizes the objective function, ϕ under the constraints, (2) to (5). Equality constraint, Eq. (2) is the system equation, in other words; though another constraint, (3) is implicit, (4) and (5) constrain $\boldsymbol{u}$ and $\boldsymbol{x}$ explicitly, meaning that $\boldsymbol{u}$ and $\boldsymbol{x}$ belong to the admissible sets, U and X, respectively. Obviously, an analytical solution to Eq. (1) is hardly possible when the optimization of a process, non-linear in nature and endowed essentially with various constraints as could be exemplified in this work (see later) is dealt with.

Consequently, the use of computer becomes indispensable; one must pay due attention in this use of computer to an algorithm which is capable of saving computation time as much as possible, because the time sometimes overruns an allowable limitation inherent in a computer unless an appropriate algorithm is used. This is true particularly when the objective function becomes complicated, having many independent variables as could easily be found in the fermentation industry.

In the present paper, the modified complex method has been adopted as the optimization algorithm. Before elaborating the point of the modification in this work, it is deemed

* when "maximize" is required, the sign of objective function is reversed.

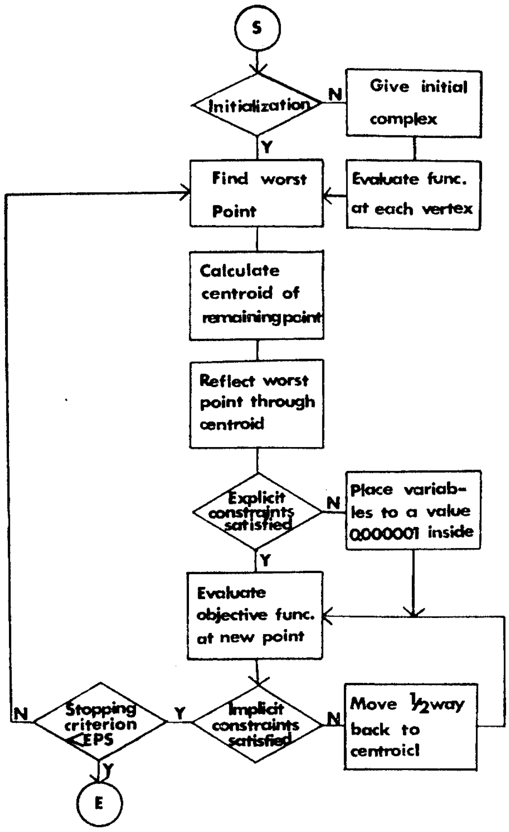

Fig. 1. Computational flow diagram of the original complex method (OPTIM).

worthy to have a quick review of the original complex method which has been developed by Box[1] (see Fig. 1).

In Fig. 1, the first step is "initialization," which means an establishment of k-dimension complex having k-vertices via generation of "random number" in the n-dimensional space, provided: k =number of vertices ($k \geqslant n+1$)

n =dimension of vector, $\boldsymbol{u}$

The objective function is then calculated at each vertex of the complex. This calculation is followed by the step to reject a vertex which gives the worst function value as shown in the figure. Then the point is replaced by a new one as follows:

$$\boldsymbol{u}_{\text{new}}=\boldsymbol{u}_{\text{c}}+\alpha_r\cdot(\boldsymbol{u}_{\text{c}}-\boldsymbol{u}_{\text{w}}) \quad (6)$$

where

$$\boldsymbol{u}_{\text{c}}=\Big(\sum_{\substack{j=1\\ j\neq w}}^{k}\boldsymbol{u}_j\Big)/(k-1) \quad (7)$$

provided: $\boldsymbol{u}_{\text{c}}$ =centroid

$\boldsymbol{u}_{\text{new}}$ =new point

$\boldsymbol{u}_{\text{w}}$ =worst point

α_r =reflection factor ($\geqslant 1$)

If the explicit inequality constraints are violated in this reflection of the worst point through the centroid, any component (variables) of the new vertex is reset to a value 0.000001 inside the constraints. If the implicit inequality constraints are violated, on the other hand, the reflected vertex is moved half-way between the reflection point *in situ* and the centroid in toward the latter until a valid point is obtained. This reset or the transfer of half-way as shown in Fig. 1 is followed by another comparison of the function values among the new vertex and remaining vertices excluding the worst point previously cited. Here again, the comparison rejects another worst point and a new vertex is located exactly by the same procedure mentioned earlier. The significance of explicit and implicit inequality constraints in Fig. 1 will be demonstrated in the calculation example appearing later on in this paper.

