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ML Classification of Cancer Types Using High Dimensional Gene Expression Microarray Data

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Abstract: Cancer is a disease caused by the abnormal growth of cells in different parts of body and is one of the top causes of death globally. Microarray gene expression data plays a critical role in the identification and classification of cancer tissues. Due to recent advancements in Machine Learning (ML) techniques, researchers are analyzing gene expression data using a variety of such techniques to model the progression rate & treatment of cancer patients with great effect. But high dimensionality alongside the presence of highly correlated columns in gene expression datasets leads to computational difficulties. This paper aims to propose the use of ML classification techniques- Linear Discriminant Analysis (LDA) & Random Forest (RF) for classifying five types of cancer (breast cancer, kidney cancer, colon cancer, lung cancer and prostate cancer) based on high dimensional microarray gene expression data. Principal component analysis (PCA) was used for dimensionality reduction, and principal component scores of the raw data for classification. Six distinct categorization performance measures were used to evaluate these approaches; RF method provided us with higher accuracy than LDA method. The method and results of this article should be helpful to researchers who are dealing with many genes in microarray data.

Keywords: principal components analysis; Linear Discriminant Analysis; Random Forest; precision; recall; F1; AUC; macro-averaged AUC; micro-averaged AUC

1. Introduction

Cancer is a disease which can start almost anywhere in the human body, in which some of the body's trillion cells grow uncontrollably and spread to other parts of the body. There are over 200 types of cancer such as colon, liver, ovarian and breast etc. [1,2]. In 2023, 1,958,310 new cancer cases and 609,820 cancer deaths were projected in the United States. [3]. This prompts a clear understanding of the underlying mechanism and characteristics of this potentially fatal disease alongside identifying the most significant genes responsible for it.

Cancer can alter the gene expression profile of the body cells. Therefore, microarray data is utilized in clinical diagnosis to recognize down or up the regulated gene expression, which is the reason for generating new biomarkers, and leading to cancer disease [4]. Microarray data analysis has been a popular approach for diagnosing cancer, and DNA microarray is a technology used to collect data on large numbers of various gene expressions at the same time [5,6]. The classification and identification of gene expression using DNA microarray data is an effective tool for cancer diagnosis and prognosis for specific cancer subtypes. Gene expression analysis can assure medical experts whether a patient suffers from cancer within a relatively shorter time than traditional methods. Recently, its analysis has emerged as an important means for addressing the fundamental challenges associated with cancer diagnosis and drug discovery [7,8]. Analysis of gene expression data involves the identification of informative genes, [9] and [10] demonstrates that cancer classification can be improved by identifying informative genes which in turn can be used to accurately predict new sample classes.

Machine learning (ML) is a branch of artificial intelligence (AI) that enables computers to "self-learn" or obtain information from training data; recognize patterns in data and develop their own predictions, improving over time without being explicitly programmed [11]. Medical researchers and clinicians are utilizing several ML techniques on medical data sets to construct an intelligent diagnosis system [12]. Massive volume of data is being generated in the medical industry thanks to the digital revolution in information technology. ML techniques are highly suited for analyzing these massive data sets, and multiple algorithms have been used to diagnose various diseases [13–15]. Numerous research has been done to classify cancer using microarray gene expression data. Golub et al. [16] suggested a strategy based on expression profiles generated by microarrays. According to ML theory, classification outcomes are dependent on the features of the input set, the training algorithm, and the system's capacity to adapt to the original data. It is necessary to evaluate the behavior of various classifiers on provided data.

Recently, several classification approaches were created in the ML domain, and many of them were utilized in cancer classification [17]. However, there are several difficulties possible to face in the microarray classification process like (a) The microarray genes expression data constitutes many highly correlated genes for just a small sample size. The small number of cancer samples compared with the number of features can degrade the performance of the classifier and increase the risk of over-fitting. (b) Various uncertainties associated with the process of acquiring microarray data, for example, fabrication, image processing etc., resulting in unexplained fluctuation in the data. (c) The majority of genes in the microarray date are redundant for classifying diverse tissue types [18,19].

The earliest detection of cancer is among the most efficient approaches to reduce cancer-related death [20–23]. The microarray's primary characteristic is its greater number of genes (p) in comparison to the number of tissues (n) [24]. In most gene expression studies selection of relevant genes to differentiate between patients with and without cancer is a common task [25–30]. Due to overestimation & various linearity issues it is difficult to categorize high-dimensional microarray data (p > n) using statistical approaches [31,32]. There is no single optimal method to examine microarray data, with its continually evolving analysis methods [33]. Various supervised and unsupervised ML techniques have also been adopted to identify the most significant genes [34–36].In microarray gene expression analysis, gene selection or feature selection (FS) is utilized to improve cancer classification performance while using fewer samples, eliminate undesired & repetitive attributes from data and ultimately counter the curse of dimensionality by identifying the most informative genes to enhance disease prediction accuracy [37,38]. ML and dimensionality reduction techniques also perform exceptionally well at classifying biologic data [39–41]. Hence it may be beneficial to use feature selection methods which can address the challenges arising from high data dimensionality and small sample size.

The remainder of this paper is structured in the following manner. Section 2 discusses the related work. Section 3 presents the materials and methods. In Section 4, we present the experimental results. Finally, in Section 5, we conclude the paper giving a discussion.

