# Modeling of Polycaprolactone Production from ε-Caprolactone Using Neural Network

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**Abstract.** In this paper, extensive study of ring-opening polymerization ε-caprolactone (ε-CL) using lipase Novozym 435 as catalyst in flask level and reactor level were conducted. The polymerization rates increase with an increase in time up to 4 h after which there has been a steep decrease for all temperature from 50 to 100 °C in the flask level. The conclusion out of flask level and reactor level study is that a uniform trend is obtained at 70 °C. A multilayer feed-forward neural network (FANN) model was trained with an error back-propagation algorithm. Reaction time, temperature were used as the input parameters and molecular weight is the output for the flask level study where as reactor impeller speed was also included for reactor level study. Two FANN models with modeling performances of 2-10-1 in the flask level and 3-9-1 FANN1 and 2-13-1 FANN2 (excluding reactor impeller speed) for the reactor level study were obtained.

**Keywords:** Biopolymer, Lipase enzyme, Molecular weight distribution, nonlinear process, Feedforward neural networks.

## 1 Introduction

Enzymatic polymerization as the name suggests is the polymerization using enzyme as the catalyst has been under scanner for the past few years. Enzymatic polymerization enables the synthesis of polymers, which otherwise are difficult to prepare. Polycaprolactone (PCL) is one of the examples of bio based aliphatic polyesters that have emerged as important materials in industrial processes that require biodegradable high performance plastics. Lipik et al. [1] synthesized a series of polymers, according to experimental design and developed a mathematical model, which can account for the real molar mass of a synthesized polymer using the main polymerization parameters as the variables. Sivalingam et al. [2] investigated the thermal degradation/modification dynamics of poly (ε-caprolactone) (PCL) in a thermogravimetric analyzer under non-isothermal and isothermal conditions. Experimental molecular weight evolution and weight loss profile were modeled using continuous distribution kinetics. Sivalingam et al. [3] investigated the thermal degradation of the poly (ε-caprolactone) (PCL), poly (vinyl acetate) (PVAC), and their mixtures in solution.

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T. Huang et al. (Eds.): ICONIP 2012, Part II, LNCS 7664, pp. 444–451, 2012.

Neural networks have been considered as one of the important empirical modelling technique for research in recent years and biotechnology is no exception. This is due in part to the simplicity of the "black-box "input-output relationship that results. Also important is the"universal approximation" capability of neural networks. Feedforward nets are easily implemented under real-time conditions. Neural networks can be applied to static systems and dynamic systems.

As far as empirical models are concerned, feedforward neural network models deserve consideration because they have the following advantages:

1. Efficient identification algorithms and structure optimisation techniques have been developed.
2. Have simple structure and relatively small number of parameters (unlike fuzzy models do not suffer from "the curse of dimensionality")
3. Can be easily incorporated into the MPC algorithms and efficiently used on-line.

FANN has its own share in the field of biopolymerization ranging from pattern recognition for design of biomaterial scaffolds [4] to chemical fibers [5]. In this paper we wish to report extensive study of ring-opening polymerization ε-caprolactone (ε-CL) using lipase Novozym 435 as the catalyst. This paper explains the comparisons in terms of the kinetic trends, homogeneity temperature effects, and feedforward neural network modeling of both the flask level production and scale up of polycaprolactone in a bioreactor from e-caprolactone using ring opening polymerization.

## 2 Material and Methods

Two different set of experiments namely the flask level and scale up level experiments carried out on the production of polycaprolactone. In flask level experiments focus was to achieve an optimum temperature at which maximum molecular weight could be achieved and these temperatures were considered for the scale up level so as to validate the reactor level study with the flask level study.

### 2.1 Experimental Set-Up

**Flask Level Experiment.** Polymerization grade ε-caprolactone purchased from Merck Private Limited, was first dried over calcium hydride and then distilled under reduced pressure in nitrogen atmosphere. Chloroform and toluene were purchased from Merck Private Limited. Toluene was dried over calcium hydride and distilled under nitrogen atmosphere. Novozyme-435 (specified activity 7000 PLU/g) was purchased from Science Technics Private Limited. All liquid chemical transfers were performed by syringe through rubber septum caps under nitrogen atmosphere. ε-CL (10 g), toluene (20 mL) and Novozyme-435 (1 g) were added to a round-bottom flask (250 mL) and the reaction was maintained at 70°C, for 4 h, with magnetic stirring. Reactions was terminated by adding chloroform and filtrated. The chloroform in filtrate was removed by rotary evaporation and polymer in the concentrated solution was precipitated in methanol. The precipitate was isolated by filtration and dried (0.1 mmHg, 50°C, 24 h). The molecular weights of the samples were determined by Gel permeation chromatography (GPC).

