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Gene selection for cancer identification: a decision tree model empowered by particle swarm optimization algorithm

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Abstract

Background: In the application of microarray data, how to select a small number of informative genes from thousands of genes that may contribute to the occurrence of cancers is an important issue. Many researchers use various computational intelligence methods to analyzed gene expression data.

Results: To achieve efficient gene selection from thousands of candidate genes that can contribute in identifying cancers, this study aims at developing a novel method utilizing particle swarm optimization combined with a decision tree as the classifier. This study also compares the performance of our proposed method with other well-known benchmark classification methods (support vector machine, self-organizing map, back propagation neural network, C4.5 decision tree, Naive Bayes, CART decision tree, and artificial immune recognition system) and conducts experiments on 11 gene expression cancer datasets.

Conclusion: Based on statistical analysis, our proposed method outperforms other popular classifiers for all test datasets, and is compatible to SVM for certain specific datasets. Further, the housekeeping genes with various expression patterns and tissue-specific genes are identified. These genes provide a high discrimination power on cancer classification.

Keyword: Gene expression, Cancer, Particle swarm optimization, Decision tree classifier

Background

Researchers have tried to analyze thousands of genes simultaneously by microarray technology to obtain important information about specific cellular functions of gene(s) which can be used in cancer diagnosis and prognosis [1]. The gene selection from gene expression data are challenging due to the properties of small sample size, high dimension and high noise. A method is needed for choosing the important subset of genes with high classification accuracy. Such method would not only enable doctors to identify a small subset of biologically relevant genes for cancers, but will also save computational costs [2].

The gene selection method can be divided into three classes, the wrapper, the filter, and the embedded approaches. Wrappers utilize learning machine and search for the best features in the space of all feature subsets. Despite their simplicity and often having the best performance results, wrappers highly depend on the inductive principle of the learning model and may suffer from excessive computational complexity because the learning machine has to be retrained for each feature subset considered [3]. The wrapper method is usually superior to the filter one since it involves intercorrelation of individual genes in a multivariate manner, and can automatically determine the optimal number of feature genes for a particular classifier. The filter approach usually employs statistical methods to collect the intrinsic characteristics of genes in discriminating the targeted phenotype class, such as statistical tests, Wilcoxon's rank test and mutual information, to directly select feature genes [4].

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This approach is easily implemented, but ignores the complex interaction among genes. Finally, the embedded method is a catch-all group technique which performs feature selection as part of the model construction process. It is similar to the wrapper method, while multiple algorithms can be combined in the embedded method to perform feature subset selection [5,6]. Genetic algorithms (GAs) [7] are generally used as the search engine for feature subset in the embedded method, while other classification methods, such as estimation of distribution algorithm (EDA) with SVM [8-13], K nearest neighbors/genetic algorithms (KNN/GA) [14], genetic algorithms-support vector machine (GA-SVM) [15] and so forth, are used to select feature subset.

Particle Swarm Optimization (PSO), developed by Kennedy and Eberhart [16], is a population-based meta-heuristic on the basis of stochastic optimization, inspired by the social behavior of flocks of birds or schools of fish [17]. PSO has been widely applied in many fields to solve various optimization problems, including gene selection [1,2,18-20]. A swarm of particles with randomly initialized positions would move toward the optimal position along the search path that is iteratively updated on the basis of the best particle position and velocity in PSO. The potential solutions, called particles, are used to represent a candidate solution for the problem. Among the classifiers given a specific search algorithm, C4.5 is a decision tree-based classifier listed in the top 10 most influential data-mining algorithms [21]. Decision trees are a linear method which is easy to interpret and understand.

This paper presents a PSO-based algorithm to address the problem of gene selection. The proposed approach is an integration of PSO searching algorithm and C4.5 decision tree classifier, called PSODT. Combining PSO with C4.5 classifier has rarely been investigated by previous researchers. The performance of our proposed method will be evaluated by 11 microarray datasets, which consist of 1 dataset from cancer patients of the M² DB in Taiwan [22] and 10 from the Gene Expression Model Selector [23]. In addition, the performance of our proposed method will be compared with other well-known classifier algorithms, such as self-organizing map (SOM), C4.5, back propagation neural network (BPNN), SVM, NaiveBayes (NB), CART decision tree, and artificial immune recognition system (AIRS). Statistical test will be employed to discriminate the difference of all the algorithms in terms of classification accuracy.

