Prediction of the size of silver nanoparticles prepared via green synthesis: A gene expression programming approach

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Abstract. This study presents a new prediction model for estimating the size of silver nanoparticles (AgNPs) prepared by green synthesis via Gene Expression Programming (GEP). First, 30 different experiments were carried out to construct the GEP models. Plant extract, reaction temperature, concentration of silver nitrate (AgNO₃), and stirring time parameters were considered as input variables and the size of AgNPs was selected as the output variable. The collected experimental data were randomly divided into eight testing sets and 22 training sets for further analysis. By considering the correlation coefficient ($R^2$), Mean Absolute Error (MAE), and Root Relative Square Error (RRSE) as the criteria, the performances of proposed models by GEP were compared. Finally, the best model (i.e., GEP-1) with $R^2 = 0.9961$, MAE = 0.2515, and RRSE = 0.0668 was proposed as a new model with simplified mathematical expressions to estimate the size of AgNPs. The results of sensitivity analysis showed that the amount of plant extract, the concentration of AgNO₃, stirring time, and reaction temperature were the most effective parameters on the size of AgNPs, respectively. The proposed model can be extended for a wide range of applications and it provides the possibility of minimum materials consumption in the preparation of the lowest-size AgNPs with regard to practical or economic constraints. 

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1. Introduction 

Silver nanoparticles (AgNPs) have desirable physical/chemical properties, including favorable optical and thermal characteristics as well as high electrical conductivity, and significant biological properties [1-3]. There are various chemical, physical, and biological methods for the synthesis of AgNPs. However, environmental hazards and high cost are the main drawbacks of the former two [4,5]. On the contrary, green synthesis has considerable advantages for the synthesis of AgNPs. Consequently, several researchers have tried to optimize the practical parameters of AgNPs by green synthesis. However, unfortunately, this technique suffers from complicated interactions among the practical parameters as well as prolonged synthesis time [6]. According to the literature [7], particle size, composition, microstructure, and morphology of AgNPs significantly affect their unique features. As
a consequence, employment of advanced optimization as well as modeling approaches to dictate the optimal properties of AgNPs is a hot topic for various studies. Accordingly, development of a detailed accurate model for the prediction of the size AgNPs will be so beneficial. The main merit of Gene Expression Programming (GEP) technique is its inherent capability to propose an equation as a mathematical function. This approach provides a systematic and efficient methodology to optimize the performance and quality of complicated engineering issues [8,9]. The main contribution of the current study is using GEP algorithm to estimate the particle size of AgNPs with regard to experimental data, including plant extract (Pe), temperature of reaction (Tr), stirring time (St), and molar concentration of AgNPs (Mc), as effective practical parameters. A sensitivity analysis was performed to evaluate the effect of each input variable on the size of nanoparticles in the investigated range.

2. Data collection and method of analysis

2.1. Data set and input/output selection
Determining the important variables of green synthesis that affect the size of AgNPs is the main part of optimization and modeling. Shabanzadeh et al. [7] investigated the green synthesis of AgNPs using Vi-tex negundo L. extract by Artificial Neural Networks (ANNs). They mentioned that the AgNPs size was mainly affected by four practical parameters, namely Pe, Tr, St, and Mc. Table 1 summarizes the details of 30 practical data that repeated based on the operational condition of literature [7]. These data have randomly been divided into testing (eight cases) and training (22 cases) sets for the development of various GEP models.

2.2. Gene Expression Programming (GEP)
Genetic Programming (GP) is an enhanced version of Genetic Algorithm (GA) proposed by Koza [10]. Moreover, to overcome the limitations of both GA and GP algorithms, a new population-based evolutionary algorithm, named Gene Expression Programming (GEP), was introduced by Ferreira [11-13]. The inherent ability of GEP to develop an equation by considering independent practical parameters as input for estimating a predefined output with acceptable accuracy distinguishes it from other modeling approaches [14-17]. The main components of GEP are terminal set, termination condition, fitness function, control parameters, and function set [10]. Figure 1 illustrates the flowchart of a typical GEP. As observed, the main component of GEP consists in the genetic operators [18-20].

