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Gene Selection using a Parallel Multi Objective Optimization Island Model Genetic Algorithm for microarray based cancer classification

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ABSTRACT

Feature selection has played a very important role in the field of data mining and meachine learning.The high performance parallel and distributed computing is used for gene expression analysis and finding the thousands of genes simultaneously. The classification and validation of molecular biomarkers for cancer diagnosis is an important problem in cancer genomics. The microarray data analysis is used for extracting the biologically useful data from the huge amount of expression data to know the current state of the cell. Most cellular processes are regulated by changes in gene expression. This is a great challenge for computational biologists who see in this new technology the opportunity to discover interactions between genes. In this paper we propose a Parallel island model multi objective optimization Genetic Algorithm for Gene Feature Selection. We have implemented PIMGA for gene feature selection to classify the cancer data sets. More importantly, the method can exhibit the inherent classification difficulty with respect to different gene expression datasets, indicating the inherent biology of specific cancers.

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INTRODUCTION

Microarray Data:

DNA microarray experiments are used for cancer classification and prediction. The microarray technology has been used in many biomedical researches. The one major problem in applying gene expression summary to cancer classification is that number of features distinguish the number of genes. Some important cancer informatics studies have exposed that the small coolection of genes selected by feature selection methods can give the good classification results. Feature Selection (FS) is a very important task in machine learning for cancer classification with the goal of identifying very important features subsets in a microarray data. It is one of the most key problems in the field of data mining and bioinformatics. The classification and validation of molecular biomarkers for cancer diagnosis is an important problem in cancer genomics. The selection of applicant genes is very essential to identify accurately the origin of cancer and treatment.With the appearance and fast development of DNA microarray technologies, making gene expression profiles for different cancer types has already become a hopeful means for cancer classification.

Multiobjective Optimization:

The multi-objective problem requires adaptation of optimization methods. The main difference with mono-objective optimization problems is that in multi-objective problems,there is not a single solution for which all criteria are optimal but a set of solutions for which there are no other solutions better for all the criteria. These solutions are called Pareto-optimal. The notion of Pareto-optimality is defined in terms of dominance.

Genetic Algorithm:

Genetic algorithms (GAs) (Goldberg, D.E., J.H. Holland, 1988), a form of inductive learning strategies are adaptive search techniques initially introduced by Holland (Holland, 1975). Genetic Algorithms are inspired from Darwin's theory of evolution. By simulating nature evolution and emulating biological selection and reproduction techniques, the GA can solve complex problems in a strong search domain. The algorithm starts with a set of randomly generated solutions called population. The population size remains constant throughout

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the genetic algorithm. At each iteration the populations are evaluated based on their fitness quality with respect to the given application domain to form new solutions called offspring which retains many features of their parents. Offsprings are formed by two main genetic algorithm operators such as crossover and mutation. Crossover operates by randomly selecting a point in the two selected parent gene structures and exchanging the remaining segments of the parents to create new offspring. Therefore, crossover combines the features of two individuals to create two similar offsprings. Mutation operates by randomly changing one or more components of a selected individual. It acts as a population perturbation operator and is a means for inserting new information into the population. This operator prevents any stagnation that might occur during the search process.

In this proposed work Parallel multi objective optimization island model Genetic Algorithm feature selection is implemented based on genetic algorithm operators and function. PIMMOGA uses two different algorithms such as contribution and entropy to find the pareto optimal solutions for ranking. Since the search space is large and requires a good diversity, island model has been proposed. Finally the parallel island model multiobjective optimization GA has been implemented by using MPI.

Related Work:

Soumen Kumar Patel, *et al* (2013) has explained a novel feature selection method which was based on Multiobjective Genetic Algorithm using rough set theory. This method proposed to choose important informative gene set, which classify the cancer dataset very efficiently. This method has used two fitness functions individually based on the concepts of strong mathematics such as rough set theory and probability theory. The lack of diversity of population is overcome by jumping gene mutation. The only drawback of this method is that the population size can be set within the range 100 to 1000 only.

Asha Gowda Karegowda (2010) has proposed a wrapper approach with genetic algorithm for generation of subset of attributes with different classifiers such as Naïve Bayes, Bayes Networks,C4.5 and Radial basis functions. The above classifiers are experimented on the Diabetes datasets, Breast cancer datasets , Heart Statlog and Wisconsin Breast cancer. The main disadvantage of this approach is that the computing time is very high for the large datasets.

In 2009, QingzhongLiu, Andrew H. Sung has proposed a new feature selection method called Recursive Feature Addition method on microarray based breast cancer data. The RFA gene feature selection method provides good classification accuracy than the other methods. In this method, serial programming is used for classification which slows down the computational speed.

Methodology:

Multi objective optimization Problem:

The multi-objective problem requires adaptation of optimization methods. The main difference with mono-objective optimization problems is that in multi-objective problems, there is not a single solution for which all criteria are optimal but a set of solutions for which there are no other solutions better for all the criteria. These solutions are called Pareto-optimal. The notion of Pareto-optimality is defined in terms of dominance.

We propose to use a GA to find all the Pareto-optimal solutions which are all interesting potential rules. They are located on a boundary known as the Pareto-front. We would like the solutions to cover the Pareto-front as well as possible to obtain a good representation of this front. This "A priori" approach offers multiple solutions to the decision maker, which can select the solution that is best suited according to nonformal additional criteria, without requiring additional searches.

Multi objective operators:

To deal with multi-objective optimization problems, different mechanisms have to be used. For example, the notion of dominance has to be and population management has to be carefully studied.