2. Related Work

ML can assist in automating intelligent processes, increasing development efficiency and accuracy, and lowering costs [42]. Over the years ML-based classifiers have been widely used in classification of cancer sub-types. Several studies tried to assess whether ML can help in oncology care, by investigating the applications of ML in cancer risk stratification, diagnoses, and medication development [17,43–45]. According to those studies, ML can help in cancer prediction and diagnosis by analyzing pathology profiles and imaging studies.

BRCA (Breast Cancer gene) genes produce proteins that help repair damaged DNA and are referred to as tumor suppressor genes since certain changes in these genes can cause cancer [46]. People born with a certain variant of BRCA tend to develop cancer at early ages. Chang, Dalpatadu, Phanord and Singh [47] fitted a Bayesian Logistic Regression model for prediction of breast cancer using the Wisconsin Diagnosis Breast Cancer (WDBC) data set [48] which was downloaded from the UCI Machine Learning Repository; precision, recall and F1-measures of 0.93, 0.89, and 0.91 were reported for the training data, and 0.87, 0.91, 0.89 for the test data, respectively.HER2 protein accelerates breast cancer cell growth and HER2 positive patients when treated with medicines which attack the HER2 protein. Gene expression patterns of HER2 are quite complex and pose a challenge to pathologists. Cordova et al. (2023) developed a new interpretable ML method in immunohistochemistry for accurate HER2 classification and obtained high precision (0.97) and high accuracy (0.89) using immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) data [49].

Kidney renal cell carcinoma (KIRC) is the most prevalent type of kidney cancer, with a survival rate of less than 5 years and 338,000 estimated number of new cases each year [50]. ICD profile of KIRC. Wang et al. (2023) correlated the immunogenic cell death (ICD) of KIRK with the heterogeneity and therapeutic complexity which is useful for developing optimal immunotherapy strategy for KIRC patients [51].

A common cancerous tumor in the digestive track is colon adenocarcinoma (COAD) and is commonly associated with fatty acids [52]; diagnosis of COAD is difficult as there are hardly any early symptoms. Li et al. (2017) used a genetic algorithm and the k-nearest neighbors clustering method to determine genes which can accurately classify samples as well as class subtypes for a TCGA RNA-seq dataset of 9066 cancer patients and 602 normal samples [53].

Lung adenocarcinoma (LUAD) is a common form of lung cancer which also gets detected in the middle/late stages and therefore is hard to treat [54]. Yang et al. (2022) used a dataset of gene expression profiles from 515 tumor samples and 59 normal tissues and split the dataset into two significantly different clusters; they further showed that using age, gender, pathological stages, and risk score as predictors of LUAD increased the prediction accuracy measures [55]. Liu, Lei, Zhang, and Wang (2022) used cluster analysis on enrichment scores of 12 stemness signatures to identify three LUAD subtypes, St-H, St-M and St-L for six different datasets [56].

Prostate adenocarcinoma (PRAD) is common in elderly men, and patients suffering from PRAD typically have good prognosis [57]. Khosravi et al. (2021) used Deep Learning ML models on an MRI dataset from 400 subjects with suspected prostate cancer combined with histological data and reported high accuracies [58].

PCA is an exploratory multivariate statistical technique for simplifying complex data sets [59–61]. It has been used in a wide range of biomedical problems, including the analysis of microarray data in search of outlier genes [62], analysis of other types of expression data [63,64] as well as cancer classification [65]. AK Oladejo, TO Oladele, YK Saheed (2018) presented two methods of dimension reduction: feature extraction (FE) and FS; one-way Anova for FE and PCA was utilized for FS [66]. The Support vector machine (SVM) and k-nearest neighbor (K-NN) were used for the classification of leukemia genome data. The obtained results gave an accuracy of 90% for SVM and 81.67% for K-NN.

MO Adebiyi, MO Arowolo, MD Mshelia, OO Olugbara (2022) applied the machine learning algorithms of RF and the SVM with the feature extraction method of LDA to the Wisconsin Breast Cancer Dataset [67]. The SVM with LDA and RF with LDA yielded accuracy results of 96.4% and 95.6% respectively. Evidence from this study shows that better prediction is crucial and can benefit from machine learning methods. This research has validated the use of feature extraction in predicting a diagnostic system for breast cancer when compared to the existing literature.

Ak, Muhammet Fatih (2020) utilized the Wisconsin Breast Cancer Dataset [48] for the comparison of most of the major machine-learning procedures for detection and diagnosis [69]. Supervised learning-decision tree, RF, multilayer perception, SVM, and linear regression (LR) were compared in both the classification and regression categories. The results revealed that under the classification algorithm, the SVM provides high accuracy; however, under the regression methodology, multilayer perception regression delivers reduced errors. Díaz-Uriarte, Ramón (2006) investigated the implication of RF for classification of microarray data (including multi-class problems) and propose a new method of gene selection in classification problems based on RF [70].

The study used simulated and nine microarray data sets and demonstrated that random forest has comparable performance to other classification methods, including diagonal discriminant analysis (DLDA), KNN, and SVM, and that the new gene selection procedure yields very small sets of genes without compromising predictive accuracy.

AC Tan, D Gilbert (2003) classified cancer using gene expression data using three distinct tree-based supervised ML techniques [71]. Seven different categories of cancer data were classified using bagged and boosted decision trees (DT) alongside C4.5 DT. The bagging DT outperforms the other two. A Sharma, S Imoto, S Miyano, V Sharma (2012) proposed a Null space-based feature selection method for gene expression data in terms of supervised classification. [72]. Scatter matrices-generated null space information were utilized as a feature selection method in removing the duplicate gene expressions. After effectively lowering the dimension of the features, classification was performed using three different types of classifiers: SVM, naïve Bayes (NB), and LDA.