The calculation is repeated until a stopping criterion assessed from the value of objective function falls within a convergence tolerance. According to Box, the stopping criterion is taken as a difference of two consecutive function values; if the difference become small enough to be within an accuracy of the computer word-length five times consecutively, the convergence tolerance is claimed to be satisfied.

In order to have a rapid rate of convergence in calculations and to secure a global optimum point with certainty, some modification has been attempted here. To elaborate the global optimum point, a special case wherein the optimum point is located in a very steep "valley" will be considered, for instance. Clearly, the usual Box procedure may overlook the point unless the following modification is attempted.

Firstly, the two kinds of stopping criteria are introduced to be free from missing the global optimum point. The 1st criterion is defined by the relative difference of the largest and smallest function values at the vertices of the complex during iterative search. The 2nd criterion is defined by the ratio of the average value of the distance between adjacent vertices to the norm of the centroid. If these criteria are satisfied simultaneously, the iteration shall be stopped.

Secondly, the modification deals with the calculation of centroid, different from that in Eqs. (6) and (7). This calculation is intended to shorten the time for iteration, i.e.[2)]

$$\boldsymbol{u}_c=\left(\sum_{i=1}^{k}\Delta f(\boldsymbol{u}_i)\cdot\boldsymbol{u}_i\right)\Big/\left(\sum_{i=1}^{k}\Delta f(\boldsymbol{u}_i)\right) \tag{8}$$

where

$$\Delta f(\boldsymbol{u}_i)=(f(\boldsymbol{u}_i)-f(\boldsymbol{u}_{\max}))/(f(\boldsymbol{u}_{\max})-f(\boldsymbol{u}_{\min})) \tag{9}$$

provided: $\boldsymbol{u}_{\max}$=point which yields maximum value of objective function

$\boldsymbol{u}_{\min}$=point corresponding to minimum value of objective function

Needless to say, except for the above-mentioned modification the program used here is exactly the same as that shown in Fig. 1. The complex program in Fig. 1 is termed "OPTIM" in this paper.

Example of Optimization for Aeration and Agitation in Penicillin Fermentation

The objective function is defined as follows:

$$\phi=(\sum_{i=1}^{M} e_i \cdot E_i + C_0 \cdot X_0) \cdot N_t + \alpha \cdot \sum_{m=1}^{N} I_m \qquad (10)$$

where

e_i =unit cost of i-th utility

E_i =utility required per batch

C_0 =cost of unit mass of raw material

I_m =investment cost of equipment including fermenter vessel, air compressor, and air filter

N_t =number of batch cycles

X_0 =raw materials expended per batch

α =empirical constant (=1.42)

In Eq. (10), utilities adopted in this work were steam, electricity and air.* Steam consumed for sterilization prior to each batch was assumed to be constant (one-sixth of the working volume of the fermenter; here the fermentation working volume was taken as constant,** while electricity expended and air consumed were assumed from the respective system equations (*cf.* Eqs. (11) to (15) later)). The empirical coefficient, α is equal to depreciation (=0.3) multiplied by Lang factor (=4.74).

In order to assume the investment cost for each equipment, a convenient power function (exponent ranging from 0.5 to 1.25 depending on the item) such as *KAF, KCP, KFA* and *KFT* must be given.

