Modeling predictive control of penicillin bioreactors via radial basis function neural networks

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Abstract

This work was directed to the application of advanced machine learning and process control tools in an industrial penicillin production bioreactor. The developed algorithms were the Principal Component Analysis (PCA) method, for reducing data dimensionality, and Radial Basis Function Neural Networks (RBFNN), directed to create a multivariable interpolation model to predict the bioreactor temperature. Regarding the process control phase, the Model Predictive Control (MPC) method was used, which aims to calculate a sequence of control actions capable of approximating the output variables with their respective set points in an optimized way. In this paper, information from a real industrial process of penicillin production was analyzed, dealing with a database composed of 27 variables to be treated. The gaussian radial base function gave the neural network model a better adaptation to the system. Finally, the control actions calculated by the MPC controller resulted in the maintenance of the controlled variables in its respective set points in a gradual manner, without impacting the stability of the system.

Keywords
Model predictive control, radial basis function, neural networks, data science, bioreactor, smart manufacturing, process systems engineering.

1. Introduction
The concept of smart manufacturing has drawn the attention of both academia and corporative world in recent years, being classified as a priority to be achieved by the main economic potencies. It consists of a series of measures that seek to promote greater connectivity between equipment and machines with a better use and interpretation of the data obtained to achieve greater competitive advantages, quality and profitability. However, due to the advancement of measurement and communication technologies, the transcendence of one era marked by the scarcity of data in industrial processes to another characterized by the excessive amount of information generated has become more evident, making data management more complex and challenging (BOGLE, 2017).

An illustration of such scenario is found in the pharmaceutical industry, where the implementation of control systems is increasingly mandatory. With the transformation of raw materials into value-added effective drugs as the main objective, it is essential that such reactions occur efficiently, which implies an unceasing search for high yields and the minimization of raw materials variability and impurities (ROGERS, HASHEMI, & IERAPETRITOU, 2013). In this way, the sector has been marked by high investments in the research and development of a multitude of new computational methodologies for systems integration and optimization, which have obtained relative success in stabilizing such processes (BOUKOUVALA, MUZZIO, & IERAPETRITOU, 2010). However, in the presence of processes with large disturbances and many variables to be manipulated, the efficiency of such control systems is compromised due to the generation of an excessive amount of data from different sources and structures at high frequencies of sampling. This difficulty enables the occurrence of operational failures and as their effects propagate they can lead to accidents and interruptions with serious consequences to workers and the environment (ISERMANN, 2006). In this sense, it is necessary to implement different process systems engineering (PSE) techniques, such as the Internet of Things (IoT) and machine learning, which have shown to be quite effective in containing and preventing faults. The former consists of the installation of sensors in unit operations to capture process information, promote

data interaction and extract intelligence to better aid decision making, whereas the latter is related to applying intelligent algorithms capable of performing deep data analysis, allowing the identification of patterns and generating forecasts, in order to assure improvement opportunities (ATZORI, IERA, & MORABITO, 2010; BENGIO, 2009; EBERLE, et al., 2016).

The main objectives of this paper are to develop a model predictive controller (MPC) and create a radial basis function neural network (RBFNN) to be applied to a fed-batch fermentation bioreactor designed to convert substrate (sugar and oil) into penicillin, in order to predict the evolution of the reactor's temperature and control the process' operation. In particular, the paper aims to:

- Evaluate the control actions performed by the controller to maintain the substrate concentration and the reactor temperature (controlled variables) at their set points, based on the manipulation of the cooling jacket temperature (manipulated variable).
- Determine the significant features of the process by applying a PCA algorithm.
- Evaluate the influence of different radial basis functions into the accuracy of the prediction model, making use of the squared sum of errors (SSE) statistical indicator.

2. Materials and Methods

The following section lists the equipment and methodologies used in this project. It starts with a description of the industrial bioreactor, highlighting its main characteristics. Subsequently, the operational procedure of the data analysis methodologies and the model predictive controller were detailed, finalizing the topic by addressing other theoretical foundations involved.

2.1 Material

The radial basis function neural network (RBFNN), the principal component analysis algorithm (PCA) and the model predictive controller (MPC) were implemented through Python® and analyzed with Microsoft Office Excel 2019®.