Degroeve, De Baets, Van de Peer and Rouz´e (2002) created a balanced train and set by randomly selecting 1000 positive instances and 1000 negative and created a test data with 281 positive and 7505 negative instances and another test data set with 281 positive and 7643 negative instances; they used SVM classifier, a NB classifier, and a traditional method for feature selection for predicting splice site and obtained improved performance. Precision obtained for these datasets ranged in 93-98% range, but the recall and F1-measures were in 25-49% range [73]. Peng, Li and Liu (2006) compared various methods of gene selection over four microarray gene expression datasets and showed that the hybrid method works well on the four datasets [74].

Sharma and Paliwal (2008) used Gradient LDA method for three small microarray gene expression datasets: acute leukemia, small round blue-cell tumor (SRBCT) and lung adenocarcinoma and have obtained higher accuracies than some competing methods [75]. Bar-Joseph, Gitter and Simon (2012) provided a discussion of how time-series gene expression data is used for identification of activated genes in biological processes and describe how basic patterns lead to gene expression programs [76]. Cho et al. (2004) proposed a modified kernel Fisher discriminant analysis (KFDA) for the analysis of the hereditary breast cancer dataset [77]. The KFDA classifier employed the mean-squared-error as the gene selection criterion. D Huang (2009) evaluated the classification performance of LDA, prediction analysis for microarrays (PAM), shrinkage centroid regularized discriminant analysis (SCRDA), shrinkage linear discriminant analysis (SLDA) and shrinkage diagonal discriminant analysis (SDDA) by applying these methods to six public cancer gene expression datasets [78].

Dwivedi (2018) used the method of Artificial Neural Network (ANN) for classification of acute cases of lymphoblastic leukemia and myeloid leukemia and reported over 98% overall classification accuracy [79]. Sun et al. (2019) used the genome deep learning method to analyze 6,083 samples from the Whole Exon Sequencing mutations with 12 types of cancer and 1991 non-cancerous samples from the 1000 Genome Project and obtained overall classification accuracies ranging in 70% - 97% [80]. A survey of feature selection literature for gene expression microarray data analysis based on a total of 132 research articles [81] was conducted by Alhenawi, Al-Sayyed, Hudaib and Mirjalili (2022). Khatun et al. (2023) developed an ensemble rank-based feature selection method (EFSM) and a weighted average voting scheme to overcome the problems posed by high dimensionality of microarray gene expression data [82]. They obtained overall classification accuracies of 100% (leukemia), 95% (colon cancer), and 94.3% for the 11-tumor dataset. Osama, Shaban and Ali (2023) have provided a review of ML methods for cancer classification of microarray gene expression data; data pre-processing and feature selection methods including filter, wrapper, embedded, ensemble, and hybrid algorithms [83].

Kabir et al. (2023) compared two different dimension reduction techniques—PCA, and autoencoders for the selection of features in a prostate cancer classification analysis. Two machine learning methods—neural networks and SVM—were further used for classification. The study showed that the classifiers performed better on the reduced dataset [84]. Another study Adiwijaya et al. (2018) utilized PCA dimension reduction method that includes the calculation of variance proportion for eigenvector selection followed by the classification methods, SVM and Levenberg-

Marquardt Backpropagation (LMBP) algorithm. Based on the tests performed, the classification method using LMBP was more stable than SVM [10].

Kharya, S., D. Dubey, and S. Soni (2013) compared the accuracy of the SVM, ANN, Naive Bayes classifier, and AdaBoost tree to identify a potent model for breast cancer prediction as observational research [85]. PCA was used to reduce dimensionality. The study found that, when compared to techniques like decision trees, regression trees, and so on, ANN came out to be the one with the most reliable approach in making real-time predictions and prognoses. Rana et al (2015) used machine learning classification algorithms, which use stored historical data to learn from and forecast new input categories, benign and malignant tumors [86]. According to this study, the random forest model demonstrated the highest accuracy of 96% to detect different cancers.

Based on previous research, the general scheme in the process of classification of microarray data for the detection of cancer can be conducted via preprocessing the data and dimensionality reduction followed by cancer classification.

3. Materials and Methods

In this article, we have used the Linear Discriminant Analysis (LDA) classifier [87] and the random forest (RF) classifier [88] on an 801 rows x 20531 columns (genes) dataset of patients with five cancer types: BRCA, KIRC, COAD, LUAD and PRAD; the dataset has no missing values. Variables in this dataset are RNA-Seq gene expression levels measured by illumina HiSeq platform. The variables are dummy named gene XX. This dataset (gene expression cancer RNA-Seq) was downloaded from the UCI Machine Learning Repository [89]. The statistical software package R (2023) was used for all data analyses and visualizations [90]. We computed Principal Component (PC) scores [91] of the data and performed the 5-level classification on an increasing number of PC's and obtained excellent classification results using just the first two components PC1 and PC2. Five cancer types are described below.

We will next provide brief descriptions of the methods of data analysis and the common measures of accuracy used in multi-level classification.