***Selection Operator*:**

We use the classical roulette selection based on the ranking notion. The probability of selection of a solution is proportional to its rank. We use the Pareto ranking (Fonseca, C.M. and P.J. Fleming, 1995). The rank of a solution corresponds to the number of solutions, in the current population, by which it is dominated for a bicriteria minimization problem.

***Replacement Operator*:**

We use the elitist nondominated sorting replacement. The worst ranked solutions are replaced by dominating solutions generated by mutation and crossover operators (offspring). The size of the population remains unchanged.

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***Archive*:**

Nondominated association rules are archived into a secondary population called the "Pareto archive" to keep track of them. It consists in archiving all the Pareto association rules encountered over generations. This archive has to be updated each time a solution is added.

***Elitism*:**

The Pareto solutions (best solutions) are not only stored permanently but also take part in the selection and may participate to the reproduction.

Multi-objective optimization, solutions quality can be assessed in different ways. Some approaches compare the obtained front with the optimal Pareto front (vanVeldhuizen, D.A. and G.B. Lamont, 2000). Others approaches evaluate a front with a reference point (Jaszkiewicz, A., 2000). Some performance measures do not use any reference point or front to evaluate an algorithm (Knowles, J.D., 2000; Zitzler, E. and L. Thiele, 1999), especially when the optimal Pareto front is not known at all. Here, we have to compare different versions of the proposed model, without knowing the true Pareto front.We propose to use two complementary types of performance indicators that allow to compare two by two Pareto fronts obtained by different algorithms: the contribution and the entropy (Basseur, M., 2002). The contribution indicator quantifies the domination between two sets of nondominated solutions. The entropy indicatorgives an idea about the diversity of the solutions found.

Contribution:

The contribution of a set of solutions $P0_1$ relative to a set of solutions $P0_2$ is the ratio of nondominated solutions produced by $P0_1$. Let C be the set of solutions in $P0_1 \cap P0_2$. Let*W*1 (respectively,*W*2) be the set of solutions in $P0_1$ (respectively, $P0_2$), which dominate some solutions of $P0_2$ (respectively, $P0_1$). Let *L*1 (respectively, *L*2) be the set of solutions in $P0_1$ (respectively, $P0_2$), which are dominated by some solutions of $P0_2$ (respectively, $P0_1$). Let *N*1 (respectively, *N*2) be the other solutions of $P0_1$ (respectively, $P0_2$ $N_i = PO_i / (C \cup W_i \cup L_i)$.

Let $P0^*$ be the set of Pareto solutions of $P0_1 \cup P0_2$. Therefore, $\| P0^* \| = \| C \| + \| W1 \| + \| N1 \| + \|N2\| + \|W2\| + \|N2\|$.

The contribution of algorithm $P0_1$ relative to $P0_2$ is stated as:

$$C(P0_1 / P0_2) = \frac{\|C\|/2 + \|W1\| + \|W2\|}{\| P0^* \|}$$

for example for the two set of solutions $P0_1$ and $P0_2$ of figure 1 where solutions of po1 and po2 are represented by circles and crosses.The contributions are $C(P0_1, P0_2) = 0.7$ and $C(P0_1, P0_2) = 0.3$

Let us remark that $C(P0_1 / P0_2) + C(P0_1 / P0_2) = 1$ and hence a contribution greater than 0.5 indicates an improvement of the pareto front.

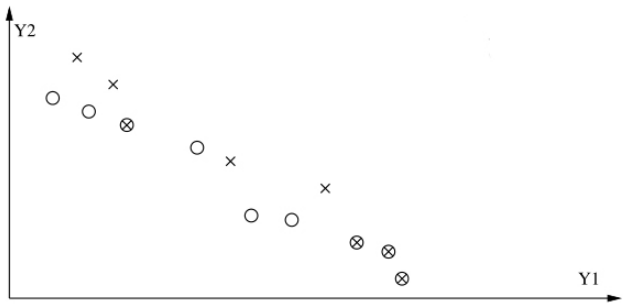

Fig. 1: Contribution (C=4,W1=4,W2=0,N1=1,N2=1).

Entropy:

The entropy allows to understand the diversity of the pareto front achieved. It is based on the definition of niche of a solution s, which represents all the solutions that are closed to the solution s.

Let $P0_1$ and $P0_2$ be two sets of solutions.

Let $P0^*$ be the set of optimal pareto solutions of $P0_1$ $P0_2$.

Let Ni be the cardinality of solutions of $P0_1 \cup P0^*$ which are in the niche of the ith solutions of $P0_1 \cup P0^*$

Let Ni be the cardinality of solutions of $P0_1$,which are in the niche of the i^{th} solutions of $P0_1 \cup P0^*$

Let c be the cardinality of the solutions of $P0_1 \cup P0^*$

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Let $\gamma=\sum_{i=1}^{c} 1/N_i$ be sum of the coefficients affected to each solution.The more concentrated is a region of the solution space, the lower will be the coefficients of its solution.

Then the following forumula is applied to evaluate the entropy E of $P0_1$ relative to the space occupied by $P0^*$

$$E(P0_1, P0_2) = -1/\log\left(\sum_{i=1}^{c} \left(\frac{1}{Ni}\frac{ni}{c}\log\frac{ni}{c}\right)\right)$$

An entropy value belongs to the interval [0,1] and the more the entropy is close to 1, the better diversified is the front.

Experimental Design:

The contribution and entropy algorithms have compared and the following parameters are used for implementating the island model.

