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Detection of colon cancer based on microarray dataset using machinelearning as a feature selection and classification techniques

ABSTRACT

Microarray data is an increasingly important tool for providing information on gene expression for analysis and interpreta-tion. Researchers attempt to utilize the smallest possible set of relevant gene expression profiles in most gene expression studies to enhance tumor identification accuracy. This research aims to analyze and predicts colon cancer data employing a machine learning approach and feature selection technique based on a random forest classifier. More particularly, our proposed method can reduce the burden of high dimensional data and allow faster calculations by combining the "MeanDecrease Accuracy" and "Mean Decrease Gini" as feature selection methods into a renowned classifier namely Random Forest, with the aim of increasing the prediction model's accuracy level. In addition, we have also shown a comparative model analysis with selection of features and model without selection of features. The extensive experimental results have demonstrated that the proposed model with feature selection is favorable and effective which triumphs the best performance of accuracy.

Keywords Colon cancer · Microarray data · Feature selection · Machine learning · Random forest · Cross validation

I. INTRODUCTION

Colon cancer is a substantial public health problem andthe global incidence of this cancer has risen quickly with population growth. World Health Organization (WHO) GLOBOCAN database study 2018 reported 1,849,518 newcases of Colorectal Cancer (CRC) and 880,792 deaths asso-ciated with CRC [1]. CRC is the third leading cause of can-cer related death in the United States, 2019 [2]. A recent study [3] indicates that approximately 25% of CRC caseshave a genetic predisposition. Golub et al. [4]. first devel-oped a generic cancer classification approach based on DNA microarray gene expression monitoring. They also proposed that such microarrays might provide a classifica- tion tool for cancer. Microarray based gene expression hasbeen widely used in the diagnosis and analysis of colon cancer. Early detection of colon cancer is very important for proper diagnosis and treatment. Microarray dataset consists of thousands of genes and the number of samples is usually small. It is a challenging task to identify the most relevant genes from such types of microarray data as not all genes have sufficient follow-up-information and many of them are redundant. Feature transformation and featureselection are the two current methods of obtaining feature genes for cancer classification based gene expression data [5]. Feature transformation is a process in which to create a new set of features from original features to achieve thepurpose of feature reduction. Although they have high discriminatory power, sometimes they do not retain the biological information of the original gene expression. Transformation of data reflects the loss of data interpret- ability and makes it impossible to identify the target genesassociated with cancer. Unlike feature transformation methods, feature selection methods do not create a new subset of features. They work by removing non-relevantor redundant features and retains the best classification accuracy. Feature selection does not involve transforma- tion of the original features thus decrease the dimension- ality problem and builds a robust learning model from theselected data [6]. Therefore, the methods of feature selec-tion have gained further interest. The most common fea- ture selection methods can be separated into three main categories: filters, wrappers, embedded techniques [7, 8].Filter methods are the process of selecting features based on some statistical performance of the features and areindependent of any subsequent machine learning algo- rithms. They are very fast computationally and rely entirelyon data set features. One of the main disadvantages is thatthey ignore correlation between features. Wrapper meth- ods are based on greedy search algorithms that search byiteratively selecting features on a specific machine learn- ing algorithm for optimal subset of features. For a datasetwith many features, they are slower than filters and com- putationally expensive. Embedded methods interact with the classification model for feature selection and are less computationally intensive and faster as compared to fil- ters and wrappers. Common embedded method includes various types of decision trees, random forest, and artificialneural networks. In this study, we proposed a method toselect variables using Mean Decrease Accuracy (MDA) andMean Decrease Gini (MDG). Then, a random forest classifier[9, 10] is constructed for colon cancer prediction.

The rest of the paper is organized as follows: Sect. 2
presents the previous work done in colon cancer detec-tion based on machine learning tools related to microarraydataset; Sect. 3 describes the architecture and methods of the proposed system. Section 4 deals with the analysis of experimental

results and discussion. Finally, the conclu- sions of this study are summarized in Sect. 5.