The operators of a gene function at level of chromosomes, hence promoting genetic diversity. It is noteworthy that GEP has a multi-gene nature and, consequently, each chromosome for one or more genes is a mathematical function. There are various methods to represent GEP output, including Karva language (the gene language), Expression Tree (ET), and mathematical functions [21-23]. Figure 2 shows a typical GEP output for an encoded chromosome with two genes as a linear string. Observing Figure 2 from left to right at the upper part shows the conversion of Karva language to ET. On the other hand, from right to left at the bottom, the figure illustrates the conversion of ET to a mathematical function [24].

To validate the randomly selected genome, the head-tail method was employed. In this methodology, every gene has two elements, i.e. a head and a tail. The former is composed of terminal and function, while the latter contains only the terminal symbols [17,25]. The GEP designer determines the head length (h) and the length of the tail (t) is calculated by Eq. (1) [26]:

$$t = h(n_{\text{max}} - 1) + 1,$$

where $n_{\text{max}}$ is the maximum number of arguments. GEP is performed in five major steps:

1. Selection of the fitness function ($f_i$) through Eq. (2) [27]:

$$f_i = \sum_{j=1}^{C_f} (M - |C_{(i,j)} - T_{(j)}|),$$

where $M$ is the selection range, $C_{(i,j)}$ represents the return value of chromosome $i$ by employing the

![Figure 1. Flowchart of a GEP.](image-url)
Table 1. Experimental data series for the synthesis of silver nanoparticles (AgNPs) by green synthesis [7] (plant extract ($Pe$), temperature of reaction ($Tr$), stirring time ($St$), and molar concentration of AgNPs ($Mc$)).

| No. | $Pe^*$ (gr) in 100 ml water | $Tr^{**}$ (°C) | $St^{***}$ (hr) | $Mc$ (mole) in 100 mL water | AgNPs size (nm) |
|-----|----------------------------|-----------------|-----------------|----------------------------|-----------------|
| 1   | 0.10                       | 25              | 48              | 0.1                        | 27              |
| 2   | 0.10                       | 30              | 48              | 0.2                        | 28              |
| 3   | 0.10                       | 40              | 48              | 0.5                        | 29              |
| 4   | 0.10                       | 50              | 48              | 1.0                        | 29              |
| 5   | 0.10                       | 60              | 48              | 1.5                        | 31              |
| 6   | 0.10                       | 70              | 24              | 2.0                        | 32              |
| 7   | 0.25                       | 25              | 24              | 0.1                        | 25              |
| 8   | 0.25                       | 30              | 24              | 0.2                        | 26              |
| 9   | 0.25                       | 40              | 24              | 0.5                        | 26              |
| 10  | 0.25                       | 50              | 24              | 1.0                        | 27              |
| 11  | 0.25                       | 60              | 12              | 1.5                        | 27              |
| 12  | 0.25                       | 70              | 12              | 2.0                        | 29              |
| 13  | 0.50                       | 25              | 12              | 0.1                        | 18              |
| 14  | 0.50                       | 30              | 12              | 0.2                        | 19              |
| 15  | 0.50                       | 40              | 12              | 0.5                        | 21              |
| 16  | 0.50                       | 50              | 6               | 1.0                        | 21              |
| 17  | 0.50                       | 60              | 6               | 1.5                        | 24              |
| 18  | 0.50                       | 70              | 6               | 2.0                        | 24              |
| 19  | 0.75                       | 25              | 6               | 0.1                        | 15              |
| 20  | 0.75                       | 30              | 6               | 0.2                        | 16              |
| 21  | 0.75                       | 40              | 3               | 0.5                        | 18              |
| 22  | 0.75                       | 50              | 3               | 1.0                        | 19              |
| 23  | 0.75                       | 60              | 3               | 1.5                        | 20              |
| 24  | 0.75                       | 70              | 3               | 2.0                        | 21              |
| 25  | 1.00                       | 25              | 3               | 0.1                        | 16              |
| 26  | 1.00                       | 30              | 1               | 0.2                        | 16              |
| 27  | 1.00                       | 40              | 1               | 0.5                        | 17              |
| 28  | 1.00                       | 50              | 1               | 1.0                        | 18              |
| 29  | 1.00                       | 60              | 1               | 1.5                        | 18              |
| 30  | 1.00                       | 70              | 1               | 2.0                        | 19              |

2. Selection of (a) terminals ($S$), (b) set of functions ($F$) to generate the chromosomes as $“F” = (Pe, Tr, St, Mc)$, (c) arithmetic operators ($+, -, \times, \div$), and (d) mathematical functions of $Exp$, $pow(10, Ln, Abs, X^2, X^3, X^4, 3Rt, Atan, and Cos$;

3. Selection of the chromosomal architecture by de-
Figure 2. Representation of GEP output for a typical chromosome with two genes through mathematical expression, Expression Tree (ET), and Karva language.

