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Application of Modified Powell's Method to Estimation of Biochemical Parameter

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Adaptation of Powell's method to estimate the parameter in biochemical system was considered. Powell's algorithm was modified to parameter estimation in differential equation system. According to the accuracy of one-dimensional search methods in the algorithm, success and faults method and second polynomial approximation method were adopted as one-directional search method. And Powell's method was slightly modified by adding non-negative constraint condition to judging step. As the results of parameter estimation in model reaction system (differential equation system), the present program was able to estimate the parameter within ± 2 % error, even if ± 10 % white noise was included in experimental data.

INTRODUCTION

For the study of the mechanism and control mode of metabolism or biochemical system, it is dispensable to understand the dynamics of the system. The first sequence in the analysis of the biochemical system is the construction of a model scheme of the real enzymatic reaction, then parameters in the model scheme should be estimated from experimental data and the appropriateness of the model scheme should be discussed. One of the most useful methods for such an analysis is based on optimization technique. Many released optimization techniques can be classified into two groups, one group is consisted of the gradient method and the other the direct search method (Jacoby et *al.*, 1972).

Since biochemical systems are generally formulated by differential equations, various gradient methods have been frequently adopted to optimization technique. However, biochemical systems are essentially large and complex, and the model scheme of such complex systems may be formulated not only by differential equation, but by another equation, i.e., algebraic, difference and variational equations (Masaki *et al.*, 1977). For the complex biochemical systems, it is very difficult to formulate an equation on the gradient of the system, and further the gradient could be evaluated only by the numerical differentiation. It has been recognized that numerical differentiation induces easily many errors in evaluation of the gradient. Therefore, the direct search method which need not to evaluate the gradient seems to be much suitable for the analysis of dynamics of complex systems.

Modified Powell's method, a typical method using conjugate direction, is well known to have an ultimate fast convergence for the parameter estimation of a general quadratic function (Powell, 1964). In the present study, it was attempted to apply modified Powell's method to the optimization of reaction parameters in a biochemical system. Since parameters in biochemical systems must not have negative values, the most effort was made to introduce a non-negative constraint into modified Powell's method. In practice, first a certain enzymatic reaction was supported to be the model scheme and it was formulated by the ordinary differential equation. The differential equation was solved numerically using a set of parameter values and calculated time-courses were obtained. Next, the calculated time-courses were regarded as experimental data and the values of parameters (rate constants) were estimated reversely by modified Powell's method from the experimental data or calculated time-course.

CALCULATION

Modified Powell's algorithm

In the formulation of the modified method, f(P) represents value of a cost-function, P_i is vector of parameter, ε_i is vector of direction, λ_i is a scalar, suffix i indicates i-th iteration and n the number of parameters.

Algorithm of modified Powell's method may be represented as follows (Powell, 1964) :

(i) Consider n-dimensional vector. For $i=1, 2, \cdots, n$ calculate λ_i so that $f(P_{i-1}+\lambda_i\varepsilon_i)$ reaches a minimum and define $P_i=P_{i-1}+\lambda_i\varepsilon_i$.

(ii) Find the integer m, $1\leqq m\leqq n$, so that $f(P_{m-1})-f(P_m)$ is a maximum, and define $\Delta=f(P_{m-1})-f(P_m)$.

(iii) Calculate $f_3=f(2P_n-P_0)$, and define $f_1=f(P_0)$ and $f_2=f(P_n)$.

(iv) If either $f_3\geqq f_1$ or $(f_1-2f_2+f_3)(f_1-f_2-\Delta)^2\geqq\Delta(f_1-f_3)^2$, use the old direction $(\varepsilon_1, \varepsilon_2, \ldots\ldots \varepsilon_n)$ for the next iteration and use P_n for the next P_0.

(v) Otherwise, defining $\varepsilon=(P_n-P_0)$, calculate λ so that $f(P_n+\varepsilon\lambda)$ is a minimum, use $\varepsilon_1, \varepsilon_2, \cdots, \varepsilon_{m-1}, \varepsilon_{m+1}, \cdots, \varepsilon_n, \varepsilon$ as the directions and $P_n+\lambda\varepsilon$ as the starting point for the next iteration, starting again from i=l.