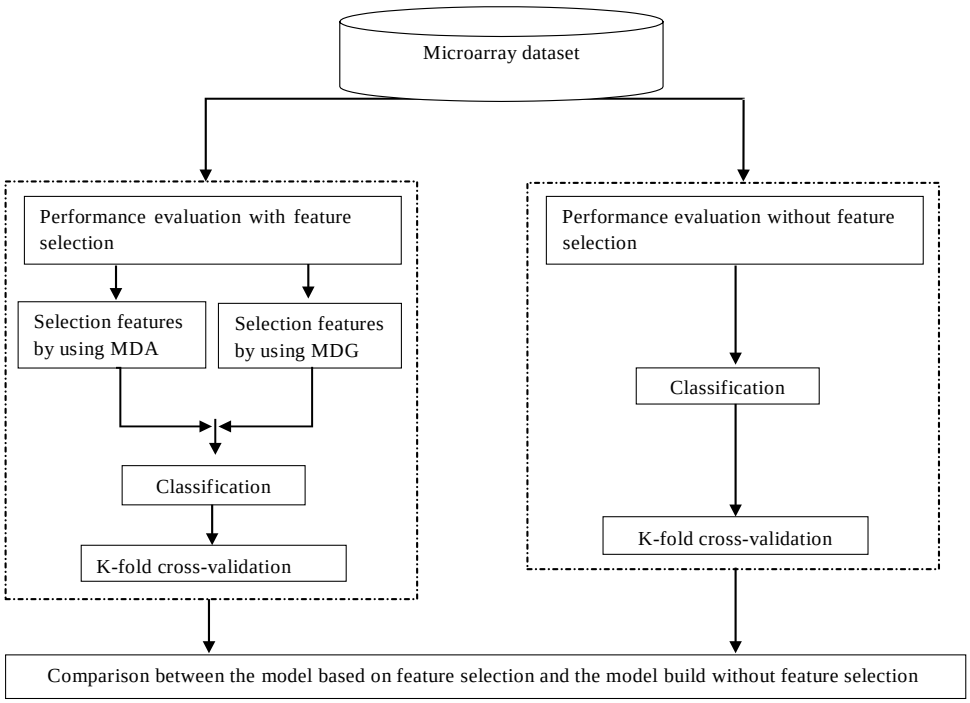
II. RELATED WORKS

Recently, a lot of research has been developed to work on healthcare data by incorporating machine learn- ing techniques with feature selection methods. Park & Kim developed a model with 20 datasets of microarray gene expressions to examine the property of the model based on sequential random k-nearest neighbor feature selection method [11]. An intelligent technique based on feature selection using t-statistic was proposed for colon cancer prediction. Authors achieved almost 85% accuracy using t-statistic feature selection method and Support Vec- tor Machine (SVM) classifier [12]. A Fuzzy Decision Tree (FDT)-based feature selection algorithm was introducedby S.A. Ludwig et al. [13] to analyze gene expression forcolon cancer data classification and achieved 80.28% accu- racy by selecting 20 features. Modified Analytic Hierarchy Process (MAHP) with Probabilistic Neural Network (PNN)was introduced in [14] as a novel aggregate gene selectionmethod for microarray data classification. The experimen-tal results demonstrated that the proposed MAHP method obtained the top accuracy of 88.89% for colon cancer diag- nosis with a benefit of inexpensive computational cost. Authors [15] used Fast Correlation Based Feature Selection(FCBFS) method with SVM as optimized by Particle SwarmOptimization (PSO) and Artificial Bee Colony (ABC) to improve cancer classification quality. They observed that the classification model based on PSO and ABC attained93.55% classification accuracy for colon cancer prognosis. Maolong et al. [5] developed a Binary Quantum-BehavedParticle Swarm Optimization (BQPSO) and SVM with leave-one-out cross validation (LOOCV) based method for cancer feature selection and classification. They con- cluded that the proposed algorithm produced the clas- sification results, with best accuracy of 93.55% and mean accuracy of 92.52% for colon cancer datasets. Authors [16] relies on the methodology that uses Information Gain (IG) for feature selection, Genetic Algorithm (GA) for feature reduction, and Genetic Programming (GP) for cancer clas- sification based on the gene expression profiles. For colon tumor classification, the suggested algorithm achieved an accuracy of 85.48%. A method of selecting features using Genetic Algorithm (GA) was proposed to select the bestsubset of features for breast cancer diagnosis system [17]. Random forest is an ensemble based classifier consist- ing of a collection of trees of classification and regression (CART). Compared to other classifiers like Adaboost, SVM, neural network, decision tree, it reduces overfitting and therefore is more accurate. It is also used as a feature selec-tion approach to rank the feature importance.

