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Mini Review

Recent Advances in Artificial Intelligence Models for Bioprocess Application

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Introduction

In the recent past, there was a paradigm shift from deterministic modelling to data-driven modelling with the increased application of different Artificial Intelligence (AI) algorithms for different subfields of bioprocess engineering.

AI models are generally trained to learn the complex nonlinear dynamic patterns of microbial and enzymatic processes and use them mainly for

A. Prediction of key process output variables,

B. Evaluating optimal operating parameters that maximizes the process performance

C. On-line monitoring and control of bioprocesses and thereby minimizing the time, effort and resources and leading to bioprocess safety and sustainability.

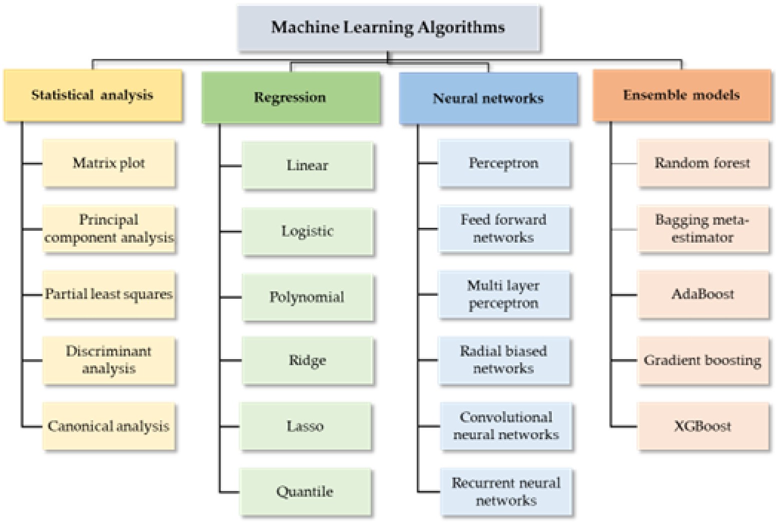

Figure 1: Classification of machine learning algorithms.

AI models can be briefly classified into four major groups based on their model structure and mathematical algorithms involved i.e., statistical analysis, regression models, neural networks, and ensemble models, they can be chosen judiciously depending on the process characteristics and application requirement. Figure 1 gives the broader outline of different AI algorithms and several of these models were used for improving the efficiency of various bioprocesses. They include the utilization of statistical models named here for data pre-processing, dimensionality reduction and also to investigate the trends, patterns, and relationships in the data [1], while regression models were used to effectively determine the underlying relationship (linear or non-linear) between the predictor and response variables [2]. Neural networks are the computing systems with interconnected nodes that mimic the functionality of neurons in human brain, and they are trained to recognize hidden patterns and correlations of several bioprocesses [3]. Ensemble modelling is another class, which considers the creation of multiple diverse models to predict an outcome, by using either different algorithms or different training data sets [4].

AI models for Different Bioprocess Domains

AI algorithms demonstrate a great potential in handling high dimensional data, recognizing the complex nonlinear data patterns, data visualization, classification etc. This section covers the recent advancements in the application of various AI tools in the field of bioprocess system engineering [5].

Prediction of key process output variables

State estimation is a primary area of focus in the application of AI in field of bioprocess engineering. Artificial Neural Networks (ANN) are the most widely used models for the prediction of important process output variables such as product conversion, yield, biomass growth etc, from the easily measurable input operating conditions such as feed flow rates, concentration , temperature, pH, rpm etc. The reported studies include ANN application for real time and off-line prediction of microalgal biomass nutrient and lutein concentrations produced by *Desmodesmus* sp [6], estimation of microbial fuel cell biofilm communities and bioreactor performance [7], performance prediction of an osmotic membrane bioreactor for simultaneous reduction of salt accumulation and membrane fouling [8] and estimation of filtration performance and membrane fouling in an osmotic membrane bioreactor [9]. Further, an Adaptive Neurofuzzy Inference Systems (ANFIS) and ANN was developed for estimating transmembrane pressure in anaerobic membrane bioreactor-sequencing batch reactor during biohydrogen production [10]. The other reported models include random forest predictor model for estimation of key chemical–biological features affecting bioreactor performance [11], Extreme Gradient Boosting (XGBoost) model for predicting the nutrient removal in an anaerobic-anoxic-oxic membrane bioreactor (A_2O-MBR) [12], gradient boosting regression model for the prediction of microbial growth curves of *Candia antarctica* for lipase production [13].

Evaluating optimal operating parameters that maximizes the process performance

Further, there is an increasing interest in the integration of AI and optimization algorithms for bioprocesses since 2009 and has been at a consistently high level since 2014. It remains a hot topic in latest bioprocess research, starting with the development of scientific methods for sensor placement, going through data storage and processing architectures, and ending with AI and optimization algorithms [14]. Several bioprocesses were optimized based on AI models, that include maximizing the insulinase production from sugarcane using ANN [15], lipase production from organic solid waste by anaerobic digestion using ANN [16], enhancing the productivity in processing of surimi with citric acid using an integrated Particle Swarm Optimization (PSO) and back propagation-ANN [17], improving bioH_2 production during the dark fermentation using multilayer perceptron ANN with response surface methodology [18]. Further, in a recent study an AI approach namely ActiveOpt is proposed to intelligently guide experiments to arrive at an optimal phenotype with minimal measured datasets [19].

On-line monitoring and control of bioprocesses

AI models can effectively capture the inherent nonlinearities of complex biochemical processes and can be used in developing efficient monitoring and control strategies. A synergetic growth is found in the application domains of AI and nonlinear control in addressing a wide variety of bioprocess monitoring and control problems [20]. Some of the reported studies include, a multivariate sensor for the on-line monitoring of a microalgal bioreactor system by integrating the Raman spectra with Support Vector Regression (SVR) to maximize the oil productivity [21,22], control of a semi-continuous batch-fed bioreactor used for yeast fermentation using a new partially supervised Reinforcement Learning (RL) algorithm [23]. Further, a low-cost, flexible, and reliable foam sensor concept for bioreactor applications was proposed for foam emergence in bioreactors based on image analysis using deep Convolutional Neural Networks (CNNs) [24]. Furthermore, process monitoring, and fault diagnosis has become an important component of advanced bioprocess operation, which involves real time detection of the occurrence of any fault (abnormal deviation), finds its root cause and brings the process back to normal operation without effecting process performance. AI algorithms proved quite effective in learning the patterns of different fault scenarios and the underlying dynamics. For instance, a random forest based classifier was used for the diagnosis of faults in a fed batch bioreactor for penicillin production [22] and in a microfabricated bioreactor automated through online characterization of adherent cell culture growth based on image analysis [25].

Conclusion and Future Scope

There is a huge scope for the application of different AI methods that effectively extracts the valuable hidden information in the experimental data and can be used to enhance the performance of various bioprocesses. Conventional bioprocess experimental approaches need to be integrated with efficient AI techniques and implement them for the development of robust and accurate representative models, and employ them for effective bioprocess optimization, monitoring, and control. The entire process requires deeper understanding of the bioprocess, systematic experimental planning and data generation, data pre-processing and key variable identification followed by appropriate model training and its implementation. The fast-growing biotechnology industry in providing alternate sustainable solutions offers great opportunities for the implementation of various AI algorithms in solving complex biochemical problems and there by leading to rapid discovery of new bioprocesses with reduced effort and resources.

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