Gene selection and classification

DNA microarray (also commonly known as DNA chip or biochip) is a collection of microscopic DNA spots attached to a solid surface and allows researchers to measure the expression levels of thousands of genes simultaneously in a single experiment. The DNA microarray is operated by

classifier approaches to compare the gene expression levels in tissues under different conditions [24]; for instance, the study of Jiang et al. [25] devised an RF-based method to classify real pre-miRNAs using a hybrid feature set for the wild type versus mutant, or healthy versus diseased classes. Batuwita and Palade [26] developed a classifier named micro-Pred for distinguishing human pre-miRNA hairpins from both pseudo hairpins and other ncRNAs. Wang et al. [27] presented a hybrid method combining GA and SVM to identify the optimal subset of microarray datasets, and claimed their method was superior to those obtained by microPred and miPred. Further, Nanni et al [28] recently devised a support vector machine (SVM) as classifier for microarray gene classification. Their method combines different feature reduction approaches to improve classification performance of the accuracy and area under the receiver operating characteristic (ROC). Park et al [29] presented a method for inferring combinatorial Boolean rules of gene sets for cancer classification and cancer transcriptome. Their study identified a small group of gene sets that synergistically contribute to the classification of samples into their corresponding phenotypic groups (such as normal and cancer) and reduced the search space of the possible Boolean rules.

Due to the high computational cost and memory usage for classifying high dimensional data, appropriate gene

Table 1 Random seed comparison

		Visual C#	U(0,1)
11_Tumors	1	96.22	97.52
	2	95.31	98.32
	3	96.72	98.04
	4	96.31	97.66
	5	97.62	97.57
	Avg.	96.44	97.82
	(Std.)	0.84	(0.35)
DLBCL	1	91.31	91.88
	2	89.70	92.22
	3	88.77	91.99
	4	88.72	92.87
	5	92.99	93.22
	Avg.	90.30	92.55
	(Std.)	1.83	(0.61)
14_Tumors	1	65.00	74.00
	2	63.00	75.00
	3	63.00	75.00
	4	63.00	74.00
	5	67.00	75.00
	Avg.	64.20	74.60
	(Std.)	1.79	(0.55)

```

01 input
02  $c_1, c_2, r_1, r_2, W, v_{min}, v_{max}$ 
03 output
04 GB
05 The fitness value of GB
06 begin
07 Initialize Population
08 while (max iteration or convergence criteria is not met) do
09   for  $i = 1$  to numbers of particles
10     Evaluate fitness value of the particle by C4.5
11     if the fitness value of  $X_i$  is greater than that of  $PB_i$ 
12       then  $PB_i = X_i$ 
13     end if
14     if the fitness value of  $X_i$  is greater than that of GB
15       then  $GB = X_i$ 
16     end if
17     for  $d = 1$  to no of genes
18        $v_{id}^{new} = w \times v_{id}^{old} + c_1 r_1 (pb_{id}^{old} - x_{id}^{old}) + c_2 r_2 (pb_d^{old} - x_{id}^{old})$ 
19       if  $v_{id}^{old} > v_{max}$  then  $v_{id}^{new} = v_{max}$ 
20       if  $v_{id}^{old} < v_{min}$  then  $v_{id}^{new} = v_{min}$ 
21       if  $sigmoid(v_{id}^{new}) > U(0,1)$ 
22         then
23            $x_{id}^{new} = 1$ 
24         else
25            $x_{id}^{new} = 0$ 
26         end if
27       next d
28     next i
29   end while
30 end
    
```

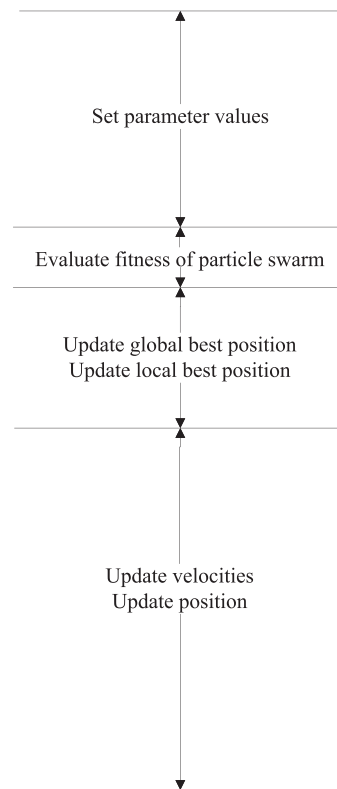


Figure 1 The proposed PSODT for gene selection.

selection procedure is required to improve classification performance. As addressed by Tan et al. [30], given the quantity and complexity of the gene expression data, it is unlikely to efficiently compute and compare the $n \times m$ gene expression matrix by manually. Instead, machine learning and other artificial intelligence techniques have potential to characterize gene expression data promptly [8,31,32].