Table 2. Predefined Gene Expression Programming (GEP) parameters for the most appropriate GEP models in the present study.

| Model | Number of chromosomes | Head size | Number of genes | Used function                                  |
|-------|------------------------|-----------|-----------------|------------------------------------------------|
| GEP-1 | 24                     | 10        | 6               | +, −, s, /, Exp, x^2, 3Rt, Atan                |
| GEP-2 | 28                     | 10        | 5               | +, −, s, /, Exp, x^2, x^3, x^4                 |
| GEP-3 | 36                     | 10        | 6               | +, −, s, /, Exp, x^2, 3Rt, Atan                |
| GEP-4 | 30                     | 9         | 4               | +, −, s, /, Exp, Ln, Pow 10, Abs, x^4          |
| GEP-5 | 19                     | 7         | 3               | +, −, s, /, Exp, x^2, 3Rt                      |
| GEP-6 | 25                     | 4         | 3               | +, s, Pow 10, x^2, 3Rt, Cos                    |
| GEP-7 | 30                     | 3         | 4               | +, −, s, x^2, 3Rt                              |
| GEP-8 | 25                     | 3         | 3               | +, −, s, Pow 10, x^2, Cos                     |
| GEP-9 | 20                     | 4         | 3               | +, −, s, x^2, x^3                              |

terminating the number of genes and chromosomes and then, enhancing the length of heads one after another in every run. By considering performance as the criterion, the testing and training processes were monitored. Table 2 presents some trials for GEP modeling:
4. Selection of the linking function;
5. Determination of genetic operators as [10,28]:

- **Mutation** [17,30]: The most efficient operator within the length of a chromosome with intrinsic modification power. Mutation is able to change the terminal or function in the head and the terminal in the tail;
- **Inversion** [17,30]: Activated in the head of a chromosome. It is able to reverse a fragment with the length of 1 to 3;
- **Transposition** [17, 31]: Including three types of Insertion Sequence (IS) transposition, responsible for the transportation of a fragment or terminal from one position to the head or other genes; Root Insertion Sequence (RIS) transposition, responsible for transportation of a fragment by preserving its function from the first position to the changed root; and gene transposition, responsible for transporting the operators of all genes to the beginning of the chromosomes.

Table 3 shows the range of GEP parameters for the proposed models in this study. The powerful GeneXproTools 5.0 software was employed to model the relation between the practical parameters of green synthesis and the particle size of AgNPs. SPSS software (version 25) was employed to analyze the collected data as input variables. This study tried to predict the
Table 3. Detailed features of Gene Expression Programming (GEP) for modeling.

| Definition of GEP parameter | Value    |
|----------------------------|----------|
| Number of chromosomes      | 19-30    |
| Head size                  | 3-10     |
| Number of genes            | 3-6      |
| Linking function           | Addition |
| Fitness function error type | RRSE     |
| Constant per gene          | 10       |
| Mutation rate              | 0.0014   |
| Inversion rate             | 0.5      |
| One-point recombination rate | 0.3     |
| Two-point recombination rate | 0.3    |
| Gene recombination rate    | 0.3      |
| Gene transposition rate    | 0.3      |
| IS transposition           | 0.5      |
| RIS transposition          | 0.5      |

Figure 3. Boxplots of practical parameters for the green synthesis of AgNPs (plant extract \(Pe\), temperature of reaction \(Tr\), stirring time \(St\), and molar concentration of AgNPs \(Mc\)).

practical parameters during the preparation of AgNPs via green synthesis. The medians of the data sets for \(Pe\) and \(Tr\), which are situated in the center of the box, indicate their symmetric distribution. On the other hand, the box plots for \(St\) and \(Mc\) are inclined towards the bottom, that is, the boxes shift to the bottom whisker. This indicates that most of the values for the data are small with a few exceptions with large values. In these cases, the average is higher than the median and close to the upper whisker. It is noteworthy that all practical parameters in the present study do not have any outliers. Table 4 statistically presents the input and output data utilized in this study.