If the annual production rate, *PO* is given, the number of batch cycles, N_t can be presented by:

$$N_t = PO/((F_r)_{max} \cdot Y \cdot V_L) \qquad (11)$$

where

PO =annual production rate, kg

$(F_r)_{max}$ =maximum product concentration, kg/m^3

V_L =working volume of fermenter, m^3

Y =relative yield

Due to paucity of appropriate data on penicillin yield (absolute value) as a function of operating variables such as volumetric coefficient of oxygen transfer, and aeration rate, etc., the use of a correlation between relative yield and volumetric coefficient of oxygen transfer multiplied by partial pressure of oxygen, $K_V \cdot p$ (which was presented by Karow *et al.*[3]) was unavoidable (see Fig. 2). Since the relative yield, Y is defined by the ratio of penicillin concentration in the broth to the maximum value ever attained, the absolute value of yield is represented by $(F_r)_{max} \cdot Y$ as seen from the denominator of Eq. (11).

Referring to the publication of Herold *et al.*[4], $(F_r)_{max}$=7.0 kg/m^3 was used. It is noted from Eq. (11) that penicillin is recovered without loss from the processes of separation and purification; however, as was referred to earlier, the assumption of 100% recovery in this "sub-optimization" does not invalidate, to any extent, the result of calculation in

* cost of water was included in that of raw material.

** see Table 1 later.

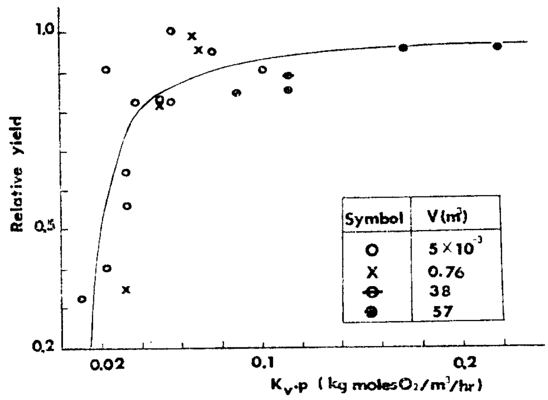

Fig. 2. Relative yield of penicillin as plotted againist $K_V \cdot p$.[2)]

this example. Briefly, the recovery efficiency is remaining to be discussed separately in the subsequent systems of separation and purification other than the aeration and agitation here.

Though the original data are scattered considerably as noted from Fig. 2, one may be permitted to draw a hyperbolic curve through the points. The function assumed is as follows:

$$Y=1.0-1.0/(a\cdot K_V\cdot p-b) \tag{12}$$

where

$$a=1.47\times 10^2$$
$$b=0.928$$

The assessment of a and b values followed the least square method for the non-linear function. The calculation was conducted by "OPTIM" in this work.

Then, a coordination of Y in Eq. (12) with operating variables via $K_V\cdot p$ is required. Though many empirical correlations between K_V and operating variables have been presented, a specific correlation presented by Cooper *et al.*[5)] will be used as shown below. The arbitrary choice of the correlation bears no particular significance.

$$K_V=0.0635\cdot(P_g/V_L)^{0.95}\cdot V_s^{0.67} \tag{13}$$

where

K_V =volumetric coefficient of oxygen transfer, kg moles O_2/m^3 hr atm

P_g =power consumption of agitation in gassed system, HP

V_s =nominal velocity of air on cross-sectional area of vessel, m/hr

Assuming that pressure inside the fermenter is kept at 0.2 Kg/cm^2 gauge, the partial pressure of oxygen, p is calculated by:

$$p=((1.2+(1.2+H_L/10.3)/2.0)\cdot 0.21 \tag{14}$$

where

H_L =liquid depth, m

p =partial pressure of oxygen, atm

Another correlation between P_g and P_0 (power requirements of agitation without aeration) modified by Fukuda *et al.*[6] will be used to have a quick calculation of N (rotation speed of impeller, 1/min).

$$P_g=2.4\cdot(P_0^2N\cdot D_i^3/QAF^{0.08})^{0.39}\cdot 10^{-3} \tag{15}$$

where

D_i =impeller diameter, cm

QAF=aeration rate, ml/min

Now, Eqs. (11) to (15) are commensurate with the system equation (or equality constraints) represented earlier by Eq. (2). Judging from the character of this problem, $K_V\cdot p$ and QAF were taken as independent variables (decision vector). Next, the explicit inequality constraints represented earlier by (4) and (5) are also taken in this example as follows:

$$0.02\leqslant K_V\cdot p\leqslant 0.2 \tag{16}$$

$$0.05\cdot V_L\leqslant QAF\leqslant 1.0\cdot V_L \tag{17}$$

On the other hand, the implicit inequality constraint appearing earlier in (3) is assumed as follows:

$$N_t\leqslant 60^* \tag{18}$$

To recapitulate, this problem is to minimize Eq. (10) under the constraints from (11) to (18).