Previous study

Some studies have proposed PSO algorithm for gene selection problems. For instance, Alba et al. [1] presented

a modified PSO (geometric PSO) for high-dimensional microarray data. Both augmented SVM and GA were proposed for comparison on six public cancer datasets. Li et al. [23] devised a method of combining PSO with a GA and adopted SVM as the classifier for gene selection. Their proposed approach used three benchmark gene expression datasets for validation: leukemia, colon cancer, and breast cancer. Mohamad et al. [19] presented an improved binary PSO combined with an SVM classifier to select a near-optimal subset of informative genes relevant to cancer classification.

Zhao et al. [33] lately presented a novel hybrid framework (NHF) for gene selection and cancer classification of high dimensional microarray data by combining the information gain (IG), F-score, GA, PSO, and SVM. Their method was compared to PSO-based, GA-based, ant colony optimization-based, and simulated annealing (SA)-based

Table 2 Microarray datasets employed in the study

Data set	Feature size	Sample size	Class size	Particle size
11_Tumors	12601	203	5	126
14_Tumors	10368	50	4	104
9_Tumors	10368	50	4	104
Brain_Tumor1	5727	60	9	57
Brain_Tumor2	12534	174	11	125
Leukemia2	5328	72	3	53
Lung_Cancer	11226	72	3	112
SRBCT	5470	77	2	55
Prostate_Tumor	10510	102	2	105
DLBCL	83	2309	4	10

```

218934_s_at <= 2.7133 (Node 2)
| 206166_s_at <= 2.5063 (Node 4)
| | 212341_at <= 10.026: Ovary (114.0) (Node 5)
| | 212341_at > 10.026: Cervix Uteri (5.0) (Node 6)
| 206166_s_at > 2.5063: Cervix Uteri (59.0) (Node 3)
218934_s_at > 2.7133: Uterus (29.0) (Node 1)
    
```

Figure 2 An illustration of partial decision tree.

Table 3 Classification accuracy for 10 microarray datasets (%)

Data set	Run no.	SVM	SOM	BPNN	C4.5	NB	CART	AIRS	PSODT
11_Tumors	1	93.85	78.76	69.38	90.31	80.3	84.73	59.61	97.52
	2	93.79	79.22	69.12	91.22	80.79	85.22	59.61	98.32
	3	94.22	78.98	69.74	90.87	80.79	84.73	56.65	98.04
	4	94.01	77.22	68.99	89.81	80.47	86.21	56.65	97.66
	5	93.60	77.81	69.21	88.72	80.30	84.73	60.59	97.57
	Avg.	93.89	78.55	69.29	90.19	80.53	85.12	58.62	97.82
	(Std.)	(0.23)	(0.90)	(0.29)	(0.98)	(0.25)	(0.64)	(1.84)	(0.35)
14_Tumors	1	60.00	40.00	28.00	48.00	72.00	56.00	54.00	74.00
	2	62.00	40.00	30.00	48.00	70.00	54.00	54.00	75.00
	3	60.00	40.00	28.00	48.00	72.00	54.00	52.00	75.00
	4	60.00	40.00	28.00	48.00	74.00	56.00	52.00	74.00
	5	62.00	40.00	29.00	48.00	70.00	54.00	54.00	75.00
	Avg.	60.80	40.00	28.60	48.00	71.60	54.80	53.20	74.60
	(Std.)	(1.10)	(0.00)	(0.89)	(0.00)	(1.67)	(1.10)	(1.10)	(0.55)
9_Tumors	1	76.00	40.00	34.00	52.00	70.00	62.00	48.00	74.00
	2	76.00	40.00	34.00	52.00	70.00	62.00	46.00	74.00
	3	76.00	40.00	34.00	52.00	70.00	62.00	46.00	74.00
	4	76.00	40.00	34.00	52.00	70.00	64.00	46.00	74.00
	5	76.00	40.00	34.00	52.00	70.00	60.00	46.00	74.00
	Avg.	76.00	40.00	34.00	52.00	70.00	62.00	46.40	74.00
	(Std.)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(1.41)	(0.89)	(0.00)
Brain_Tumor1	1	49.20	18.33	15.00	41.67	41.67	30.00	33.33	56.34
	2	49.71	19.72	15.21	41.89	41.33	28.33	35.00	57.22
	3	49.06	18.34	15.30	42.00	41.67	30.00	31.67	57.31
	4	48.78	17.78	15.23	41.79	41.67	33.34	30.00	56.96
	5	49.22	18.40	15.00	41.98	40.67	30.00	35.00	57.33
	Avg.	49.19	18.51	15.15	41.87	41.40	30.33	33.00	57.03
	(Std.)	(0.34)	(0.72)	(0.14)	(0.14)	(0.43)	(1.83)	(2.17)	(0.41)
Brain_Tumor2	1	83.03	50.00	25.28	74.12	81.61	71.24	48.28	85.75
	2	83.77	48.21	25.22	73.98	85.06	71.84	47.7	86.22
	3	83.21	49.77	25.28	74.22	84.48	70.11	44.83	86.52
	4	83.70	49.21	25.31	74.29	81.61	71.24	45.98	86.13
	5	84.01	49.80	25.30	74.22	83.33	69.54	48.28	85.70
	Avg.	83.54	49.40	25.28	74.17	83.22	70.79	47.01	86.06
	(Std.)	(0.41)	(0.73)	(0.03)	(0.12)	(1.59)	(0.94)	(1.54)	(0.34)
Leukemia2	1	93.89	60.86	50.10	90.29	93.06	84.72	47.22	100.00
	2	94.22	60.73	50.01	90.33	93.06	84.72	44.44	100.00
	3	93.71	60.80	50.22	90.21	94.44	83.33	48.61	100.00
	4	93.72	60.78	50.19	90.76	93.06	84.72	45.67	100.00
	5	93.80	62.09	50.31	90.52	94.44	81.94	47.22	100.00
	Avg.	93.87	61.05	50.17	90.42	93.61	83.89	46.63	100.00
	(Std.)	(0.21)	(0.58)	(0.12)	(0.22)	(0.76)	(1.24)	(1.61)	(0.00)
Lung_Cancer	1	98.27	68.19	39.14	90.29	93.06	73.61	57.72	100.00
	2	98.22	68.27	39.24	90.31	93.06	73.61	55.78	100.00