3.1. Principal Components Analysis (PCA)

PCA is a dimension-reduction technique which creates new and uncorrelated linear combinations of original variables (principal components); the values of the principal components are called PC-Scores and can be used in place of the original variables for further analyses such as Multiple Linear Regression (MLR) or Discrimination and Classification. Using PC-Scores instead of original variables as predictors eliminates the problem of multicollinearity. PCA was performed using the correlation matrix which normalizes the input variables.

3.2. Linear Discriminant Analysis (LDA)

LDA is itself a dimension-reduction technique which is used for separating a dataset into 2 or more subgroups, and for classification of new data into these subgroups. LDA is typically one of the methods used for multi-level classification problems. The LDA method involves computing separating hyperplanes for classification purposes [92] (pp. 587–590). We used the function prcompfast of the R-package Morpho to first perform PCA of the gene expression microarray dataset at hand and the PC-Scores were used as input variables for LDA. All computations were performed on a Windows 10 PC with AMD Ryzen Threadpiper1950X 16-Core Processor and 128 GB usable RAM.

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3.3. Random Forest (RF)

The RF method is a decision-tree based method that can be used for classification (categorical response) or regression (continuous response) problems. It randomly selects a subset of rows (samples) and a subset of columns (features) at a time and fits decision trees a very large number of times to predict Y and then uses a voting mechanism to predict Y values. Random forest is known to be highly accurate [93].

3.4. Training and Test Datasets

In ML literature, it is common practice to randomly split the available dataset into Training and Test datasets and report the accuracy measures of prediction for both datasets. Typically, higher accuracy measures are obtained for the training set than the test set. The entire raw dataset was used to compute PC-Scores by using the fast-PCA method of the R-package Morpho. A dataset of 801 rows and 25 PC-scores was created, and then this dataset of PC-scores was randomly split into an 80% training set and 20% test set. The LDA and RF methods were used on the training set of PC-Scores and the accuracy measures given below were computed for both training and test sets.

3.5. Accuracy Measures for Multi-Level Classification

All accuracy measures are computed from the confusion matrix which is a cross-tabulation of observed *Y* and predicted Y values.

Overall Accuracy (OA) = sum of diagonal elements of CM/sum of all elements of CM
Precision_j = j-th diagonal element of CM/sum of j-th column of CM
Recall_j = j-th diagonal element of CM/sum of j-th row of CM
F1_j = harmonic mean of Precision_j and Recall_j

The following accuracy measures are computed for each level by calculating the one vs all binary confusion matrices:

Area Under the Curve (AUC)
Macro- and micro-averages of AUC
Explanations of the accuracy measures and computational details are provided in [52].

4. Results

PCA was run on the entire 801 rows x 20531 genes data set, and trial-and-error showed that just the first two principal components were sufficient for classification purposes. The genes with highest absolute loadings are shown in Table 9.

A scatterplot of the first two PC-scores for the entire dataset is shown in Figure 1. A clear separation between BRCA and KIRC cancer sub-types with some overlap between COAD, LUAD and PRAD is seen in Figure 1.