Procedure of Calculation

The procedure of calculation is shown in Figs. 3 and 4. It is remarked from Fig. 3 that the main program "AEROPT" executes only the reading of input data, linking the optimizing program "OPTIM" to the subsequent subprograms, "FPC," "COS," and "AGNR." This arrangement is to impart universality to "AEROPT," leaving individual cost estimation required and ancillary calculations of the least square method, etc. entirely to the subprograms.

In Fig. 4, the subprogram "FPC" carried out an assessment of *a* and *b* values by the least square method as mentioned previously, while another subprogram "COS" deals with calculation of the objective function. If the optimal values of $K_V\cdot p$ and QAF are obtained by the iterative search, the rotation speed of impellers, N is evaluated by the last subprogram "AGNR," using the Regula-Falsi method.[7] It goes without saying that "OPTIM" appearing in Figs. 1, 3 and 4 is the core program. These programs are packaged such that the application to the aeration and agitation process other than that exemplified here can be made with ease.

* The implicit constraint here originates from that the annual working period assumed as 7,200 hr is divided by the period of working time for one batch, taken as 120 hr.

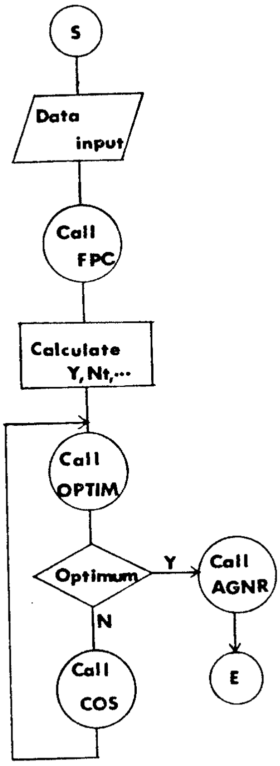

Fig. 3. Flow diagram of main program.

Actual data on the relative yield shown in Fig. 2 and in addition, data summarized in Table 1 were read from data cards. This operation was followed by the calculation via "OPTIM," "COS," and "AGNR." (*cf.* Fig. 1)

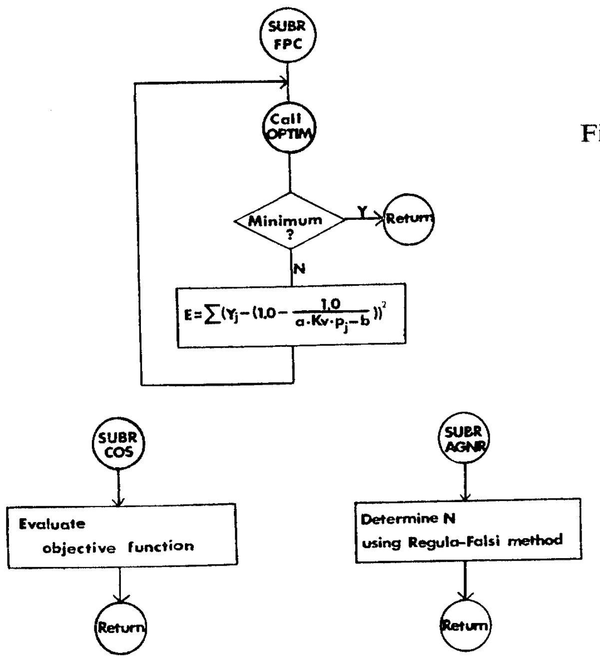

Fig. 4. Flow diagram of subprograms.

