Synopsis of the thesis entitled

Medical Diagnosis of Breast Tumor Using Kernel Machines

Submitted by

Shah Pooja Jitendra

(Registration No.: FOTE/945)

Guided by

Dr. Trupti Pankaj Shah

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Introduction:

Recently after skin cancer, breast cancer is the second most hazardous cancer diagnosed in women worldwide and becomes the reason for death. Breast cancer is a cancer that forms in the cells of the breasts. It can occur in both men and women, but it's far more common in women. There are different sign and symptoms of breast cancer like: a breast lump or thickening that feels different from the surrounding tissue, change in the size, shape or appearance of a breast, changes to the skin over the breast such as dimpling, a newly inverted nipple, peeling, scaling, crusting or flaking of the pigmented area of skin surrounding the nipple (areola) or breast skin, redness or pitting of the skin over your breast like the skin of an orange. It is alarming that the incidence rate of breast cancer is increasing each year and upraising with the time. As per the survey of WHO, each year 2.1 million women are impacting with breast cancer and also large number of women die due to deficiency in early diagnosis and early treatment [1]. In 2018, it is estimated that about 627,000 women lost their lives, that is approximately 15% of all cancer deaths among women [1]. As per the survey report of WHO, in 2020, 2.3 million women were diagnosed with breast cancer, and 685,000 were died worldwide [https://www.who.int/news-room/fact-sheets/detail/breast-cancer]. Mortality in women due to breast cancer is around 1 in 38, i.e., 2.6%. American Cancer Society (ACS) also surveyed that out of 268,600 cancerous women, 41,670 women died due to breast cancer [https://www.medicalnewstoday.com/articles/37136]. As per the report by WHO, if early diagnosis provides to the cancer patient then 96% of women may live for an average of 5 years.

Medicine advances on all fronts to improve the condition of the patients and defeat this disease of the century. It is most essential to identify and cure breast cancer in its early stage. With the help of computer aided technologies and artificial intelligence, it is possible to make early diagnosis of this panic disease. Various machine learning algorithms are used to determine whether a cancer gene is benign or malignant. Benign cancers are non-cancerous in nature or do not endanger human life, whereas malignant cancers are cancerous and cause death. Machine learning is an emerging technique which provides an efficient way to enhance the knowledge in data in order to improve the performance of the disease predictive models. There are several Machine Learning (ML) algorithms like Support Vector Machine (SVM), Artificial Neural Network (ANN), Extreme Learning Machine (ELM), Deep Learning (DL) etc. Using these algorithms, Artificial Intelligence (AI) is built into the machines. The basic requirements for any intelligent behaviour is learning. Most of the researchers today agree that there is no intelligence without learning. Therefore, ML is one of the major braches of AI.

In this study, we proposed several predictive models and implemented these models on Wisconsin Breast Cancer (WBC) (Original) and Wisconsin Diagnostic Breast Cancer (WDBC) dataset. These datasets are benchmark datasets of the University of California and are available at Irvine (UCI) Machine Learning repository [2].

<u>Importance:</u>

Medical science is home to a vast variety of applied mathematics studies. In the field of medical science, an interesting and diverse variety of applied mathematics research is being conducted. Soft computing approaches are being used in medical science by researchers worldwide. The thesis is concerned with the diagnosis of breast cancer through the application of various soft computing approaches, with a particular emphasis on kernel-based methodologies.

AI, ML or Data mining techniques can help doctors to locate the best cancer therapies within an overabundance of possibilities. Capturing data from various databases related to the condition, AI assists physicians in identifying and selecting the right drugs for the right patients. AI also supports decision-making processes for existing drugs and expanded treatments for other conditions, as well as expediting clinical trials by finding the right patients from a variety of data sources. AI in healthcare is a broad phrase that refers to the use of ML algorithms and software. As well as AI is use to simulate human cognition in analysis and presentation and comprehension of complex medical and health care data. Classification as an important role in medical science where data mining technique is used to diagnose and analyse disease at an early stage. The earlier detection of the disease followed by proper medical treatment might save the life of the patient. That is why such analysis is very much essential in the field of medical science as well as in Bioinformatics.

