Appl Biochem Biotechnol (2010) 162:1350–1361
DOI 10.1007/s12010-009-8895-2

Evaluation of Lipase Production by Genetic Algorithm and Particle Swarm Optimization and Their Comparative Study

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Received: 3 October 2009 / Accepted: 21 December 2009 /
Published online: 23 January 2010

Abstract This paper presents the nature-inspired genetic algorithm (GA) and particle swarm optimization (PSO) approaches for optimization of fermentation conditions of lipase production for enhanced lipase activity. The central composite non-linear regression model of lipase production served as the optimization problem for PSO and GA approaches. The overall optimized fermentation conditions obtained thereby, when verified experimentally, have brought about a significant improvement (more than 15 U/gds (gram dry substrate)) in the lipase titer value. The performance of both optimization approaches in terms of computational time and convergence rate has been compared. The results show that the PSO approach (96.18 U/gds in 46 generations) has slightly better performance and possesses better convergence and computational efficiency than the GA approach (95.34 U/gds in 337 generations). Hence, the proposed PSO approach with the minimal parameter tuning is a viable tool for optimization of fermentation conditions of enzyme production.

Keywords Optimization · Lipase · Fermentation · Genetic algorithm · Particle swarm optimization

Introduction

Lipases are glycerol ester hydrolases (E.C. 3.1.1.3), which hydrolyze ester linkages of glycerides at water–oil interface [1]. The increasing demand of lipases in swiftly growing biotechnology industries is attributed to their efficiency in catalyzing hydrolysis along with various reverse reactions, such as esterification, transesterification, and aminolysis, in organic solvents [2]. Moreover, the endowed substrate specificity, regioselectivity, and

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enantioselectivity of microbial lipases contribute to their catalytic activity under mild temperature conditions with reduced side products at low waste treatment costs [3]. The activity retainment in organic solvents and their catalytic promiscuity extend their range of application as the commercial biocatalysts in industry with surpass of applications [4–9].

Thermostable fungal lipases such as lipases secreted by *Rhizopus oryzae* are quite stable under non-natural conditions such as high temperatures and nonaqueous organic solvents [10] and thus highly advantageous for industrial biotechnological applications. The relatively prohibitive cost of native enzyme has been the chief obstacle hindering more rapid expansion of industrial lipase technology on a large scale. Production of *Rhizopus* lipases through solid-state fermentation (SSF), by utilizing agricultural residues as substrates, represents one of the promising options for production of bulk inexpensive lipases as far as energy requirements, volumetric productivity, and product recovery are concerned [11, 12]. Even though some work has been done on *Rhizopus* lipases, these research efforts have been directed mainly toward production of lipases by submerged fermentation [13, 14], utilization of traditional gradient-based approaches for selection of solid-state fermentation conditions [15, 16], determination of kinetic parameters, structural characterization [17], sequencing, and cloning of lipase genes [18, 19]. Several authors reported the statistical optimization of lipase production. Rathi et al. [20] utilized statistical approach for the medium optimization of hyperthermostable lipase production from *Burkholderia cepacia.* An enhanced productivity was reported with extracellular lipase production by *Bacillus sphaericus* through sequential optimization of culture medium by statistical approach [21]. The superiority of response surface methodology (RSM) over one-variable-at-a-time (OVAT) approach was also demonstrated with optimization of lipase production by *R. oryzae* KG-10 [22] and *Serratia marcescens* SB08 [23].

Evolutionary and swarm intelligence based optimization approaches such as genetic algorithm (GA) and particle swarm optimization (PSO) have attracted a great deal of attention in recent times. With their better global search abilities, these techniques successfully overcome the local optima obstacle and thus replace the traditional gradient optimization approaches [24]. These optimization approaches can find global optima more quickly through cooperation and competition among the population of potential solutions of the search space even for complex optimization problems such as fermentation process [25]. GA, originally developed by Holland, is a computerized search and optimization technique works based on the "survival of the fittest" concept of natural selection namely Darwinian evolution [26]. PSO, proposed by Kennedy and Eberhart in 1995, is a swarm intelligence optimization based on the simulation of the social behavior of birds within a flock, whose basic thinking was to find the optimal value through cooperation and sharing information among individuals of swarm [27]. Compared to other evolutionary computational algorithms, PSO is easy to implement, faster at achieving high-quality solutions, and more flexible in balancing global and local exploration [28]. Liua et al. [29] utilized neural network and quantum-behaved particle swarm optimization algorithm for optimization of culture conditions of hyaluronic acid production by *Streptococcus zooepidemicus.* The optimization of α-amylase and protease production through genetic algorithm and particle swarm optimization approaches was reported by Skolpapa et al. [30].

The present research work focuses on the utilization of GA and PSO approaches for optimization of fermentation conditions of lipase production due to their robustness in solving the non-linear problems. As far as we are aware, this is the first report on optimization of fermentation conditions for lipase production through GA and PSO approaches.