These steps are repeated until the convergence is satisfied.

One-directional search

In above mentioned modified Powell's method, the problem can be reduced to one-directional search. In the present program, three methods, ***A, B*** and C of one-directional search were combined and used.

A. *Second polynomial approximation method*

It has been recognized that a function can be generally approximated by second polynomial in neighborhood of the extremal value. Then, the true extremal value can be approximated by extremal value of second polynomial defined by three values of the function at least (Box *et al.*, 1969). Therefore, following manipulation of values of the function gives approximated extremal point,

minimum point = -v/w,

$$w=2(A(f(C)\ \text{--f(B))}\ +B(f(A)\ \text{-f(C))}\ +C(f(B)\ \text{--f(A)))/}$$
$$(A-B)(B-C)(A-C),$$
$$v=-1/2w(A+B)+(f(A)-f(B))/(A-B),$$

where A, *B* and C are the values of argument, f(A), f(B) and f(C) represent the values of the function.

B. Success and faults method

An upper bound to the length of step along one-direction is not limited in the conjugate direction methods. Therefore, in the present study, following algorithm of iteration is used to determine the length of step (Rosenbrok, 1960). The principle of this method is to select a step of arbitrary length, h, from the starting point x_0 and to evaluate the value of the function, f. If $f(x_0+h)\leqq f(x_0)$, then this trial is defined to be Success, and h is multiplied by factor 2. The other case, this trial is defined to be Faults, and h is multiplied by factor $-1/2$. This trial is repeated until the change in length of step is less than α.

C. Fibonacci search

If interval L which includes the point minimizing the function could be found, Fibonacci search gives the most narrow interval including minimizing point after N-evaluations, among various one-directional searches (Kiefer, 1953). The algorithm of Fibonacci search is formulated as follows : Assumed that interval *[a,, b,]* contains minimizing point and N is the number of evaluation. In N-th evaluation, interval is denoted by $L(N)$ and the maximum interval of uncertainly $[a_N, b_N]$ in which the minimizing point should be sought is defined by

$$d_{N-1}=1/2L(N-1),\quad d_N=1/2L(N-1)+\alpha,$$

and $$[a_N, b_N] = [a_{N-1}, a_{N-1}+d_{N-1}],$$

or $$[a_{N-1}+d_{N-1}, b_{N-1}],$$

according to whether

$$f(a_{N-1}+d_{N-1})\leqq f(a_{N-1}+d_N),$$

or $$f(a_{N-1}+d_{N-1})>f(a_{N-1}+d_N).$$

In (N-ii)-th evaluation, $i=(N-2),\cdots,$ 1 intervals $L(N-i)$ and $[a_{N-i}, b_{N-i}]$ are defined by

$$d_{N-i}=(A_i/A_{i+2})L(N-1-i),$$

and $$[a_{N-i}, b_{N-i}]=[a_{N-1-i}, b_{N-1-i}-d_{N-i}],$$

or $$[a_{N-1-i}+d_{N-i}, b_{N-1-i}],$$

according to whether

$$f(a_{N-1-i}+d_{N-i})\leqq f(b_{N-1-i}-d_{N-i}),$$

or $$f(a_{N-1-i}+d_{N-i})>f(b_{N-1-i}-d_{N-i}),$$

where A_i is the i-th Fibonacci sequence which is represented by

$$A_0=A_1=1,$$
$$A_N=A_{N-1}+A_{N-2}\qquad (N\geqq 2).$$

In first evaluation, d_1 is defined by

$$(A_{N-2}/A_N)L_1,\quad L_1=[a_1, b_1].$$

Modified judgement for new direction vector

In the present study, it was attempted to optimize the parameters in biochemical system represented by ordinary differential equation. It is well known that the parameters can not have negative value in biochemical system. Consequently it becomes to be the most important problem when the values of parameters have negative sign in the calculation process.