AI can assist medical practitioners in a variety of patient care and intelligent health systems. There are already a number of research studies suggesting that AI can perform as well as or better than humans at key healthcare tasks, such as diagnosing disease. AI techniques ranging from machine learning to deep learning are prevalent in healthcare for disease diagnosis, drug discovery, and patient risk identification. Numerous medical data sources are required to perfectly diagnose diseases using AI techniques, such as ultrasound, magnetic resonance imaging, mammography, genomics, computed tomography scan, etc.

<u>Literature survey:</u>

In 2003, H. X. Liu et al., used SVM to classify breast cancer data and achieved 96.71% accuracy with Polynomial kernel and 97.07% accuracy with Radial Basis Function (RBF) kernel [3]. In 2004, Statistical Neural Network topologies such as Radial Basis Networks (RBNs), General Regression Neural Networks (GRNNs) and Probabilistic Neural Nets (PNNs) were investigated on WBC dataset by T. Kiyan et. al. [4]. In 2004, P.R. Innocent et al. conducted a study of fuzzy methods for medical diagnosis in nursing assessment using Type-II fuzzy sets [5]. In 2005, X. Fu et al. used SVM with rule extraction and obtained 97.51% accuracy [6]. In 2009, E. D. Ubeyli proposed an integrated view of ANFIS to detect breast cancer and tested the model on the WBC dataset [7]. In 2009, M. F. Akay built SVM classifier and obtained 99.51% classification accuracy [8]. In 2009, on the WBC dataset, M. Karabatak et. al. presented an automatic diagnostic system for breast cancer diagnosis that was built on

ANNs based on Association Rules (AR) [9]. The proposed AR+NN model was compared with NN model. In the test set 3-fold cross validation method was applied on WBC dataset and achieved 95.6% of classification accuracy.

In 2009, M. S. Apostolopoulou et. al. described about NN with L-BFGS optimization algorithm on breast cancer dataset, SPECT heart problem, Australian credit approval problem, Yeast problem and Escherichia coli problem [10]. In 2009, I. Maglogiannis et. al. used SVM based classifiers for breast cancer diagnosis and prognosis data [11]. They made the comparison of SVM classifier with Bayesian classifiers and ANN. In 2010, S. S. Naghibi. et al. designed a hierarchical fuzzy neural system with Extended Kalman Filter (EKF) [12]. This model is applied to the WBC dataset. The model is compared with Hierarchical Fuzzy Neural System (HFFN)+ EKF and FNN and obtained the results. In 2010, A. Osareh et al. used SVM, k-nearest neighbours, Probabilistic Neural Network classifiers and PCA and 96.33% accuracy is obtained with RBF kernel [13]. In 2011, F. Baig et al. designed a control system using fuzzy logic for the normality of human function in the human brain and also made a medical diagnosis of brain tumor and haemorrhage [14]. In 2011, H. L. Chen et. al. built SVM classifier and used a roughest (RS) based feature selection algorithm to remove the redundant features [15]. They achieved 99.41% accuracy. In 2011, A. Fallahi et. al. applied the Relief algorithm for reducing the dimension of breast cancer data [16]. Then Bayesian network classifier is applied for classification and 98.1% accuracy is obtained. In 2012, G. I. Salama et. al. authors used fusion of multi classifier to classify three different breast cancer datasets [17]. They used MLP, Naive Bayes (NB), Sequential Minimal Optimization (SMO) and Instance based for k-nearest neighbour (IBK) with PCA and 10-fold CV.