Materials and Methods

Materials and Microorganism

p-Nitrophenyl palmitate was procured from Sigma, USA. The culture media components were purchased from Hi Media Laboratories, Mumbai, India. Dimethyl sulfoxide (DMSO) and all other reagents were of AR grade and procured from Merck, India. A lipolytic fungal strain of *R. oryzae* NRRL 3562 was isolated from the local soil of AGFE Department, IIT Kharagpur, and maintained on potato dextrose agar medium. The 3-day-old spore suspension of 6×10^5 spores/ml of *R. oryzae* NRRL 3562 was used as an inoculum.

Solid-State Fermentation

Sieved, medium-sized wheat bran was moistened with Czapek-dox medium (supplemented with 5% glucose and 10% coconut oil) in different solid to liquid ratio (1:0.5–1:2.5) with a moisture % of 60–100, and pH (5–7) was taken in a 100-ml Erlenmeyer flask and autoclaved at 121 °C for 20 min. The autoclaved substrate was inoculated with 6×10^5 spores/ml and incubated at different incubation time (3–7 days) and temperature (25–40 °C). After incubation period, the fermented biomass was soaked in 30% DMSO in Tris–HCl (30 mM, pH 8.0) and placed for 2 h at 30 °C. The soaked fermented biomass was squeezed through cheese cloth and was centrifuged at 6,987×*g* for 10 min at 4 °C. The clear supernatant obtained after centrifugation was used as the extracellular enzyme.

Lipase Assay

Lipase activity was determined spectrophotometrically using *p*-Nitrophenyl palmitate as the substrate [9]. One unit (U) of enzyme is defined as the amount of enzyme that liberates 1 μmol of *p*-nitrophenol per minute under the assay conditions. Enzyme activity is expressed in U/gds (gram dry substance).

Optimization Methodology

Optimization is the act of obtaining the best result possible or the effort for achieving the optimal solution under a given set of circumstances. The traditional optimization methods approaches are not robust and found hard to solve complex non-linear problems such as fermentation process by inclining toward a local optimal solution [31]. Due to the fact that the present research work has intended to optimize the lipase production through evolutionary and swarm intelligence-based optimization approaches such as GA and PSO. In a general case of optimization, the problem must first be formulated as a mathematical model, and then the system to be optimized must be defined [32]. Hence, in the present work, the experimentally validated lipase production non-linear RSM model has been utilized for the optimization purpose, which gives the relationship between several explanatory variables and one or more response variables by through a second-order polynomial quadratic equation [33].

Lipase production through solid-state fermentation mainly depends upon the process variables namely temperature (°C), liquid to solid ratio, pH, and incubation time (day). The non-linear RSM model of lipase production based on central composite design

with an adjusted R^2 value of 95.0% (data not shown) can be written in uncoded form as follows:

$$\begin{aligned}\mathrm{La} = {} & -842.551 + 31.6692^{\circ} + 103.673B + 75.2450C + 41.1417D - 0.381250AB + \\ & 1.10875AC - 0.156125AD + 0.687500BC + 2.93375BD + 4.61875CD - 0.508562A^2 - \\ & 35.9412B^2 - 13.0713C^2 - 6.66031D^2\end{aligned} \tag{1}$$

where A, B, C, and D represent the input process parameters namely temperature (°C), liquid to solid ratio, pH, and incubation time (day), respectively.

Evolutionary Intelligence-Based Optimization Approach

In the present study, a binary-coded GA was used to optimize the fermentation process of *R. oryzae* NRRL 3562. Genetic algorithms are search and optimization procedures, extensively used in the optimization of various problem domains [34, 35]. The operation of GA begins with a randomly generated initial population (N) of strings (that is, binary-coded individuals) (Fig. 1). The fitness of each individual string is evaluated with respect to the given objective function. Then, this initial population is operated by the three GA-parameters —reproduction, crossover (P_c), and mutation (P_m)—for creating a better solution. Reproduction facilitates the formation of mating pool selected from the population based on the fitness value. The mating pairs participating in crossover were selected randomly and exchanged properties between the two parents to form two children solutions. The local minima (if any) can be avoided with mutation, which brings a local change to the solution. This new population is further evaluated and tested for some termination criteria. As there are four process variables, each variable is represented with the help of ten bits. Therefore, 40 bits are used to represent a GA string as shown below.

$$\underbrace{10\ldots11}_{A}\,\underbrace{01\ldots01}_{B}\,\underbrace{11\ldots10}_{C}\,\underbrace{01\ldots10}_{D}$$

Swarm Intelligence-Based Optimization Approach

Due to the simple concept, easy implementation, and quick convergence, nowadays, PSO has gained much attention in solving many complex problems [36, 37]. In the present study, MOPSO-CD [38], a variant of PSO and has been utilized for the optimization problem of lipase production. The present approach incorporates the crowding distance (the average distance of its two neighboring solutions) [39] and mutation operators in to the simple PSO, which affects the global best criteria and enhances the exploring capability of algorithm by preventing the premature convergence problem of PSO algorithm [40]. Based on the global best value, the crowding distance operator deletes the non-dominant solution of the repository. The working procedure of the particle swarm optimization is summarized in Fig. 2. At each generation, the adjustment of the flight of each particle is based on the subdivision of the swarm. The velocity and position vectors changes are done like the following.

