



Interval-value Based Particle Swarm Optimization algorithm for cancer-type specific gene selection and sample classification



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ABSTRACT

Microarray technology allows simultaneous measurement of the expression levels of thousands of genes within a biological tissue sample. The fundamental power of microarrays lies within the ability to conduct parallel surveys of gene expression using microarray data. The classification of tissue samples based on gene expression data is an important problem in medical diagnosis of diseases such as cancer. In gene expression data, the number of genes is usually very high compared to the number of data samples. Thus the difficulty that lies with data are of high dimensionality and the sample size is small. This research work addresses the problem by classifying resultant dataset using the existing algorithms such as Support Vector Machine (SVM), K-nearest neighbor (KNN), Interval Valued Classification (IVC) and the improvised Interval Value based Particle Swarm Optimization (IVPSO) algorithm. Thus the results show that the IVPSO algorithm outperformed compared with other algorithms under several performance evaluation functions.

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1. Introduction

Cancer classification using gene expression data usually relies on traditional supervised learning techniques, in which only labeled data (i.e., data from a sample with clinical follow-up) can be exploited for learning, while unlabeled data (i.e., data from a sample without clinical follow-up) are disregarded [1]. Recent research in the area of cancer diagnosis suggests that unlabeled data in addition to the small number of labeled data can produce significant improvement in terms of accuracy by using a technique called semi supervised learning. Indeed, semi supervised learning has proved to be effective in solving different biological problems including protein classification, prediction of transcription factor–gene interaction and gene-expression based cancer subtype discovery. Microarray technology allows simultaneous measurement of the expression levels of thousands of genes within a biological tissue sample. An important application of gene expression is to classify samples according to their gene expression profiles, such as the diagnosis or the classification of different types or subtypes of cancer [2,3]. Different classification methods from statistical and machine learning have been applied to the classification of cancer. However, high dimensionality and possibly a small number of noisy samples pose great challenges to the existing methods. The main approach to this problem was based on the existing algorithms to analyze gene expression data. Most of

the classifiers involve complex models containing numerous genes. This has limited the interpretability of the classifiers and this lack of interpretability hampers the acceptance of diagnostic tools. Classification models based on numerous genes can also be more difficult to transfer to other assay platforms, which may be more suitable for clinical application. Several researchers pointed out that the classifiers might be developed to contain a small number of genes that provide classification accuracy comparable to that achieved by models that are more complex [4]. Moreover, some more complex algorithms based on numerous genes for classification often overfit the data [5].

Prior to classification, a variety of gene selection strategies have been used. The aim of gene selection is to select a small subset of genes from a larger pool [6,7]. Gene selection methods are classified into three types: (1) filter methods, (2) wrapper methods and (3) embedded methods. Filter methods evaluate a subset of genes by looking at the intrinsic characteristics of data with respect to class labels, while wrapper methods evaluate the goodness of a gene subset by the accuracy of its learning or classification. Embedded methods are generally referred to as algorithms, where gene selection is embedded in the construction of the classifier. In the gene selection process, an optimal feature subset is always relative to a certain criterion. Every criterion measures the discriminating ability of a gene or a subset of genes to distinguish different class labels. To measure the gene–class relevance, different statistical and theoretical measures such as the t-test, entropy and mutual information are typically used, and different metrics including the Euclidean distance and correlation coefficient are employed to calculate the gene–gene redundancy [11,15].

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In filters, the characteristics in the feature selection are uncorrelated to those of the learning methods, therefore they have a better generalization property [1]. The filters, wrapper and embedded are then analyzed to identify the most frequently appearing genes which would correspond to the most predictive genes [2]. The Genetic Algorithm combined with a Support Vector Machine classifier is used for selecting predictive genes and for final gene selection and classification. The analysis of gene expression data is to identify the sets of genes as classification or diagnosis platforms. Machine learning techniques, such as artificial neural networks (ANNs), present a more flexible ‘model-free’ approach for classification and frequently yield good results [6]. The advantage of selecting a combination of genes with small redundancy, favors the selection of mutually uncorrelated genes. The selected set of paired genes was used as a new feature set for the classification.