III. METHODOLOGY

Figure 1 shows this study's methodology. The process starts with data collection. The first phase data was then transferred for classification purposes to the second phase. In the third phase, we applied two MDI and MDG-based feature selection algorithms that were used to train and test the data. We performed a comparative design study

Fig. 1 Framework of the pro-posed model



without selecting features and models that used featureselection in the final research phase.

Phase 1 data acquisition
Colon cancer gene expression data has been obtained from [18] in the data acquisition phase. The datasets are made up of 62 cases (tests) and 2000 genes (attrib-utes) from patients with colon cancer. Among them are40 tumor biopsies (marked as abnormal) and 22 normal.Colon tumor sample data can be seen in Table 1.

Phase 2 evaluation of classificationwithout feature selection
In this phase, a RF classifier with tenfold cross-validation was performed with all the attributes to evaluate the per-formance of the model.

Phase 3 evaluation of classification with featureselection
MDA and MDG ware performed as feature selection tech- niques with an end goal to pick the significant important features. At that point, we built a robust model by utilizing the selected features and performed a similar procedure as described in the above phase.

Phase 4 comparative analysis
In this phase, we compared the model's output withoutselection of features and the model with selection of fea- tures. We used recall, precision, accuracy, and F1-score metrics to assess the reliable performance of the clas- sification. Such output measures are extracted from the confusion matrix, which is used for evaluating classifier performance. Representation of confusion matrix and the

Table 1 Colon tumor data samples

No	Attribute_1	Attribute_2	Attribute_3	Attribute_4	Attribute_5	...Attribute_2000	Class
1	8589.416	5468.2407	4263.4077	4064.9358	1997.893	...28.70125	Abnormal
2	9164.254	6719.5293	4883.4487	3718.159	2015.2214	...16.77375	Normal
3	3825.705	6970.3613	5369.9688	4705.65	1166.5536	...15.15625	Abnormal
4	6246.4487	7823.534	5955.835	3975.5642	2002.6132	...16.085	Normal
.....	.....	.....	.....	.....	.....	.....	.....
62	7472.01	3653.934	2728.2163	3494.4805	2404.6655	...39.63125	Normal

Table 2 Confusion matrix

Actual class	Predicted class	
	Positive	Negative
Positive	True positive, TP	False negative, FN
Negative	False positive, FP	True negative, TN

Table 3 Performance measure representation

Performance metrics	Formula
Recall	$\frac{TP}{TP+FN}$
Precision	$\frac{TP}{TP+FP}$
F1-score	$\frac{2*TP}{2*TP+FP+FN}$
Accuracy	$\frac{TP+TN}{TP+TN+FP+FN}$

formula for the measurement of performance metrics are shown in Tables 2 and 3 respectively.
Recall also known as sensitivity is the ratio of correctly predicted positives cases to the all observations in actual class. The precision metric indicates the correct positive outcomes out of all the positive outcomes. The accuracy ofa classifier is simply the ratio of correctly predicted class tototal class. F1-score is estimated by applying the weighted
average over precision and recall. In case we have an une-
ing the values of x_j. A variable is considered to be as more important whose exclusion (or permutation) decrease the accuracy of random forest. That's why variables with a large mean decrease in accuracy are more important for classification.

3.5.2 Mean decrease gini
Mean Decrease Gini is a forest-wide weighted average of the decrease in the Gini Impurity which is a metric used in decision trees to determine how a variable splits between the parent and child nodes. It can be defined as averaging the total decrease in node impurity across all the trees thatforming the forest. We can calculate variable importance (VI) for variable x_j for MDG method as described by the following equation [21]:

ven class proportion, F1-score is generally more valuable than precision because it takes both false positives and false negatives into account.

$$VI(x_j) = \frac{1}{n_{tree}} \sum_{k=1}^{n_{tree}} 1 - \sum_{k=1} Gini(j)^k \quad (2)$$

Feature selection algorithms description
Feature selection plays an important role for interpreta- tion and prediction. It also makes the classification pro-cess easier rather than incorporating unnecessary features.Feature selection discovers the most significant features for microarray or high dimensional dataset, reducing the classifier's workload and accordingly improves the classifi- cation accuracy. For feature selection, two indices are con-sidered in this paper: Mean Decrease Accuracy (MDA) andMean Decrease Gini (MDG) [19]. These two techniques takeinto account the importance of variable's impurity and theimportance of out-of-bag (OOB) error [20].