Table 3 Classification accuracy for 10 microarray datasets (%) (Continued)

	3	97.43	67.85	39.17	90.22	93.06	73.61	57.72	100.00
	4	97.47	68.33	38.79	90.54	91.67	73.61	55.56	100.00
	5	97.12	68.12	39.01	90.31	93.06	73.61	57.72	100.00
	Avg.	97.70	68.15	39.07	90.33	92.78	73.61	56.90	100.00
	(Std.)	(0.51)	(0.19)	(0.18)	(0.12)	(0.62)	(0.00)	(1.13)	(0.00)
SRBCT	1	96.62	67.67	83.08	78.00	80.52	87.01	51.95	92.49
	2	95.42	68.07	83.19	78.66	80.52	85.12	53.64	93.21
	3	96.01	68.31	82.86	78.21	79.22	85.42	53.05	93.08
	4	95.55	67.90	82.99	77.97	81.82	87.01	53.24	92.82
	5	96.01	67.21	83.01	77.90	81.82	88.32	51.95	93.10
	Avg.	95.92	67.83	83.03	78.15	80.78	86.58	52.77	92.94
	(Std.)	(0.47)	(0.42)	(0.12)	(0.31)	1.09	1.31	0.77	(0.29)
5 Prostate_Tumor	1	88.04	66.71	56.62	88.14	62.75	82.35	51.96	94.10
	2	87.91	67.51	56.77	88.14	62.75	83.33	52.94	94.64
	3	87.11	66.88	56.49	88.18	61.76	82.35	52.94	94.21
	4	88.23	67.02	56.80	88.14	62.75	82.35	52.75	94.49
	5	87.03	68.07	56.92	88.14	61.76	82.35	51.96	94.11
	Avg.	87.66	67.24	56.72	88.15	62.35	82.55	52.51	94.31
	(Std.)	(0.55)	(0.55)	(0.17)	(0.02)	0.54	0.44	0.51	(0.24)
DLBCL	1	88.42	51.47	35.88	79.34	85.11	73.49	50.6	91.88
	2	88.71	52.28	34.71	79.21	86.75	69.88	53.01	92.22
	3	89.09	51.77	34.98	79.44	85.11	69.88	54.93	91.99
	4	88.68	51.29	35.06	79.83	84.34	69.88	53.37	92.87
	5	88.97	51.49	35.78	79.20	85.11	69.88	54.21	93.22
	Avg.	88.77	51.66	35.28	79.40	85.28	70.60	53.22	92.55
	(Std.)	(0.26)	(0.39)	(0.52)	(0.26)	0.88	1.61	1.65	(0.61)