The subprogram "FPC" executed the curve fitting of the experimental data[3] by the least square method. Whether the sum of squared differences, E was minimal or not was determined by the stopping criteria decreasing below a value of 0.005. The subprogram "COS" carried out calculation of objective function via Eqs. (10) to (14). The subprogram "AGNR" executed the determination of rotation speed of impellers by a trial and error method, using the Regula-Falsi method.[7]

Results and Discussion

The specified condition used for this optimization is summarized in Table 1, whereas the optimization result is shown in Table 2. Final values of the objective function are summarized in the latter table by changing the number of vertices, the convergence tolerance and the initial point independently.

Despite the various conditions employed, the final value of the objective function approaches nearly the identical value of (1.062 to 1.065) $\times 10^8$ Yen in this example, though the 3rd order below the decimal point changed slightly from 2 to 5.

Table 1. Specified condition for optimization.

Annual production rate	50,000	kg
Fermenter volume (nominal)	200	m^3
Working volume of fermenter	140	m^3
Utility data		
Air	0.28	Yen/m^3
Electricity	3.35	Yen/Kw hr
Steam (6.0 Kg/cm^2 gauge)	635	Yen/ton
Raw material	5,000	Yen/m^3
Coefficient of cost estimation		
KAF (*QA*(m^3/min)=20~35)	24.0$\times 10^3$	
(*QA*(m^3/min)=35~70)	200.0 〃	
KCP	540.0 〃	
KFA (*FKW*(Kw)=10~50)	28.0 〃	
(*FKW*(Kw)=50~200)	5.2 〃	
KFT	980.0 〃	

Table 2. Comparison of optimal computations under various conditions.

Number of vertices	Initial point $K_V \cdot p$	Initial point *QAF*	Initial objective function	EPS*	Final point $K_V \cdot p$	Final point *QAF*	Final** objective function	Number of iteration
			$\times 10^8$				$\times 10^8$	
	0.107	24.96	1.106					
3	0.119	15.79	1.075	0.005	0.116	10.52	1.063	24
	0.096	24.71	1.108	0.001	0.119	9.64	1.062	36
	0.107	24.96	1.106					
	0.119	15.79	1.075	0.005	0.116	9.77	1.062	40
4	0.104	18.94	1.08[illegible]	0.001	0.115	10.26	1.063	40
	0.096	24.71	1.108					
	0.093	32.46	1.131					
3	0.140	24.80	1.107	0.005	0.130	11.65	1.065	39
	0.049	32.25	1.168					

* convergence tolerance

** The final objective function is obtained when the two criteria decrease below EPS; the 1st criterion is $|(\phi_{max}-\phi_{min})/\phi_{max}|$ and 2nd one is $r_{av}/||a||$, provided:

r_{av}=average value of the distance between adjacent vertices

$||a||$=norm of centroid

Generally, it is difficult, in solving the non-linear optimization problem, to confirm whether the point whose stopping criteria satisfy the convergence tolerance is really optimal or not. Accordingly, the search should be carried out repeatedly under various conditions even when the modified complex method is used.

Actually, the above-mentioned difference in the value of the 3rd order below the decimal point depending on the initial condition reflects really the difficulty in judging the optimal point. For convenience, in this example the optimal point was assumed to be 1.062×10^8 Yen.

In this connection, one may urge that difference between the initial and final values of the objective function in Table 2 is so small, depreciating the applicability of this optimization. However, it should be mentioned that the initial points selected here are originally located near the optimal point, referring to the previous attempt,[8] in which the thorough-search method was used instead of the modified complex method.

The above argument will be made clear from Fig. 5 which illustrates the pattern of convergence behavior in this procedure; the ordinate is the value of the objective function, while the abscissa represents the number of iterations. It is evident from this iteration pattern that the objective function becomes larger than 1.3×10^8 Yen during the iteration, implying that the optimal value mentioned earlier ($=1.062\times10^8$) is considerably smaller than an arbitrary point which should satisfy both the explicit and implicit inequality constraints in this demonstration.