Mean decrease accuracy
MDA is also called permutation importance. OOB erroris a subsampling technique used to calculate predictionerror and then evaluate the variable importance. MDA is a method that is usually described as a decrease in the model accuracy from permuting the values in each feature.The formula for Mean Decrease Accuracy [21] is
It simply records the decrease in Gini Impurity for all
variables from 1 to n_{tree} . A variable with higher Mean Decrease in Gini indicates higher variable importance.

Classification algorithm description

In this study, a renowned classification algorithm for the prediction model namely random forest was evaluated in the prediction of colon cancer. RF is a combined classi-fier formed by combining a collection of unpruned deci-sion trees, i.e., CART (classification and regression trees). A detailed overview of CART procedure can be found in Chang and Wang [22] and Harb et al. [23]. The RF pre- diction when conducting classification analysis is the unweighted majority of individual trees class votes. Fig- ure 2 represents a RF model's architecture for predicting the class of colon.

Random forest algorithm description [24]
For the original dataset D(X, Y), RF constructs the basic decision trees:

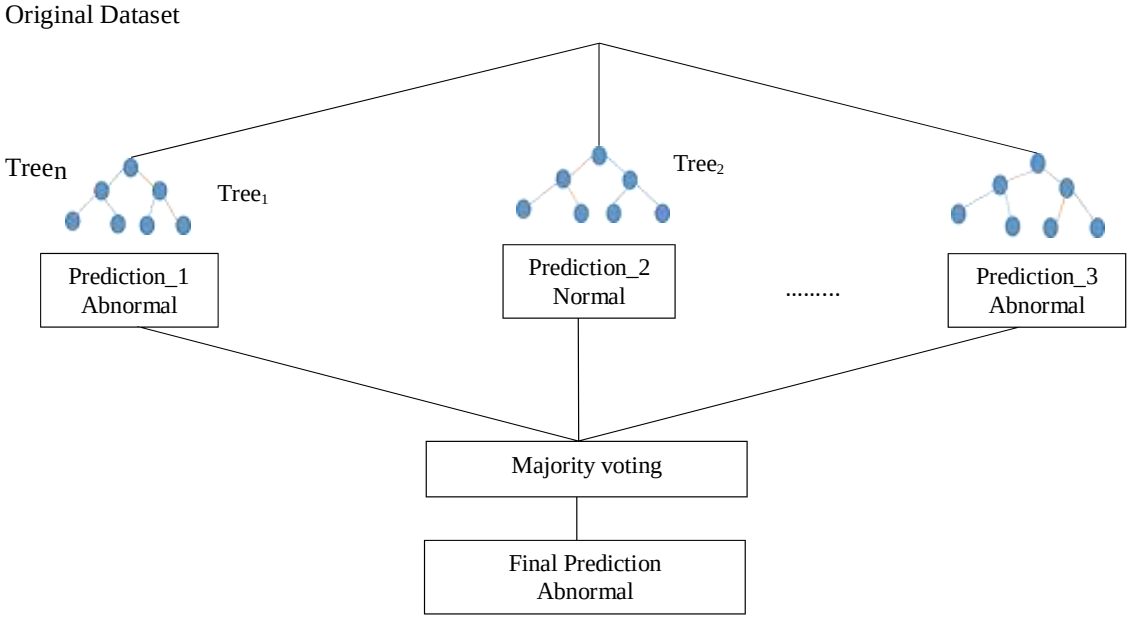


Fig. 2 Architecture of random forest classifier

$D(X, Y) = x_1, y_1 \ , \ x_2, y_2 \ \ldots\ldots\ x_n, y_n$ (3)

- for i = 1 to k

where, n is the number of training observations con-sists of a set of instances whose class membership is known, K is the number of class and $(x_i, y_i) \epsilon (X, Y)$. Find an optimal classifier $h_K(X)$ that minimizes the error with respect to the original dataset, then the combined clas- sifier can be described as:

- Keep the fold f_i as a validation set and the remain-ing k-1 folds in the training set.
- Fit a model on the training set and evaluate theaccuracy of the model on the validation set.

