

**TABU SEARCH FOR PARAMETER IDENTIFICATION  
OF AN FERMENTATION PROCESS MODEL**

Kalin Kosev<sup>1</sup>, Tania Trenkova<sup>2</sup>, Olympia Roeva<sup>1</sup>

<sup>1</sup>Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences

105 Acad. G. Bonchev Str., Sofia 1113, Bulgaria

E-mails: [kalin.kosev@yahoo.com](mailto:kalin.kosev@yahoo.com), [olympia@biomed.bas.bg](mailto:olympia@biomed.bas.bg)

<sup>2</sup>National Institute of Meteorology and Hydrology - Bulgarian Academy of Sciences

66 Tzarigradsko shose Blvd., Sofia 1784, Bulgaria

E-mail: [ttrenkova@gmail.com](mailto:ttrenkova@gmail.com)



**Abstract**

*In this paper the problem of parameter estimation using tabu search algorithm is examined. A case study considering the estimation of the parameters of a nonlinear dynamic model of E. coli fermentation is taken as a test problem. The parameter estimation problem is stated as a nonlinear programming problem. This problem is known to be frequently ill-conditioned and multimodal. Thus, traditional (gradient-based) local optimization methods fail to arrive at satisfactory solutions. To overcome this limitation, the use of tabu search algorithm is explored. Parameters of the TS algorithm are tuned based on several pre-tests. The model parameter estimates with high accuracy are obtained applying proposed tuned TS.*

**Key words:** Tabu search, Parameter identification, Fermentation Processes

**1. INTRODUCTION**

Mathematical optimization can be used as a computational engine to arrive at the best solution for a given problem in a systematic and efficient way [12]. In the context of fermentation processes, coupling optimization with suitable simulation modules opens a whole new area of opportunities. Fermentation processes are complex highly nonlinear dynamic systems and their modeling and optimization is a complicated and rather time consuming task. This mathematical problem is a big challenge for traditional local optimization methods. As an alternative to surmount the parameter estimation difficulties the global optimization methods are used.

Global optimization methods can be roughly classified as deterministic and stochastic strategies [12]. There are many different kinds of stochastic methods for global optimization, but the following groups must be highlighted: adaptive stochastic methods; clustering methods; evolutionary computation; simulated annealing, tabu search and other metaheuristics [12].

Tabu search (TS) is a metaheuristic algorithm that can be used for solving combinatorial optimization problems attributed to Fred W. Glover [9]. TS uses a local or neighborhood search procedure to iteratively move from a solution  $x$  to a solution  $x'$  in the neighborhood of  $x$ , until some stopping criterion has been satisfied. To explore regions of the search space that would be left unexplored by the local search procedure, TS modifies the neighborhood structure of each solution as the search progresses.

TS is dramatically changing our ability to solve problems of practical significance. Current applications of TS span the realms of resource planning, telecommunications, VLSI design, financial analysis, scheduling, space planning, energy distribution, molecular engineering, logistics, pattern classification, flexible manufacturing, waste management, mineral exploration, biomedical analysis, environmental conservation and scores of others [14]. TS has been widely used for combinatorial optimization [16] but its use is very limited in continuous optimization [4, 10, 11, 15].

In this study a TS algorithm examined in solving the parameter estimation problem of *E. coli* fermentation process is proposed. Applying the TS algorithm a set of optimal model parameters values are obtained.

## 2. STATEMENT OF THE PARAMETER IDENTIFICATION PROBLEM

Parameter estimation problem of fermentation processes models is stated as minimizing a cost function. The cost function measures the goodness of the model fit with respect to a given experimental data set, subject to the dynamics of the system (acting as a set of differential equality constraints) plus possibly other algebraic constraints [5]. Generally, the formulation is:

Find  $p$  to minimize

$$J = \int_0^{t_f} (y_{exp}(t) - y_{mod}(p, t))^T W(t) (y_{exp}(t) - y_{mod}(p, t)) dt \rightarrow \min \quad (1)$$

subject to

$$f\left(\frac{dX}{dt}, x, y, p, v, t\right) = 0 \quad (2)$$

$$x(t_0) = x_0 \quad (3)$$

$$h(x, y, p, v) = 0, \quad g(x, y, p, v) \leq 0 \quad (4)$$

$$p^L \leq p \leq p^U \quad (5)$$

where  $J$  is the cost function to be minimized,  $p$  is the vector of decision variables of the optimization problem, the set of parameters to be estimated,  $y_{exp}$  is the experimental measure of a subset of the (so-called) output state variables,  $y_{mod}(p, t)$  is the model prediction for those outputs,  $W(t)$  is a weighting (or scaling) matrix,  $x$  is the differential state variables,  $v$  is a vector of other (usually time-invariant) parameters that are not estimated,  $f$  is the set of differential and algebraic equality constraints describing the system dynamics (i.e., the nonlinear process model), and  $h$  and  $g$  are the possible equality and inequality path and point constraints that express additional requirements for the system performance. Finally,  $p$  is subject to upper and lower bounds acting as inequality constraints.

Because of the nonlinear and constrained nature of the system dynamics, these problems are very often multimodal. Therefore, if this problem is solved via standard local methods, such as the standard Levenberg-Marquardt method or Nelder-Mead Simplex search method, it is very likely that the solution found will be of local nature. To avoid this fact metaheuristic TS algorithm is realized.

### 3. BACKGRAUND OF THE TABU SEARCH ALGORITHM

A pseudo code of TS is presented as:

**Step 1. Initialization**

Set  $k = 1$   
Generate initial solution  $S_0$   
Set  $S_1 = S_0$ , then  $G(S_1) = G(S_0)$

**Step 2. Moving**

Select  $S_c$  from neighborhood of  $S_k$   
IF move from  $S_k$  to  $S_c$  is already in TL THEN  
     $S_{k+1} = S_k$   
    GOTO Step 3  
END IF  
IF  $G(S_c) = G(S_0)$  THEN  
     $S_0 = S_c$   
END IF  
Delete the TL move in the bottom of TL  
Add new Tabu Move in the top of TL  
GOTO Step 3

**Step 3. Next iteration**

Set  $k = k + 1$   
IF  $k = N$  THEN  
    STOP  
ELSE  
    GOTO Step 2  
END IF

TS starting from one initial solution and iteratively generate new solution to search through its neighborhood. The search space of a TS heuristic is simply the space of all possible solutions that can be considered during the search.

Closely linked to the definition of the search space is that of the neighborhood structure. At each iteration of TS, the local transformations that can be applied to the current solution, denoted  $S$ , define a set of neighboring solutions in the search space (the neighborhood of  $S$ ) [7, 8].

In general, for any specific problem, there are many possible neighborhood structures. This follows from the fact that there may be several plausible neighborhood structures for a given definition of the search space [7, 8].

In TS, acceptance of moving to other solution in neighborhood is deterministic. Records of move, called Tabu Move, are kept in a list, called Tabu List (TL). The TLs are historical in nature and form the Tabu search memory. The role of the memory can change as the algorithm proceeds. At initialization the goal makes a coarse examination of the solution space, known as 'diversification', but as candidate locations are identified the search is more focused to produce local optimal solutions in a process of 'intensification'. In many cases the differences between the various implementations of the Tabu method have to do with the size, variability, and adaptability of the Tabu memory to a particular problem domain [2, 3, 6].

Before generating the neighborhood, TS move will be checked in TL. After new solution neighborhoods generated, the best solution on its iteration will be chosen as the parent for the next solutions generation.