The new velocity "$V[i]$"

$$V[i] = W \times V[i] + R_1[\mathrm{P}_{\mathrm{best}}(i) - P(i)] + R_2 \times [A(\mathrm{G}_{\mathrm{best}}) - P(i)] \tag{2}$$

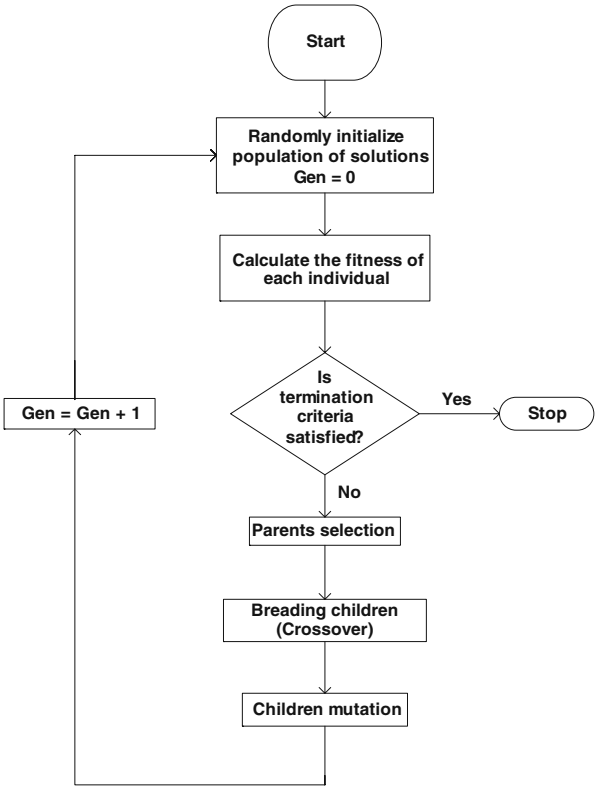

Fig. 1 Flow chart of simple genetic algorithm

where W is the inertia weight, which is equal to 0.4, R_1 and R_2 are the random numbers in the range of [0–1], $P_{best}(i)$ is the best position that the particle i reached and, $A(G_{best})$ is the global best guide for each dominated solution

1. The new position of "$P[i]$"

$$P[i] = P[i] + V[i] \tag{3}$$

The parameters, namely, swarm size, number of generations, inertia weight (W), social components R_1 and R_2, and repository size, play an important role in the present approach.

Results and Discussion

Optimization determines the values of independent variables that result in an optimal value of a dependent variable. In solid-state fermentation, the fermentation variables such as temperature, solid to liquid ratio, pH, and incubation time play a vital role on the enzyme production. From the OVAT approach (Table 1), a lipase activity of 80.42 U/gds was obtained with the selected parameters of 35 °C temperature of solid to liquid ratio of 1:4, pH of 6.0, and incubation time of 5 days (data not shown). The effect of fermentation variables on lipase production was also reported by several researchers by utilizing the