2.2 Penicillin Bioreactor

Figure 3.1 shows the fed-batch industrial bioreactor (FBSTR) for penicillin production. The configuration of the bioreactor is consistent with the traditional 100,000 L bioreactor available in previous literatures (SHULER & KARGI, 2002). The bioreactor has a tank radius of 2.1 m with three Rushton impellers with internal diameters of 1.7 m and is operated at a fixed agitation of 100 rpm. The vessel is equipped with pH, temperature, dissolved oxygen, foaming and pressure sensors, and off-line measurements of penicillin, nitrogen and viscosity. Samples were collected every 24 hours and the phenylacetic acid measurements were taken every 12 hours (GOLDRICK, STEFAN, LOVETT, MONTAGUE, & LENNOX, 2015).

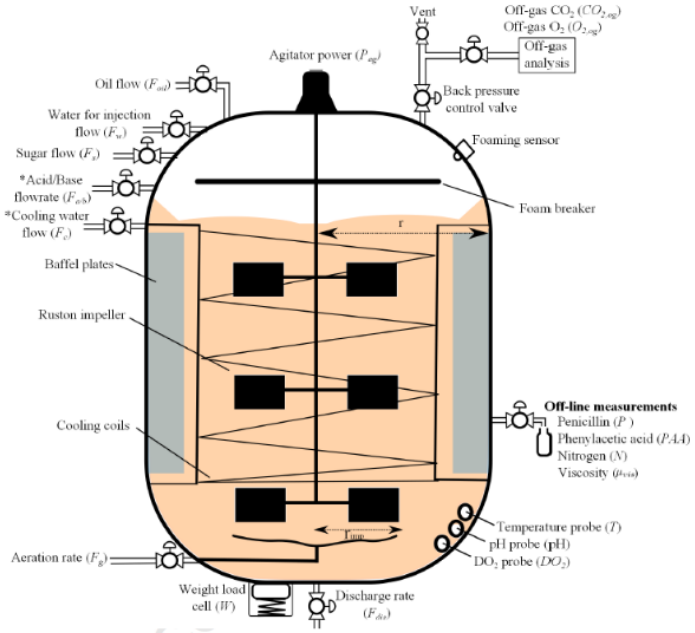

Figure 1. Fed-batch industrial penicillin bioreactor configuration.

2.3 Mole and Energy Balances

This process involves a fed-batch bioreactor (FBSTR). For the purpose of this paper, the mole and energy balances of the aforementioned reactor were employed, as shown by the following equations.

$$\frac{dC_S}{dt} = \frac{F}{V} \cdot (C_{SF} - C_S) - r_S \quad (1)$$

$$\rho C_P V \frac{dT}{dt} = F\rho C_P (T_F - T) + \Delta H_R r_S + UA(T_C - T) \quad (2)$$

2.4 Rate Law

The kinetic mechanism for the proposed reaction is represented by the following Arrhenius relationship.

$$r_S = k_S C_S \quad (3)$$

$$k_S = A_P \cdot \exp\left(-\frac{Ea}{R} \cdot \frac{1}{T}\right) \quad (4)$$

2.5 Principal Component Analysis (PCA)

The first step of the PCA algorithm is the standardization of the variables to ensure that each variable contributes to the analysis in an equal manner and avoids biased results. Mathematically, the standardization (z) can be expressed by the following equation:

$$z = \frac{\text{Value} - \text{Mean}}{\text{Standard Deviation}} \quad (5)$$

Next, comes the computation of the covariance matrix which enables to understand how the input variables interact amongst each other. The next equation expresses the covariance mathematical expression between two variables.

$$\text{Cov}(x, y) = \frac{\sum(x_i - \bar{x}) \cdot (y_i - \bar{y})}{N - 1} \quad (6)$$

Finally, the last step of the PCA algorithm implementation is the computation of the eigenvectors and eigenvalues of the covariance matrix to identify the principal components which are new variables that are constructed as linear combinations or mixtures of the initial variables.

2.6 Radial Basis Function Neural Network (RBFNN)

Regarding the radial basis function neural network, each neuron inputs are collected from other neurons or from bias terms and their strength or magnitude is evaluated. These inputs are then summed and compared with a threshold level

to determine the output value as shown in Equation (7). Then, the summation term suffers a nonlinear transformation, which can be the sigmoidal transformation according to Equation (8) below.

$$z = \sum w_i x_i + b \tag{7}$$

$$f(z) = \frac{1}{1 + e^{-z}} \tag{8}$$

For this paper, the sigmoidal function was replaced by different radial basis functions. These have several advantages including their easy design process, strong tolerance to noise and enhanced online learning ability. The summation term is described by Equation (9), where the term R refers to the radial basis function to be employed and Ci expresses the coordinates of the hidden poles (nodes). The radial basis functions employed in this work were the Gaussian, the thin plate spline, the multiquadratic, and the inverse multiquadratic.

