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IHO-CBC: Biomarker Discovery Based on Improved Hybrid Optimization Algorithms for Cancer Classification

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Abstract
For the early detection of cancer, highly sensitive and specific biomarkers are needed. Bio-fluid biomarkers are particularly useful because they can be used for non-biopsy tests. Although the altered human activities of cancer cells have been observed in many studies, little is known about cancer biomarkers for cancer screening. Cancer classification with a highly efficient tool is essential in this era. When a gene is selected from microarray datasets, many problems are addressed, like diminishing the number of inappropriate and noisy genes. This paper proposed the Improved Hybrid Optimization in Cancer Biomarker classification (IHO-CBC) Model for cancer biomarker detection. The microarray datasets are pre-processed and training using Feedforward Neural Network (FFNN). The Enhanced Binary Black Hole (E-BBH) Algorithm for best features is selected. The Classification has been done with the Hybrid method E-BBH-FFNN. E-BBHO is a novel optimization algorithm that improves the accuracy of the Classification by identifying the optimal weights and biases. The stability improvement with ensemble methods is particularly noticeable for small signature sizes (a few samples of genes), which is most relevant for designing a diagnosis or prognosis model from a gene signature. The experimental results show that the E-BBH-FFNN outperforms the performance metrics like mean square error (MSE), AUC, and F-Score.

Keywords: Gene selection, E-BBHA, E-BBH-FFNN, FFNN, Microarray cancer dataset

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I. INTRODUCTION

Cancer is a worldwide leading cause of morbidity and mortality [1,2]. It is defined as the the disease of uncontrolled cell division in any of the cell types or organs in the human body, with a capacity to spread to other tissues by invasion and metastasis. Nowadays, all optimization issues are solved by bio-inspired computation and swarm intelligence-based algorithms such as feature selection (FS), data clustering, etc. These features can cause incorrect algorithmic modeling and overfitting problems [1]. Because there isn't an FS approach, present models fail to capture data patterns precisely. The FS's foremost objective is to improve classification performance by choosing a small number of pertinent or important characteristics. To tackle these issues, a well-organized global search approach is necessary [2]. In this research, Binary Black Hole Algorithm is proposed to tackle the concerns of feature selection in biological data. In machine learning, feature selection should

be regarded as a pre-processing stage in the previous dataset to the Classification utilized to attain optimal performance with diminished memory necessities and a short training period.

For challenging tasks, novel metaheuristic techniques are reassuring [3]. In recent times, the most well-known technique, the black hole heuristic method, has been established for solving the issues of NP-hard of data clustering difficulties and hard or complex optimization [4]. The black hole heuristic method is based on the phenomenon of black holes, and for an optimization issue, the initial population of candidate solutions starts first. A population-based approach calculates an objective function for them [5]. Three dissimilar physical assets of a black hole are angular momentum, mass, and charge. Like any other charged object in a given region, other charged things are expelled by a charged black hole [6, 7].

An effective and uncomplicated global search method is necessary for solving the issues of FS. This technique was found by modeling the performance of a black hole in space [8, 9]. The BHA contains superior optimal performance, fast convergence, and a single parameter. Based on this, the attraction of gravitational will engulf us whole while you near a black hole [10], which has been utilized to address an assortment of issues such as detection of spam, clustering, difficulties in optimization, optimum digital overcurrent relay coordination, and multi-objection reactive power dispatch [11, 12, 13, 14, 15]. The BBHA was integrated with a NN classifier and used with other text datasets to confirm its applicability and generalization. While compared to other techniques performance of NN gives a better experimental result, as does the proposed E-BBHA wrapper-based feature selection technique; in terms of CPU time, it surpasses the BPSO and GA, the number of parameters utilized in the model's configuration, and the number of selected optimal features. Moreover, in the literature performance of the proposed E-BBHA is greater than another algorithm. This study is divided into four sections: Section II is described related works, followed by section III, research methodology, then section IV explains the discussion of results, and finally, section V discusses the conclusion.