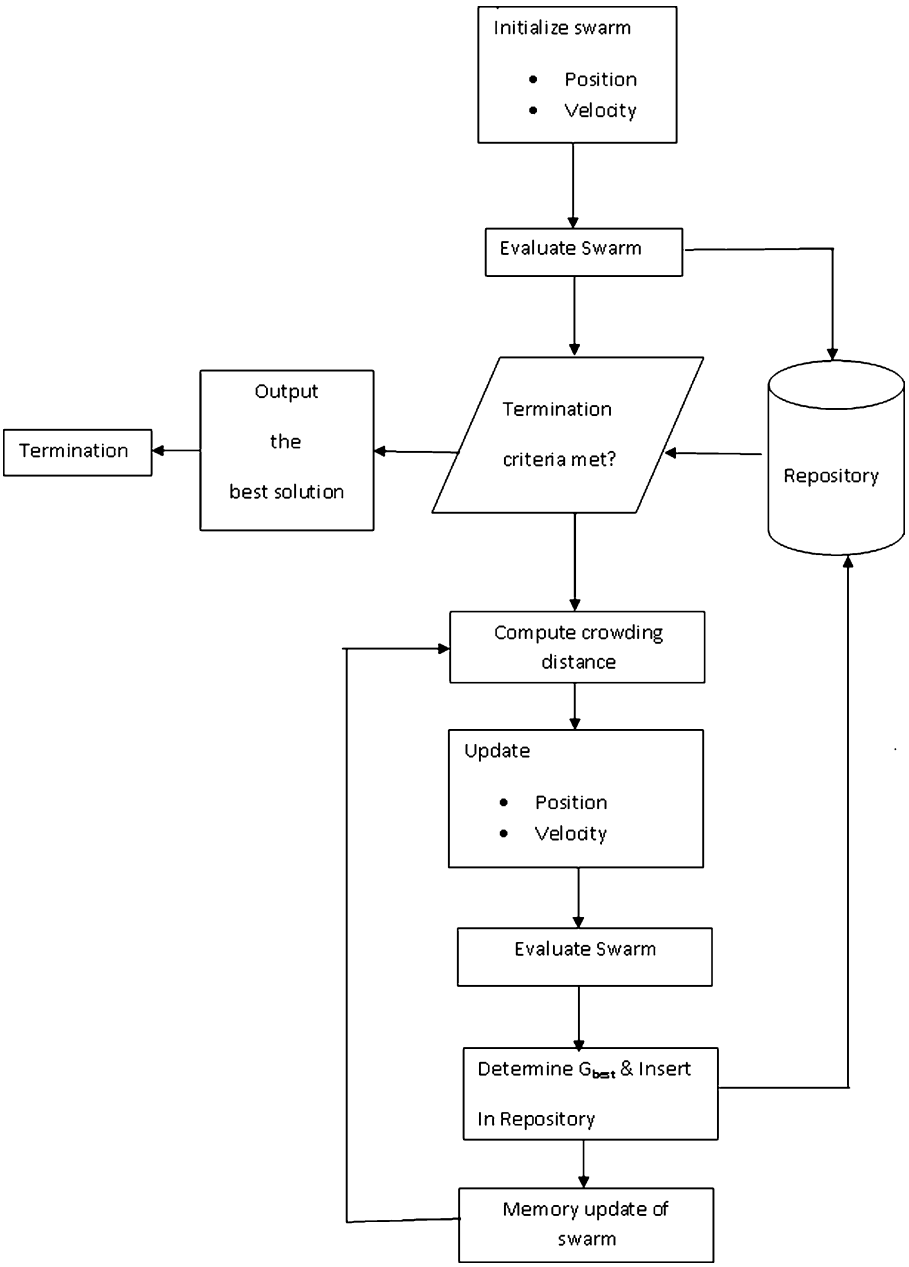

Fig. 2 Sequence of events in particle swarm optimization

OVAT and statistical gradient-based approaches. OVAT approach is helpful if the variables are independent of each other. But in case of any system such as fermentation process, the variables exert their influence on the process. The level of one variable may well modify the influence of other variable, which can lead both to compensatory and to seducingly poor results, whereas the gradient-based optimization approaches will stuck to local optima due

Table 1 Experimental and predicted lipase activity (U/gds) with optimal variable conditions of OVAT, GA, and PSO approaches.

Approach	Parameters of lipase production				Lipase activity (U/gds)	
	Temperature (°C)	*L*/*S*	pH	Incubation time (day)	Predicted	Experimental
OVAT	35.0	1.4	6	5	–	80.42
GA	35.6	1.5	5.29	4.82	96.89	95.34
PSO	35.58	1.49	5.28	4.83	96.91	96.18

to the premature convergence. Hence in the present work, the evolutionary and swarm intelligence-based global optimization approaches, which are capable of handling the local optima problem with their parallel search [41], are utilized for optimization of lipase production.

Evolutionary Intelligence-Based Optimization Approach

In the present study, lipase activity (La) model of *R. oryzae*3562 was posed as an optimization problem for maximizing the lipase activity. The maximization problem was converted to minimization problem as given below.

$$\text{Minimize} = \frac{1}{\text{Maximize(La)}}$$

$$\text{subject to } 30 \leq 40.1 \leq B \leq 2.5 \leq C \leq 6.4 \leq D \leq 6.$$

where La indicates lipase activity (Eq. 6), and *A*, *B*, *C*, and *D* represent the uncoded values of the variables temperature, liquid to solid ratio, pH, and incubation time, respectively. A systematic study was conducted to determine the GA parameters responsible for optimal value of lipase activity. In the present study, tournament selection of size 2, uniform crossover probability (p_c) of 0.5, bit-wise mutational probability (p_m) of 0.0009, population size of 80, and maximum number of generations of 337 were employed in search of optimal values of the process parameters for the solid-state fermentation of *R. oryzae* NRRL 3562. The results of parametric study conducted to determine the optimal parameters are shown in Fig. 3. The convergence toward optimal value of GA across the generations was presented in Fig. 4. As the evolution search proceeds through the generations, the maximum number of population falls in the group of 90–100 U/gds. From Fig. 4, it was observed that more than 85% of the population was consistently above 90 U/gds (Fig. 4) after generation number 200.The optimum values of process parameters are seen to be equal to 35.6 °C, 1.5, 5.29, and 4.82 days for temperature, liquid to solid ratio, pH, and incubation time, respectively. Moreover, the maximum value of lipase activity for *R. oryzae* NRRL 3562 is found to be equal to 96.89 U/gds. Thus, this optimized set of variables was chosen for the experimental model validation. The extracelluar lipase production under the stated conditions resulted in the lipase activity of 95.34 U/gds with a % deviation of −1.63. Compared with the OVAT approach (80.42) (Table 1), the lipase activity has been increased to more than 15 U/gds through GA optimization approach. The enhanced results were also reported in case of glucansucrase and protease production with GA approach. Singh et al. utilized an integrated approach of ANN-GA for optimization of fermentation medium for