In wrapper type methods, feature selection is “wrapped” around a learning method and a feature is directly judged by the estimated accuracy of the learning method [11]. One can often obtain a set with a very small number of non-redundant features, which gives high accuracy, because the characteristics of the features match well with the characteristics of the learning method [14]. Wrapper methods can use different performance metrics and objective functions. And also the wrapper methods select the “minimum” subset of features that provides the highest sensitivity. Embedded methods differ from other feature selection methods in the way that feature selection and learning interact [14]. In contrast to filter and wrapper approaches, in embedded methods the learning part and the feature selection part cannot be separated – the structure of the class of functions under consideration plays a crucial role [22].

2. Experiments

In this section, we evaluate the discriminative performance of our selected gene set on different classifiers. We also compare the performance of our proposed classification method to a wide range of standard classifiers: Support Vector Machine (SVM), K Nearest Neighbor (KNN), Particle Swarm Optimization (PSO) and Interval Value Classification (IVC). A set of experiments is conducted on the dataset by varying the number of genes selected to receive the highest classification accuracy.

2.1. Results on the leukemia dataset

To evaluate the performance of the proposed method in practice, this research used the datasets containing gene expression profiles from patients with acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia (AML). The leukemia dataset is collected from the UCI Repository. In the leukemia dataset 72 samples are used for the training set and 32 samples are used as the testing set. This dataset have compared with the leukemia dataset that contains the ALL/AML types. The ALL portion of the dataset is derived from two cell types, B-cells and T-cells, while the AML part is split into two types as bone marrow (BM) samples and peripheral blood (PB). The correctly classified instance for the leukemia dataset is 8.0 and incorrectly classified instance is 1.0. The comparison has been done with proposed IVPSO and several existing algorithm such as SVM, KNN, IVC. It has been found that the proposed algorithm is better than the existing algorithm for classifying the leukemia datasets. Table 2.1 shows the results for the leukemia dataset and Fig. 2 shows the performance comparison of existing and proposed algorithms for the leukemia dataset.

2.2. Results on the breast cancer dataset

To further test the performance of the proposed method the breast cancer dataset is used for comparison, and it is collected from the UCI Repository. Here the dataset consists of 69 samples from human cancer cell lines. The breast cancer dataset spans nine classes and gene

Table 2.1

Performance comparison of existing and proposed methods for the leukemia dataset.

Algorithms/performance metrics	TP rate	FP rate	Precision	Accuracy
Support Vector Machine	70.97	28.61	43.75	69.01
K-Nearest Neighbor	80.27	22.2	90.0	71.28
Interval Valued Classification	85.0	60.0	94.4	78.26
Particle Swarm Optimization	90.0	22.6	83.35	81.8
Interval Value based Particle Swarm Optimization	100	0.0	90.0	96.88

expression levels were measured for 769 genes. The prediction accuracy of 74.86 is reported in reference using one-versus-the rest IVC with 150 selected genes. To test the proposed algorithm on an external dataset, 43 samples are used for the training dataset while 18 samples as the testing dataset. Based on 150 genes selected and 12 genes selected by PSO, the classification accuracy report of all the compared algorithms can be predicted. The correctly classified instance for the breast cancer dataset is 7.2 and incorrectly classified instance is 2.8. Consistent with the results on the breast cancer dataset in this experiment, the proposed method also achieved the highest classification accuracy. Thus Table 2.2 shows the results for the breast cancer dataset and Fig. 3 shows the performance comparison of existing and proposed algorithms for the breast cancer dataset.

2.3. Results on the lung cancer datasets

The performance of the proposed algorithm is calculated by using the lung cancer dataset and it can be collected from the UCI Repository which consists of 61 samples from human cancer cells. In the lung cancer dataset, the class and gene expression levels were measured for 462 genes. The prediction accuracy of IVC is 70.55 with 72 instances and 32 attributes. To test the proposed algorithm, a dataset of 43 samples was used for the training dataset and 32 samples as the testing dataset. The correctly classified instance for the lung cancer dataset is 7.2 and the incorrectly classified instance is 2.8. Consistent with the results on the lung cancer dataset in this experiment, the proposed method also achieved the highest classification accuracy. Thus Table 2.3 shows the results for the lung cancer dataset and Fig. 4 shows the performance comparison of existing and proposed algorithms for the lung cancer dataset.