While central to TS, tabus are sometimes too powerful: they may prohibit attractive moves, even when there is no danger of cycling, or they may lead to an overall stagnation of the searching process. It is thus necessary to use algorithmic devices that will allow one to cancel tabus [7, 8]. These are called aspiration criteria. The simplest and most commonly used aspiration criterion (used in here presented TS implementation) consists in allowing a move, even if it is tabu, if it results in a solution with an objective value better than that of the current best-known solution (since the new solution has obviously not been previously visited) [7, 8]. The search has to be stopped at some point, i.e. the termination criterion has to be defined. The most commonly used stopping criteria in TS are [7, 8]: after a fixed number of iterations (or a fixed amount of CPU time); after some number of iterations without an improvement in the objective function value (the criterion used in most implementations); when the objective reaches a pre-specified threshold value (used here).

#### 4. PARAMETER IDENTIFICATION OF *ESCHERICHIA COLI* FED-BATCH FERMENTATION MODEL

The optimization problem consists of the estimation of 3 kinetic parameters of a nonlinear dynamic model formed by 3 ordinary differential equations (6) – (8) describe the alteration of the process variables with time.

The mathematical formulation of the nonlinear model of *E. coli* fermentation is described according to the mass balance as follows [13]:

$$\frac{dX}{dt} = \mu_{max} \frac{S}{k_s + S} X - \frac{F}{V} X \quad (6)$$

$$\frac{dS}{dt} = -\frac{1}{Y_{SX}} \mu_{max} \frac{S}{k_s + S} X + \frac{F}{V} (S_{in} - S) \quad (7)$$

$$\frac{dV}{dt} = F, \quad (8)$$

where:  $X$  is the concentration of biomass, [g/l];  $S$  – concentration of substrate (glucose), [g/l];  $F$  – feeding rate, [l/h];  $V$  – bioreactor volume, [l];  $S_{in}$  – initial concentration of substrate in the feeding solution, [g/l];  $\mu_{max}$  – maximum values of the specific growth rates, [h<sup>-1</sup>];  $k_s$  – saturation constant, [g/l];  $Y_{SX}$  – yield coefficient, [g.g<sup>-1</sup>].

The global optimization problem is stated as the minimization of a distance measure  $J$  between experimental and model predicted values of the state variables, represented by the vector  $y$ :

$$J = \sum_{i=1}^n \sum_{j=1}^m \left\{ \left[ y_{exp}(i) - y_{mod}(i) \right]_j \right\}^2 \rightarrow \min, \quad (9)$$

where  $n$  is the number of data for each variable,  $m$  is the number of variables,  $y_{exp}$  represents the known experimental data, and  $y_{mod}$  is the vector of states that corresponds to the predicted theoretical evolution using the model with a given set of the 3 parameters.

In order to increase the performance of the TS algorithm it is necessary to provide the adjustments of the parameters depending on the considered problem. With the appropriate choice of the algorithm settings the accuracy of the decisions and the computing time could be optimized to a considerable degree. Parameters of the regarded algorithm are tuned based on several pre-tests according considered here parameter identification problem. After tuning procedures the main TS parameters are set to the optimal settings, presented in the Table 1.

**Table 1.** Tabu Search parameters

| Parameter                                | Value                                                   |
|------------------------------------------|---------------------------------------------------------|
| Simplex edge length (SEL)                | $0.1 * \min(\text{upper limits} - \text{lower limits})$ |
| Ratio of accepting diversification point | 1                                                       |
| Maximum number of iteration              | $100 * \text{number of variables}$                      |
| Termination accuracy                     | $10^{-6}$                                               |
| Number of tabus in TL (TN)               | $5 * \text{number of variables}$                        |
| TR radius                                | $0.01 * \text{SEL}$                                     |
| Region radius                            | $2 * \text{SEL}$                                        |
| Number of best points saved in TL        | $\text{TN} / 2.5$                                       |

All the computations are performed using a PC/Pentium IV (3.00 GHz) platform running Windows XP. Based on real experimental data for *E. coli* MC4110 fed-batch fermentation process a model parameter identification is performed applying TS algorithm. The experiment is carried out in the *Institute of Technical Chemistry, University of Hannover* [1]. On the basis on feeding rate data, off-line measurements of biomass and on-line measurements of substrate (glucose) parameter estimation of mathematical model Eq. (6) – Eq. (8) is carried out. The received parameter estimates are presented in Table 2.