- Calculate the model's accuracy by averaging the accu- racy of all k-fold cross-validation cases.

$h = h_1(X), h_2(X), \ldots\ldots h_K(X)$
(4)

K-fold cross-validation description
Cross-validation is a resampling procedure used to eval- uate machine-learning models on a limited data sample. The method has a single parameter called k which cor- responds to the number of groups to be divided into a given data sample. Therefore, the technique is often referred to as k-fold cross-validation. When the specific value of k is chosen to be 10 then the model is calledtenfold cross-validation.
K-fold cross-validation is carried out according to the following steps:

- Spilt the whole dataset into k equal parts where eachspilt of the data is called a fold. Let $f_1, f_2, \ldots\ldots f_k$ be the name of each fold.

IV. RESULTS AND DISCUSSION

This section explains briefly the experimental results obtained in the three phases namely evaluation of classification phase without feature selection, evaluation of classification phase with feature selection, and comparative analysis phase. For experimental testing, we haveconsidered each of the 2000 genes to classify the wholedataset into two classes: normal and abnormal. Table 4shows the confusion matrix and the performance analysiswith respect to recall, precision, F1-measure, and accuracyscores across the two different classes is shown in Table 5. As can be seen in Tables 4 and 5, the results of our classification model based on random forest that can correctly detect 52 items out of a total of 62 items, resulting in a weighted recall, precision, and F1-score of 83.68%, 83.87%, and 83.68% respectively. The overall accuracy of

Table 4 Confusion matrix of the model without feature selection

Actual class	Predicted class	
	Abnormal	Normal
Abnormal	36	4
Normal	6	16

Table 5 Performance analysis of the model without feature selection

Class	Recall	Precision	F1-score	Accuracy (%)
Abnormal	0.85714	0.90	0.8780	
Normal	0.80	0.72727	0.7619	83.871
Weighted measure (%)	83.68	83.87	83.68	

this model is 83.871% using all genes. We have applied mean decrease accuracy and mean decrease gini as a feature selection procedure to remove the most irrelevantand redundant genes from the whole dataset. The aim isto identify a subsets of discriminatory genes that improvesthe performance of learning models. Figure 3 shows theselection of top 20-genes.

From Fig. 3, the outcomes indicate that the top 20-genes selected by the two feature selection methods, the top 7-genes (M26383, H43887, U19969, T48804, X68277, H49870, and R80966) are common among these

Table 6 Confusion matrix of the model with feature selection

Actual class	Predicted class	
	Abnormal	Normal
Abnormal	39	1
Normal	2	20

40. Considering the common 7-genes, the total numberof top selected genes is 33 that has been used to build up a robust learning method. The final confusion matrix and the performance metrics based on the top selected 33 genes are depicted in Tables 6 and 7 respectively.

The model based on the top 33 selected genes can correctly detect 59 samples out of 62 samples with an accuracy of 95.161%. The models also achieved the weighted recall, precision, and F1-score of 95.16% and 95.12% respectively. Table 8 exemplifies the comparative study ofthe model with and without feature selection.

The results in Table 8 demonstrate that when using the model with feature selection, all the analysis metrics outperformed their counterparts without the model without feature selection. The graphical representation of the overall results of the model

based on the performance metrics is as shown in Fig. 4. Table 9 shows the comparison of ourproposed method with existing approaches.
From Table 9, it proves that the performance of our method is better than all other methods which have lowerperformance on this gene expression data.