2.4. Results on blood cancer datasets

The performance of the proposed algorithm is also measured using the blood cancer datasets and it can be collected from the NCBI database. Blood cancer is an umbrella term for cancers that affect the bone marrow, blood and lymphatic system. In this dataset a total of 399 instances and 18 attributes were used. In this analysis, the data are based on class distribution. In 339 instances, to test the proposed algorithm a dataset of 48 samples were used for the training dataset and 36 samples as the testing dataset. The correctly classified instance is 7.8 and the incorrectly classified instances are 2.2. Consistent with the results on the blood cancer dataset with this experiment, the proposed method also achieved the highest classification accuracy. Thus Table 2.4 shows the results for the blood cancer dataset and Fig. 5 shows the

Table 2.2

Performance comparison of existing and proposed methods for breast cancer dataset.

Algorithms/performance metrics	TP rate	FP rate	Precision	Accuracy
Support Vector Machine	71.26	29.45	70.75	71.87
K Nearest Neighbor	76.8	27.24	75.95	67.29
Interval Valued Classification	80.1	25.24	75.66	74.86
Particle Swarm Optimization	82.8	20.86	79.87	84.63
Interval Value based Particle Swarm Optimization	90.16	17.17	83.9	92.24

Table 2.3
Performance comparison of existing and proposed methods for lung cancer dataset.

Algorithms/performance metrics	TP rate	FP rate	Precision	Accuracy
Support Vector Machine	71.30	28.4	71.4	70.55
K Nearest Neighbor	77.8	26.24	73.95	65.29
Interval Valued Classification	79.19	24.08	76.67	79.03
Particle Swarm Optimization	83.27	21.03	79.83	80.02
Interval Value based Particle Swarm Optimization	89.24	19.42	82.12	94.68

performance comparison of existing and proposed algorithms for the blood cancer dataset.

2.5. Discussion

From the experimental results it is inferred that for the leukemia dataset the proposed IVPSO algorithm performs 29.03% better than the SVM algorithm, 19.73% better than the KNN algorithm, 15% better than the IVC algorithm and 10% better than the PSO algorithm. For the breast cancer dataset the proposed IVPSO algorithm performs 20.96% better than the SVM algorithm, 14.82% better than the KNN algorithm, 11.16% better than the IVC algorithm and 8.16% better than the PSO algorithm. And for the lung cancer dataset the proposed IVPSO algorithm performs 20.11% better than the SVM algorithm, 12.82% better than the KNN algorithm, 11.26% better than the IVC algorithm and 6.69% better than the PSO algorithm. Finally, for the blood cancer dataset the proposed IVPSO algorithm performs 18.78% better than the SVM algorithm, 11.4% better than the KNN algorithm, 30.78% better than the IVC algorithm, and 3.72% better than the PSO algorithm. Thus Fig. 1 shows the comparison of accuracy for the leukemia, breast cancer, and lung cancer and blood cancer datasets for the existing and proposed algorithms.

- (1) The accuracy of the classification is highly dependent on the classification method. For instance, with the gene set selected by the PSO method, the IVPSO classifier has an accuracy of 96.88% on the ALL–AML dataset, the average classification accuracy.

IVPSO is 96.88% > SVM is 69.01% > KNN is 71.28% > IVC is 82.6%. It is observed that proposed IVPSO method gets the best performance.

- (2) The accuracy of the classification is also highly dependent on the selected gene set. When the genes are selected by the PSO method, the SVM classifier has an accuracy of 91.41% on the ALL–AML-3 dataset. On the same dataset with the gene set selected by the IVR method, the accuracy of SVM is 97.27%. This significant differential accuracy between the gene selection method of PSO and IVC also occurs in the other classifiers.
- (3) It achieves better performance than any of the other classifiers. It is conceivable that feature selection raises the accuracy since it can reduce the number of insignificant dimensions, thereby overcoming the curse of dimensionality. This appears to be the case for the KNN and SVM classifier methods. The accuracy of KNN, Decision Tree and SVM is improved on the two datasets with genes selected by the PSO method.
- (4) Remarkably, with the aid of feature selection, IVC achieves a 96.88% accuracy on the ALL–AML dataset and 92.24% accuracy

Table 2.4
Performance comparison of existing and proposed methods for the blood cancer dataset.