**Table 2.** Results of the model parameter estimation

| Parameter            | Tabu Search results |         |
|----------------------|---------------------|---------|
|                      | average             | best    |
| $J$                  | 9.3952              | 6.6408  |
| CPU time (s)         | 42.5625             | 45.3438 |
| Number of iterations | 371                 | 384     |
| $\mu_{\max}$         | 0.4965              | 0.4797  |
| $k_s$                | 0.0314              | 0.0175  |
| $1/Y_{sx}$           | 2.0193              | 2.0099  |

The parameter estimation presented in Table 2 are adequate and meet the physical sense, they bear. Fig. 1 and Fig. 2 present simulation results for the considered best decision vector. As can be seen the correlation between the experimental and predicted model concentrations of the process variables is very good.

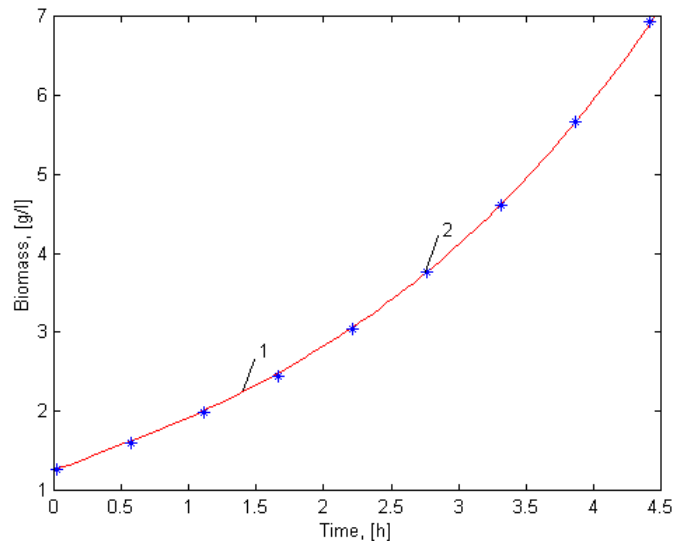


**Fig. 1.** Experimental (2) and model predicted data (1) for biomass.

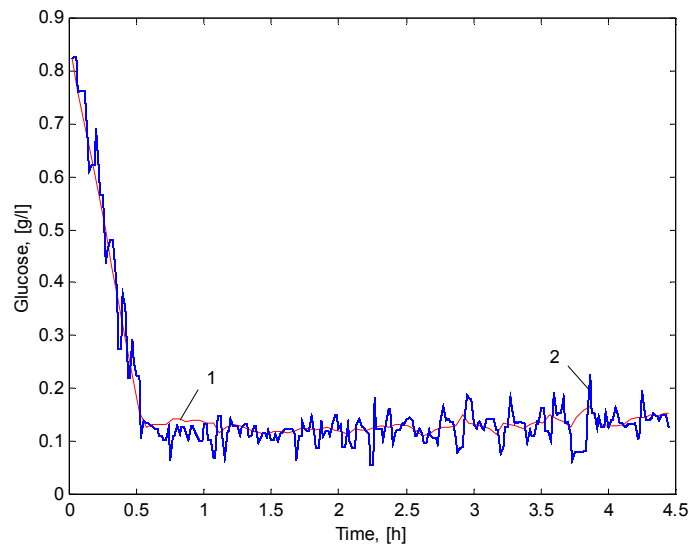


**Fig. 2.** Experimental (2) and model predicted data (1) for glucose.

The results show that TS algorithm manages to find solution accuracy which is commensurate to a solution obtained by a genetic algorithm for example. Compared to the results presented in [13] it can be shown that the presented here TS algorithm achieved optimization criterion accuracy closer to observed by genetic algorithm. In the same time the TS is around four-five times better than examined

genetic algorithm. For the solution of considered problem TS needs approximately 45 s and achieves  $J = 6.64$ . In comparison genetic algorithm solves the problem for around 200 s and obtains  $J = 6.54$ .