$$z = \sum w_i \cdot R\|x_i - C_i\|^2 + b \tag{9}$$

In order to compare the accuracy of the different models, the squared sum of the errors was employed, which is described by Equation (10).

$$SSE = \sum (y_i - \hat{y}_i)^2 \tag{10}$$

2.6 Model Predictive Control (MPC)

For the model predictive controller, such procedures culminate in the objective functions described by Equations (11) and (12), which can also be subjected to multiple constraints.

$$\min_{\Delta u(k)} \sum_{i=1}^{P} \left\| C_S{}^{SP}(k+i) - \widehat{C_S}(k+i) \right\|^2 + \|\Delta T_C(k+i)\|^2 \tag{11}$$

$$\min_{\Delta u(k)} \sum_{i=1}^{P} \left\| T^{SP}(k+i) - \widehat{T}(k+i) \right\|^2 + \|\Delta T_C(k+i)\|^2 \tag{12}$$

With the design equations, the Python algorithm was developed through the GEKKO® package. The programmed changes in the reactor temperature's set-point is shown in Figure 2, which also illustrate its upper and lower limits of 330 and 270 K, respectively. In order to quantify the performance of the controller, different metrics were implemented, which can be found in Equations (13) to (15).

$$IAE = \int_0^{\infty} |e(t)|dt = \sum_{i=0}^{n} \left| SP(i) - \widehat{T}(i) \right| \Delta t_i \tag{13}$$

$$ISE = \int_0^{\infty} e(t)^2 dt = \sum_{i=0}^{n} (SP(i) - \widehat{T}(i))^2 \Delta t_i \tag{14}$$

$$ITAE = \int_0^{\infty} t|e(t)|dt = \sum_{i=0}^{n} t(i) \cdot \left| SP(i) - \widehat{T}(i) \right| \Delta t_i \tag{15}$$

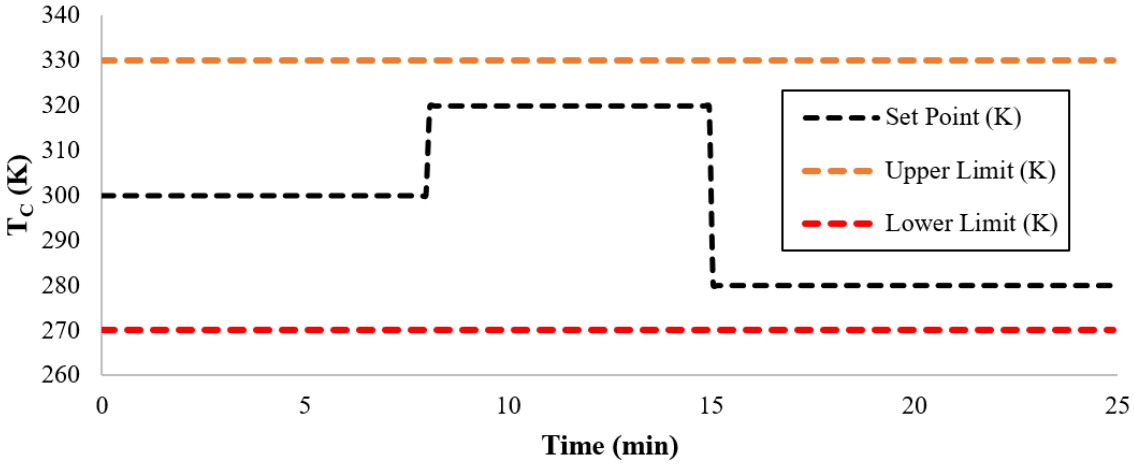

Figure 2. Penicillin bioreactor temperature set-point schedule.

3. Results and Discussion

Regarding the radial basis function neural network algorithm for the FBSTR reactor, the simulation was done considering a database of 1131 lines. From the PCA algorithm, it was possible to observe from Figure 3 below that approximately 95% of the batches' information could be explained by 11 variables out of 27.