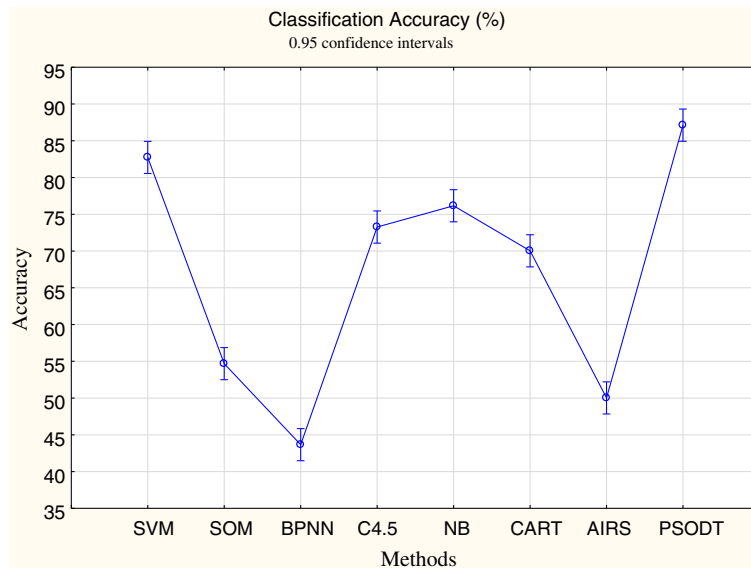


Figure 3 95% confidence interval of the mean for classification accuracy.

The inertia weight (w) was set at 0.4. Random factors, r_1 and r_2 , are within [0, 1] interval. The process was repeated until either the fitness of the given particle was 1.0 or the number of the iterations was achieved by the default value of $T = 100$. Table 2 shows the summarization of microarray dataset characteristics.

Cross-validation

To guarantee the impartial comparison of the classification results and avoid generating random results, this study adopted a five-fold cross-validation strategy. Cross-validation is a statistical method by dividing data into two segments for evaluating and comparing learning algorithms. One part used to learn or train a model and the other used to validate the model. Stone [38] and Geisser [39] employed cross-validation as means for choosing proper model parameters, as opposed to using cross-validation purely for estimating model performance [40-42]. K -fold cross-validation is used to evaluate algorithms. In this study we set $K = 5$, and the details are stated as follows: in each iteration, the algorithms apply K folds of data to earn one or more models, and subsequently the learned models are asked to predict the data in the validation fold. The performance of the algorithm on each fold is tracked by its accuracy. Upon completion, the K samples of the accuracy is available for validation.

An illustration of the resulting cancer classifier structure

Figure 2 demonstrates a sample decision tree for classifying three female cancers (i.e., ovary, cervix uteri and uterus). The genes causing cancers led to a classification tree with four terminal nodes (or clusters of cancer). For instance, 218934_s_at, 206166_s_at and 212341_at are identified as splitters. 218934_s_at are strongly associated with the three cancers; the first branch of the tree is based on 218934_s_at: a high score (i.e., 218934_s_at > 2.7133) implies the occurrence of uterus cancer (Node 1). When 218934_s_at <= 2.7133 (Node 2), 206166_s_at > 2.5063

Table 7 The arrays of cancers

#	Cancer	Sample size
1	Bladder	94
2	Liver	107
3	Cervix Uteri	148
4	Prostate	166
5	Lung	222
6	Brain	250
7	Lymph Node	280
8	Kidney	301
9	Ovary	331
10	Colon	437
11	Blood	503
12	Bone Marrow	676
13	Breast	1817

implies the occurrence of cervix uteri cancer (Node 3), and when 206166_s_at <= 2.5063 (Node 4) and 212341_at <= 10.026, it implies the occurrence of ovary cancer (Node 5); otherwise, 212341_at > 10.026 implies again the occurrence of cervix uteri cancer (Node 6).

Benchmark results with other classification algorithms

To confirm effectiveness of our proposed PSODT, this study compares its accuracy with the other seven popular classification algorithms (i.e., SVM, SOM, BPNN, C4.5, BN, CART, and AIRS). Table 3 shows the accuracy of our proposed method as compared to the other four algorithms. Five-fold cross-validation is applied on the datasets and the average and standard deviations were obtained. Our proposed method was superior to the others, except it is compatible to SVM for two datasets, 9_Tumors and SRBCT. The stability (convergence) shows that the standard deviation of PSODT is less than 1%. Figure 3 shows the averaged classification accuracy in 95% confidence interval (with respect to the 10 datasets) which indicates that

Table 6 CPU time (in sec.)