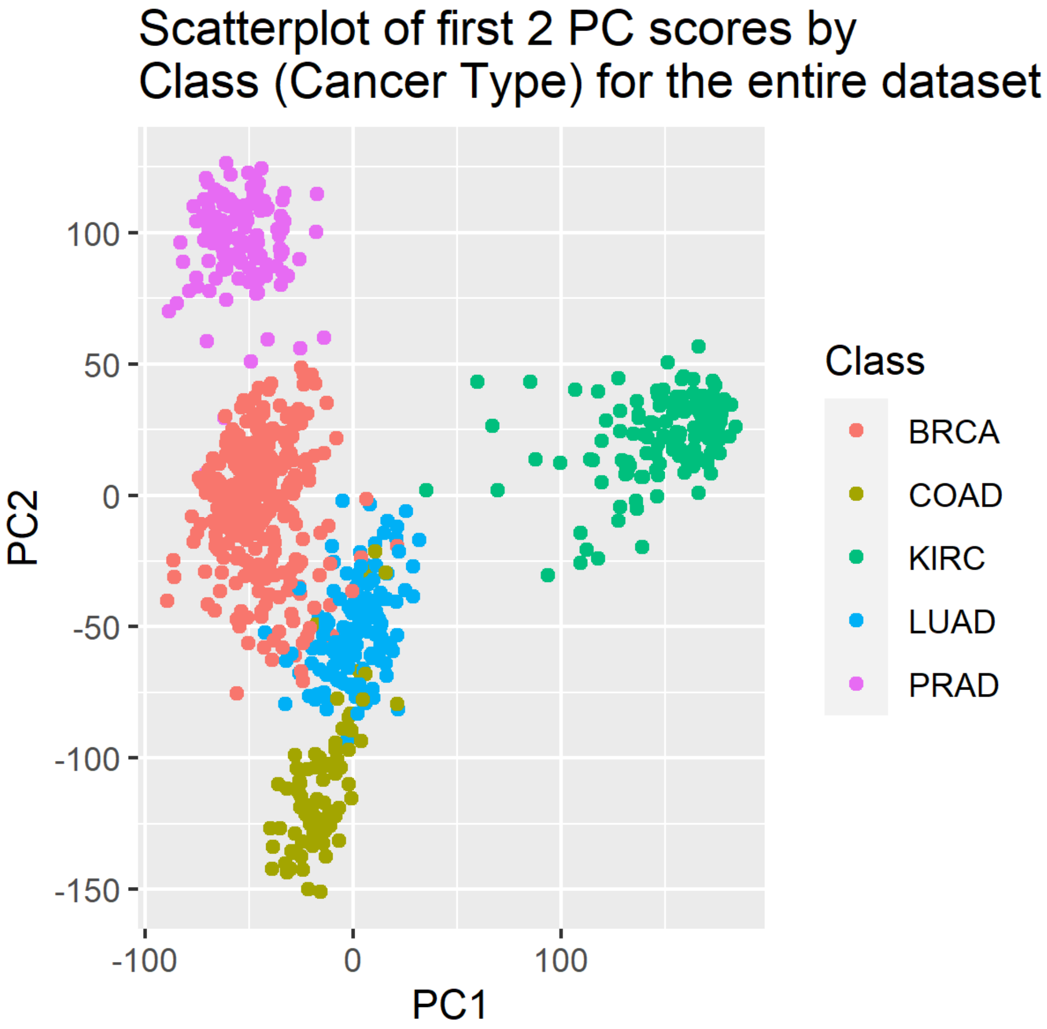


Figure 1. Scatterplot of PC2 vs PC1 for the Entire Data**.**

Figures 2–5 show plots of the confusion matrices for the LDA and RF classifiers for training and test sets, respectively. Tables 1–8 show that all measures of multi-level accuracy are high for both training and test datasets and both LDA and RF methods.

Accuracy Measures for the LDA Classifier for Training Data

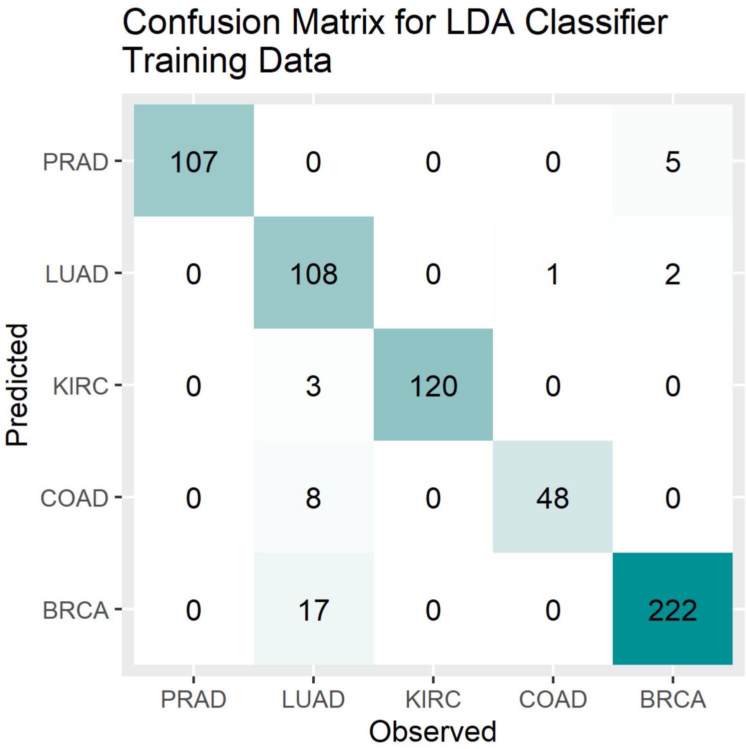


Figure 2. Confusion Matrix Plot for the LDA Classifier – Training Data.

Table 1. Precision, Recall, F1 and AUC Measures for the LDA Classifier – Training Data**.**

	Precision	Recall	F1	AUC
BRCA	0.97	0.93	0.95	0.96
COAD	0.96	0.84	0.9	0.92
KIRC	1	0.97	0.98	0.98
LUAD	0.77	0.95	0.85	0.95
PRAD	1	0.97	0.99	0.99

Table 2. Macro- and Micro-Averaged AUC Measures for the LDA Classifier – Training Data**.**

Macro average AUC	0.94	0.93	0.94	0.95
Micro average AUC	0.94	0.94	0.94	na
OA	0.94			
na: no micro-averaged AUC exists in the ML literature				

Accuracy Measures for the LDA Classifier for Test Data

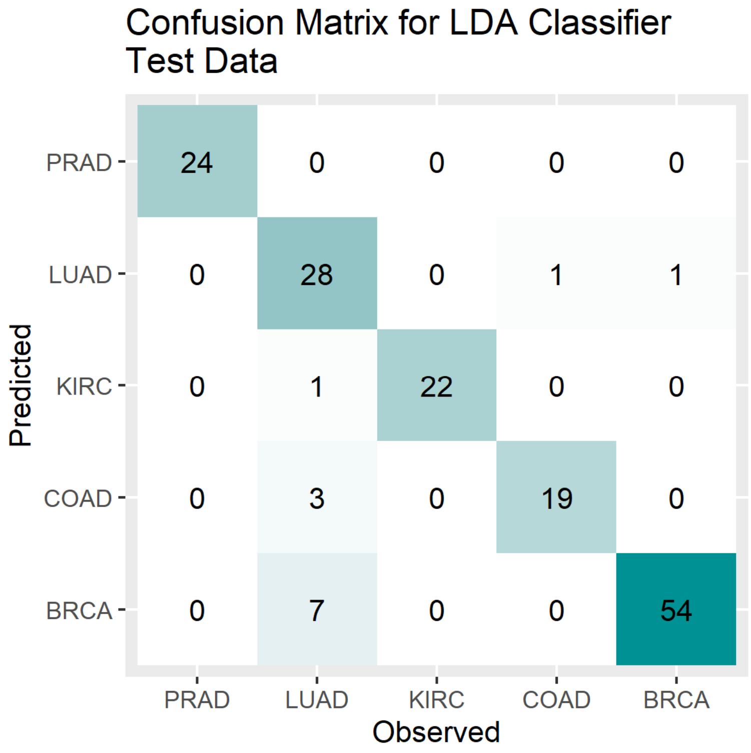


Figure 3. Confusion Matrix Plot for the LDA Classifier – Test Data.