Algorithms/performance metrics	TP rate	FP rate	Precision	Accuracy
Support Vector Machine	66	22.2	70	66.66
K Nearest Neighbor	72	25	72.3	72.82
Interval Valued Classification	56.25	43.75	81.2	78.26
Particle Swarm Optimization	78.6	22.1	79.2	80.26
Interval Value based Particle Swarm Optimization	81.26	18.19	83.6	90.86

on the breast cancer dataset. For the SVM method, it is possible to achieve very high accuracy on most of the microarray datasets [24]. However, the best performance on the experimental datasets does not outperform the IVPSO method.

From the results shown in Tables 2.1–2.4, it is inferred that the IVPSO is the best method for sample classification based on gene expression. It achieves better performance than any of the other classifiers. This appears to be the case for the SVM, KNN and IVC classifier methods. The accuracy of SVM, KNN and IVC is improved on the four datasets with genes selected by the different methods. For the SVM method, it is possible to achieve very high accuracy on most of the microarray datasets [24]. These four datasets have smaller sample sizes than those of the other datasets, so one may conclude that multiclass classification based on gene expression can be effectively solved when the sample size is large. Although it is widely used in text categorization in order to perform very well for tissue classification based on gene expression using the standard feature selection method [24]. From the experimental results above, this research concludes that the proposed approach is superior to other methods. This may be due to the following advantages: interval-value based particle swarm optimization, minimum redundancy of the selected gene subset and simple classifiers.

The experimental results show that our proposed method has superior performance. Consecutively, in this work a new classification algorithm is proposed to classify the leukemia datasets. The tables and graphs represent the comparison of performance measures for the datasets such as leukemia, breast cancer, lung cancer and blood cancer. We analyzed and compared the performance of existing classification algorithms such as SVM (Support Vector Machines), KNN (K Nearest Neighbor), and Interval-valued Classification (IVC), Particle Swarm Optimization (PSO) and the proposed PSO-IVC (Particle Swarm Optimization–IVC). The performance is evaluated by using the parameters such as accuracy, precision, true positive rate and false positive rate. From the experimental results it is inferred that the proposed method works better than the existing systems for classifying the datasets.

3. Gene selection and tissue sample classification methods

The particle swarm optimization is a computational method which optimizes a problem by continuously trying to enhance a candidate solution with regard to a given measure of quality. In every iteration process, each candidate solution is calculated by the objective function being optimized, deciding the fitness of that solution. Every particle preserves its position, composed of the candidate solution and its evaluated fitness, and its velocity.

3.1. Gene selection

Based on the Interval Value Based Particle Swarm Optimization, we present a method to select the genes & tissue.

Algorithm IVPSO

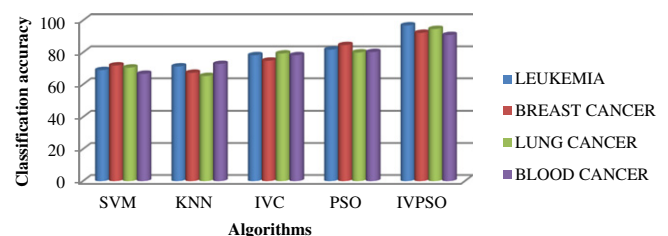


Fig. 1. Comparison of accuracy on the leukemia, breast cancer, lung cancer and blood cancer datasets.

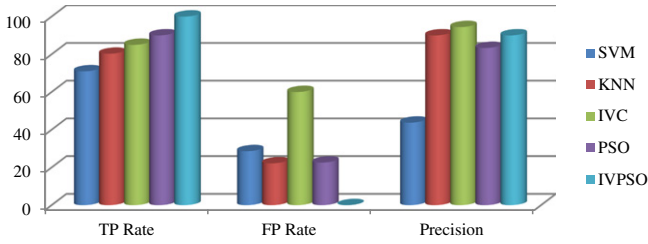


Fig. 2. Performance comparison of existing and proposed methods for the leukemia dataset.

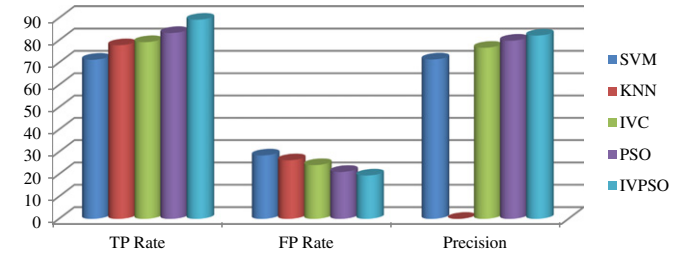


Fig. 4. Performance comparison of existing and proposed methods for the lung cancer dataset.