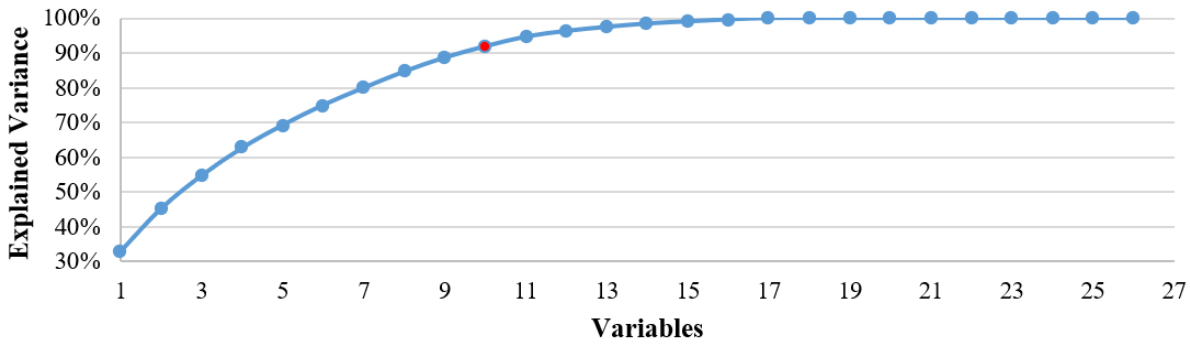

Figure 3. PCA algorithm explained variance chart.

Figure 4 illustrates the obtained RBFNN training and test results for every radial basis function. The application of the gaussian radial basis function resulted in the smallest SSE (54.61). With the establishment of the optimum number of variables, the MPC algorithm for the FBSTR reactor was created in Python®, through the GEKKO® package. The simulation was done considering a prediction horizon (P) of 25 min, as shown in Figure 4. The temperature range of the cooling jacket (T_C) is situated between 270 and 330 K, satisfying the specifications determined by the problem. With the control actions calculated by the controller, it is observed that substrate consumption happened smoothly, where the output concentration (C_S) reached the value of 1.0 mol/L approximately after 20 min. Likewise, it is noted that the reactor temperature (T) reached the set points established by the algorithm satisfactorily, having reached the value of approximately 290 K at the end of the prediction horizon P (Figure 5). Finally, regarding the performance of the controller, it obtained promising values of IAE (119.92), ISE (1535.68) and ITSE (1412.87), which were in average 40% lower than the obtained values for PI and PID controllers.

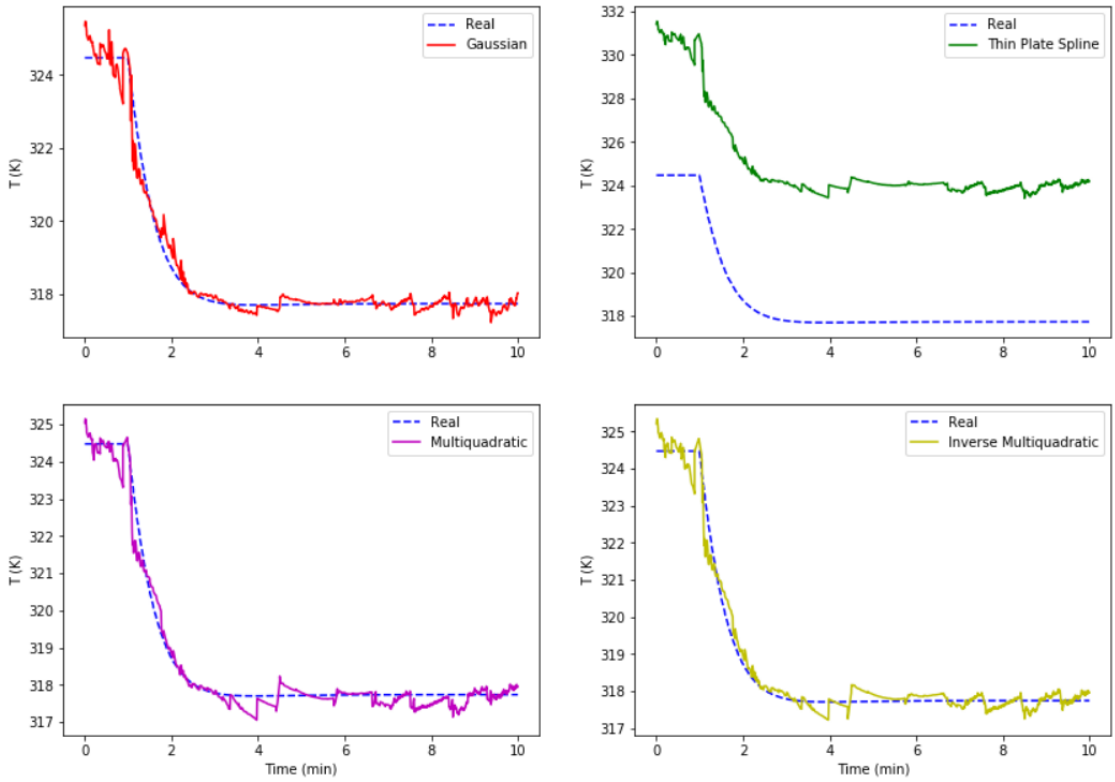

Figure 4. Radial basis function neural network (RBFNN) fitting results.