To determine the magnitude and direction of the relationship between practical parameters, Bivariate Correlation Analysis (BCA) was employed. BCA first performs a careful analysis of the way of measuring the practical data and then, determines any highly correlated pairs. Highly negative or positive correlation coefficients among the pairs decrease the accuracy of the developed GEP model, significantly, and complicate the evolving issues in explaining the effect of explanatory practical parameters on the size of AgNPs as the outcome. For example, in case of significant interdependency between the variables, the effect of each input parameter may be exaggerated, resulting in the evolution of multi-collinearity [33]. Table 5 presents the correlation matrix of practical parameters by calculating Pearson’s coefficient. As indicated in the table, there are not any significant correlations between the independent variables of \(Pe\), \(Tr\), and \(Mc\). However, there is considerable dependency between the \(Mc\) and \(Tr\) as well as \(St\) and \(Pe\).

3. Result and discussion

The presence of outlier practical data negatively affect clear understanding of the relationships between variables. Hence, identification and elimination of outlier data from the original data set leads to higher accuracy during GEP analysis. There are various techniques to detect the outliers, e.g., statistical and box plot approaches [32]. Figure 3 indicates the box plot for four

Table 4. Explanation of the statistical distribution of practical parameters in the development of Gene Expression Programming (GEP) models.

| Parameter | Unit | Minimum | Maximum | Mean | Standard deviation |
|-----------|------|---------|---------|------|-------------------|
| \(Pe\)    | gr   | 0.1     | 1       | 0.52 | 0.332             |
| \(Tr\)    | ºC   | 25      | 70      | 45.833| 16.192            |
| \(St\)    | hr   | 1       | 48      | 15.666| 16.595            |
| \(Mc\)    | mL   | 0.1     | 2       | 0.883| 0.703             |
Table 5. Correlation coefficients of the practical variables for green synthesis of AgNPs: experimental data series for the synthesis of silver nanoparticles (AgNPs) by green synthesis\(^7\) (plant extract (Pe), temperature of reaction (Tr), stirring time (St), and molar concentration of AgNPs (Mc)).

| Parameters | Pe   | Tr   | St    | Mc    |
|------------|------|------|-------|-------|
| Pe         | 1    | 0    | -0.845 | 0     |
| Tr         | 0    | 1    | -0.186 | 0.993 |
| St         | -0.845 | -0.186 | 1    | -0.191 |
| Mc         | 0.993 | -0.191 | 1    |       |

To study the multi-collinearity between the practical parameters, a Principal Component Analysis (PCA) can be employed. PCA is an approach to dimension reduction in which the correlated variables are transferred from a multi-dimensional space to a lower-dimension space to remove the correlation of variables. The uncorrelated variables in the new space are called the principal component\(^34\)-\(^36\). To ensure the possibility of performing PCA, the Kaiser Mayer Olkin (KMO)\(^37\) factor should be adopted as the as criterion, calculated via Eq. (3).

\[
KMO = \frac{\sum_{i \neq j} r_{ij}^2}{\sum_{i \neq j} r_{ij}^2 + \sum_{i \neq j} a_{ij}^2},
\]

where \(r_{ij}\) and \(a_{ij}\) are the correlation coefficient and the practical correlation coefficient of variables \(i\) and \(j\), respectively. When the KMO factor is lower than 0.7, the dependency between the practical parameters is unreal and the data are not appropriate for PCA analysis\(^32\). The KMO factor of the current study was estimated at 0.502. Therefore, there was no need to use PCA for the correction of the interaction between the practical parameters. The KMO analysis revealed that the presence of considerable dependency between some of the practical parameters in Table 4 was a consequence of the nature of the BCA analysis, not a causality or linear association of \(Mc\) with \(Tr\) or \(St\) with \(Pe\). Thus, the practical parameters are independent from each other and appropriate for the subsequent analysis by GEP.