1. Initialize N number of particles in the swarm, each particle having a position x_i and velocity v_i . Let pBest be the best known position of particle i and gbest as the best known position of the entire swarm
2. Initialize the particle's position x_i
3. For each particle $i = 1, 2, \dots, N$
4. Calculate fitness value for every particle
5. If fitness value is better than the best fitness value (pBest)
6. Set current value as the new pBest
7. Until a termination criterion is met
8. Select the particle with best fitness value of all particles as the gbest
9. For every particle
10. //Calculation of particle velocity
11. $v_i(t + 1) = wv_i(t) + c_2r_2[\bar{x}_i(t) - x_i(t)] + c_2r_2[g(t) - x_i(t)]$ //Where, the index of the particle is represented by i , $v_i(t)$ is the velocity of particle i at time t , $x_i(t)$ is the position of particle i at time t ; the parameters w , c_1 , and c_2 are coefficients
12. Update particle position
13. $x_i(t + 1) = x_i(t) + v_i(t + 1)$

Until some stopping conditions are met.

4. Preliminaries

4.1. Microarray dataset

A microarray dataset is a gene expression data, in which each column represents a gene and each row represents a sample with a class label. Let $G = \{g_1, \dots, g_n\}$ be a set of genes and $U = \{s_1, \dots, s_m\}$ be a set of samples. The corresponding gene expression matrix can be represented, as m is the number of samples and n is the number of genes. The matrix X is composed of m row vectors $i = 1, 2, \dots, m$. Each vector in the gene expression matrix may be regarded as a point in n -dimensional space, and each of the n columns consists of an m -element expression vector for a single gene.

4.2. Particle Swarm Optimization

Particle Swarm Optimization was first proposed by Kennedy and Eberhart in 1995 [13]. PSO is a population based evolutionary algorithm inspired by the social behavior of bird flocking or fish schooling. In the

description of PSO, the swarm is made up of a certain number of particles (similar to population of individuals in EAs). At each iteration, all the particles move in the problem space to find the global optima. Each particle has a current position vector and a velocity vector for directing its movement.

The particle swarm optimization is a computational method which optimizes a problem by continuously trying to enhance a candidate solution with regard to a given measure of quality. In every iteration process, each candidate solution is calculated by the objective function being optimized, deciding the fitness of that solution. Every particle preserves its position composed of the candidate solution and its evaluated fitness along with its velocity. Furthermore, it considers the best fitness value, which has been accomplished during the process of the algorithm that which is referred to as the individual best fitness, and the candidate solution that achieved this fitness, which is referred to as the individual best position. At last, the PSO algorithm maintains the best fitness value accomplished among all particles in the swarm, called the global best fitness, and the candidate solution that achieved this fitness, called the global best position or global best candidate solution.

$$v_{id}^{k+1} = w \cdot v_{id}^k + c_1 \cdot rand_1() \cdot (p_{id}^k - x_{id}^k) + c_2 \cdot rand_2() \cdot (p_{gd}^k - x_{id}^k) \quad 1$$

$$x_{id}^{k+1} = x_{id}^k + v_{id}^{k+1} \quad 2$$

$$\vec{p}_{id}^{k+1} = \begin{cases} \vec{x}_i^{k+1} : Fitness(\vec{x}_i^{k+1}) > fitness(\vec{p}_i^{k+1}) \\ \vec{p}_i^k : Fitness(\vec{x}_i^{k+1}) > fitness(\vec{p}_i^k) \end{cases} \quad 3$$

$$\vec{p}_i^{k+1} = \arg \max_{p_i} \vec{p}_i^{k+1} \quad 4$$

PSO optimizes a problem by having solutions, here dubbed particles, and moving these particles around in the search-space according to simple mathematical formulae over the particle's position and velocity. Each particle's movement is influenced by its local best known position and is also guided toward the best known positions in the search-space, which are updated as better positions are found by other particles. This is expected to move the swarm toward the best solutions. Although the proposed method was originally designed for microarray data analysis,

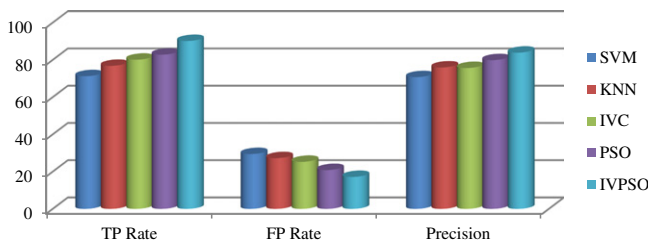


Fig. 3. Performance comparison of existing and proposed methods for the breast cancer dataset.