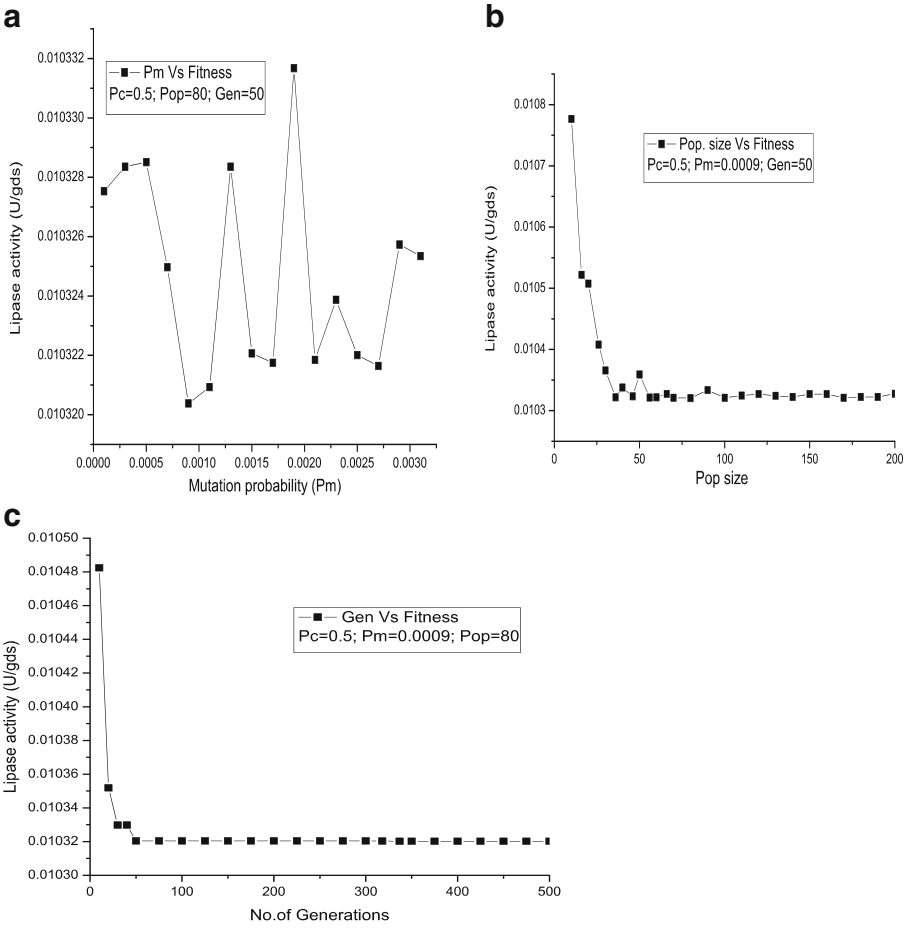

Fig. 3 Results of parametric study of GA. **a** Mutation probability (P_m) vs fitness, **b** population size vs fitness, **c** maximum number of generations vs fitness

the production of glucansucrase, which results a 6.0% increase of glucansucrase activity over the regression-based prediction [42]. The maximized product concentration was observed in case of protease production in a bubble column bioreactor using *Pseudomonas* sp. RAJR 044 by using GA approach [43].

Swarm Intelligence-Based Optimization Approach

Swarm size plays a very important role in PSO, and robustness and computation cost of algorithm are also affected by it. Small population size may result in local convergence; large size will increase computational efforts and may make slow convergence. So an appropriate population size can maintain the effectiveness of the algorithm. In PSO, the balance between the global and local exploration abilities is mainly controlled by the inertia weight [28]. In the present study, a particle size of 100, inertia weight (W) of 0.4, archive size of 500, and maximum number of generations of 46 were employed in the search criteria. The parametric study result of PSO to determine the optimal fermentation