Validation of every developed model was performed by considering the coefficient of determination \((R^2)\), Mean Absolute Error (MAE), and Root Relative Square Error (RRSE) as the criteria, defined through Eqs. (4)-(6)\(^38\).

\[
R^2 = \frac{(n \sum t_i \alpha_i - \sum t_i \sum \alpha_i)^2}{(n \sum t_i^2 - (\sum t_i)^2)(n \sum \alpha_i^2 - (\sum \alpha_i)^2)}
\]

\[
RRSE = \sqrt{\frac{\sum_{i=1}^{n} (t_i - \bar{o}_i)^2}{\sum_{i=1}^{n} (t_i - \frac{1}{n} \sum_{i=1}^{n} t_i)^2}}
\]

\[
MAE = \frac{\sum_{i=1}^{n} |t_i - \bar{o}_i|}{n},
\]

where \(t\) is the target value, \(o\) is the predicted value, and \(n\) is the number of data within the testing and training phases. \(R^2\) closer to 1 and MAE and RRSE closer to zero indicate better fit of the developed model\(^39\). The statistical characteristics of nine appropriate models for the training and testing data sets are given in Table 6.

As indicated, the values of \(R^2\) for the proposed model range between 0.9856-0.9983 and 0.9795-0.9993

Table 6. Correlation coefficient \((R^2)\), Mean Absolute Error (MAE), and Root Relative Square Error (RRSE) amounts for nine appropriate GEP models.

| No. | Training | Testing | MAE Training | RRSE Training | MAE Testing | RRSE Testing |
|-----|----------|---------|--------------|---------------|-------------|--------------|
| GEP-1 | 0.9883 | 0.9961 | 0.1403 | 0.041 | 0.2545 | 0.0668 |
| GEP-2 | 0.9902 | 0.9798 | 0.4055 | 0.0988 | 0.6428 | 0.1616 |
| GEP-3 | 0.9954 | 0.9963 | 0.2586 | 0.0693 | 0.3193 | 0.0951 |
| GEP-4 | 0.9905 | 0.9930 | 0.3834 | 0.0971 | 0.4185 | 0.1026 |
| GEP-5 | 0.9857 | 0.9895 | 0.5101 | 0.1195 | 0.4114 | 0.1129 |
| GEP-6 | 0.9814 | 0.9915 | 0.4795 | 0.1206 | 0.4877 | 0.1274 |
| GEP-7 | 0.9826 | 0.9906 | 0.5220 | 0.1316 | 0.5018 | 0.1297 |
| GEP-8 | 0.9855 | 0.9855 | 0.4724 | 0.1200 | 0.5310 | 0.1450 |
| GEP-9 | 0.9827 | 0.9884 | 0.5153 | 0.1316 | 0.5138 | 0.1342 |
Figure 4. Various statistical indices for training and testing data series in Gene Expression Programming (GEP) models: (a) Correlation coefficient ($R^2$), (b) Mean Absolute Error (MAE), and (c) Root Relative Square Error (RRSE).

Figure 5. Expression Tree (ET) of the GEP-1 model.

in the training and testing phases, respectively. Moreover, the minimum amounts of MAE and RRSE are equal to 0.1403 and 0.041 in the training phase and 0.2545 and 0.0068 in the testing phase, respectively. Figure 4 compares the values of $R^2$, MAE, and RRSE for nine better GEP models. GEP-1, GEP-3, and GEP-4 show higher accuracies than other models for the prediction of AgNPs size.

Table 7 summarizes the mentioned nine better GEP models. The relatively large size of GEP models shows the complicated space for the practical parameters of green synthesis. Figures 5-7 illustrated
Table 7. The equations extracted from the nine Gene Expression Programming (GEP) models with experimental data series for the synthesis of silver nanoparticles (AgNPs) through green synthesis [7] (plant extract (Pe), temperature of reaction (Tr), stirring time (St), and molar concentration of AgNPs (Mc)).