## 5. CONCLUSION

In this work a TS algorithm is proposed for a parameter identification of a nonlinear model of fed-batch cultivation process of *E. coli*. Parameters of the TS algorithm are tuned based on several pre-tests. The model parameter estimates with high accuracy are obtained applying proposed tuned TS. Based on the performed numerical experiments it can be drawn the following conclusions:

1. The TS algorithm finds sufficiently accurate solution of the given problem.
2. The TS algorithm is characterized by fast convergence, which is a big advantage in online applications.
3. The TS algorithm can be used as a metaheuristic method for finding good initial conditions for start of classical optimization methods. These methods are characterized by high accuracy if the solution search starts from good initial conditions.

## ACKNOWLEDGEMENTS:

This work has been partially supported by the Bulgarian National Scientific Fund under the Grants DID 02/29 "Modeling Processes with Fixed Development Rules (ModProFix)" and DMU 02/4 "High Quality Control of Biotechnological Processes with Application of Modified Conventional and Metaheuristics Methods".

## REFERENCES

1. Arndt, M., Hitzmann, B. (2001) Feed forward/feedback control of glucose concentration during cultivation of *Escherichia coli*, Proceedings of the 8th IFAC Int. Conf. on Comp. Appl. in Biotechn., Quebec City, Canada, pp. 425-429.
2. Balicki, J. (2007) Tabu Programming for Multiobjective Optimization Problems, International Journal of Computer Science and Network Security, 7(10), pp. 44-51.
3. Battiti, R., Tecchiolli, G. (1994) The Reactive Tabu Search, ORSA Journal on Computing, 6(2), pp. 126-140.
4. Chelouah, R., Siarry, P. (2000). Tabu search applied to global optimization, European Journal of Operational Research, 123, pp. 256-270.
5. Christodoulos, A.F., Pardalos, P.M. (2004) Frontiers in Global Optimization, Springer, 597 p.
6. Dave, P.H., Dave, H.B. (2007) Design and Analysis of Algorithms, Pearson.
7. Gendreau, M. (2002) An introduction to tabu search, In Handbook of Metaheuristics, (F. Glover and A. Gary (Eds.)), Kluwer Academic Publishers, pp. 37-54.
8. Gendreau, M., Potvin, J.-Y. (2010) Handbook of Metaheuristics, Springer, 648 p.
9. Glover, F., Laguna, M. (1997) Tabu Search, Kluwer Academic Publishers, Boston.
10. Lin, B., Miller, D.C. (2004a) Solving heat exchanger network synthesis problems with tabu search, Computers and Chemical Engineering, 28, pp. 1451-1464.

Journal of International Scientific Publications:  
Materials, Methods & Technologies, Volume 6, Part 2

11. Lin, B., Miller, D.C. (2004b) Tabu search algorithm for chemical process optimization, Computers and Chemical Engineering, **28**, pp. 2287-2306.
12. Moles, C.G., Mendes, P., Banda, J.R. (2003) Parameter Estimation in Biochemical Pathways: A Comparison of Global Optimization Methods, Genome Research, **13**, pp. 2467-2474.
13. Roeva, O., Pencheva, T., Hitzmann, B., Tzonkov, St. (2004) A Genetic Algorithms Based Approach for Identification of *Escherichia Coli* Fed-batch Fermentation, Bioautomation, **1**, pp. 30-41.
14. Srinivas, M., Rangaiah, G.P. (2007) A study of differential evolution and Tabu search for benchmark, phase equilibrium and phase stability problems, Computers and Chemical Engineering, **31**, pp. 760-772.
15. Teh, Y.S., Rangaiah, G. P. (2003) Tabu search for global optimization of continuous functions with application to phase equilibrium calculations, Computers and Chemical Engineering, **27**, pp. 1665-1679.
16. Youssef, H.M., Sait, S., Adiche, H. (2001) Evolutionary algorithm, simulated annealing and tabu search: A comparative study, Engineering Applications of Artificial Intelligence, **14**, pp. 167-181.