Table 3. Confusion Matrix Plot and Accuracy Measures for the LDA Classifier – Test Data.

	Precision	Recall	F1	AUC
BRCA	0.98	0.97	0.97	0.98
COAD	1	0.94	0.97	0.97
KIRC	1	1	1	1
LUAD	0.92	1	0.96	0.99
PRAD	1	0.96	0.98	0.98

Table 4. Macro and Micro averaged AUC for the LDA Classifier – Test Data.

Macro average	0.94	0.93	0.94	0.98
Micro average	0.94	0.94	0.94	na
OA	0.94			
na: no micro-averaged AUC exists in the ML literature				

Accuracy Measures for the RF Classifier for Training Data

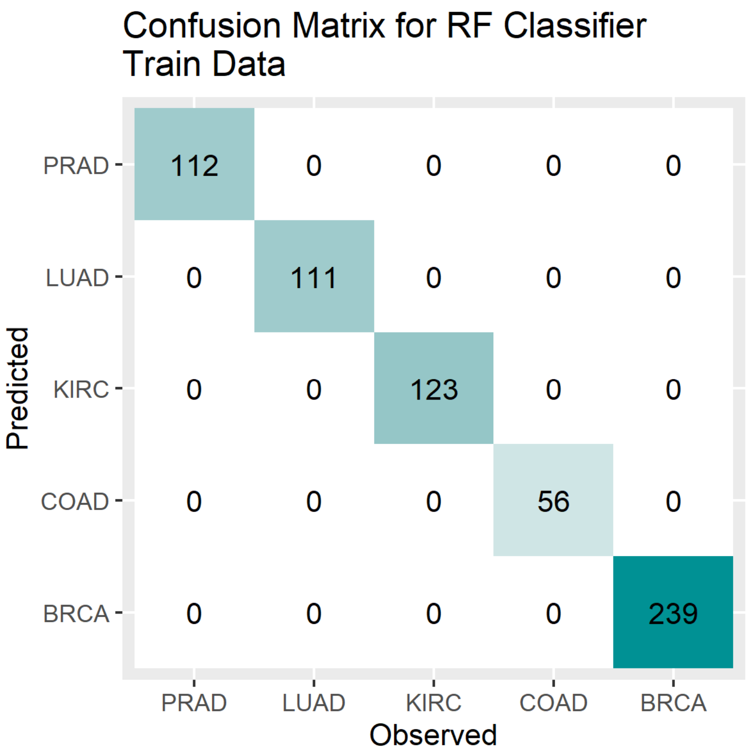
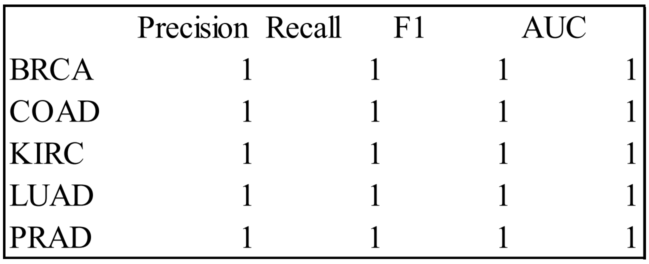


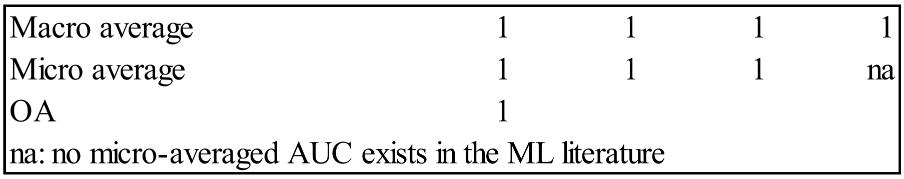
Figure 4. Confusion Matrix Plot for the RF Classifier – Training Data.

Table 5. Precision, Recall, F1 and AUC Measures for the RF Classifier – Training Data.



	Precision	Recall	F1	AUC
BRCA	1	1	1	1
COAD	1	1	1	1
KIRC	1	1	1	1
LUAD	1	1	1	1
PRAD	1	1	1	1

Table 6. Macro and Micro averaged AUC for the RF Classifier – Training Data.