Data set	SVM	SOM	BPNN	C4.5	NB	CART	AIRS	PSODT
11_Tumors	6.63	33.57	252.10	27.53	36.21	110.75	50.90	1203.80
14_Tumors	0.63	3.90	31.16	2.06	5.70	10.62	14.12	139.53
9_Tumors	0.63	4.57	36.08	3.21	5.21	14.21	15.69	164.05
Brain_Tumor1	1.17	5.24	42.14	3.93	5.73	17.66	10.37	186.45
Brain_Tumor2	8.35	38.11	295.33	35.49	32.02	160.34	45.73	1348.20
Leukemia2	0.53	2.86	23.73	1.43	5.51	8.33	20.51	101.29
Lung_Cancer	0.98	5.64	44.21	3.13	9.12	19.88	21.00	198.62
SRBCT	0.31	2.77	21.23	1.37	5.52	8.53	14.99	99.10
Prostate_Tumor	1.12	8.37	64.40	2.87	13.08	18.34	34.66	300.58
DLBCL	0.30	1.64	13.66	1.11	3.22	5.90	15.21	58.06

Table 8 Classification accuracies for each run using PSODT

Data set	Run no.	Classification accuracy (%)	No. selected genes
13 cancer	1	97.26	135
	2	98.72	100
	3	97.25	134
	4	97.79	135
	5	97.39	126
	Avg.	97.68	126
	(Std.)	(0.62)	(15.02)

PSODT outperformed the other algorithms. This study used two-way ANOVA to determine whether the eight algorithms were significantly different in terms of average classification accuracy. The result fulfills the ANOVA assumptions on normality, homoscedasticity and independence. In ANOVA analysis, the classification algorithms defined as “factor”, whereas the datasets were defined as “block”. Table 4 lists the ANOVA results for average classification accuracy. The results showed significant differences of classification accuracy among the 8 algorithms. Further, to determine if each pair of the five algorithms differed from each other, Fisher’s test was used in this study, as shown in Table 5. The p-values demonstrate that our proposed method exhibits differences in mean classification accuracy as compared with the other algorithms, except it is compatible with SVM. Table 6 shows the computational time for each algorithm. Although the time consumed by the proposed tree based algorithm is significantly larger than the others, it is within a reasonable range even for the large-sized datasets.

In summary, SVM classification method which is generally considered as one of the most powerful machine learning classifiers is based on the statistical learning theory [43]. However, the structure of SVM is a black box system which does not provide insights on the reasons of a classification or explanations similar to ANN. SOM is one of the categories of ANN algorithms for supervised learning. BPNN is a common type of ANN and capable to recognize complex patterns in data. However, all these abovementioned classifiers are black box systems

and nonlinear models. NB classifier considers each of these features to contribute independently to the probability, regardless of the presence or absence of the other features. CART may be no good binary split on an attribute that has a good multi-way split [44], which may lead to inferior trees. AIRS have many parameters that is not easy to find the optimum combination of parameters. Instead, C4.5 is a classifier that creates a decision tree based on rules, and is a linearly method simple to understand and interpret. This study integrates the nonlinear search capability of PSO and linearly separable advantage of DT.

Model justification by a clinical dataset

This study investigated a set of clinical practice data including 13 actual cancer cases from the M² data bank in Taiwan [22]. The raw intensity data of cancer (CEL files) generated using Affymetrix HG-U133A and HG-U133 plus 2.0 platforms were retrieved from Array Express and Gene expression omnibus (GEO). Arrays performed with samples other than human clinical specimens, such as cell lines, primary cells, and transformed cells, were excluded.

All raw data of microarray (5,335 samples) were pre-processed using three different algorithms: Affymetrix Microarray Suite 5 (MAS5), robust multi-chip average (RMA), and GC-robust multi-chip average (GCRMA) as implemented in the Bioconductor packages. RMA and GCRMA processed data on a multi-array basis. All of the arrays of the same platform were uniformly pre-processed to reduce variance. The cancer microarray consisted of 13 cancer types, namely, bladder, blood, bone marrow, brain, breast, cervix uterus, colon, kidney, liver, lung, lymph node, ovary, and prostate. The information of each cancer is shown in Table 7.

Table 8 presents the classification accuracy of PSODT for each run and the number of genes selected. The accuracy of PSODT and SVM were 97.26 and 72.46, respectively. The test results on the 13 cancer microarrays for all benchmark algorithms are shown in Table 9. The results indicated that PSODT outperformed the SVM and other benchmark methods.

To perform a five-fold cross-validation, we selected five independent sets of cDNA clones (refer to supplementary

Table 9 Classification accuracy for 13 sets of cancer microarray (%)

Data set	Run no.	SVM	SOM	BPNN	C4.5	NB	CART	AIRS	PSODT
13 cancer	1	72.46	52.60	42.58	93.14	94.21	91.42	50.41	97.26
	2	72.46	52.77	41.77	93.25	93.78	90.54	52.31	98.72
	3	72.51	51.39	42.59	93.26	93.60	91.77	53.33	97.25
	4	72.51	52.60	42.33	93.25	94.81	92.04	53.85	97.79
	5	73.62	52.60	43.33	93.25	94.02	91.09	53.71	97.39
	Avg.	72.71	52.39	42.52	93.23	94.08	91.37	52.72	97.68
	(Std.)	(0.51)	(0.56)	(0.56)	(0.05)	(0.47)	(0.59)	(1.43)	(0.62)

Tables one to five of Appendix three at [34]). A total of 453 cDNA clones were selected at least once. Among the lists of cDNA clones, a number of them were selected multiple times. The genes being selected multiple times (with Frequency ≥ 4) indicate that the expression levels of these genes provide a high discrimination power among the tumors of different anatomical origin. Therefore, these genes are likely to be the tissue-specific genes. Alternatively, such expression differences may be generated result from organ- or tissue-specific malignant transformation.