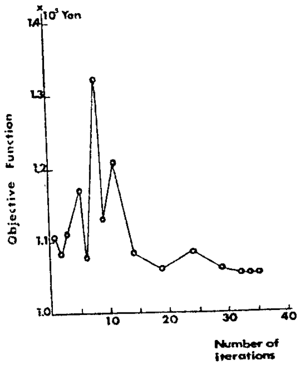

Fig. 5. Convergence of iterative search in the modified complex method (OPTIM).

Iteration here is defined as number of calculating the objective function by calling the subprogram "COS." Accordingly, at the start of the computation, the value of the objective function was present, corresponding to the 1st, 2nd, and 3rd iterations as shown in the figure (*cf.* the 1st row for the number of vertices=3 in Table 2). The objective function value in the figure, thereafter, was taken from that corresponding to a new point assumed by the repetitive manipulation as mentioned earlier in the modified complex method.

The next item of significance of this optimization is that the cost of fermenter which occupies around 50% of the total expenditures of the aeration and agitation was left intact in this example. If the fermenter volume could have been employed as another independent variable in view of a more comprehensive optimization program of the fermentation process, the merit of this sub-optimization of aeration and agitation should have been more revealed. This interesting aspect will be discussed separately.

In comparison with the complete (or thorough) search method which may require an enormous repetitions of calculation (more than thousands), this optimization program is considered to be more efficient for saving the time required for calculation.

The data in Table 3 suggest that the choice of aeration and agitation intensities more economic to a specific fermentation (*cf.* Fig. 2) does not agree with that of securing the maximum product concentration. Even though one may criticize that optimal result in the table, N=48 rpm for instance, seems to be incompatible with practical experience, the controversial point has originated actually from the use of Fig. 2 in this work. Undoutedly, the demonstration which may be subjected to the above-mentioned criticism does not de-

Table 3. Optimal results.

Objective function	1.062×10^8 Yen
Fixed cost	0.642×10^8 Yen
Raw material cost	0.382×10^8 Yen
Running cost	0.038×10^8 Yen
Independent variables	
$K_V\cdot p$	0.116 kg moles O_2/m^3hr
QAF	9.77 m^3/min
	(0.07 vvm)
Dependent variables	
P_g	77.78 HP
N	48 rpm
(two sets of impellers, $D_t/D_i=3$)	

preciate the applicability of the modified complex method to the optimization in the fermentation process.

Nomenclature

a	=empirical constant
$\|\|a\|\|$	=norm of centroid
b	=empirical constant
C_0	=cost of unit mass of raw material
D_i	=impeller diameter, cm, m
D_t	=vessel diameter, m
e_i	=unit cost of i-th utility
E_i	=utility required per batch
f	=vector-valued function
FKW	=power required for motor, Kw
F_r	=product concentration, kg/m^3
g	=vector-valued function
H_L	=liquid depth, m
I_m	=investment cost of m-th unit equipment
k	=number of vertices of the complex
KAF	=coefficient of cost estimation of air filter
KCP	=coefficient of cost estimation of air compressor
KFA	=coefficient of cost estimation of agitator
KFT	=coefficient of cost estimation of vessel
K_V	=volumetric coefficient of oxygen transfer, kg moles O_2/m^3 hr atm
N	=rotation speed of impeller, rpm
N_t	=number of batch cycles
p	=partial pressure of oxygen, atm
P_g	=power requirements of agitation in gassed system, HP
P_0	=power requirement of agitation without aeration, HP
PO	=annual production rate, kg
QA	=air delivery rate of compressor, m^3/min
QAF	=aeration rate, m^3/min, ml/min exclusively in Eq. (15)
r_{av}	=average value of the distance between adjacent vertices
U	=admissible set of decision vectors

V_L = working volume of fermenter, m^3
X = admissible set of state vectors
X_0 = raw materials expended per batch
Y = relative yield

Vector
$\boldsymbol{u}$ = decision vector
$\boldsymbol{x}$ = state vector

Subscript
c = centroid
max = maximum
min = minimum
new = new point
w = worst point

Greek letters
α = empirical constant
α_r = reflection factor

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