Macro average	1	1	1	1
Micro average	1	1	1	na
OA	1			
na: no micro-averaged AUC exists in the ML literature				

Accuracy Measures for the RF Classifier for Test Data

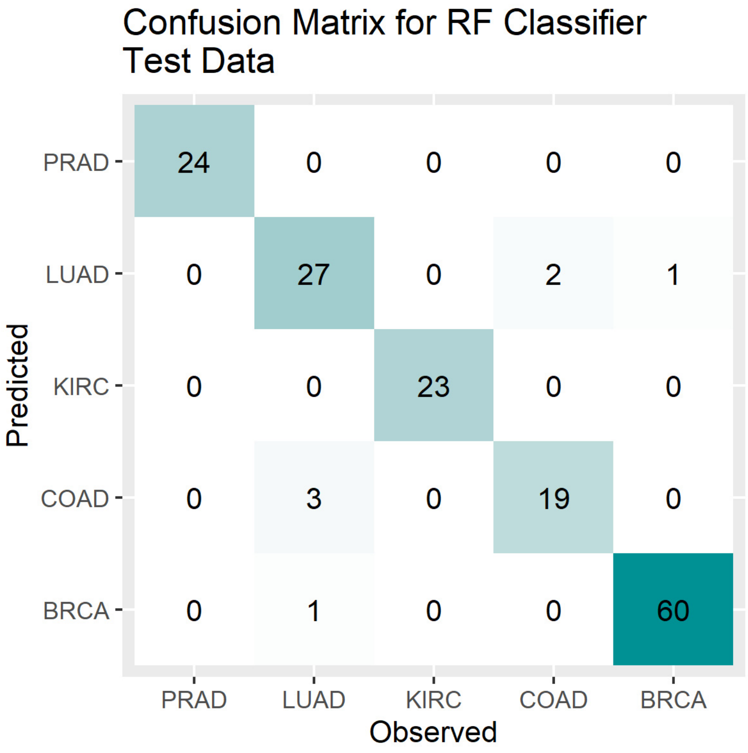


Figure 5. Confusion Matrix Plot for the RF Classifier – Test Data.

Table 7. Precision, Recall, F1 and AUC Measures for the RF Classifier – Test Data.

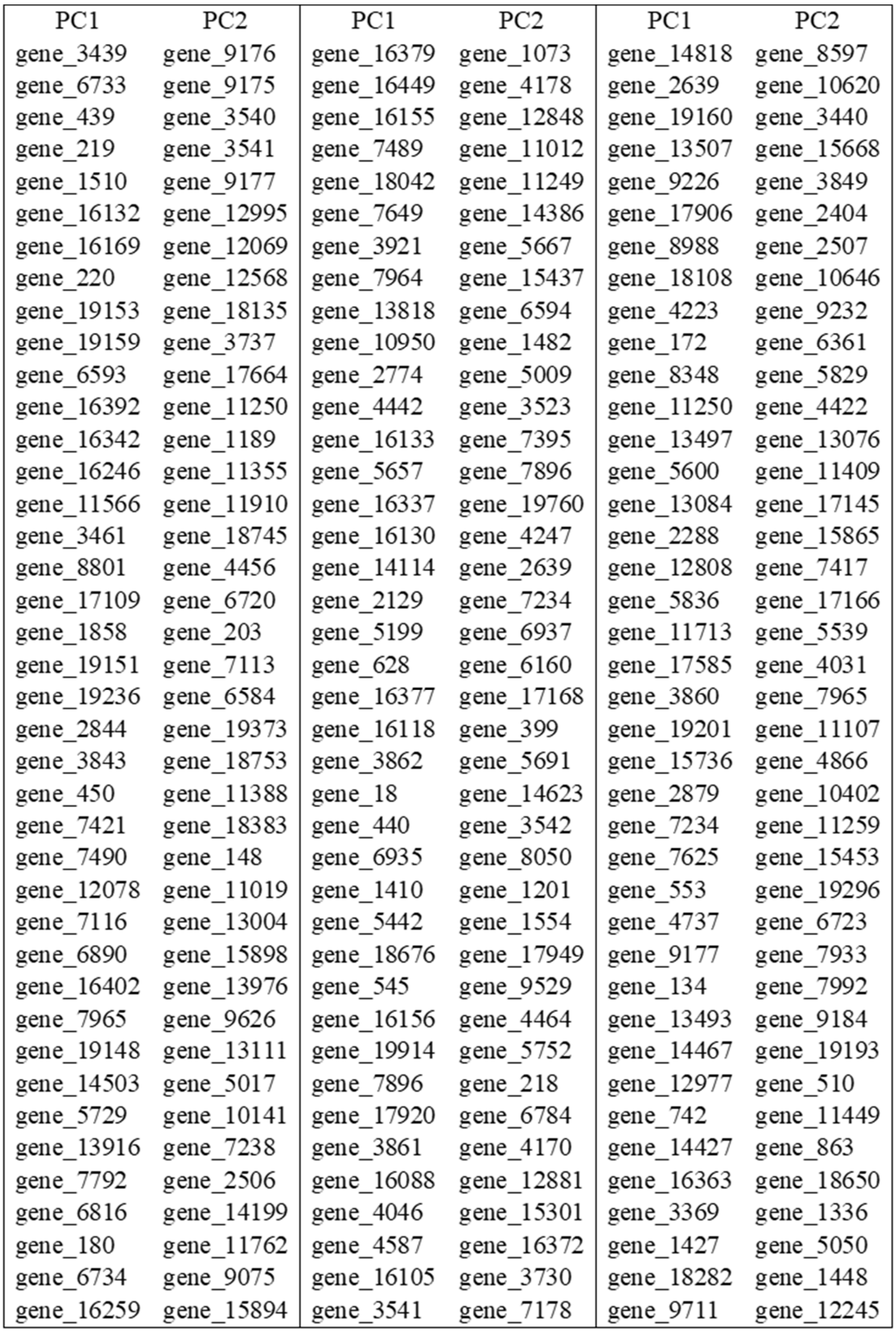
	Precision	Recall	F1	AUC
BRCA	0.95	1	0.98	0.99
COAD	0.88	0.94	0.91	0.96
KIRC	1	1	1	1
LUAD	0.97	0.88	0.92	0.94
PRAD	1	0.96	0.98	0.98

Table 8. Macro and Micro averaged AUC for the RF Classifier – Test Data.