1. Population size is 1000
2. Selection in population is 4⁄6 (400)
3. Global mutation rate is 0.5
4. Crossover rate is 0.8
5. Selection in Pareto archive (elitism) is 0.5
6. Minimal number of generations are 500

The stopping criterion used is the nonamelioration. Once the minimal number of generations has been overpassed and after taking the best solution for all 10 generations, the iteration stops. For further improving the computing time, we have used clustered machine comprised of six workstations with Intel Core i5 processor with NVIDIA Graphics processor (Oiso, M., Y. Matumura, 2011) and 1GB main memory.The fig 6 shows the pseudo code for the parallel Island model. The sequential GA has implemented using the following pseudo code which is shown in Fig 7.

```
1. Island Model(A,n,μ)
2. begin
3. Concurrently for each of the i ? 1 to n subpopulations
   Initialize(Pi, μ);
4. For each no of generation ? 1 to A do
5. Concurrently for each of the i ? 1 to n subpopulations do
6. Sequential _GA(Pi, Gi)
7. od;
8. For i ? 1 to n do
9. For each neighbour j of i
10. Migration (PiPj),
11.Assimilate (Pi);
12.od
13.od
14.problem solution = best individual of all subpopulations;
15.End
```

Fig. 2: Island model Pseudocode.

```
1. Sequential_GA (Pi,Pj)
2. Begin
3. For generation ? 1 to Gi do
4. Pnew ? P?
5. For offspring ? 1 to Max_offspring do
6. Pα ? selection (Pi)
7. Pβ ? selection (Pi)
8. Pnew = pnew ? crossover (Pα, Pβ)
9. Od
10. Fitness_calculation(Pi ? Pnew)
11. Pi ? Reduction (Pi ? Pnew)
12. Mutation (Pi);
13. Fitness_calculation(Pi)
14. End
```

Fig. 3: Sequential GA.

Parallel Island model Multi-Objective Genetic Algorithm:

The population generation is one of the basic steps in multi-objective genetic algorithm. The Parallel Genetic Algorithm (Zdenek Konfrst, 2004) has been classified into three main models: global, fine cellular and island. The global model uses parallelism to speed up the sequential GA. This model uses a global shared population and the fitness evaluation is done on different processors. The cellular model seeks to exploit the fine-gained, massively parallel architectures. The population is separated into a large number of very small subpopulations, which are maintained by different processors. In the island model, the population is divided into a few large independent subpopulations called islands. Each processor evolves their population using a parallel

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GA. For each island, some solutions rarely migrate to another island. We choose the island model for Parallel multi objective optimization GA.

Island Model:

The island model is implemented in parallel programming and many islands are connected by using ring topology (Fig. 4). This model typically runs on a parallel multi-objective GA. In this, each processor is called an island with independent populations and Pareto archives (Fig.5). Each GA starts with its proper parameters such as population, parameters of GA. Periodically each island sends some solutions from its Pareto archive randomly selected to the neighboring island. The island model has four steps:

1. Each island model creates its population.
2. Each model develops its population for a global number of generations and updates its archives for every generation.
3. Each island sends some solutions of its Pareto archive to the neighboring island according to the migration policy.
4. Finally, the island receives all the migrating solutions and replaces its worst solutions by those immigrants according to the ranking.

At the end, a specific island waits for all the others to finish their execution and collects all the final Pareto archives to create the global Pareto archive. This island model has been implemented by using parallelization tools like Open MPI (August, A.D., 2010; Quinn, M.J., 2004).

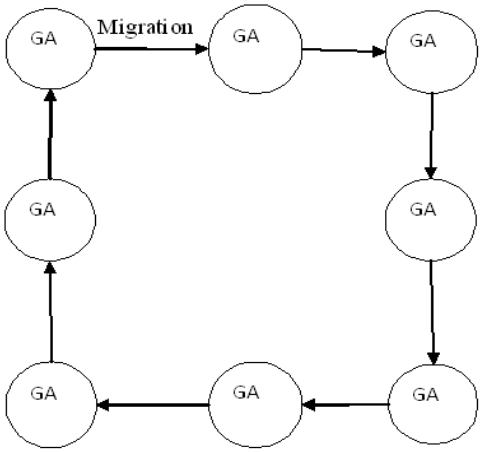

Fig. 4: Island model Ring Topology connection.

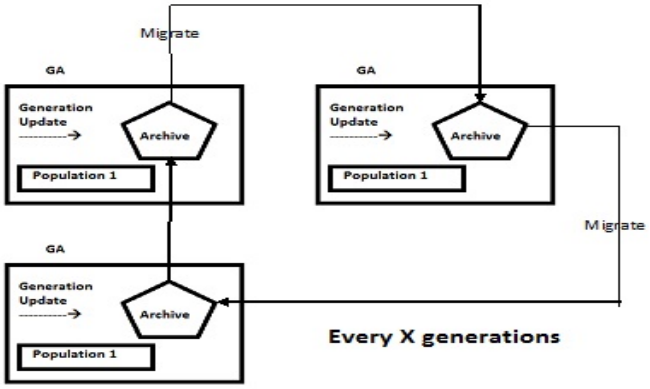

Fig. 5: Island Model.

Experiments:

Our proposed method has been implemented in parallel computing. The measured run times for 4,8,16,32 processors are shown in the table 1.The best features have been taken from CPMOGA gene feature selection method and compared with the existing feature selection methods using the orange data mining tools using python scripting language.

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Table 1: Measured run time.