Conclusions

We proposed a novel method to identify tissue-specific genes as well as housekeeping genes with altered expression patterns that provide a high discrimination power on cancer classification. These genes may play as an important role in diagnosis and/or pathogenesis of various types of tumors. Eleven cancer datasets were used to test the performance of the proposed method, and a five-fold cross-validation method was used to justify the performance of our proposed method. Our proposed approach achieved a higher accuracy as compared with all the other methods.

This proposed method has integrated with the nonlinear search capability of PSO and linearly separable advantage of DT to apply to microarray cancer datasets for gene selection. Hawse have identified representative cancer genes (453 genes) from numerous microarray data (65,000 genes) that can reduce costs. In addition, we compared our proposed method with four well-known algorithms using a variety of datasets (diverse sizes and numbers of classes and features). Consequently, our proposed method outperformed all the other benchmark methods and is compatible to SVM for certain specific datasets.

Further studies to be further conducted are suggested as follows. First, PSO may result in better solutions by optimizing parameter settings; therefore, self-adaptation parameters of particle size, number of iterations, and constant weight factors are worth developing. Second, adding hybrid search algorithms in PSO algorithm may improve its performance; for example, swarms with mixed particles may further enhance the effectiveness. Third, the improvement in the execution time for large-sized data sets could be treated as a research subject in the future.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

KHC, KJW and AMA designed all the experiments and wrote most of this paper. KSC discussed and refined the paper. MLT, WCC, KPT and KMW interpreted the results. TSY and NCT guided the whole project. All authors read and approved the final manuscript.

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References

1. Alba E, et al: Gene selection in cancer classification using PSO/SVM and GA/SVM hybrid algorithms. *IEEE C Evol Computat* 2007, **9**:284–290.
2. Li S, Wu X, Tan M: Gene selection using hybrid particle swarm optimization and genetic algorithm. *Soft Comput* 2008, **12**:1039–1048.
3. Ahmad A, Dey L: A feature selection technique for classificatory analysis. *Pattern Recogn Lett* 2005, **26**:43–56.
4. Su Y, Murali TM, et al: RankGene: identification of diagnostic genes based on expression data. *Bioinformatics* 2003, **19**:1578–1579.
5. Kahavi R, John GH: Wrapper for feature subset selection. *Artif Intell* 1997, **97**:273–324.
6. Li X, Rao S, Wang Y, Gong B: Gene mining: a novel and powerful ensemble decision approach to hunting for disease genes using microarray expression profiling. *Nucleic Acids Res* 2004, **32**:2685–2694.
7. Zhao XM, Cheung YM, Huang DS: A novel approach to extracting features from motif content and protein composition for protein sequence classification. *Neural Netw* 2005, **18**:1019–1028.
8. Brown MP, et al: Knowledge-based analysis of microarray gene expression data by using support vector machines. *Proc Natl Acad Sci U S A* 2000, **97**:262–267.
9. Evers L, Messow CM: Sparse kernel methods for high-dimensional survival data. *Bioinformatics* 2008, **24**:1632–1638.
10. Hua S, Sun Z: A novel method of protein secondary structure prediction with high segment overlap measure: support vector machine approach. *J Mol Biol* 2001, **308**:397–407.
11. Oh JH, Gao J: A kernel-based approach for detecting outliers of high-dimensional biological data. *BMC Bioinforma* 2009, **10**:S7.
12. Saey Y, et al: Feature selection for splice site prediction: a new method using EDA-based feature ranking. *BMC Bioinforma* 2004, **5**:64.
13. Zhu Y, Shen X, Pan W: Network-based support vector machine for classification of microarray samples. *BMC Bioinforma* 2009, **10**:S21.
14. Li L, Darden TA, et al: Gene assessment and sample classification for gene expression data using a genetic algorithm/k-nearest neighbor method. *Comb Chem High T Scr* 2001, **4**:727–739.
15. Li L, Jiang W, et al: A robust hybrid between genetic algorithm and support vector machine for extracting an optimal feature gene subset. *Genomics* 2005, **85**:16–23.
16. Kennedy J, Eberhart R: Particle swarm optimization. *IEEE Int Conf Neural Networks - Conf Proc* 1995, **4**:1942–1948.
17. Robinson J, Rahmat-Samii Y: Particle swarm optimization in Electromagnetics. *IEEE Trans Antennas Propag* 2004, **52**:397–407.
18. Chen LF, et al: Particle swarm optimization for feature selection with application in obstructive sleep apnea diagnosis. *Neural Comput Appl* 2011, **21**(8):2087–2096.
19. Mohamad MS, et al: Particle swarm optimization for gene selection in classifying cancer classes. Proceedings of the 14th International Symposium on Artificial Life and Robotics; 2009:762–765.