This paper's key contribution is as follows:

- To propose the Enhanced BBHA, a binary version of the BHA for solving discrete problems based on the hyperbolic tangent function
- Dataset training using FFNN
- The proposed E-BBHA is based on a wrapper-based FS approach, and it is applied with five diverse microarray datasets to examine the performance of the E-BBHA wrapper-based FS method with a single classifier FFNN, which is a sort of ANN.
- Finally, the accuracy, region behind the ROC curve, CPU time, Mean Square Error, and F-Score of the proposed E-BBHA wrapper-based technique is evaluated using various parameters.

II BACKGROUND STUDY

Abdallah, M. et al. [1] a simulation of the cell membrane potential effect using field-effect transistors (FET) with a high aspect ratio of micropillars in the gate region, where charges were present on the micropillar surface. It was discovered that the drain current altered when the voltage was applied. The Ion Measuring Field Effect Transistors (IMFET) sensing method might be ascribed to a change in the threshold current owing to surface charges,

affecting the semiconductor channel's effective potential. The findings demonstrated that the IMFET sensor design might categorize cancer cells based on their distinct principal ion concentrations in solutions. The simulations revealed encouraging findings that micropillars boosted the IMFET devices' sensitivity in detecting the ion exchange activity of sick cells. IMF chips may be made at a minimal cost; hence would be economical for point-of-care applications.

AlShamlan, H. et al. [2] Cancer Biomarker Rule Discovery (CBRD) is a method that helps biologists and physicians standardize data for diagnosis by eliminating duplicate and noisy data. The project also focuses on dimensionality reduction and acquiring guidelines to choose a certain gene, which is the most crucial phase. Then, via visualization, make the outcome clear to the target user. Ultimately, the Rule Discovery procedure will provide a rule that precludes such ambiguity by identifying the dominating qualities that create the outcome in question.

Doungpan, N. et al. [8] The Gene-set-based Gene Co-expression Network (gGCN) created for each gene-set supplied network data useful for discovering gene subnetwork cancer biomarkers. The cross-validation of identified gene subnetwork biomarkers performed marginally better in the Classification of independent lung cancer datasets than identified gene subnetwork biomarkers derived from gene-gene interaction (GGI), protein-protein interaction (PPI), and minimum spanning of the interaction (MST)-gene co-expression network (GCN) data. Integrating GCN into the network-based strategy resulted in the identification of subnetworks including both known and putative lung cancer-related genes that have biological value.

Kwon, L. et al. [12] The authors' findings demonstrate that the photonic crystal enhanced fluorescence (PCEF) platform is very sensitive, particularly in the on-resonance state. They can detect anti-E7 antibody concentrations as low as 6 pM in serum. The PCEF platform may be used for accurate quantitative cancer diagnosis and therapy monitoring by overcoming the above-described difficulties. This will need to occur in tandem with identifying and characterizing clinically important biomarkers and developing cancer therapy medicines, which will need sensitive and particular biosensors to accurately follow the treatment's progression.

O'Keefe et al. [17] The microfluidic architecture offer a straightforward DNA detection method with excellent sensitivity. This parallelized Dhrm-platform allows discrimination of uncommon methylated variants with frequencies as low as 0.0001% and investigation of DNA methylation heterogeneity in its entirety. We expect this technique to bring fresh insights into the consequences of methylation heterogeneity on cancer and increase cancer detection sensitivity.

Sahu, B. et al. [19] This study introduces a unique hybrid model for diverse microarray datasets based on a modified mutant firefly method (MMFA) and the support vector machine (SVM). To strengthen the ing model. The model's performance was achieved by comparing its performance to that of two different metaheuristic models. Specifically, MMFA-DT and MMFA-NB employ the same datasets, meta-search technique, learning model, and validation scheme. All datasets' features within the range [0,1] were scaled using normalization methods to eliminate computational inconsistencies. Using ten cross-validations, MMFA was then

used in the massive dataset to identify the highlighted subset of genes. The outcome of this generates fresh re-ranked highlighted genes.