No of Processors	Run time(H)
4	3.50
8	1.78
16	0.90
32	0.45
No of Processors	Run time(H)

We have done this experiment on four publicly available microarray cancer datasets (Alexandre Mendes, 2011) available at Kent Ridge Bio-medical Data Set Repository (http://datam.i2r.a-star.edu.sg/datasets/krbd/).The existing feature selection methods are applied for this cancer data sets and classification accuracy are measured using Orange data mining and machine Learning tool.The feature selection methods (Aboul Ella Hassaneian, 2003; Kemal Polat, 2005) like Novel Hybrid, Wrapper approach, Consistency Subset Selection (CON) (Yu, L., H. Liu, 2004), Correlated Feature Selection (CFS) (Hall, M.A., 1999), Single Objective Genetic Algorithm (SOGA) (Goldberg, D.E., J.H. Holland, 1988), Multi-Objective GA (MOGA) and the proposed Parallel Multiobjective optimization Island model GA(PIMMOGA) are applied on this four cancer data sets. It is then measured by various classification methods like Random Forest, K-NN, Classification tree, SVM,CN2 rules and Interactive Tree builder in Orange tool. Our proposed CPMOGA feature selection method provides better classification accuracy than the other feature selection algorithm and the computing time is very less than the other methods. Table 2 shows the classification accuracy of various methods. The Cross-fold validation is used for measuring the classification accuracy in terms of time which is available at Orange tool and CPMOGA is implemented by us. From Table 2 we observe that the proposed method is better than other methods in terms of time consuming, feature selection and classification accuracy. Our executing system consists of core i5 processor with NVIDIA Graphics processor running at 4 GHz clock frequency.

Table 2: Classification accuracy (%) of Breast cancer data set sub types.

Breast cancer Data set Sub types	Feature SelectionMethods	Data Mining Classifier					
		SVM	Naïve bayes	kNN	CT	CN2	RF
Breast cancer	Wrapper Approcah	62	54	58	54	45	51
	CON	61	53	59	55	48	53
	CFS	60	53	60	57	48	51
	SOGA	62	51	61	56	48	50
	MOGA	69	59	63	55	49	48
	CPMOGA	76	72	72	78	50.5	54
	Novel Hybrid	65	55	65	89	50	51
DLBCL	Wrapper Approcah	62	52	55	53	43	50
	CON	60	52	53	53	48	53
	CFS	60	53	60	57	48	51
	SOGA	69	65	67	58	54	66
	MOGA	72	74	75	71	64	68
	CPMOGA	73	74.5	76	76	69	72
	Novel Hybrid	61	61	69	71	64	68
Lung	Wrapper Approcah	64	65	61	68	46	56
	CON	69	66	61	53	46	57
	CFS	69	65	67	58	54	66
	SOGA	73	67	67	65	56	66
	MOGA	76	73	71	73	55	57
	CPMOGA	76.5	73.5	72	76	67	68
	Novel Hybrid	74	75	74	73	63	61
prostate	Wrapper Approcah	74	76	73	72	56	59
	CON	73	74	72	70	57	55
	CFS	70	72	74	70	54	51
	SOGA	68	69	67	68	52	57
	MOGA	72	73	70	68	66	67
	CPMOGA	74	75	71	73	68	70
	Novel Hybrid	69	70	70	71	65	65

Some statistical measurements like True Positive Rate, False Positive Rate of the classifiers are calculated using equation (4), (5).

$$TPR = TP / P = TP / (TP+FN) \quad (4)$$

$$FPR = FP / N = FP / (P+TN) \quad (5)$$

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Here the TP is positive object classified as positive, FP is positive object classified as negative, TN is negative object classified as negative and FN is negative object classified as positive.

Results:

The ROC curves visualized by orange data mining tool for the existing feature selection methods for different classifiers. It shows the classification performance of the different classifier. The proposed ROC curve is shown in Fig.6 to Fig 29. From the graph we observed that the true positive rate is better than the existing methods. Our proposed method curves indicates that the best features are taken and provides accurate classification performance on the breast cancer data set.

ROC Curve of Breast Cancer Data sets for Data mining classifiers:

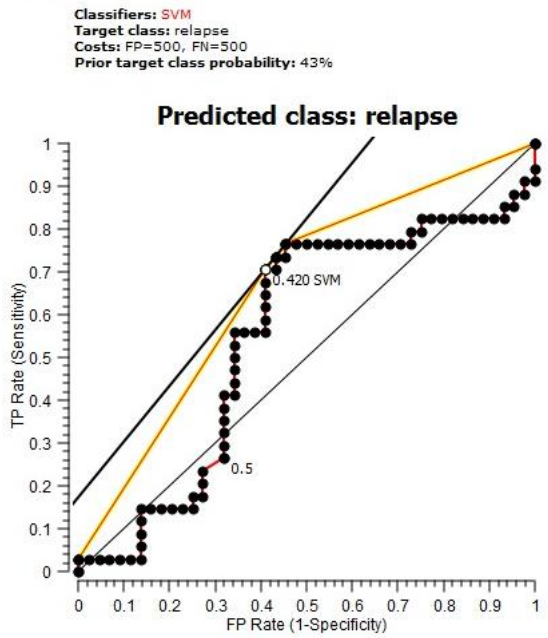

Fig. 6: ROC Analysis for SVM Classifier.