20. Shen Q, Shi WM, Kong W: **Hybrid particle swarm optimization and tabu search approach for selecting genes for tumor classification using gene expression data.** *Comput Biol Chem* 2008, **32**:52–59.
21. Wu X, et al: **Top 10 algorithms in data mining.** *Knowl Inf Syst* 2008, **14**:1–37.
22. Cheng WC, et al: **Microarray meta-analysis database (M2DB): a uniformly pre-processed, quality controlled, and manually curated human clinical microarray database.** *BMC Bioinforma* 2010, **11**:421.
23. GEMS Dataset: 2012, <http://www.gems-system.org/>.
24. Dudoit S, Fridlyand J, Speed TP: **Comparison of discrimination methods for the classification of tumors using gene expression data.** *J Am Stat Assoc* 2002, **97**:77–86.
25. Jiang P, et al: **MiPred: classification of real and pseudo microRNA precursors using random forest prediction model with combined features.** *Nucleic Acids Res* 2007, **35**:W339–W344.
26. Batuwita R, Palade V: **MicroPred: effective classification of pre-miRNAs for human miRNA gene prediction.** *Bioinformatics* 2009, **25**:989–995.
27. Wang Y, et al: **Predicting human microRNA precursors based on an optimized feature subset generated by GA-SVM.** *Genomics* 2011, **98**:73–78.
28. Nanni L, Brahnam S, Lumini A: **Combining multiple approaches for gene microarray classification.** *Bioinformatics* 2008, **28**:1151–1157.
29. Park I, Lee KH, Lee D: **Inference of combinatorial Boolean rules of synergistic gene sets from cancer microarray datasets.** *Bioinformatics* 2010, **26**:1506–1512.
30. Tan PN, Steinbach M, Kumar V: *Michael Steinbach, and Vipin Kumar. Introduction to Data Mining.* 1st edition. Addison Wesley, Boston, MA, USA; 2005.
31. Brazma A, Vilo J: **Gene expression data analysis.** *FEBS Lett* 2000, **480**:2–16.
32. Golub TR, et al: **Molecular classification of cancer: class discovery and class prediction by gene expression monitoring.** *Science* 1999, **286**:531–527.
33. Zhao W, et al: **A novel framework for gene selection.** *Int J Adv Comput Technol* 2011, **3**:184–191.
34. TOM laboratory: *TOM laboratory*; 2013. <http://tom.im.ntust.edu.tw/>.
35. Kennedy J, Eberhart RC, Shi Y: *Swarm Intelligence.* San Francisco, CA, USA: Morgan Kaufman; 2001.
36. Shi Y, Eberhart RC: *A Modified Particle Swarm Optimizer.* Anchorage Alaska: IEEE International Conference on Evolutionary Computation; 1998:69–73.
37. Tan S: **Neighbor-weighted k-nearest neighbor for unbalanced text corpus.** *Expert Syst Appl* 2005, **28**:667–671.
38. Stone M: **Cross-validated choice and assessment of statistical predictions.** *J Royal Stat Soc* 1974, **36**:111–147.
39. Geisser S: **The predictive sample reuse method with applications.** *J Am Stat Assoc* 1975, **70**:320–328.
40. Larson S: **The shrinkage of the coefficient of multiple correlation.** *J Educ Psychol* 1931, **22**:45–55.
41. Mosteller F, Turkey JW: *Data analysis, including statistics. Handbook of Social Psychology.* Reading, MA: Addison-Wesley; 1968.
42. Mosteller F, Wallace DL: **Inference in an authorship problem.** *J Am Stat Assoc* 1963, **58**:275–309.
43. Cortes C, Vapnik V: **Support-vector networks.** *Mach Learn* 1995, **20**:273–297.
44. Kononenko I: *A counter example to the stronger version of the binary tree hypothesis.* ECML-95 workshop on Statistics, machine learning, and knowledge discovery in databases; 1995:31–36.

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