Tanvir, R. et al. [21] Cancer genes undergo mutations. Using a stage-specific co-expression network analysis of breast cancer to identify trajectory-specific biomarkers, this study demonstrates a computational pathway for identifying biomarkers that endure during these transitions. In addition, stage-specific biomarkers, which are network biomarkers that are exclusively connected with a single stage and no other stages, are also discovered utilizing this approach. Using this approach, 25 distinct trajectories and 83 stage-specific biomarkers were identified.

Tanvir, R. et al. [25] Modeling and assessing the dynamical connection based on gene expression patterns is challenging, and many inference approaches provide predictions with very poor accuracy. This research proposes a unique l2-norm regularised dynamic smooth network reconstruction (lrSNR) approach for reconstructing the structure of time-varying regulatory networks from microarray genetic data, including dynamic time series. The novel approach combines l2-norm penalty parameter learning with Bayesian information criterion controlling to boost computation efficiency. Experiments demonstrate that the suggested lrSNR method significantly reduces computing time and increases network inference precision. SNR surpasses three current techniques in discovering genuine network edges and computation time. Utilizing dynamic genetic network reconstruction, lrSNR is useful for discovering cancer biomarkers or oncogenes due to its favorable inference performance and detective capability.

III. MATERIALS AND METHODS

This section is discussed with the proposed IHO-CBC framework. The microarray datasets are imported and pre-processed using the Multi-layer Perception (MLP) model. The datasets are trained with FFNN, and Classification is done with the E-BBHA algorithm. The classification accuracy has been optimized by using the E-BBHO algorithm.

3.1 Datasets

The microarray datasets are Lung cancer, Leukemia, Colon Cancer, Leukemia, and SRBCT. The Gene's features of all the datasets are 1000, and attributes are nearly 7000.

3.2 Black Hole Algorithm

To start the black hole, attract the stars around it after completing the initialization phase. In this situation, randomly produced new stars and sited in the search space, causing a new search to begin. An initial population of potential solutions to an optimization issue is used to start the black hole algorithm and a determined objective function for each [12].

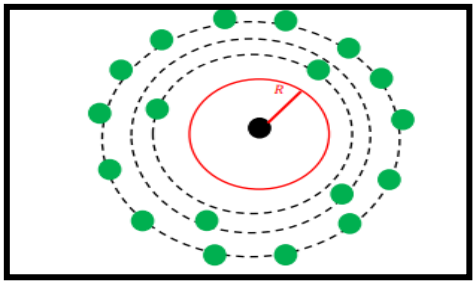

Figure 1: The basic diagram of a Black hole [Ref:31,32]

3.3 Enhanced Binary Black Hole Algorithm (E-BBHA)

The fitness function assesses all of the stars' fitness levels to assist them in becoming more fit. In all BBHA iterations, the highest fitness value in a star is referred to as a black hole. Consider the following equations:

$$X_{id}(t+1) = X_{id}(t) + \text{rand} \times \left(X_{bh} - X_{id}(t)\right) \; i = 1,2,\dots,N$$

$$s\left(X_{id}(t+1)\right) = \text{abs}\left(\tanh\left(X_{id}(t+1)\right)\right)$$

Moving towards the XBH using equation 1, a star may reach a location with a maximum fitness value than the XBH. Otherwise, their fitness values are similar, but there are fewer features. A star may pass the event horizon as it approaches the black hole. In this instance, the black hole will devour this star and generate a new star in the search space at random to replace it.

$$X_{id}(t+1) = \begin{cases} 1 & \text{if } S\left(X_{id}(t+1)\right) > \text{rand} \\ 0 & \text{otherwise} \end{cases}$$

Where fi refers to fitness values of the ith star

And f_{BH} refers to a black hole

$$R = \frac{fBH}{\sum_{i=1}^{N} fi}$$

The BHA was mainly intended for continuous-valued spaces. However, the main issue in discrete combinatorial optimization is FS, having discrete binary integers as opposed to continuous numbers as values. The motive of algorithm 1 is to introduce a binary BHA called BBHA. The binarization method is the proposed system that falls within the first of these categories. After the continuous iteration in the first group, only two steps are added with no changes to the operators. The Hyperbolic Tangent function is utilized to adjust the position of stars in the proposed technique, as stated in Equations (1) and (2).