In 2012, consistency based feature selection was proposed by A. M. Thandar et. al. to find the best subset of features [18]. Also proposed method improved performance of the RBFN by reducing irrelevant features. The authors made use of many medical dataset including breast cancer and lymphography as well as dataset on sick-thyroids and hepatitis. In their conclusion, authors claimed that prior to employing consistency-based feature selection, RBFN was not ideal. They also led to the conclusion that using the consistency method, accuracy was improved as well as an overall time was reduced. Their accuracy with RBFN was 74.71% where as their accuracy with the proposed consistency based RBF was 85.19%. In 2013, R. Fakoor et. al. have studied about how to increase prediction and diagnosis of cancer using deep leaning [19]. They implemented unsupervised feature learning technique to classify different types of cancers like breast cancer, colon cancer, leukemia, prostate cancer etc., using gene expression with sparse autoencoder, starked autoencoder, stack autoencoder with fine tuning and PCA+softmax/SVM for Gaussian kernel. In 2013, M. Rana et al. proposed an expert system using fuzzy logic to diagnosis of haemorrhage, brain tumor, cardiac disease, and thyroid [20]. In 2014, J. B. Awotunde et al. proposed a medical diagnosis system using fuzzy logic for malaria disease [21]. In 2015, a deep belief network-based Computer-Aided Detection (CAD) approach for identifying breast cancer was developed by A. M. Abdel-Zaher et. al. [22], where they employed Deep Neural Network (DNN) as a classifier model and used recursive feature elimination for feature selection. The experiment was carried out on the WBC dataset and resulted with an accuracy of 99.68%.

The sluggish convergence and constant being caught at the local minima are two major drawbacks of the Artificial Neural Network (ANN) classifier. To solve this challenge, in 2015, the Differential Evolution algorithm was employed by H. T. Tike Thein to find the best or nearbest ANN parameter values [23]. Using the WBC dataset, the authors proposed and tested an island-based training model with an ANN, in which they found 99.97% classification accuracy. In 2016, for the different dataset like WDBC, WPBC and WBC data set, S. Aalaei et. al. employed ANN with GA-based feature selection and a PS (Particle Swarm)-classifier to diagnose breast cancer [24]. In this they proposed wrapper feature selection method based on genetic algorithm. This method is evaluated using Particle Swarm Optimization algorithm based classifier and obtained 96.70% accuracy for WBC dataset, while for the WDBC data set, they achieved 97.30% accuracy and 79.2% accuracy for WPBC dataset. In 2016, M. A. Madkour et al. developed a model using Fuzzy logic for the diagnosis of Flu [25]. They had also implemented this model for common Measles, German measles, Mumps, Chickenpox, Whooping cough, Common cold and Meningitis.

In 2017, RBFNN and BPN (Back Propagation Neural Network) approaches were tested by S. Vijayalakshmi to see how they performed [26]. It was developed utilising the WBCD, WDBC, and WPBC datasets for analysis. In 2017, M. W. Huang et. al. built a SVM classifier and obtained 96.57% accuracy with linear kernel and 98.25% accuracy with Radial Basis Function kernel along with Genetic Algorithm (GA) as feature selection technique [27]. In 2018, N. Liu proposed hybrid algorithm for breast cancer diagnosis and achieved 98.04% accuracy for WBC dataset and 98.83% accuracy for WDBC dataset [28]. In 2018, R. Siouda et. al. proposed optimized RBF-NN for classification of breast cancer WBCD [29]. The first phase involves the application of the k-means clustering algorithm to identify the RBF centres. The width of the RBFs is further optimized using Particle Swam Optimization (PSO) in the second phase. They compared propagation and PSO+k-mean networks. They claimed with 97.82% classification accuracy for classification of breast cancer. In 2019, C. H. Shravya et. al. used Logistic Regression, SVM, k-Nearest Neighbour and achieved 92.7% accuracy [30]. In 2019, H. Dhahri et. al. authors have studied about feature reduction technique Principal Component Analysis with Genetic Programming (GP) [31]. They prepared their model in four different stages like data pre-processing, feature selection, ensemble ML algorithm, parameter optimization. They used PSO, GA, Best first, Evolutionary search and compared their classification accuracy. In 2020, M. Tiwari et. al. implemented various models such as SVM,

KNN, MLP, ANN etc. and obtained 99.3% accuracy for ANN model and 97.3% for CNN model for WDBC dataset [32].