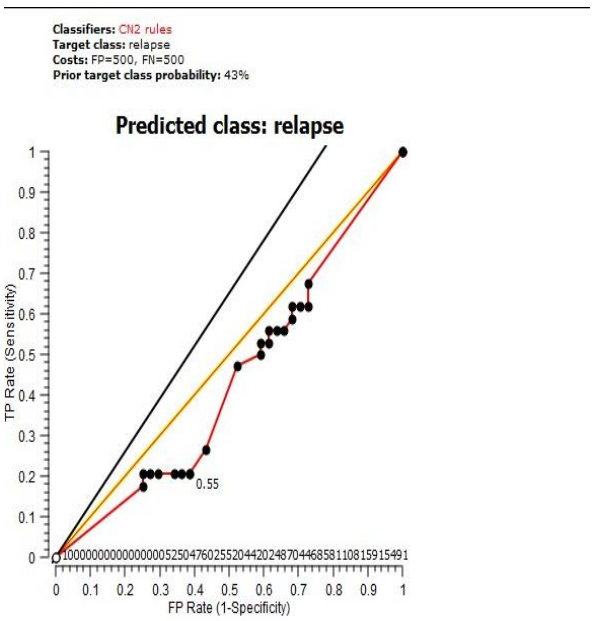

Fig. 7: ROC Analyses for CN2 Classifier.

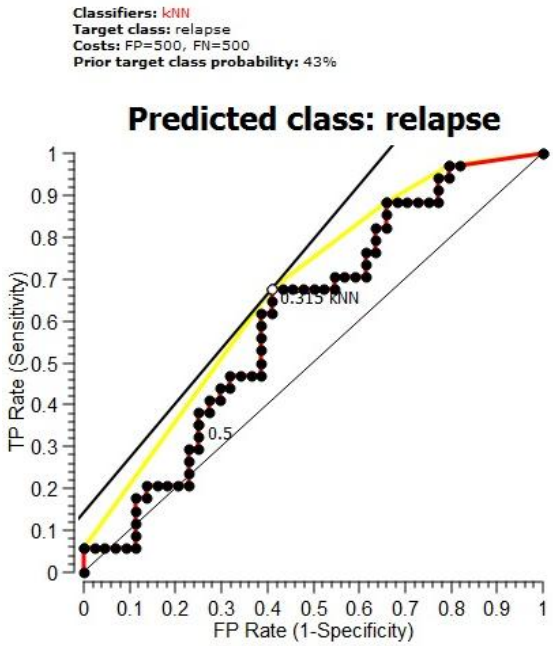

Fig. 8: ROC Analysis for kNN Classifier.

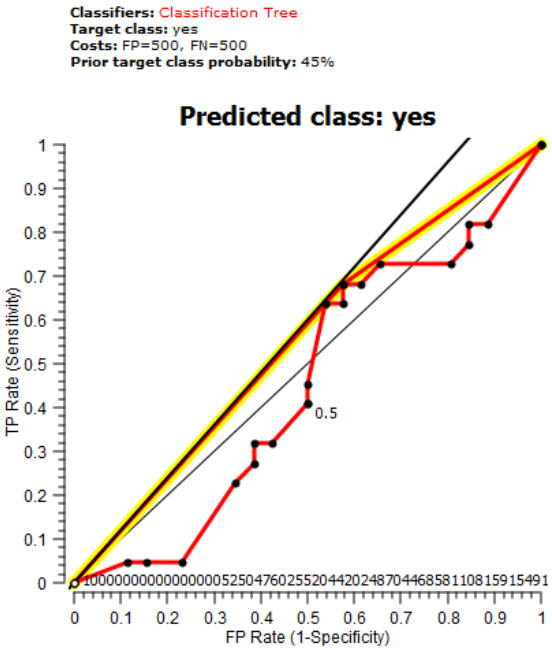

Fig. 9: ROC Analysis for Classification Tree.

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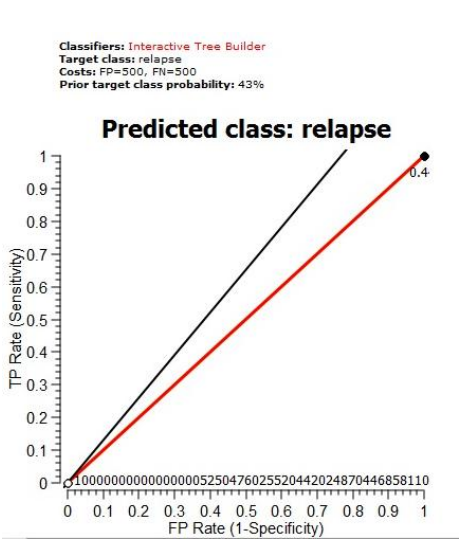

Fig. 10: ROC Analysis for ITB rules Classifier.

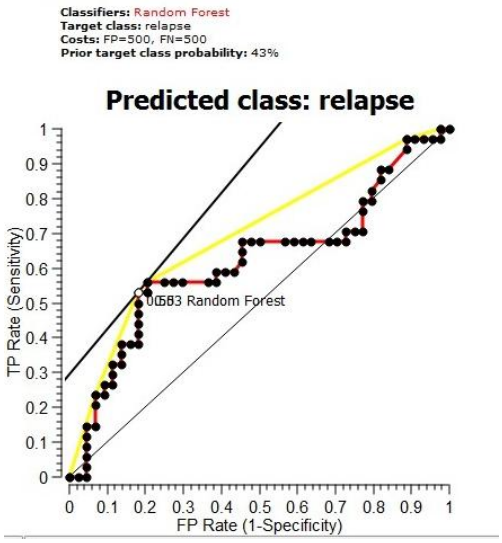

Fig. 11: ROC Analysis for Random Forest Classifier.