$$S\left(X_{id}(t+1)\right) = \text{abs}\left(\tanh\left(X_{id}(t+1)\right)\right)$$

$$X_{id}(t+1) = \begin{cases} 1 & \text{if } S\left(X_{id}(t+1)\right) > \text{rand} \\ 0 & \text{otherwise} \end{cases} \rightarrow (1), (2)$$

Where rand denotes the uniform random number among 0 and 1, here utilized instead of the rand threshold in Equation 1, because it outperforms other transference functions like the sigmoid function, it was chosen for this implementation. Only the number of stars in BBHA needs to be set. The proposed algorithm addresses some drawbacks of conventional optimization algorithms, such as sluggish convergence rates and the necessity for many parameter adjustments.

3.4 Feed Forward Neural Network (FFNN)

Artificial Neural Networks' main strategy is the Feed Forward Neural Network (FNN) approach. Each layer is made up of a specific number of neurons. Here, the output vector of h neurons in the hidden layer is denoted by T, whereas o= T denotes the output vector of m neurons in the output layer. The letters HB and OB stand for hidden and output neuron biases, respectively. Figure 2 expressions a single hidden layer MLP network with x = (x1, x2,..., xn) T as an input vector in the input layer containing n neuron values. (s1, s2,..., sh) T denotes the output vector of h neurons in the hidden layer, whereas o = (o1, o2,..., om) T represents the output vector of m neurons in the output layer.

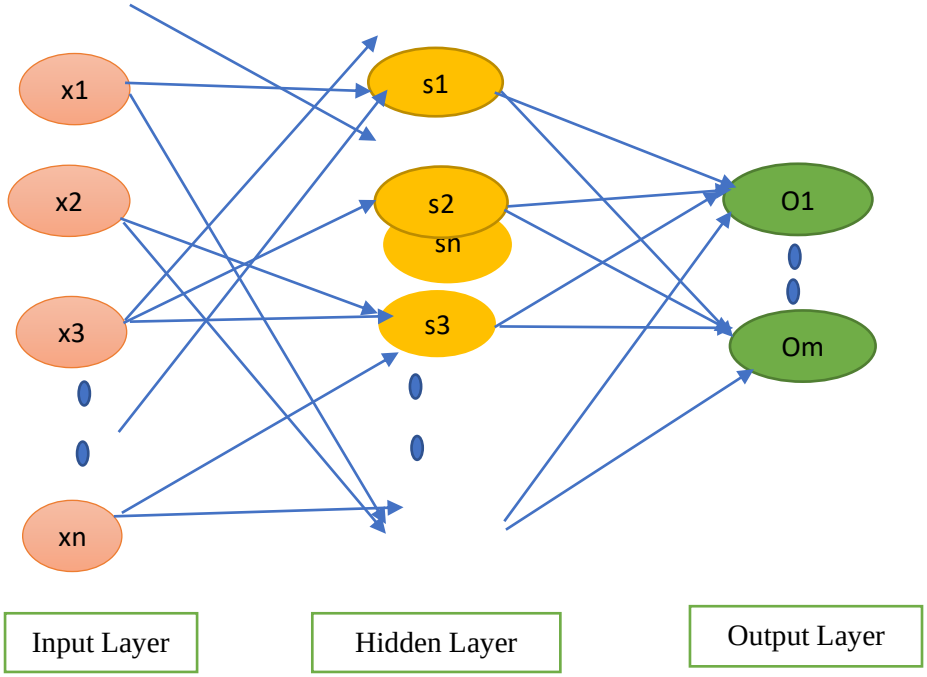

Figure 2: MLP structure with a single hidden layer [Ref:31]