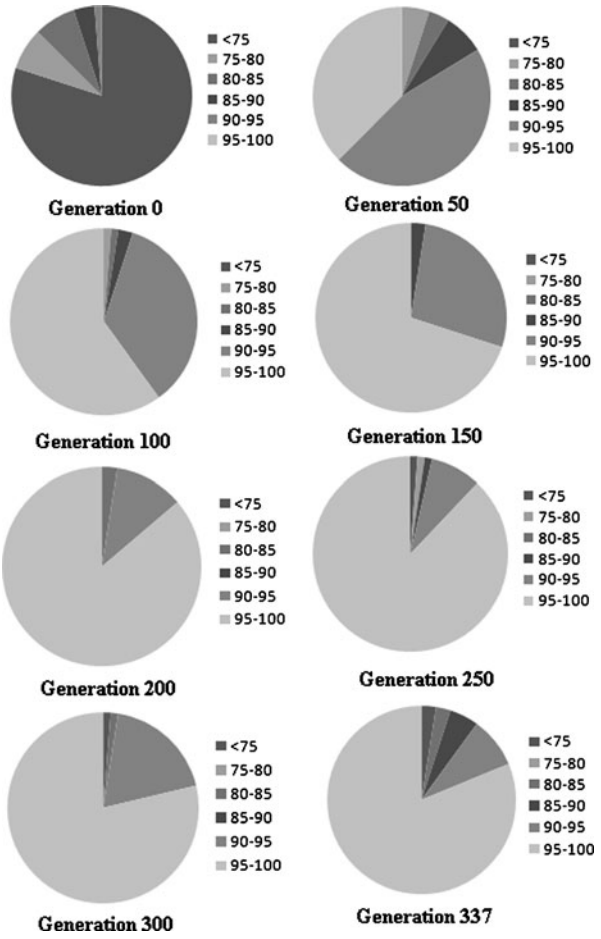

Fig. 4 Population profile at different generations in the genetic algorithm

parameters for lipase production is depicted in Fig. 5. The optimal lipase activity of 96.91 U/gds was obtained with the fermentation variables of 35.58 °C temperature, solid to liquid ratio of 1.49, pH of 5.28, and incubation time of 4.83 days. To confirm the feasibility of the PSO predicted fermentation variables, experiments were conducted in triplicates. The experimental lipase activity of 96.18 U/gds was in close agreement with the PSO predicted value (96.91 U/gds), with a % deviation of −0.76. Moreover, optimization through PSO approach brought about a significant improvement (more than 15 U/gds) in lipase activity, when compared with the OVAT approach (80.42 U/gds) (Table 1). The simple structure of PSO also helps for enhanced productivities of α-amylase and protease by optimizing the fed-batch culture of recombinant *Bacillus subtilis* ATCC 6051a [30].

Comparison Between GA and PSO

While applying PSO and GA, a number of parameters are required to be specified. An appropriate choice of the parameters affects the speed of convergence of the algorithm. The optimal parameters of GA were found to be population size 80, max. generations 337, cross-over probability 0.5, and mutation probability 0.0009. In case of PSO the optimal

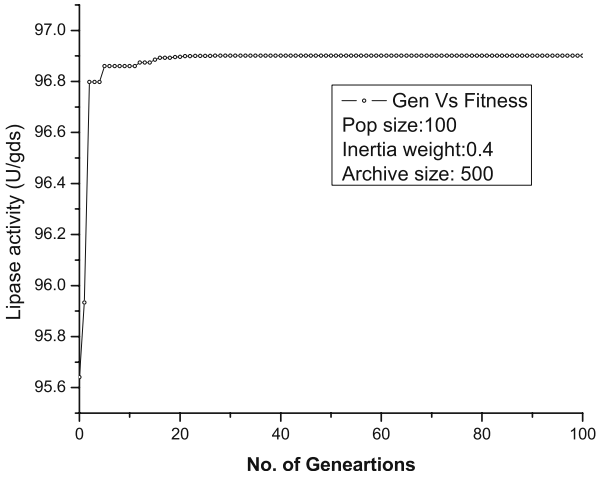

Fig. 5 Variation of objective function value with the number of generations in particle swarm optimization

parameters of particle size, max. generations, inertia weight, and archive size were found to be equal to 100, 46, 0.4, and 500, respectively. The convergence rate of objective function (lipase activity (U/gds)) with the number of generations for PSO and GA is shown in Fig. 6. It is clear from Fig. 6 that, for the optimization problem considered, PSO converges at a faster rate (around 46 generations) compared to that for GA (around 337 generations). Moreover, the computational time for optimized response in case of PSO (0.06 s) was found to be lesser than the GA approach (0.34 s).While comparing the optimized results with optimal parameters (Table 1) of PSO with the GA approach, the optimal lipase activity and parameters obtained by PSO approach are slightly better than the GA approach. The higher convergence rate of PSO over GA is also reported with fed-batch optimization of α-amylase and protease production [38]. The simple structure associated with the minimal parameter tuning helps PSO approach to converge faster than GA [44]. The lipase production through solid-state fermentation by *Rhizopus rhizopodiformis* and *Rhizomucor pusillus* using olive oil cake and sugar cane bagasse mixture as a substrate resulted a lipase