ROC Curve of DLBCL Cancer Data sets for Data mining classifiers:

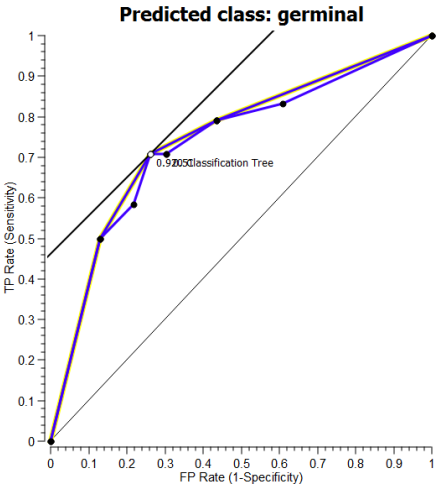

Fig. 12: ROC Analysis for CT Classifier**.**

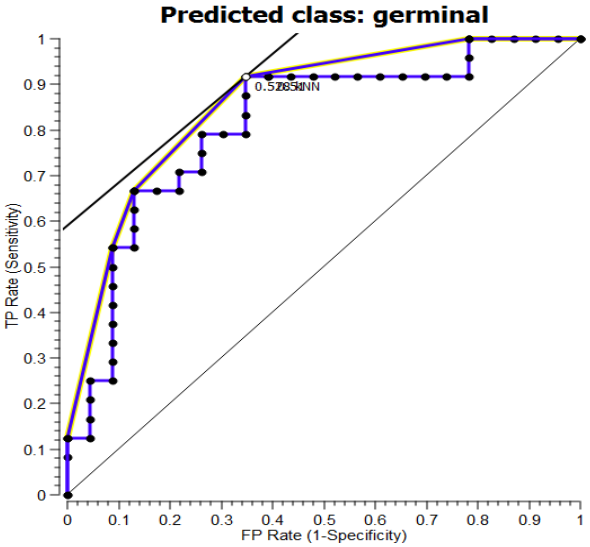

Fig. 13: ROC Analysis for kNN Classifier.

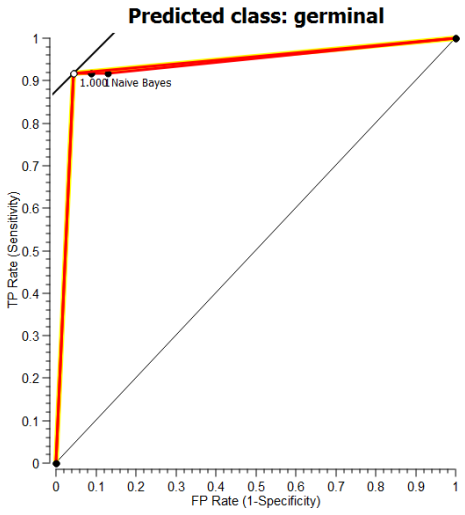

Fig. 14: ROC Analysis for NB Classifier.

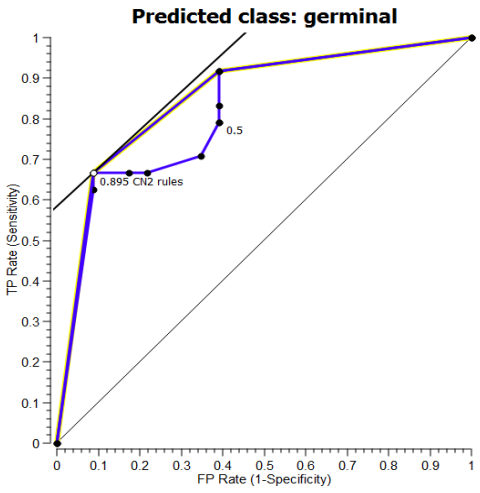

Fig. 15: ROC Analysis for CN2Classifier.

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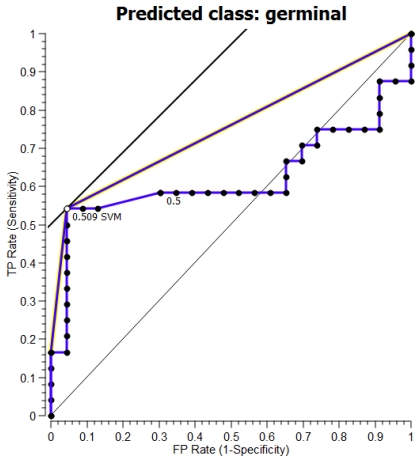

Fig. 16: ROC Analysis for SVM rules Classifier.

ROC Curve of Prostate Cancer Data sets for Data mining classifiers:

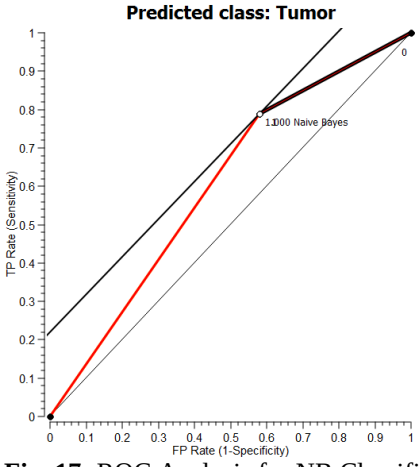

Fig. 17: ROC Analysis for NB Classifier**.**

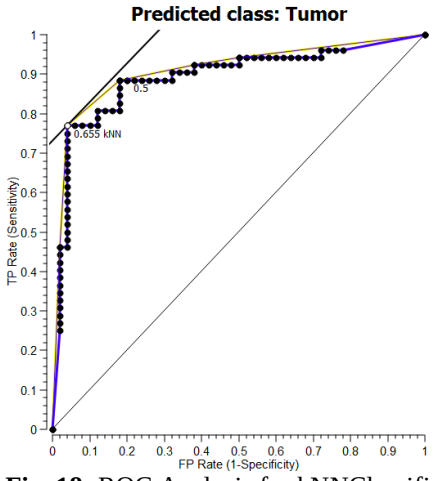

Fig. 18: ROC Analysis for kNNClassifier.