3.5 Training using FFNN

The initial phase of the proposed system is arbitrarily initialization of BBHA's, which are utilized to make for NN training with candidate solutions. If the fitness value of the overall finest solution remains unaffected after the completion of three iterations from the half-worst population, the complementary module will create additional candidate solutions. In terms of fitness value, complementary-based solutions may outperform prior solutions; the old solutions will be replaced with new solutions that are opposed. Suppose the fitness value of the original complementary-based solution is lower than the origin after to re-initialize the solution without comparing fitness. In that case, the E-BBHO approach is employed, and BHA is used to identify optimal solutions using the recently produced solutions. Figure 3 depicts the overall methodology model.

At the initial stage of BBHA, the star's location in the main population is arbitrarily initialized. In this scenario, our suggested approach is evaluated by one FFNN classifier. The FFNN classifier's accuracy is used for biological data, and the FFNN classifier's accuracy is utilized for text and image datasets. E-BBHA-FFNN is a proposed wrapper strategy based on BBHA integration with NN, whereas E-BBHA-FFNN is a proposed wrapper technique that depends on the FFNN classifier combination. The BBHA specifications call for a population of 10 stars to be iterated 100 times.

In conclusion, the BBHA wrapper-based FS method is selected as the finest performance in the star. This star's position reveals which features have been picked. To prevent unexpected consequences and assure impartial assessment of classification performances, the FFNN approach's ability for specified features is assessed 100 times using optimization algorithms. Below is algorithm one, the approach of applying BBHA for FS.