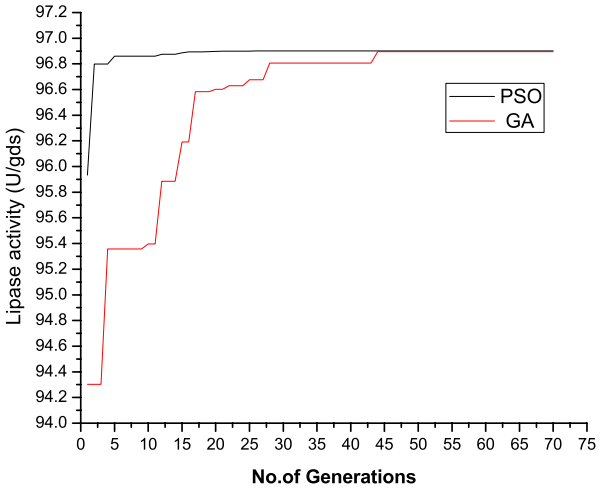

Fig. 6 Comparison of PSO vs GA

activity of 79.6 and 20.24 U/gds, respectively [45]. The lipase activity of 40 and 30.3 U/gds was reported by Kempka et al. [46] and Gombert et al. [47] through solid-state fermentation by *Penicillium verrucosum* and *Penicillium restrictumusins*. Recently, Sun and Xu [18] utilized wheat flour with wheat bran as a substrate for lipase production through SSF by *Rhizopus chinensis* and achieved a lipase activity of 24.447 U/gds. Therefore, the present approach results in a lipase activity of more than 15 U/gds than the previous reports.

Conclusion

In the present study, nature-inspired optimization approaches such as genetic algorithm and particle swarm optimization have been utilized to optimize the fermentation conditions of lipase production. For exploration, both the approaches utilized the interior search space of non-linear RSM model of lipase production. Compared with OVAT approach (80.42 U/gds), the proposed GA (95.34 U/gds) and PSO (96.18 U/gds) approaches brought a significant improvement in lipase activity. The results show that the PSO (96.18 U/gds in 46 generations) has obtained slightly better performance and possesses better convergence property than the GA (95.34 U/gds in 337 generations). The simple structure associated with minimal parameter tuning helps the PSO in outperforming the GA. Therefore, the present nature-inspired optimization approaches may replace the traditional gradient-based optimization approaches and giving new dimensions in the optimization studies of industrial enzyme production.

Acknowledgment The financial support from the Ministry of Human Resource Development, Government of India is acknowledged gratefully.

References

1. Reis, P., Holmberg, K., Watzke, H., Leser, M. E., & Miller, R. (2009). *Advances in Colloid and Interface Science, 147–148*, 237–250.
2. Mala, J. G. S., & Takeuchi, S. (2008). *Anal. Chem. Insights, 3*, 9–19.
3. Aloulou, A., Rodriguez, J. A., Fernandez, S., van Oosterhout, D., Puccinelli, D., & Carrière, F. (2006). *Biochimica et Biophysica Acta, 1761*, 995–1013.
4. Hasan, F., Shah, A. A., & Hameed, A. (2006). *Enzyme and Microbial Technology, 39*, 235–251.
5. Kumari, A., Mahapatra, P., Garlapati, V. K., & Banerjee, R. (2009). *Biotechnol Biofuels, 2*, 1.
6. Jegannathan, K. R., Abang, S., Poncelet, D., Chan, E. S., & Ravindra, P. (2008). *Critical Reviews in Biotechnology, 28*(4), 253–264.
7. Mahapatra, P., Kumari, A., Garlapati, V. K., Banerjee, R., & Nag, A. (2009). *Biocatalysis and Biotransformation, 27*(2), 124–130.
8. Kumari, A., Mahapatra, P., Garlapati, V. K., Banerjee, R., & Dasgupta, S. (2009). *Food Technology and Biotechnology, 47*(1), 13–18.
9. Mahapatra, P., Kumari, A., Garlapati, V. K., Banerjee, R., & Nag, A. (2009). *Journal of Molecular Catalysis. B, Enzymatic, 60*, 57–63.
10. Kumari, A., Mahapatra, P., Garlapati, V. K., & Banerjee, R. (2008). *Bioprocess and Biosystems Engineering, 31*, 291–298.
11. Sun, S. Y., Xu, Y., & Wang, D. (2009). *Bioresource Technology, 100*(9), 2607–2612.
12. Singhania, R. R., Patel, A. K., Soccol, C. R., & Pandey, A. (2009). *Biochemical Engineering Journal, 44* (1), 13–18.
13. Shukla, P., Garai, D., Zafar, M., Gupta, K., & Shrivastava, S. (2007). *J Appl Sci Environ Sanit, 2*(3), 93–103.
14. Essamri, M., Deyris, V., & Comeau, L. (1998). *Journal of Biotechnology, 60*, 97–103.
15. Mateos Diaz, J. C., Rodriguez, J. A., Roussos, S., Cordova, J., Abousalham, A., Carriere, F., et al. (2006). *Enzyme and Microbial Technology, 39*, 1042–1050.