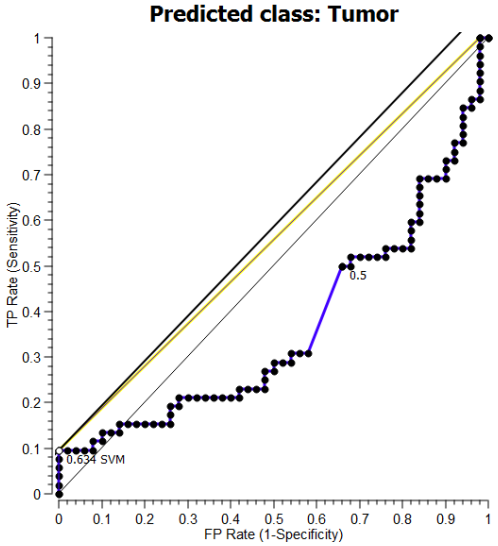

Fig. 19: ROC Analysis for SVM Classifier**.**

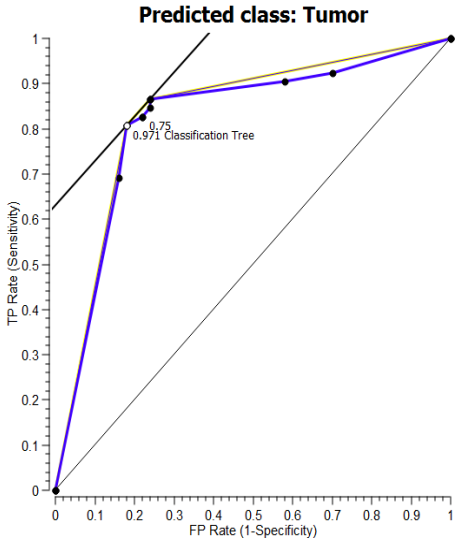

Fig. 20: ROC Analysis for CT Classifier.

ROC Curve of Lung Cancer Data sets for Data mining classifiers:

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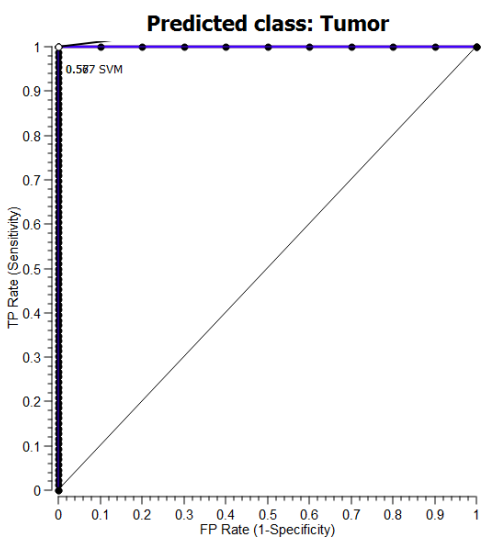

Fig. 21: ROC Analysis for SVM Classifier**.**

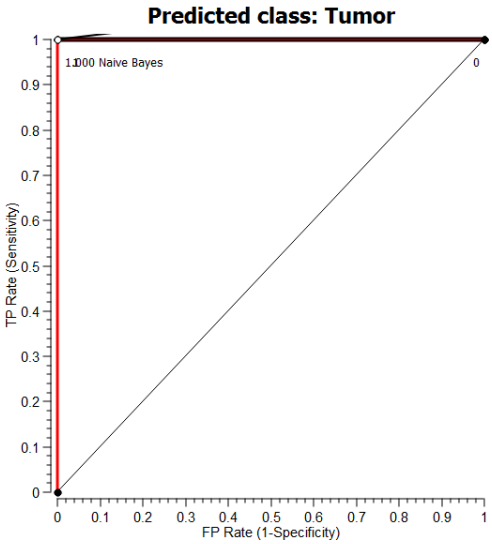

Fig. 22: ROC Analysis for NB Classifier.

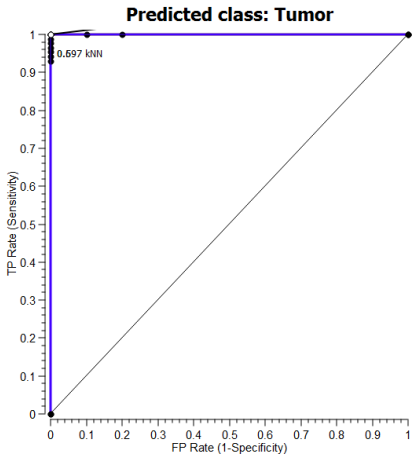

Fig. 23: ROC Analysis for kNN Classifier**.**

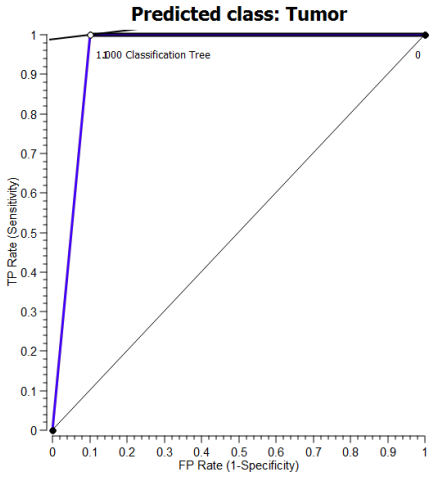

Fig. 24: ROC Analysis for CT Classifier.