Brief about our work:

As mentioned in the above literature survey, most of the researchers have focused on the diagnosis of the breast cancer and proposed various predictive models. Their models have also been implemented on WDBC and WBC datasets for classification of tumor into benign or malignant. These datasets are available on UCI Machine Learning Repository, Irvine, CA: University of California, School of Information and Computer Science (http://archive.ics.uci.edu/ml).

Wisconsin Diagnostic Breast Cancer (WDBC) dataset was introduced in November 1995. This dataset contains 569 samples of patients out of which 357 benign and 212 malignant cases. This dataset contains 32 features including class distribution and patient's ID. The class attribute '4' is used for malignant (M) and '2' is used for benign (B). Measurements of features of this dataset are obtained with the help of digitised image of Fine Needle Aspirate (FNA) of a breast mass. These features describe the characteristic of the cell nuclie. The features of this datasets are radius (mean of distances from the centre to points on the parameter), texture (standard deviation of grey-scale values), perimeter, area, smoothness (local variation in radius length), compactness (perimeter2/area-1), concavity (severity of concave portions of the contour), concave points (number of concave portions of the contour), symmetry and fractal dimension ('coastline approximation'-1).

Wisconsin Breast Cancer (WBC) (Original) dataset from the University of California at Irvine (UCI) Machine Learning repository is used to test the proposed model. Dr. William H. Wolberg of the University of Wisconsin Hospitals in Madison provided this breast cancer database. He evaluated breast tumor biopsies for 699 patients up to July 15, 1992; each of nine features (attributes) was scored on a scale of 1 to 10. There are 699 rows and 11 columns in all. Among the 699 samples in the WBC dataset, 458 were benign and 241 were malignant. The WBC dataset has nine features and contains 699 samples. The patient's ID and class properties are included in all of these aspects. Nine characteristics (attributes) of WBCD are shown in Table 1. Both dataset have output corresponding to inputs.

No.	Attributes	Range
1	Clump Thickness (CT)	1-10
2	Uniformity of cell size (UCS)	1-10
3	Uniformity of cell shape (UCSH)	1-10
4	Marginal Adhesion (MA)	1-10
5	Single Epithelial cell size (SEC)	1-10
6	Bare Nuclei (BN)	1-10
7	Bland Chromatin (BC)	1-10
8	Normal Nucleoli (NN)	1-10
9	Mitoses (Mit)	1-10
	Class	2 for Benign 4 for Malignant

Table 1 Wisconsin Breast Cancer (WBC) Dataset

We have also constructed various predictive models along with the time analysis for classification of breast tumor using various soft computing techniques like Artificial Neural Network (ANN), Deep Neural Network (DNN), Support Vector Machine (SVM), Radial Basis Neural Network (RBFN) and Adaptive Neuro Fuzzy Inference System (ANFIS). We trained the proposed models using various optimization techniques like Stochastic Gradient Descent (SGD), Adaptive Moment Estimation (Adam) and Limited-memory Broyden Fletcher Goldfarb Shanno (L-BFGS). Moreover, we have proposed various feature reduction techniques like Principal Component Analysis (PCA), Independent Component Analysis (ICA), Relief Based algorithm in data pre-processing. The comparative analysis of the performance of the classification accuracy obtained by the various researchers in their models with our respective proposed models is carried out and we find that the predictive models proposed by us gives highest classification accuracy in just few seconds.

Organization of the thesis:

The layout of the thesis along with the proposed methodologies used in constructing the predictive models for classification of breast cancer (described in chapters 3 to 6) is as follows.

Chapter 1: Introduction

This chapter mainly deals with the motivation as well as literature survey of the breast cancer.