16. Rodriguez, J. A., Mateos, J. C., Nungaray, J., González, V., Bhagnagar, T., Roussos, S., et al. (2006). *Process Biochemistry, 41*, 2264–2269.
17. Hiol, A., Jonzo, M. D., Rugani, N., Druet, D., Sarda, L., & Comeaua, L. C. (2000). *Enzyme and Microbial Technology, 26*, 421–430.
18. Sun, S. Y., & Xu, Y. (2008). *Process Biochemistry, 43*, 219–224.
19. Lorenzo, M. D., Hidalgo, A., Haas, M., & Bornscheuer, U. T. (2005). *Applied and Environmental Microbiology, 71*(12), 8974–8977.
20. Rathi, P., Goswami, V. K., Sahai, V., & Gupta, R. (2002). *Journal of Applied Microbiology, 93*(6), 930–936.
21. Aravindan, R., & Viruthagiri, T. (2007). *Journal of Chemical Technology and Biotechnology, 82*(5), 460–470.
22. Shukla, P., Garai, D., Zafar, M., Gupta, K., & Shrivastava, S. (2009). *Journal of Applied Science and Management, 2*(3), 93–103.
23. Venil C.K., Kamatshi N.S., Lakshmanaperumalsamy P. (2009) *Internet J Microbiol 7*(1), 29–33.
24. Tang, W. J., & Wu, Q. H. (2009). *Transactions of the Institute of Measurement and Control, 31*, 495. doi:10.1177/0142331208094044.
25. Back, T. (1996). *Evolutionary algorithms in theory and practice*. New York: Oxford University Press.
26. Holland, J. H. (1992). *Adaptation in natural and artificial systems*. Cambridge: MIT Press.
27. Kennedy J., Eberhart R.C. (1995) Particle swarm optimization. In IEEE International conference on neural networks (Perth, Australia). IEEE Service Center, Piscataway, NJ, pp. 1942–1948
28. Shi Y., Eberhart R.C. (1998) Parameter selection in particle swarm optimization. In Evolutionary programming VII: Proceedings of the seventh annual conference on evolutionary programming. New York, pp. 591–600
29. Liua, L., Sunc, J., Zhanga, D., Dua, G., Chenb, J., & Xuc, W. (2009). *Enzyme and Microbial Technology, 44*, 24–32.
30. Skolpap, W., Nuchprayoon, S., Scharer, J. M., Grisdanurak, N., Douglas, P. L., & Moo-Young, M. (2008). *Chemical Engineering Science, 63*, 4090–4099.
31. Ashlock, D. (2006). *Evolutionary computation for modeling and optimization*. New York: Springer.
32. Pierre, D. A. (2002) Optimization. In J. Trefil (ed.), *McGraw-Hill Encyclopedia of Science and Technology*, 9th ed. (pp. 479–485). New York: McGraw-Hill Inc.
33. Myers, R. H., Montgomery, D. C., & Anderson-Cook, C. M. (2009). *Response surface methodology: Process and product optimization using designed experiments*. Hoboken: Wiley.
34. Goldberg, D. E. (1989). *Genetic algorithms in search, optimization and machine learning*. Reading: Addison-Wesley.
35. Fogel, & David, B. (2006). *Evolutionary computation: Toward a new philosophy of machine intelligence* (3rd ed.). Piscataway: IEEE Press.
36. Trelea, I. C. (2003). *Inform Process Lett, 85*(6), 317–325.
37. Angeline P.J. (1998) Evolutionary optimization versus Particle swarm optimization: philosophy and performance differences. In Evolutionary programming VII: Proceedings of the seventh annual conference on evolutionary programming, San Diego, CA, USA
38. Raquel C., Naval P. (2005) An effective use of crowding distance in multiobjective particle swarm optimization. In Proceedings of the 2005 conference on genetic and evolutionary computation. Washington DC, USA, pp. 257–264
39. Deb K., Agrawal S., Pratab A., Meyarivan T. (2000) A fast elitist non-dominated sorting genetic algorithm for multiobjective optimization: NSGA-II. In Proceedings of parallel problem solving from nature VI Conference, pp. 849–858.
40. Coello C., Pulido G., Salazar M. (2004) Handling multiobjectives with particle swarm optimization. In IEEE Transactions on evolutionary computation, 8, pp. 256–279
41. Eiben, A. E., & Smith, J. E. (2003). *Introduction to evolutionary computing*. Heidelberg: Springer.
42. Singh, A., Majumder, A., & Goyal, A. (2008). *Bioresource Technology, 99*, 8201–8206.
43. Dutta, J. R., Dutta, P. K., & Banerjee, R. (2005). *Process Biochemistry, 40*, 879–884.
44. Eberhart, R. C., & Shi, Y. (1998) Comparison between genetic algorithms and particle swarm optimization. In Evolutionary Programming VII: Proceedings of the seventh annual conference on evolutionary programming. San Diego, CA, USA
45. Cordova, J., Nemmaoui, M., Ismaıli-Alaoui, M., Morin, A., Roussos, S., Raimbault, M., et al. (1998). *Journal of Molecular Catalysis. B, Enzymatic, 5*, 75–78.
46. Kempka, A. P., Lipke, N. L., Pinheiro, T. L. F., Menoncin, S., Treichel, H., Freire, D. M. G., et al. (2008). *Bioprocess and Biosystems Engineering, 31*, 119–125.
47. Gombert, A. K., Pinto, A. L., Castilho, L. R., & Freire, M. G. D. (1999). *Process Biochemistry, 35*, 85–90.