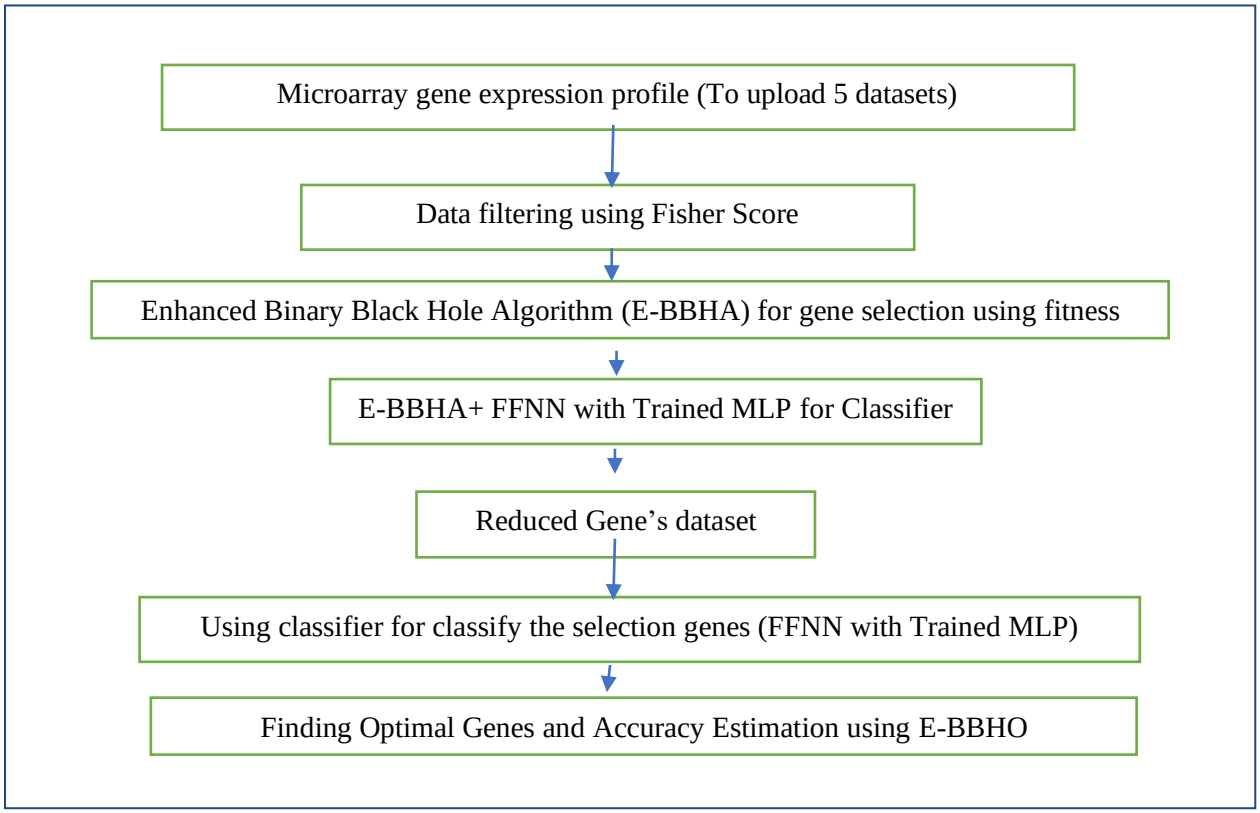

Figure 3: IHO-CBC Architecture

ALGORITHM 1: A new hybrid algorithm E-BBHA-FFNN with Trained MLP

Input: Rand number of stars (200), number of iterations 100
Output: Binary Black hole (E-BBHA)
The fitness value of a black hole
Begin
Initialize a population of stars (1000)
for j=1 to numbers of stars
Evaluate fitness value of the stars (j) by 10-fold CV FFNN with Trained MLP and save in fitness array(f)
next j
The star with the most remarkable fitness value is chosen as the black hole
While (max iteration or convergence criteria is not met) **do**
For a=1 to the number of stars
Evaluate fitness value of the star (Xa) by 10-fold-CV FFNN with Trained MLP
if (fitness of Xa>fitness of X_{BH}) Then
X_{BH} = Xa
else if ((fitness of Xa>fitness of X_{BH}) and (|Xa |<|X_{BH}|)) **then**
X_{BH} = Xa
end if
Replace the new fitness value of the star (Xa) with the previous value

Update fitness array (f) and Calculate:

$$R = \frac{fBH}{\sum_{i=1}^{N} fi}$$

if

$$R = \frac{fBH}{\sum_{i=1}^{N} fi}$$

Then

Replace Xa with a new start in an optional location in the search scope

end if next a

for i=1 to numbers of stars

for d=1 to the number of features

$X_{id}^{new} = X_{id}^{old} + rand * (X_{BH} d - X_{id}^{old})$

if abs (tanh (Xid^{new})) > rand Then

$X_{id}^{new} = 1$

else

$X_{id}^{old} = 0$

end if next d

next i

end while **end** /* end of E-BBHA algorithm*/

if the fitness value of X_{BH} remains unchanged in the worst five iterations (5)

For i=1 to half the number of the stars with the worst fitness values

Xidopposite =Xmax + Xmin - X_{id}^{old} /* The position of the worst stars changes using balancing*/

if the balancing-based star's fitness value ($X_{id}^{opposite}$)< fitness value of $X_{id}^{old,}$ then

$X_{id}^{new} = X_{id}^{opposite}$

else

$X_{id}^{new} = X_{id}^{old} + \alpha . N$

end

end end

End

3.6 Optimization

This section explains how to train a single-layer MLP using a proposed binary version of a black hole-based algorithm. Here, three main mechanisms are utilized: BHA, Complementary-Based Learning Components, and the Random Walk. Mainly MLP is trained using a Random Walk component that establishes the appropriate weighting and bias values to reduce total MLP error and boost its accuracy. In the first phase, randomly created a group of weight and bias values are comprised of the possible solutions. The MLPs contain a candidate weight, and bias is improved, as a result, is the minimum cost. The MSE is the cost function represented by Equation. (5), with Equations. (3-4) used to compute the neural network output. EBBHA offers the advantage of finding the best solution globally. For gene selection, we use EBBHA, and for sample classification, we use FFNN with MLP. EBBHA-