**Reactor Level Experiments.** The scale up production of polycaprolactone from e-caprolactone was carried out using an Infors-HT Labfors bioreactor. The temperatures

that were considered for the experiment was 60°C, 70°C and 80°C and the reactor impeller speed were 250, 500, 750 and  to 1000 rpm.

### 2.2 Feed Forward Neural Networks

In this study, feed forward neural network (FANN) were developed and trained by the Levenberg-Marquardt optimisation algorithm with regularisation and "early stopping". In order to determined the number of hidden nodes in the hidden layer, neural networks with different numbers of hidden neurons were trained on the training data and tested on the testing data. The network with the lowest sum square error (SSE) on the testing data was considered as having the best network topology. In assessing the developed models, MSE and r value on the unseen validation data is used as the performance criterion as shown in Table 2.

**Flask Level Study (FANN)**

$$Y(t) = fn[u1(t), u2(t)] \tag{1}$$

Therefore in this case study, the number of hidden neuron used in the models for FANN is 10.

**Reactor Study**
FANN1 (with reactor impeller speed) .

$$Y(t) = fn[u1(t), u2(t), u3(t)] \tag{2}$$

FANN2 (without reactor impeller speed).

$$Y(t) = fn[u1(t), u2(t)] \tag{3}$$

where

u1(t)= temperature
u2(t)= impeller speed
u3(t) = reaction time

Therefore in this case study, the number of hidden neuron used in the models for FANN1 and FANN2 are 9 and 13 respectively.

## 3 Results and Discussion

### 3.1 Experimental Results

**Flask Level Experiments.** Figure 1 shows the variation of molecular weight with reaction time for toluene as solvent at various temperatures (50–100°C) with a volume ratio of 1:2 of $\varepsilon$-caprolactone: toluene being taken. The polymerization rates increase with an increase in time up to 4 h after which there has been a steep decrease for all temperature from 50 to 100°C. Hence the molecular weight is found to be the maximum at a temperature of 70°C for the 4th hour. The important feature of using toluene as the solvent is that the polymerizations using toluene gave a solution in which $\varepsilon$–CL and polymer were soluble and the catalyst remained insoluble.

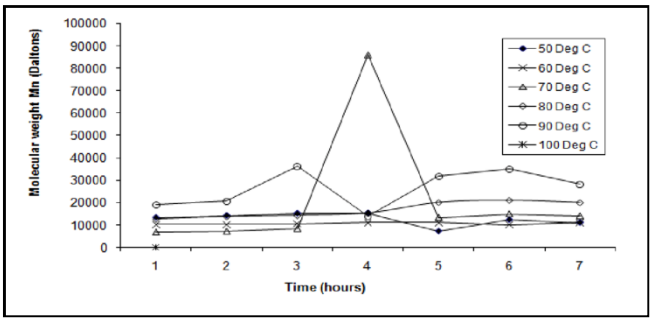


**Fig. 1.** Effect of temperature on Molecular weight for flask level study

**Reactor Level Experiments.** As mentioned earlier the following plots explain the time-temperature and time- reactor impeller speed relationships. This is to prove that the behavior of the bio-polymerization of e-caprolactone changes depends on the two parameters.

Figure 2 indicates the variation of molecular weight with reaction time at impeller speed (500 rpm) for the temperatures of 60°C, 70°C, 80°C.

Figure 3 shows the variation of molecular weight with reaction time at 60°C, indicates that the trend for all the impeller speeds namely 250, 500, 750, 1000 rpm is uniform.

