

## **Artificial Neural Network (ANN): Application in media optimization for industrial microbiology and comparison with response surface methodology (RSM)**

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### **ABSTRACT**

*In recent, artificial neural network (ANN) has been applied for media production for different bioprocesses and enzyme production. Some important studies described comparative account of response surface methodology (RSM) and artificial neural network (ANN). Numerous reports described better production of enzymes and biomolecules by using ANN as compared to RSM. Besides microbiology, ANN has been used in different scientific optimization processes successfully. An introduction to ANN has been given in this review. This review focuses on some studies in which ANN has been used for microbial production of biomolecules using ANN and also described the comparison with RSM.*

**Keywords:** artificial neural network, response surface methodology, microbiology, enzyme production

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### **INTRODUCTION**

Media optimization is an crucial step in microbiology for production of industrially important biomolecules. Initially researchers used *one-variable-at-a-time* approach for media optimization in microbiology. Even, these days also some times this approach is used. This traditional approach of *one-variable-at-a-time* method for media optimization requires several sequential experiments to find the optimal conditions. The optimization of media constituents or biological transformation is generally expensive, labourious and time consuming [1; 2] and can be used only if there is no interaction between the variables [3]. Moreover, the complexity of microbial processes and variable responses to different nutrients adds to the unreliability of the traditional approach [1]. In last decades, researchers used response surface methodology (RSM) to optimize media. RSM is a statistical tool used to elucidate the interaction of independent variables and relationship among responses [4]. Response surface methodology (RSM) emerged as most common method used for media optimization [1; 2; 5]. Central composite rotatable design (CCRD), Plackett-Burman and Box-Behnken were used widely. In RSM, a number of factors and their interactions regulating the common response can be studied. RSM has been used both at small and large scale for the optimization of production of various bio-molecules [1], but many research groups have reported used of artificial neural networks (ANN) as the mathematical or statistical modeling tool in a wide range of biotechnology applications particularly optimization of bioprocesses, media optimization for various biomolecules production and to increase enzyme yield from different source microorganisms. ANN consists of dense interconnected computing units that are simple models for complex neurons in biological systems [6]. ANN is biologically motivated and mimics human brain. ANN consisting of a large network of neurons which are connected with connection link [7; 8; 9]. These neurons

have an activation function to elucidate the output. Commonly nonlinear activation functions such as sigmoid and step functions are used. ANNs are trained by experience, when applied a new input to the network it can generalize from past experiences and produce a new result [8; 9]. The simple structure of ANN normally consists of an input layer, a hidden layer and an output layer [5; 9; 10; 11]. By applying algorithms that mimic the processes of real neurons, the network can learn to solve many types of problems. It provides a mathematical alternative to the quadratic polynomial for representing data derived from statistically designed experiments. ANN is also able to handle a large amount of data to approximate functions to any desired degree of accuracy, thus make it attractive as empirical model [2]. ANN has been used in different filed of science including physics, chemistry and management also. ANN has also been used in predicting the secondary structures of globular proteins (Girish K. Jha, I.A.R.I., New Delhi). Following studies by different researchers described use of ANN and gave an idea that it is better than RSM in particular cases.

#### **Citric acid production**

Recently, Ricca et al. [7] have successfully applied the artificial neural network (ANN) for optimization of media constituents by solid state bioconversion. Authors reported significance of ANN approach for citric acid production from oil palm empty fruit bunches using *Aspergillus niger*. They have compared the results obtained from both RSM and ANN. Authors reported building of ANN model using MATLAB software. The coefficients determination ( $R^2$ ) value was 0.997 and 0.985 for ANN and RSM, respectively. These coefficients determination showed the superiority in terms of non linear behaviors. After validation process, maximal production of citric acid was obtained from ANN. From the data and results analysis, authors reported that ANN better approach than RSM.

#### **L-asparaginase production**

Baskar et al. [12] have reported use of artificial neural network (ANN) linked genetic algorithm for optimal production of L-asparaginase by *Enterobacter aerogenes* MTCC 2823. Authors also compared the coefficient of determination of RSM and ANN. The workers used three neurons in input, three in hidden and one in output layer to observe the media constituents dependent production of L-asparaginase. Though authors report accurate predictions of results from RSM model and ANN model, but ANN showed more accuracy and better prediction with experimental results. The coefficient of determination ( $R^2$ ) was higher in case of ANN (0.984) as compared to RSM (0.871). Authors clearly mentioned that ANN based BPN provided better results and accurate predictions than CCD of RSM. The optimal production of L-asparaginase was found to be 18.72 IU/ml using ANN.