FFNN with MLP is the name of the proposed technique. Below are the precise steps of the proposed approach:

$$S_j = \sum_{i=1}^{n} w_{ij}x_i + hb_j \quad j = 1,2,\dots,h$$

$$o_k = f(o_k) = \frac{1}{1 + e^{-o_k}}$$

$$MSE = \frac{1}{n}\sum_{i=1}^{n}(c - o)^2 \rightarrow (3), (4), (5)$$

Step 1 N solutions (stars) are randomly produced; each of the stars encodes a group of MLP with the values of weights and biases.
Step 2 MSE criteria are used to evaluate the goodness of each solution. In the training dataset, each of the stars is involved. MLP's MSE has been calculated. The best solution is chosen as the star with the lowest MSE. Their fitness levels are evaluated and likened to past star placements. The star has a maximum fitness value in the opposed position; then it will be involved in the population, afterward performed
Step 3: Identifying the new location for stars is referred to as the E-BBHO, whose complementary positions aren't as good as their initial positions.
Step 4. Then Step 3 will be carried out if this is not the case.

IV EXPERIMENTAL RESULTS AND DISCUSSION

The IHO-CBC framework has been developed using Python programming language. The Experiments on five benchmark microarrays are used to test the efficacy of our proposed technique.
Our result was analyzed using the framework of the proposed Classification.
TPB: the prediction is category b, and the reality is category b.
TNb: the prediction is other classes of category B; the reality is other classes of category b.
FPb: the prediction is category B; the reality is other classes of category b.
FNb: the prediction is other classes of category B; the reality is category b.
Each category was used as a positive sample to determine the overall accuracy, precision, and recall values. Equation (13) may be used to represent the precision as follows:

$$\text{Accuracy} = \frac{\text{Number of samples correctly classified}}{\text{number of samples for all categories}} \qquad (13)$$

The precision of a particular category may be interpreted as a prediction of the accuracy of the sample, as shown in Equation (14):

$$\text{Precision}_i = \frac{TP_b}{TP_b + FP_b} \qquad (14)$$

The recall of a particular category may be regarded as the amount to which the properly predicted sample of category d covers the sample of category d in the sample set, as shown in Equation (15),

$$\text{Recall}_i = \frac{\text{TP}_b}{\text{TP}_b + \text{FN}_b} \quad (15)$$

F measure is calculated by giving the Equation.

$$\text{F} - \text{Measure} = 2.\frac{\text{Precison. recall}}{\text{Bprecison} + \text{recall}} \quad (16)$$

The model proposed in this study has been used for training and testing on the selected microarray dataset, and the results are shown in Table 1. Training and testing have involved FF Neural Networks.

Table 1: Training and testing values with the 10 Epoch

Epoch	**Training Loss**	**Validation Loss**	**Training Accuracy**	**Testing Accuracy**
1	0.3856	0.2131	0.8710	0.9410
2	0.1980	0.1633	0.9401	0.9602
3	0.1877	0.1400	0.9631	0.9604
4	0.1654	0.1206	0.9641	0.9702
5	0.1071	0.1014	0.9651	0.9701
6	0.0833	0.0554	0.9685	0.9709
7	0.0727	0.0436	0.9715	0.9707
8	0.0641	0.0349	0.9743	0.9704
9	0.0569	0.0250	0.9769	0.9709
10	0.0415	0.0223	0.9783	0.9808