In modified Powell's algorithm, it may be that the values of parameters will become negative in judging step of new direction vector. In order to replacement of the vector ε_m by new direction vector $\varepsilon=(P_n-P_0)$, the following procedure was proposed in Powell's method: The direction vectors $\varepsilon_1, \varepsilon_2, \cdots, \varepsilon_n$ should be chosen to make the corresponding determinant as large as possible. Therefore, if new direction was adopted by replacement of one of old direction vectors, it will be proved that the direction which should be discarded, is $\varepsilon_m, 1\leqq m\leqq n$ where m is such that $f(P_{m-1})-f(P_m)$ is maximum.

Because $f(P_i)$ is a minimum in the direction ε_i, if ε_i is scaled, so that

$$\varepsilon_i A\varepsilon_i=1,$$

where $\boldsymbol{A}$ is the coefficient matrix which defined by

$$\mathrm{f(P)}=\boldsymbol{P^tAP+BP+C.}$$

The displacement from P_{i-1} to P_i is

$$[f(P_{i-1})-f(P_i)]\,\varepsilon_i=\lambda_i\varepsilon_i\,.$$

The direction can be defined by the iteration as

$$P_n-P_0=\mu\varepsilon,$$

where $\varepsilon A\varepsilon=1$.

Replacement of the vector ε_i by the vector ε effects the multiplication of directions by λ_i/μ. Consequently, the direction which λ_i is largest will be discarded, and new direction will be sited the direction ε_m.

Obviously this replacement should be made only if A, $\geqq\mu$. For the calculation of μ, the function f_1, f_2 and f_3 defined in algorithm are used with second polynomial approximation. Finally, criterion can be evaluated by following equation. Only if

$$f_3\geqq f_1,$$

or

$$(f_1-2f_2+f_3)(f_1-f_2-\Delta)\geqq 1/2\Delta(f_1-f_3)^2,$$

where $\Delta=\max_{\mathrm{m}}(f(P_{m-1})-f(P_m))$,

new direction should not be used for the next iteration.

It was known that in this step, negative value of $2P_n-P_0$ appeared frequently. Then, in the present program, this step was modified as follows: If $2P_n-P_0$ had negative value, $2P_n-P_0$ was replaced by non-negative vector in the same direction. And, instead of evaluation of $f_3\geqq f_1$ or $(f_1-2f_2+f_3)\ (f_1-f_2-\Delta)\geqq 1/2\Delta(f_1-f_3)^2$, μ was calculated actually by second polynomial approximation from f_1, f_2 and f_3 which was evaluated by non-negative vector. This process is diagramed in Fig. 1. Then, direction ε_i was replaced by a new direction ε, if $\lambda_i\geqq\mu$,

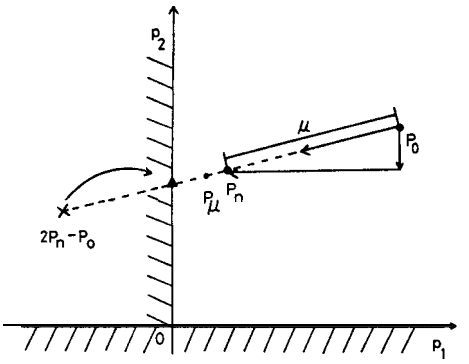

Fig. 1. Diagram of modified routine for judgement on new direction vector in parameter space. Both axes p_1 and p_2 indicate elements of the parameter vector, P_0 is the starting point and P_n is the end point of parameter vector in an iteration, P_n-P_0 is the vector of new direction, P_μ shows minimizing point on new direction vector and permissible region is first quadrant.

where $\lambda_i=\max_i(f(P_{i-1})-f(P_i))$.

This modification was added to the original judging step. And only if negative condition arises in calculation, this modification process was executed in the present program.

In the present study, calculation was executed by FACOM M-200 in Computer Center of Kyushu University.