Chapter 2: Mathematical preliminaries

<u>Chapter 3: The Ultimate kernel machine based on Support</u> <u>Vector Machines</u>

In machine learning, Support Vector Machines are supervised learning models with associated learning algorithms that analyse data for classification, regression analysis and outliers detection. This algorithm has a good generalisation ability, better performance, and a robust mathematical theory. Machine learning, optimization techniques from operations research, and kernel functions from functional analysis are all combined in this approach. It is often referred to as a large margin classifier.

When it comes to diagnose breast cancer, SVM has proven to be extremely effective. To build the cost-effective kernel machine for breast cancer diagnosis, the tools of PCA and k-fold Cross-Validation (CV) techniques are employed. The model is implemented on WDBC and WBC datasets to check the condition of the tumor for its malignancy. Classification accuracy and time computation are obtained and comparative experimental results are analysed under different conditions. For WBC dataset, 100% accuracy is obtained using Polynomial kernel in just 0.03 second.

<u>Chapter 4: Regularized Deep Neural Network with hybrid</u> <u>approach of Independent Component Analysis</u>

The history of Deep Learning can be traced back to 1943, when Walter Pitts and Warren McCulloch created a computer model based on the neural networks of the human brain. They used a combination of algorithms and mathematics they called "threshold logic" to mimic the thought process. Deep learning is part of a broader family of machine learning methods based on artificial neural networks with representation learning. Learning can be supervised, semi-supervised or unsupervised. A Deep Neural Network (DNN) is an Artificial Neural Network with multiple layers between the input and output layers. There are different types of neural networks but they always consist of the same components: neurons, synapses, weights, biases, and functions. These components functioning similar to the human brains and can be trained like any other ML algorithm. Complex DNNs have many layers, hence the name "deep" networks. One of the main advantages of deep learning lies in being able to solve complex problems that require discovering hidden patterns in the data and/or a deep understanding of complex relationships between a large number of interdependent variables. It not only has the ability to tackle nonlinear programming problems with the restrictions of equality and inequality, but it also has a greater overall performance.

In this study, we investigate the use of Regularized Deep Neural Network (R-DNN) for the prediction of breast cancer. A variety of optimization techniques, such as Limited-memory Broyden Fletcher Goldfarb Shanno (L-BFGS), Stochastic Gradient Descant (SGD), Adaptive Moment Estimation (Adam), and activation functions like as Tanh, Sigmoid, and Rectified Linear Unit (ReLu) are used in the simulation of R-DNN. The Independent Component Analysis (ICA) approach is used to identify the most effective features to be used in the study. To measure the efficacy of the model, training and testing of the proposed network is carried out using the WDBC and WBC dataset from the University of California at Irvine (UCI) Machine Learning repository. The detailed analysis of the accuracy is carried out and compared to the accuracy of other author's model. We find that the proposed network attains the highest accuracy.

<u>Chapter 5: A Hybrid Approach of Adaptive Neuro Fuzzy</u> Inference System and Novel Relief Algorithm

An adaptive neuro-fuzzy inference system or Adaptive Network-based Fuzzy Inference System (ANFIS) is a kind of artificial neural network that is based on Takagi– Sugeno fuzzy inference system. The technique was developed in the early 1990s [33][34]. Since it integrates both neural networks and fuzzy logic principles, it has potential to capture the benefits of both in a single framework. Its inference system corresponds to a set of fuzzy IF–THEN rules that have learning capability to approximate nonlinear functions [35]. Hence, ANFIS is considered to be a universal estimator [36].

ANFIS blends advantages of both Artificial Neural Networks and Fuzzy Logic in a single framework. It provides accelerated learning capacity and adaptive interpretation capabilities to model complex patterns and apprehends nonlinear relationships. It is possible to identify two parts in the network structure, namely premise and consequence parts. In more details, the architecture is composed by five layers. The first layer takes the input values and determines the membership functions belonging to them. It is commonly called fuzzification layer. The second layer is responsible of generating the firing strengths for the rules. The role of the third layer is to normalize the computed firing strengths, by dividing each value for the total firing strength. The fourth layer takes as input the normalized values and the consequence parameter set. The values returned by this layer are the defuzzificated ones and those values are passed to the last layer to return the final output.