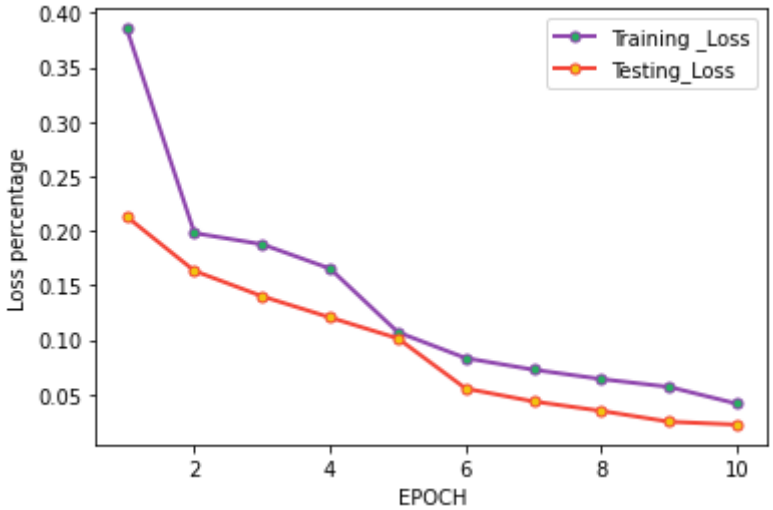

Fig 4: Training and testing loss

The proposed model is trained with loss values, as shown in Fig 4. In X-axis denotes the Epoch number, and Y-axis denotes the loss value.

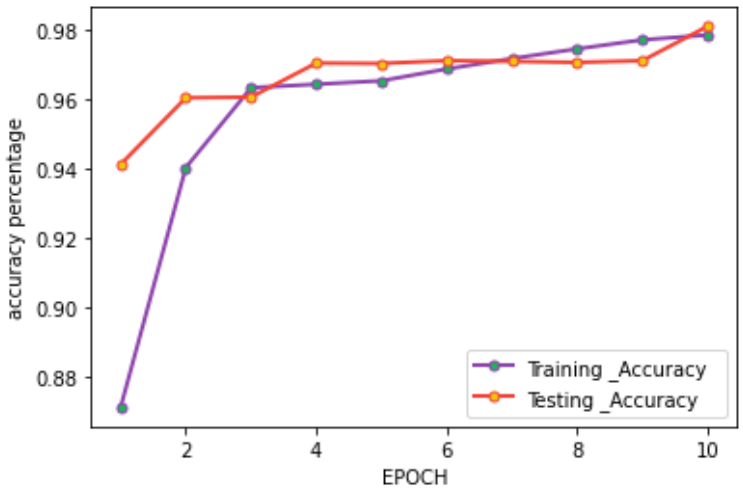

Fig 5: Training and testing Accuracy.

The CNN-ResNet has trained with 10 Epochs with Training, and the testing accuracy is shown in Fig 5. The X-axis denotes the Epoch number, and Y-axis denotes the accuracy.

Table 2: Microarray Datasets

Datasets	**No. of Genes (Features /Attributes)**	**No. of Samples (Instances)**	**No. of Class Distribution**	**Sample Per Class**
Lung Cancer	1000 /7219	96	2	Cancer, Normal
Leukemia_1	1000 /7219	72	2	AML, ALL
Colon Cancer	1000 /2000	62	2	Cancer, Normal
Leukemia_2	1000 /7129	52	2	AML, ALL
SRBCT	1000 /2308	47	2	EWS, NB

Table 3: Overall performance proposed model

Datasets	**Hybrid Enhanced BBHA-FFNN**			
	MSE [Mean Square Error]	**AUC [Area Under Curve]**	**F-Score**	**Accuracy**
Lung Cancer	0.024	0.75	74.83%	98.05%
Leukemia_1	0.017	0.61	79.20%	97.60%

Colon Cancer	0.016	0.78	81.78%	98.75%
Leukemia_2	0.017	0.06	78.78%	97.20%
SRBCT	0.768	0.81	72.19%	97.15%

V. CONCLUSION

We proposed the IHO-CBC method for cancer biomarker detection. The systematic analysis discussed here indicates the trends from the reported studies that have attempted to identify cancer biomarkers using machine learning as a data-mining or classification technique. We have described the dataset as training using FFNN, and the Classification was done using the hybrid E-BBHA-FFNN method. Finally, the Classification has improved by using the E-BHHO algorithm. E-BBHA-FFNN was proposed as a strategy to locate biomarkers and attains the maximum classification accuracy with a small number of essential genes. This method uses an Enhanced BBHA to select genes, and for sample categorization, FFNN with cross-validation is used. According to microarray results, the proposed technique got the maximum classification accuracy with the fewest informative genes. Further to improve the classification accuracy and biomarker detection.

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