GEP-1 \[42.704 - 2Pe + Pe^4 + 1.302(\frac{Pe^5}{5} + Pe^3) + \frac{16Pe^4}{7^{14.144MC(-4.055+St)+0.445St^2}} - \frac{8.575}{7^2} \tan[0.336MC - 0.336Pe - 20.578A\tan[Pe] + A\tan[MC^2(-10.094 + St)^2] + A\tan[\left(-\frac{0.872}{7^1} + A\tan[MC^3]^2\right)]^2 |\]

GEP-2 \[37.234 + 20.295MC + Pe(-28.276 + Pe(11.709 + Pe)) + \frac{3.362}{7^{4.632 - 2MC(1.111 + Tr)}}\]

GEP-3 \[29.608 - 2Pe + Pe^4 + \frac{16Pe^4}{7^{14.144MC(-4.055+St)+0.445St^2}} - \frac{48.423}{7^2} + A\tan[0.809MC - 0.809Pe - 20.784A\tan[Pe]]\]

GEP-4 \[15.731 - 0.0837e^{MC} + e^{-0.062Pe} + 24.32e^{-10Pe + 2Pe} - MC - 2Pe + \frac{0.1137e^{(8.738 + 7^1)A\tan[St]}}{0.3377e^{Tr}} + Ab[0.082 + MC - Pe + St]\]

GEP-5 \[24.692 - 3.107MC + Pe(-29.792 + 14.538Pe) + 0.23Tr\]

GEP-6 \[10.253 + 10^{Cos[Pe]^2} + 10^{Cos[2Pe]} + 2.172MC + Pe\]

GEP-7 \[30.576 + 2.221MC + Pe(-29.14 + 13.584Pe)\]

GEP-8 \[29.938 + 2.148MC + (-23.381 + 0.974 \times 10^{Pe} - Pe)Pe\]

GEP-9 \[10.688 + 2MC + 10.236(1.397 - Pe)^2 + Pe + 2Pe^3\]

**Figure 6.** Expression Tree (ET) of the GEP-3 model.
the sub-ETs of GEP-1, GEP-3, and GEP-4 models, respectively. The number of genes (sub - ETs) is 6 for GEP-1, 8 for GEP-2, 6 for GEP-3, and 4 for GEP-4 models. Suppose $m$ is the maximum number of iterations, $n$ is the number of chromosomes, and $O(e)$ indicates the complexity of each GEP model. Then, time complexity of our strategy is $O(mne)$, since in each iteration, the GEP model is executed for each chromosome.

Table 8 compares the actual and predicted sizes of AgNPs for GEP-1, GEP-3, and GEP-4 models. The results confirm that the proposed models are unable to predict the size of AgNPs with an acceptable precision.

Figure 8 illustrates the actual and predicted values of AgNPs size for GEP-1, GEP-3, and GEP-4 in the testing and training phases. As shown, there is reasonable agreement between the experimental and predicted values for the GEP-1, GEP-3, and GEP-4, especially in the training phase. However, some deviations are observed from the linear trend, especially in GEP-3 and GEP-4 during the testing phase. Accordingly, GEP-1 is proposed as the most appropriate model for the estimation of the size of AgNPs prepared by green synthesis.

A sensitivity analysis is performed by changing an output/input and keeping all other parameters constant [40]. To estimate the relative influence of every
Table 8. Comparison of the actual and predicted AgNPs sizes with GEP-1, GEP-3, and GEP-4 models.