**Comparison on Flask and Reactor Level.** On comparing the results of flask level with the reactor level, Figure 1 which is the plot of molecular weight against the conversion for polymerizations carried out at 50 -100 °C in the flask level, shows a trend where in the maximum molecular weight is obtained at 4hr for 70°C, but when carried out in reactor level the results are not the same. The maximum output of more than 3000 daltons is obtained at 80°C, but the fact to be noted is that the trend followed in case of 80°C is not steady. So the conclusion out of the two studies of flask level and reactor level is that a uniform trend is obtained at 70°C and higher molecular weight (even though not maximum in case of the reactor level) is obtained .

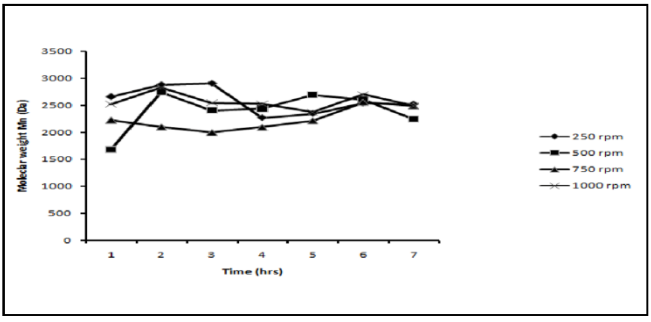


**Fig. 2.** Effect of Temperature on Molecular weight at of 500 RPM impeller speed

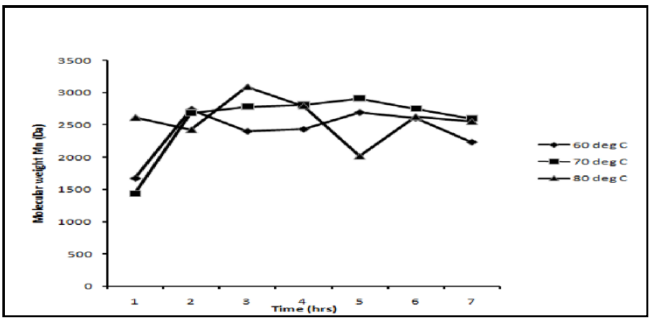


**Fig. 3.** Effect of impeller speed on molecular weight at a constant temperature of 60 Deg C

### 3.2 Molecular Weight Prediction Using Feed Forward Neural Network (FANN)

**Flask Level Study.** Figure 4 shows the plot comparing the predicted output with the actual output in flask level study which reveals the scaled molecular weight distribution for each sample. The plot shows that the experimental data and the predicted data match almost close to each other. The plot represent that the actual and predicted data are much synchronized and the plots are seen to be overlapping because of their similarity and it is the sign of an excellent representation of the process.

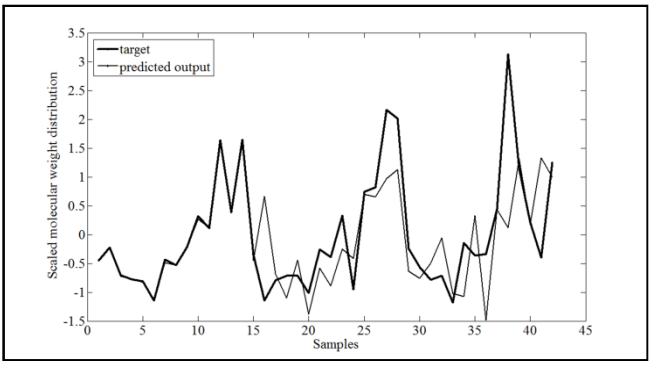


**Fig. 4.** Plot comparing the predicted output with the actual output for flask level study

**Table 1.** Correlation Coefficient Value and MSE for flask level study

| Data | NN (with flask level study) | |
|---|---|---|
| | Correlation Coefficient, *r* | MSE |
| Training | 0.916 | 0.144 |
| Testing | 0.957 | 0.269 |
| Validation | 0.938 | 0.081 |