Macro average	0.96	0.96	0.96	0.96
Micro average	0.96	0.96	0.96	na
OA	0.96			
na: no micro-averaged AUC exists in the ML literature				

In Table 9 we provide the variables (genes) with high absolute loadings on the first two PC-scores; such a table can be very useful for selection of features (genes).

Table 9. Significant genes with highest absolute loadings on the first two PC-scores.



PC1	PC2	PC1	PC2	PC1	PC2
gene_3439	gene_9176	gene_16379	gene_1073	gene_14818	gene_8597
gene_6733	gene_9175	gene_16449	gene_4178	gene_2639	gene_10620
gene_439	gene_3540	gene_16155	gene_12848	gene_19160	gene_3440
gene_219	gene_3541	gene_7489	gene_11012	gene_13507	gene_15668
gene_1510	gene_9177	gene_18042	gene_11249	gene_9226	gene_3849
gene_16132	gene_12995	gene_7649	gene_14386	gene_17906	gene_2404
gene_16169	gene_12069	gene_3921	gene_5667	gene_8988	gene_2507
gene_220	gene_12568	gene_7964	gene_15437	gene_18108	gene_10646
gene_19153	gene_18135	gene_13818	gene_6594	gene_4223	gene_9232
gene_19159	gene_3737	gene_10950	gene_1482	gene_172	gene_6361
gene_6593	gene_17664	gene_2774	gene_5009	gene_8348	gene_5829
gene_16392	gene_11250	gene_4442	gene_3523	gene_11250	gene_4422
gene_16342	gene_1189	gene_16133	gene_7395	gene_13497	gene_13076
gene_16246	gene_11355	gene_5657	gene_7896	gene_5600	gene_11409
gene_11566	gene_11910	gene_16337	gene_19760	gene_13084	gene_17145
gene_3461	gene_18745	gene_16130	gene_4247	gene_2288	gene_15865
gene_8801	gene_4456	gene_14114	gene_2639	gene_12808	gene_7417
gene_17109	gene_6720	gene_2129	gene_7234	gene_5836	gene_17166
gene_1858	gene_203	gene_5199	gene_6937	gene_11713	gene_5539
gene_19151	gene_7113	gene_628	gene_6160	gene_17585	gene_4031
gene_19236	gene_6584	gene_16377	gene_17168	gene_3860	gene_7965
gene_2844	gene_19373	gene_16118	gene_399	gene_19201	gene_11107
gene_3843	gene_18753	gene_3862	gene_5691	gene_15736	gene_4866
gene_450	gene_11388	gene_18	gene_14623	gene_2879	gene_10402
gene_7421	gene_18383	gene_440	gene_3542	gene_7234	gene_11259
gene_7490	gene_148	gene_6935	gene_8050	gene_7625	gene_15453
gene_12078	gene_11019	gene_1410	gene_1201	gene_553	gene_19296
gene_7116	gene_13004	gene_5442	gene_1554	gene_4737	gene_6723
gene_6890	gene_15898	gene_18676	gene_17949	gene_9177	gene_7933
gene_16402	gene_13976	gene_545	gene_9529	gene_134	gene_7992
gene_7965	gene_9626	gene_16156	gene_4464	gene_13493	gene_9184
gene_19148	gene_13111	gene_19914	gene_5752	gene_14467	gene_19193
gene_14503	gene_5017	gene_7896	gene_218	gene_12977	gene_510
gene_5729	gene_10141	gene_17920	gene_6784	gene_742	gene_11449
gene_13916	gene_7238	gene_3861	gene_4170	gene_14427	gene_863
gene_7792	gene_2506	gene_16088	gene_12881	gene_16363	gene_18650
gene_6816	gene_14199	gene_4046	gene_15301	gene_3369	gene_1336
gene_180	gene_11762	gene_4587	gene_16372	gene_1427	gene_5050
gene_6734	gene_9075	gene_16105	gene_3730	gene_18282	gene_1448
gene_16259	gene_15894	gene_3541	gene_7178	gene_9711	gene_12245

5. Discussion

We have demonstrated successful application of PCA for dimensionality reduction on a dataset with a very large number of genes collected from a much smaller number of subjects. PCA results showed that the first 50 components (PC) cumulatively explained 71% of all variability present in the 801 × 20532 gene expression data, with the first two PC's explaining only 26% of total variability. The first two PC's, however, were sufficient for classification of cancer sub-types with high accuracy. This can be seen from the plot of the first two components by of cancer sub-type. LDA was able to classify each of the five cancer-subtypes with high accuracies except for LUAD which had a precision of 77% for the training set. The RF method was able to classify each sub-type with very high accuracy. The

PCA loadings on 20532 genes were sorted in order of magnitude and genes (features) important for classification were identified. Our results are not generalizable, but the proposed classification method should be very helpful to researchers and clinicians working with gene expression microarray data of very high dimensionality. It should be noted that high accuracy is achieved by the LDA and the RM classifiers using just the first two PC-Scores even though only 26% of variability was explained by the first two components.

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