| No. | Actual AgNPs size (nm) | Predicted AgNPs (nm) |
|-----|------------------------|-----------------------|
|     |                        | GEP-1 | GEP-3 | GEP-4 |
| 1   | 27.39                  | 27.54 | 27.73 | 27.59 |
| 2   | 28.44                  | 28.27 | 28.18 | 27.98 |
| 3   | 28.83                  | 29.07 | 28.88 | 28.87 |
| 4   | 29.31                  | 29.43 | 29.77 | 29.79 |
| 5   | 30.98                  | 30.90 | 30.71 | 30.70 |
| 6   | 31.79                  | 31.65 | 31.54 | 31.23 |
| 7   | 24.62                  | 24.07 | 24.28 | 24.52 |
| 8   | 25.77                  | 25.10 | 25.02 | 24.99 |
| 9   | 26.08                  | 25.90 | 25.81 | 25.99 |
| 10  | 26.84                  | 26.83 | 26.75 | 26.98 |
| 11  | 27.49                  | 27.83 | 27.63 | 27.76 |
| 12  | 28.53                  | 28.55 | 28.51 | 28.64 |
| 13  | 18.23                  | 18.46 | 18.65 | 19.30 |
| 14  | 19.21                  | 19.24 | 19.20 | 19.82 |
| 15  | 20.67                  | 20.63 | 20.60 | 20.87 |
| 16  | 21.32                  | 21.40 | 22.15 | 21.79 |
| 17  | 23.78                  | 23.39 | 23.20 | 22.77 |
| 18  | 24.12                  | 24.03 | 24.09 | 23.66 |
| 19  | 15.37                  | 5.40  | 15.49 | 15.95 |
| 20  | 16.43                  | 16.53 | 16.22 | 16.49 |
| 21  | 17.83                  | 17.90 | 17.86 | 17.51 |
| 22  | 19.33                  | 19.06 | 18.83 | 18.55 |
| 23  | 19.85                  | 20.28 | 19.88 | 19.54 |
| 24  | 20.74                  | 20.75 | 20.80 | 20.43 |
| 25  | 15.64                  | 15.60 | 15.63 | 14.73 |
| 26  | 16.44                  | 16.44 | 16.46 | 16.44 |
| 27  | 17.31                  | 17.19 | 16.38 | 16.93 |
| 28  | 17.55                  | 7.94  | 17.05 | 17.38 |
| 29  | 18.47                  | 18.38 | 18.04 | 18.36 |
| 30  | 18.72                  | 18.72 | 18.97 | 19.26 |

practical parameter on the AgNPs size, sensitivity analysis of the most appropriate model, i.e., GEP-1, was carried out (Figure 9). As shown, plant extract, concentration of AgNO₃, and stirring time had positive effects on reducing the AgNPs size with plant extract being the most effective parameter. Furthermore, reaction temperature, with negligibly negative effect within the investigated range, had the minimum effect on the size of AgNPs.

Figure 10 illustrates the effects of two most influential parameters (Mc and Pe) on the AgNPs size in 3D profiles. As shown, decreasing Pe from 1
Figure 9. Sensitivity analysis of the practical parameters for the green synthesis of AgNPs (plant extract ($Pe$), temperature of reaction ($Tr$), stirring time ($St$), and molar concentration of AgNPs ($Mc$)).

Figure 10. 3D profiles of AgNPs changes with changes in the most important parameters (plant extract ($Pe$) and molar concentration of AgNPs ($Mc$)) for green synthesis when other practical parameters ($Tr$ (temperature of reaction) = 40°C and $St$ (stirring time) = 12 hr) are constant.

The result indicates that 0 caused a severer enhancement in AgNPs size, even at higher levels of $Mc$ (e.g., 1.5). That is, $Pe$ is the major parameter in the synthesis and any increase in $Pe$ leads to a significant decrease in the AgNPs size.

4. Conclusion

AgNPs size is a crucial physical/chemical property that significantly affects the quality of products. Unique characteristics of green synthesis as an appropriate alternative to the conventional methods encouraged us to estimate AgNPs size prepared through green synthesis. In summary, this study tried to employ Gene Expression Programming (GEP) for the estimation of AgNPs size on the basis of experimentally collected data. Various functions and architectures of modeling under different preparation conditions were compared to find the most appropriate GEP model. The results showed that GEP-1 had the best performance in the prediction of particle size with RRSE, $R^2$, and Mean Absolute Error (MAE) equal to 0.0668, 0.9061, and 0.2545, respectively. Also, sensitivity analysis of GEP-1 revealed that plant extract and concentration of AgNO$_3$ were the most effective parameters on the size of AgNPs.

Nomenclature

- **GEP**: Gene Expression Programming
- **$Pe$**: Plant extract
- **$Tr$**: Temperature of reaction
- **$St$**: Stirring time
- **$Mc$**: Molar concentration of AgNPs
- **$R^2$**: Correlation coefficient
- **MAE**: Mean Absolute Error
- **RRSE**: Root Relative Square Error
- **ET**: Expression Tree
- **$h$**: Head of gene
- **$t$**: Tail of gene
- **RIS**: Root Insertion Sequence transposition
- **IS**: Insertion Sequence
- **BCA**: Bivariate Correlation Analysis
- **PCA**: Principal Component Analysis
- **KMO**: Kaiser-Meyer-Olkin

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