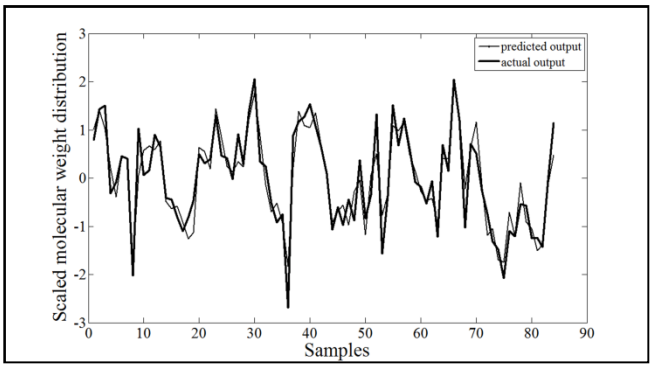


**Fig. 5.** Plot comparing the predicted output with the actual output with reactor impeller speed

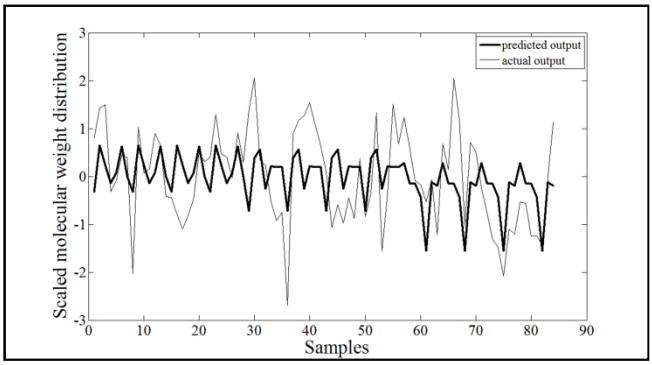


**Fig. 6.** Plot comparing the predicted output with the actual output without reactor impeller speed

SSE, RMSE and R values are the renowned method of assessment for neural network model. The values of MSE and R value are 0.081 and 0.938, respectively from Table 1 shows that intricate process like biopolymerization can be modeled and generalized excellently. ANOVA (analysis of variance) is a statistical method that is capable to test whether or not the means of several groups of data are all equal. In this work, one-way ANOVA is chosen for assessing the data. One-way ANOVA demonstrates the relation of mean of the flask level study between the experimental and predicted data for all the temperatures. The p-value (performance of the analyzed data) for One-way ANOVA is 0.6129 which is higher than significant value which should be less than 0.05 or 0.01, the reason being that range for the molecular weight range between flask, and neural network model is different.

**Reactor Level Study.** Figure 5 & 6 shows the plot comparing the predicted output with the actual output with and without reactor impeller speed respectively revealing the scaled molecular weight distribution for each sample. MSE and R values can be seen in the Table 2. Table 3 shows One-way ANOVA the relation between mean of the reactor level study with (FANN1) and without impeller speed (FANN2). Hence

the standard ANOVA table determines the sums of squares, degrees of freedom, mean squares (SS/df), F statistic, and p value. The F statistic was used to do a hypothesis test to find out if the molecular weights obtained from the two experiments one with impeller speed and the other without impeller speed are the same. Anova1 returns the p value from this hypothesis test. Based on the results, it is seen that p-value is higher because of the range for the molecular weight range between reactor, and neural network model is different.

**Table 2.** Correlation Coefficient Value and MSE

| Data | NN1(with impeller speed) | | NN2(without impeller speed) | |
|---|---|---|---|---|
| | Correlation Coefficient, *r* | MSE | Correlation Coefficient, *r* | MSE |
| Training | 0.958 | 0.082 | 0.399 | 0.829 |
| Testing | 0.938 | 0.31 | 0.632 | 0.458 |
| Validation | 0.989 | 0.037 | 0.744 | 0.796 |

**Table 3.** ANOVA plots for the reactor study

| p-value for One-way ANOVA for FANN1 | p-value for One-way ANOVA for FANN2 |
|---|---|
| 0.568 | 0.8126 |

## 4 Conclusion

Molecular weight is found to be the maximum at a temperature of 70°C for the 4th hour with a uniform trend for 50 to 100°C in the flask level.. The maximum output of more than 3000 daltons is obtained at 80°C. The inference from flask level and reactor level study is that a uniform trend and higher molecular weight (even though not maximum in case of the reactor level) is obtained at 70°C. Two FANN models were obtained one with the inclusion and other with exclusion of reactor impeller speed. The results showed that a 2-10-1 in the flask level and 3-10-1 FANN1 and 2-13-1 FANN2 arrangement for the reactor level study gave best performance. Results show that FANN1 performs better FANN2.

**Acknowledgement.** This work was supported by the Universiti Sains Malaysia (USM) RU Grant (USM-RU) 814076.

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