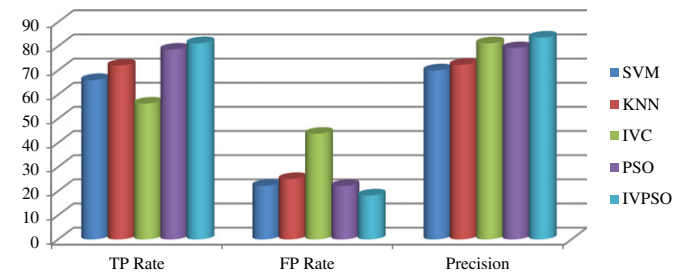


Fig. 5. Performance comparison of existing and proposed methods for the blood cancer dataset.

it can be applied to the data from the next generation sequencing technologies.

$$\vec{p}_i^{k+1} = \arg \max_{x_{pi}} \vec{p}_i^{k+1} x_{id}^{k+1} = x_{id}^k + v_{id}^{k+1}. \quad 5$$

Eqs. (1) and (2) describe the velocity and position update of a given particle i at a certain iteration k . Eq. (1) calculates a new velocity v_i for each particle (potential solution) based on its previous velocity, the particle's location at which the best fitness so far has been found $p_{Best\ i}$, and the population global (or local neighborhood, in the neighborhood version of the algorithm) location at which the best fitness so far has been achieved. Individual and social weights are represented by means of '1 and 2' factors respectively. Finally, positions are random numbers in range $\{0, 1\}$, and represent the inertia weight factor. Eq. (6) updates each particle's position x_i in solution Space.

4.3. Assessment metrics in the leukemia datasets.

Usually, the accuracy rate in Eq. (6) is the most frequently used measure in assessment metrics. But in the framework of the leukemia datasets, the accuracy is a proper measure, because it distinguishes between the numbers of correctly classified examples of different classes.

$$\text{Acc} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FN} + \text{FP} + \text{TN}} \quad 6$$

$$\text{TP rate} = \frac{\text{TP}}{\text{TP} + \text{FN}} \quad 7$$

$$\text{FP rate} = \frac{\text{FP}}{\text{FP} + \text{TN}} \quad 8$$

$$\text{Pre} = \frac{\text{TP}}{\text{TP} + \text{FP}} \quad 9$$

$$\text{True positive rate (TPR)} = \text{TP/P} \quad 10$$

$$P = (\text{TP} + \text{FN}) \quad 11$$

where, P is Positive and TP is the True Positive.

5. Conclusion and future prospects

This research work proposed a combination method of Particle Swarm Optimization and interval valued classification based gene selection and sample classification. This approach reduces the number of genes selected and increases the classification accuracy in terms of correctly and incorrectly classified instances. Many methods have been proposed to solve this problem. But in this research work, performance analysis has been done on various classifiers such as the SVM, KNN, PSO, IVC and IVPSO. The proposed gene selection method can improve the performance of the IVPSO classification method to achieve an accuracy

of 96.88%. Based on the classification and comparison results, the proposed algorithm performs better than other algorithms. The correctly and incorrectly classified instances also have been detected. For all the datasets the proposed algorithms perform better than the existing methods in the case of numerical datasets. From the experimental analysis it is inferred that for all the datasets the proposed IVPSO algorithm performs better than the existing classification algorithms.

The proposed classification technique can be easily extended to any other applications different from the leukemia dataset problem. In future, this method can be combined with any evolutionary algorithms to get a new and more powerful classification algorithm, and it can also be extended along with different classification techniques. In the future it can also be solved on other datasets, and in the future it can be extended to modify the Interval Value based Particle Swarm Optimization algorithm to obtain more effective results by using different parameters. IVPSO classification, for instance, can be well suited for gene selection and different filtering techniques. Since this task requires rapid model updates with high level of accuracies, IVPSO can be a good choice.

Conflict of interest

The authors declare that there are no conflicts of interest.

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