ESTIMATION OF PARAMETERS

The accuracy of one-directional search method

In order to investigate accuracy of three methods of one-directional search, the parameters of following Rosenbrock's function

$$f(X)=100(x_2-x_1^2)^2+(1-x_1)^2+90(x_4-x_3^2)^2+(1-x_3)^2 +10.1(x_1-1)^2+(x_4-1)^2+19.8(x_2-1)(x_4-1)$$

were optimized using the program described above. The results of the optimization are shown in Table 1. The number in first column indicates the trial number in success and faults routine. Case 1 is for that in which only success and faults method was used as one-directional search. In Case 2, the success and faults method and Fibonacci search were used together. In Case 3, the success and faults method and second polynomial approximation were used. In Case 4, three methods were simultaneously used. As can be seen in Table 1, the minimum point of Rosenbrock's function was accurately estimated except for the Case 1. In all cases, the monotonous decreasing in the cost function was not realized by simple increasing of the trial number in success and faults routine. Typical examples of the mode of the decreasing in the cost function are shown in Fig. 2. As can be seen in Fig. 2, Cases 3 and 4

Table 1. Optimized values of Kosenbrock's function in four cases of one-directional search.

	No.*	x_1	x_2	x_3	x_4	Cost function	CPU time	No.**
Minimum point		1.0	1.0	1.0	1.0			
Case 1	5	0. 96	0.92	0.80	0. 69	0.17×10	**0.97** sec	13
	7	0.89	0.79	1.1	1.2	0.40×10^{-1}	1.13 sec	13
	10	-1. 3	1.7	0.30	0.072	0.68 x 10	1.14 sec	25
	11	1.0	1.0	1.0	1.0	0.25×10^{-7}	1.07 sec	15
	30	1.0	1.0	1.0	1.0	0.37×10^{-9}	0.97 sec	14
Case 2	5	0.83	0.73	1.0	1.0	0. 69	1.04 sec	15
	10	1.0	1.0	1.0	1.0	0.17×10^{-8}	1.04 sec	14
	30	1. 0	1. 0	1.0	1.0	0.52×10^{-11}	0.99 sec	12
Case 3	5	1. 0	1.0	1.0	1.0	0. 16 **x10-3**	1.18 sec	20
	10	1.0	1.0	1.0	1.0	0.78×10^{-16}	1.03 sec	13
	30	1. 0	1. 0	1.0	1.0	0.29×10^{-11}	1.04 sec	12
Case 4	5	1.0	1.0	1.0	1.0	0.40×10^{-12}	1.12 sec	14
	10	1.0	1.0	1.0	1. 0	0.71×10^{-16}	1.05 sec	12
	30	1.0	1.0	1.0	1.0	0.12 x10-s	1.03 sec	11

*: Trial number in success and faults routine.
**: Number of optimization.
Case 1: success and faults.
Case 2: success and faults + Fibonacci search.
Case 3: success and faults + second polynomial approximation.
Case 4: success and faults + Fibonacci search + second polynomial approximation.

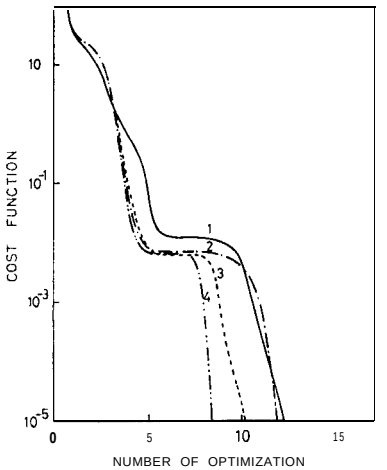

Fig. 2. Changes in the cost function with iteration.
1 : success and faults (ll-iterations).
2: success and faults (lo-iterations) +Fibonacci search.
3: ***success*** and faults (10-iterations) + second polynomial approximation.
4: success and faults (lo-iterations) +Fibonacci search + second polynomial approximation.

gave considerably good convergence. The success and faults method followed by second polynomial approximation (Case 3) was found to be the best among four cases, because the number of evaluation of the cost function was fewer

than other cases.

Estimation of rate constants in a model reaction system

In order to investigate the efficiency of the program developed in the present study, the parameter estimation was carried out using a supposed model of the reaction system. The time-courses were first calculated using the model system and to the value on the time-course at each time was added the randomly chosen value which was supposed to be the experimental error. The resulted values on time-courses synthesized as above were regarded as the experimental data. The values of parameters were estimated from the imaginary experimental data. Finally the efficiency was evaluated by the difference between the supposed parameter and the estimated parameter.