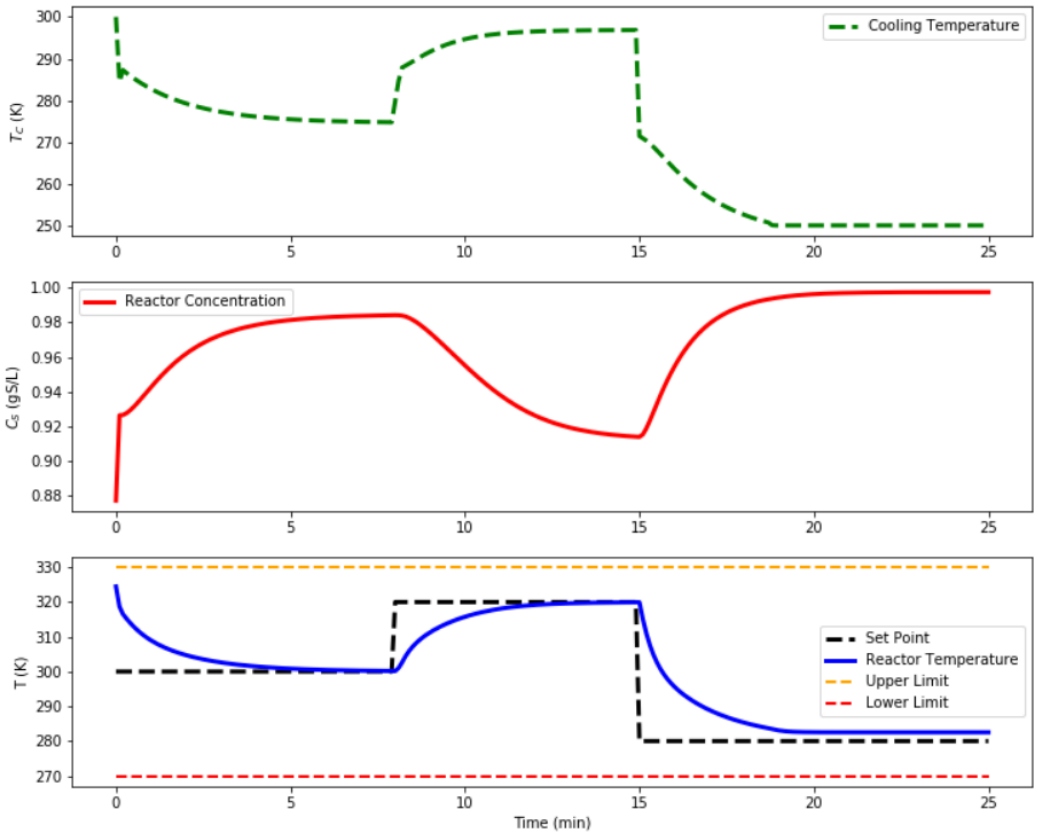

Figure 5. Model predictive control simulation for the penicillin bioreactor.

4. Conclusions

Based on the obtained results, it can be concluded that the implementation of the neural network and the MPC controller via Python® were both satisfied and similarly successful. It was possible to observe the importance of such tools in the chemical process industry, not only related to the control of processes, but also through the deep analysis of the data that allows corporations to achieve higher quality and profitability margins.

Regarding the development of the neural network, it was found through the principal components analysis (PCA) algorithm that the optimal number of variables that explained 95% of the data behavior was equal to 11, which decreased the computational effort to perform its calculations and simplified the interpretation of results. Such variables were the flowrates of sugar, soybean oil, phenylacetic acid, acid and base, dilution water, removed broth, aeration, pH and temperature.

In addition, the application of the gaussian radial basis function resulted in a better fit to the experimental data, since the SSE value was the lowest among the other functions. Finally, the control actions calculated by the MPC controller resulted in the maintenance of the controlled variables (substrate concentration, reactor temperature) in its respective set points in a gradual manner, without impacting the stability of the system or exploring it, which would compromise the integrity of the raw materials and, consequently, the quality of the final product. Another point to note was that the control actions were performed within the specified limits, and that it performance metrics were superior when compared with other controller types.

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