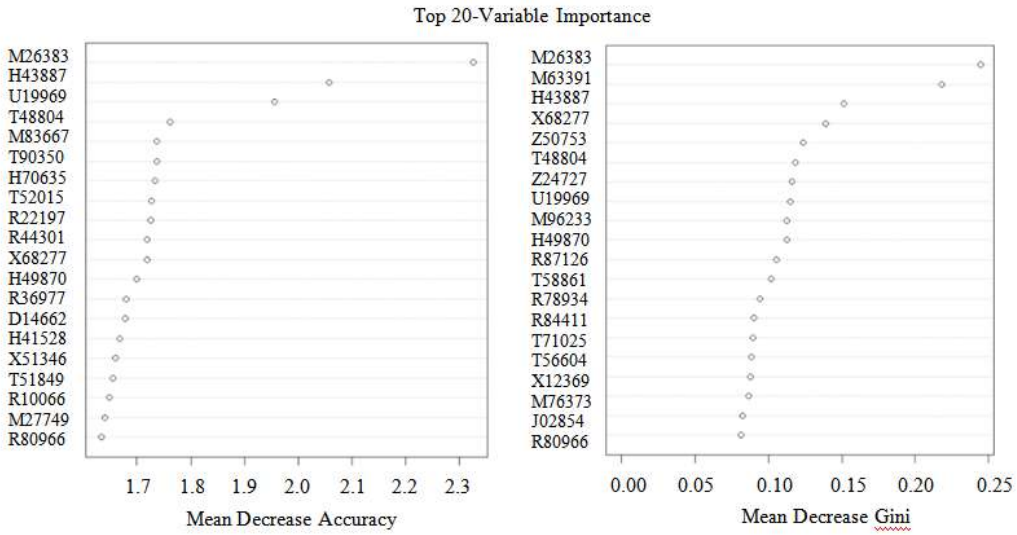


Fig. 3 Feature selection result

Table 7 Performance analysis of the model with feature selection

Class	Recall	Precision	F1-score	Accuracy (%)
Abnormal	0.95122	0.975	0.9629	
Normal	0.95238	0.90909	0.9302	95.161
Weighted measure (%)	95.16	95.16	95.12	

Table 8 Comparative analysis of the model

	Evaluation criteria			
	Weighted precision (%)	Weighted recall (%)	Weighted F1-score (%)	Accuracy (%)
Model without feature selection	83.87	83.68	83.68	83.871
Model with feature selection	95.16	95.16	95.12	95.161

Performance of the prediction with and without feature selection
Without feature selection with feature selection

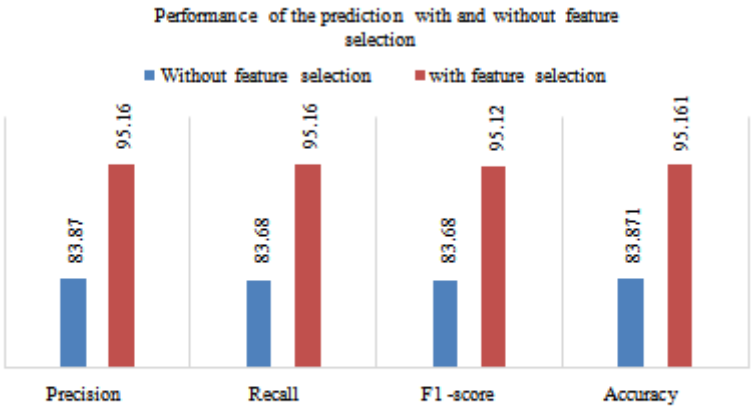


Fig. 4 Graphical comparison of the model for different evaluation criteria

Table 9 Performance comparison among different methods

Publication	Method	No. of attrib-utes	Accuracy
Simone A. Ludwig et al. [13]	FDT	20	80.28%
Nguyen T et al. [14]	MAPH + PNN	5	88.89%
Lingyun Gao et al. [15]	FCBFS + SVM	14	93.55%
Salem H et al. [16]	IG + GA + GP	60	85.48%
Proposed method	MDA + MDG + RF	33	95.16%

V. CONCLUSION

In this examination, we assessed the utilization of machinelearning techniques for the order of classification of colon cancer prediction/prognosis dependent on the variation in gene expression. We additionally examined to discover the dependability of the most significant gene expression or patterns from a natural point of view. For this reason, we have presented the results of our experiments with and without feature selection algorithm. We also compared the attributes identifiers of top 33 selected genes with those obtained from 2000 genes. We achieved the best predic-tion accuracy by applying the feature selection methodscomprising 33-genes rather than every one of the 2000 genes. From the analysis of experimental results, we may infer that the combination of different types of feature selection methods and classification models can give goodoutcomes in the field of detecting and classifying several categories of cancer. In future we will extend our researchthat can integrate more sophisticated methods for featureselection.

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Compliance with ethical standards
Conflict of interest On behalf of all authors, the corresponding au-thor states that there is no conflict of interest.

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