A. Reaction system

The model of reaction system was supposed to be open system consisted of four steps of first-order reaction with five rate constants. The model system is illustrated in Fig. 3, where A, B, C and D indicate reactants and k_i the rate constant.

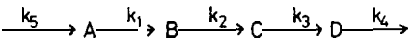

Fig. 3. Reaction model. For calculation of time-courses, $k_1=1.0$; $k_2=0.5$; $k_3=0.5$; $k_4=0.3$; $k_5=10.0$ were used, A, B, C and D: reactants.

The rate constants, $k_1=1.0$, $k_2=0.5$, $k_3=0.5$, $k_4=0.3$ and $k_5=10.0$ were adopted for the calculation of time-courses. For optimization, the cost function f was defined by

$$f(\boldsymbol{X})=\sum_{i}^{M}\sum_{j}^{N}(X_e(i,j)-X_c(i,j))^2$$

where $X_e(i, \mathrm{j})$ is the value of imaginary experimental data of i-th reactant at time j, and $X_c(i, \mathrm{j})$ is the optimized value of i-th reactant at time j. M is

Table 2. Imaginary experimental data synthesized from calculated time-course.

Concentration \ Time		0.0	3.0	6.0	9.0	12.0	15.0	18.0	21.0	24.0	27.0	30.0
0% error	A	100.0	14.5	10.2	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
	B	20.0	51.2	28.5	22.0	20.4	20.1	20.0	20.0	20.0	20.0	20.0
	C											
	D	10.0 10.0	46.8 38.3	37.8 58.3	26.9 54.4	22.45.7 2	20.39.5 6	20.2 36.2	34.6 20.0	20.0 33.9	20.0 33.6	33.20.04
±2.5% error	A	97.5	14.3	10.4	10.0	10.0	10.1	9.8	9.8	9.9	10.0	9.8
	B											
	C	20.9.8 0	52.47.3 5	27.37.4 9	22.27.2 1	22.19.9 1	20.20.2 4	20.20.3 4	20.20.5 4	20.5 20.3	20.20.5 2	20.3 19.6
	D	10.1	37.8	56.9	54.1	44.7	39.8	36.9	35.0	34.5	34.2	33.0
±5% error	B	95.0	14.1	10.5	10.1	10.1	10.2	9.5	9.6	9.8	9.9	9.6
	C	20.9.0 6	47.8 53.7	27.36.9 2	22.27.5 1	22.19.5 1	20.20.3 2	20.6 20.6	20.8 20.7	20.9 20.6	20.9 20.4	20.19.25
	D	10.2	37.2	55.5	53.9	43.7	40.0	37.6	35.4	35.2	34.9	32.5
±10% error	A	90.0	13.8	10.7	10.1	10.2	10.5	9.1	9.1	9.5	9.9	9.2
	B											
	C	20.1 9.2	56.2 48.9	35.25.9 9	22.3 28.1	21.18.6 9	20.4 19.8	21.2 21.0	21.5 21.7	21.2 21.9	20.7 21.9	21.1 18.4
	D	10.5	36.0	52.8	53.4	41.7	40.5	38.9	36.2	36.5	36.3	31.7

the total number of reactants and N the number of observation (time).

B. *Imaginary experimental data with error*

By considering real experimental data with error, the imaginary experimental data were set by introducing the random values of which the maximum was bounded at $\pm 0, \pm 2.5, \pm 5$ and $\pm 10\%$, respectively, of the values on the calculated time-courses (see row of 0 % error in Table 2).

C. ***Reversely estimation of rate constant***

The rate constants, $k_1, \cdots, k_5$ which had been originally supposed in the reaction model, were reversely estimated by the present program from the above mentioned imaginary experimental data. In the present program, Runge-Kutta-Gill method was adopted for solving the differential equations of the model, and the combined method of success and faults method and second polynomial approximation was used for one-directional search. The estimated rate constants after convergence are shown in Table 3. In the case of 0% error, the estimated value has no any difference from the postulated value after 8 iterations. In the cases of $\pm$ 2.5 % and $\pm$ 5 % errors, convergence was so fast that after 7 and 8 iterations convergence was completed, and the difference between estimated and postulated value was not more than 2 % in relative value. The maximum difference in the case of $\pm$ 10 % error was found to be -1.52 % in relative value, indicating modified Powell's method is excellent for the estimation of reaction parameter from the experimental data which include the white noise.