Proposed ROC for different classifiers:

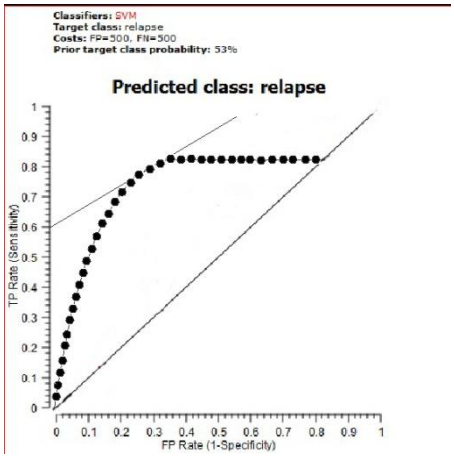

Fig. 24: Proposed ROC for SVM**.**

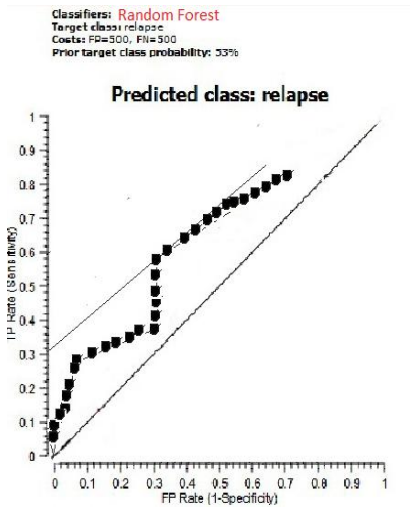

Fig. 25: Proposed ROC for RF**.**

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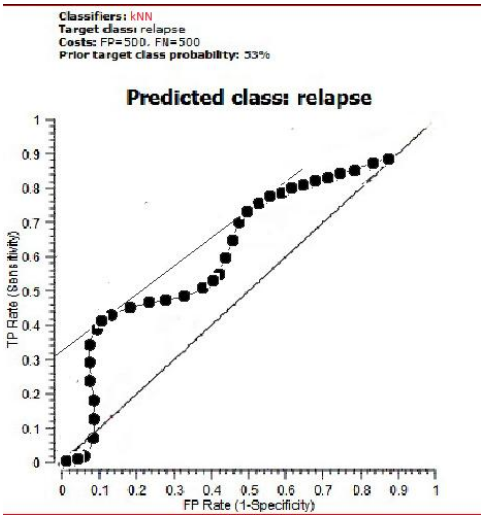

Fig. 26: Proposed ROC for kNN**.**

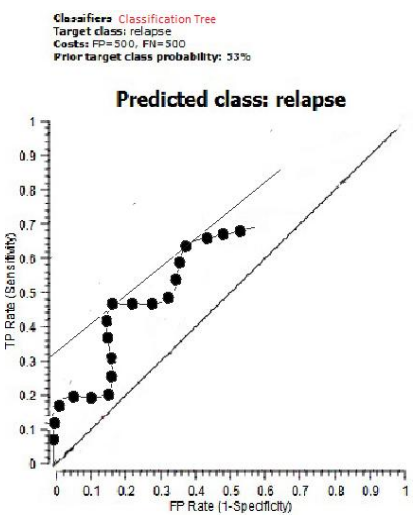

Fig. 27: Proposed ROC for CT**.**

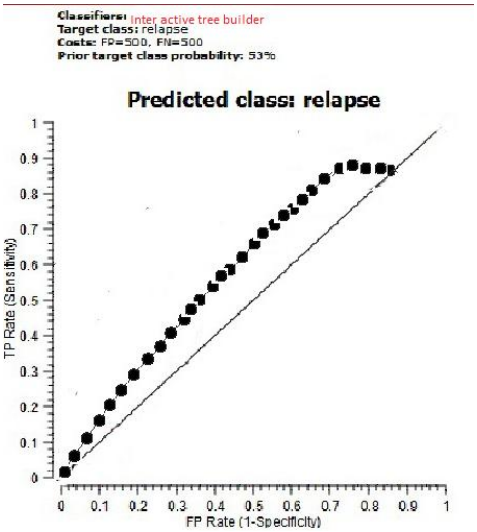

Fig. 28: Proposed ROC for ITB**.**

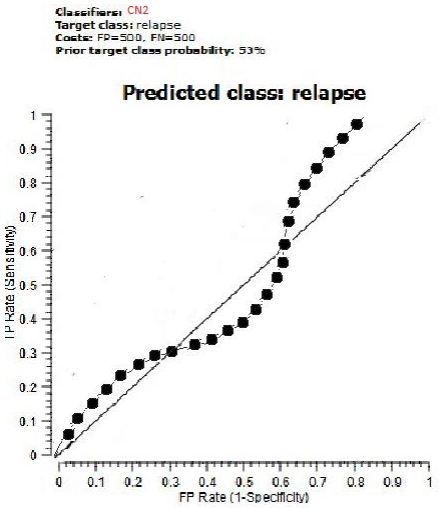

Fig. 29: Proposed ROC for CN2.

Conclusion and Future Work:

In the above work the Parallel multiobjective optimization Island model genetic algorithm has been implemented and best features are selected in short time. The gene feature selection is very important in cancer classification. This method uses the island model for generating the best population. The multiple islands are implemented in parallel which has substantially reduced the execution time in the process of best feature selection. In this work standard microarray data sets are taken from Kent Ridge Bio-medical Data Set Repository. In future real time data from cancer patients has to be taken. The classification accuracy should also be clinically verified.

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