#### **Actinomycin V production**

Singh et al. [13] also reported use of artificial neural network (ANN) and genetic algorithm (GA) for optimization of media constituents for production of actinomycinV from *Streptomyces triostinicus*. Workers conducted the experiments by using central composite design (CCD), and the resultant data was employed to generate artificial neural network model. Concentrations of five media constituents were used as inputs to the neural network model, and the response (antibiotic yield) was treated as output of the model. The response (antibiotic) yield obtained by the ANN and GA was much higher (36.7%) as compared to yield obtained from the response surface methodology (RSM). Authors reported that ANN-GA hybrid methodology has considerably improved the product yield. They have recommended ANN approach to be used for modeling and optimization of other bioprocesses.

#### **Production of Scleroglucan**

Desai et al. [5] reported comparison of ANN/GA and RSM for optimal production of biopolymer scleroglucan. Production of scleroglucan was studied as a function of four independent variables. The predictive capabilities and generalization ability of both ANN and RSM proved superiority of ANN/GA. The higher yield of scleroglucan was obtained with ANN.

#### **Triterpenoid production from *Antrodia camphorata* ATCC 200183**

Lu et al. [14] have reported comparison of ANN and RSM for production of triterpenoid from *Antrodia camphorata* ATCC 200183. Authors compared these two models for optimal production of intracellular triterpenoids by optimizing inoculum size and media constituents. The Root mean squares error,  $R^2$ , and standard error of prediction shown by ANN were 0.31%, 0.99%, and 0.63%, respectively, while RSM shown 1.02%, 0.98%, and 2.08%, respectively. These data pointed out the better fitness and prediction accuracy of ANN as compared to RSM. The experimental yield of triterpenoid was  $64.79 \pm 2.32$  mg/l using ANN/GA designed medium and this was in good accord with the predicted value. The workers recommended that the same optimization process may be used to optimize numerous genetic and environmental factors that can also affect the triterpenoid production from *Antrodia*

*camphorate*. Authors also suggested that this process may also be used for improved production of biologically active metabolites from potent medicinal fungi by changing the fermentation parameters.

#### Enhanced lipase production

Haider et al. [15] reported enhanced production of lipase from a soil microorganism. Authors also compared ANN-GA and RSM for modeling and optimization of lipase production. According to these workers, ANN model, developed based on back propagation algorithm, were highly accurate in predicting the system and the coefficient of determination ( $R^2$ ) was found to be close to 0.99. After optimization of media constituents using ANN-GA maximal production of lipase (7.69 U/ml in terms of lipolytic activity) was obtained from 72 h old culture. This yield was found to be higher (8.8%) than the maximal values predicted by response surface methodology (RSM).

#### Biosurfactant Production

Pal et al. [16] described comparative studies on production of a biosurfactant from *Rhodococcus erythropolis* MTCC 2794. Authors compared ANN-GA and RSM to optimize media constituents for enhanced production of the biosurfactant. ANN and RSM models were developed by combining the quantity of four media constituents as independent input variables and biosurfactant yield was calculated as output variable. ANN-GA and RSM were compared for their predictive and generalization ability. ANN-GA was found to be more precise and constant in predicting optimized conditions and maximum yield than RSM. The value of correlation coefficient was found to be approximately 0.99 for ANN-GA. The workers also stated that ANN-GA based models could be used accurately for sensitivity analysis. The biosurfactant yield was found to be 3.5-fold higher using ANN-GA mediated optimized media.

#### Enhanced Synthesis of Marine Biosurfactant

Recently, Sivapathasekaran and Sen, [17] reported employment of an improved resilient back-propagation neural network modeling combined with genetic algorithm to optimize the process variables for maximal production of lipopeptide biosurfactant *Bacillus circulans*. The workers used to optimize four independent parameters, agitation, aeration, temperature and pH. Authors reported improved ANN-GA modeling and optimization using MATLAB v.7.6 and the experimental design was obtained using Design Expert v.7.0. They have developed ANN model using the advanced neural network architecture known as resilient back-propagation algorithm. The workers reported approximately 52% enhanced biosurfactant production using the ANN based optimization strategy.

In industrial microbiology, optimization of media constituents is a routine research work and both ANN and RSM based model are used. Recently, Narasimhan and Shivakumar [18] reported production of chitinase from *Bacillus subtilis* using Plackett-Burman design. Loc et al. [19] reported production of recombinant NPRC10 protease at fermentor scale. Use of ANN and RSM can be useful in such type of studies. Recently, Unakal et al. [20] reported use of banana waste for  $\alpha$ -amylase synthesis from *Bacillus subtilis*. In such type of studies ANN and RSM can be used and this may provide better yield of desired protein.

### CONCLUSION

ANN has emerged as a new modeling tool for optimization of production of useful microbial products. It has been reported in numerous studies to give better yield of products as compared to RSM. In last few years ANN has been used widely in different areas including chemistry, finance, physics and biological sciences. Numerous reports on media optimization using ANN make convenient to understand its applicability for different biological responses particularly in microbiology. Keeping in mind the examples, mentioned in the manuscript, it can be concluded that ANN can be used more widely in microbiology and industrial biotechnology.

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