DISCUSSION

In the present program, one-directional search is the key part to convergence and accuracy of parameter estimation. As shown in Table 1 and Fig. 2, linear relationship cannot be found between increase in the trial number in success and faults routine and decrease of the cost function. Especially in Case 1, accuracy of estimation was insufficient at trial 5, 7 or 10, whereas the trial number 11 showed a good accuracy. Therefore, only using of the success

Table 3. Difference between true (supposed) value and optimized (estimated) value.

		Rate constant					cost function	No.*
		k_1	k_2	k_3	k_4	k_5		
True value		0.100 x 10	0.500	0.500	0.300	0.100 x 10^2		
Optimized value	$\pm 0\%$ error	0.100~10	0.500	0.500	0.300	0.100 $\times 10^2$	0.20 $\times 10^{-12}$	8
	Difference	$\simeq 0\%$	$\simeq 0\%$	$\simeq 0\%$	- 0 %	$\simeq 0\%$		
	12.5% error	0.101 $\times$ 10	0.497	0.498	0.302	0.101 x 10^2	0.15 x 10^2	7
	Difference	+1.0%	-0.62%	-0.34%	+0.60%	+0.59%		
	$\pm 5\%$ error	0.102 $\times$ 10	0.494	0.497	0.304	0.101 $\times 10^2$	0.58 $\times 10^2$	9
	Difference	+2.0%	-1. 2%	-0.68%	+1.2%	+1.2%		
	$\pm 10\%$ error	0.993	0.499	0.492	0.299	0.992 x 10	0.25 x 10^3	27
	Difference	-0.74%	-0.24%	-1.5%	-0.40%	-0.84%		

*: Number of optimization.

and faults method thought to give insufficient value at a small trial number. This is because the success and faults routine has possibility that a wide interval was always held during calculation or contained no minimizing point at a small number of trial. Accordingly, the method in which success and faults method is followed by other one-directional method, such as Cases 2, 3 and 4, was expected to be better with regard to the convergence.

In biochemical system, it has been recognized that there must be non-negative value of parameters. However, there may be the possibility in modified Powell's method that parameter takes negative value on judging step for new direction vector. Therefore, judging step was modified as described previously. As a result, the appearance of the negative value of parameter was almost removed from the process of computation. Thus, the revised program was able to be applied to the optimization of the value of parameters in differential system.

For differential system, the value of parameters was estimated by the program from imaginary experimental data including some error. As shown in Table 2, in spite of the existence of the errors, the difference between the values of the postulated and estimated parameters did not increase beyond 2 %. The negative value of parameter never appeared in the calculation in all cases providing for the modified judging step. Thus, it was concluded that even if data have some experimental error (white noise), the present program can be sufficiently used for the estimation of the parameters in differential equation.

REFERENCES

Box, M. J., D. Davies and W. H. Swann 1969 ***Non-linear Optimization Techniques.*** Imperial Chemical Industries Limited (England)

Jacoby, S. L. S., J. S. Kowalik and J. T. Pizzo 1972 ***Iterative Methods for*** Nonlinear ***Optimization Problems.*** Prentice-Hall, New Jersey (U.S.A.)

Kiefer. J. 1953 Sequential minimax search for a maximum. *Proc.* ***A.M.S.*** 4: 502-505

Masaki. A., Y. Aso, D. Koga and K. Hayashi 1977 Computer analysis of lysozyme-catalyzed reaction with chitooligosaccharide. ***J. Fac. Agr., Kyushu Univ., 21:*** 47-66

Powell, M. J. D. 1964 An efficient method for finding the minimum of a function of several variables without calculating derivatives. ***The Computer Journal, 7: 155-162***

Rosenbrock. H. H. 1960 An automatic method for finding the greatest or least value of a function. ***The Computer Journal, 3: 175-184***