The proposed model introduces a hybrid strategy of effectively diagnosing breast cancer by using a novel Relief algorithm for feature selection with an Adaptive Neuro-Fuzzy Inference System. The efficiency of this proposed hybrid model and the ANFIS model without using any feature selection technique are estimated using WBC dataset. The study finds that the new hybrid model has attained highest accuracy of 99.30% and is ideal for detecting breast cancer.

<u>Chapter 6: Ensemble Based Lasso Ridge Radial Basis</u> <u>Function Network</u>

Radial Basis Function Networks (RBFNs) are a commonly used type of artificial neural network for function approximation problems. RBFNs are distinguished from other neural networks due to their universal approximation and faster learning speed. An RBF network is a type of feed forward neural network composed of three layers, namely the input layer, the hidden layer and the output layer. The first layer corresponds to the inputs of the network, the second is a hidden layer consisting of a number of RBF non-linear activation units, and the last one corresponds to the final output of the network. Activation functions in RBFNs are conventionally implemented as Gaussian functions. The input layer is not a computation layer, it just receives the input data and feeds it into the special hidden layer of the RBF network. The computation that is happened inside the hidden layer is very different from most neural networks, and this is where the power of the RBF network comes from. The output layer performs the prediction task such as classification or regression.

RBF neural network architecture, which includes Lasso and Ridge Regularisation and Ensemble learning, is used in the proposed approach. This has several advantages, including greater approximation capabilities and shorter processing times. Various RBF networks come together to form an ensemble. This study uses ensemble RBF networks to detect breast cancer. We achieved 100% of classification accuracy for diagnosis of breast cancer.

Conclusion:

The predictive models based on various soft computing techniques like Support Vector Machines, Deep Neural Network, Adaptive Neuro Fuzzy Inference System and Radial Basis Function Network along with different optimization techniques and different architectures are built and implemented on WDBC and WBC datasets for classification of breast cancer. The comparative analysis of the performance of the classification accuracy obtained by the various researchers in their models with our respective proposed models is carried out. The proposed predictive models attained highest classification accuracy in very less time.

Future scope:

If the large amount of clinical data, pathological data, genomic data and images of mammogram are available for Indian women, we can design the computer aided expert system can be built using deep learning techniques. Such expert system can assist the medical professionals to predict the breast cancer in early stage and may reduce the laboratory cost for further investigation.

List of publications:

- Pooja J. Shah and Trupti P. Shah, Regularized Deep Neural Network in Identification of Breast Cancer, Solid State Technology, 2020, Vol. 63, No. 6, Pp. 22704-22713.
- Pooja Shah and Trupti Shah, Identification of Breast Tumor Using Hybrid Approach of Independent Component Analysis and Deep Neural Network, International Journal Of

Intelligent Systems And Applications In Engineering, 2021, Vol. 9, No. 4, Pp. 209-219, doi: https://doi.org/10.18201/ijisae.2021473642.

 iii. Pooja J. Shah and Trupti P. Shah, The Ultimate Kernel Machine for Diagnosis of Breast Cancer, International Journal of Applied Pattern Recognition, 2022, Vol. 7, No. 1, Pp. 1-14, doi: 10.1504/JJAPR.2022.122259

Manuscript under communication:

- Pooja J. Shah, Trupti P. Shah, "A Hybrid Approach of Adaptive Neuro Fuzzy Inference System and Novel Relief Algorithm in Breast Cancer Detection" in "Journal of Advances in Engineering Sciences and Applied Mathematics".
- Pooja J. Shah, Trupti P. Shah, "Ensemble Based Lasso Ridge Radial Basis Function Network in Diagnosis of Breast Cancer" in "Bulletin of Mathematical Sciences".

List of papers presented in conferences:

- i. "Diagnosis of Breast Cancer by Using Artificial Neural Network", at a two days' National conference on STEM (Science, Technology, Engineering and Mathematics), held on September 27-28, 2019, at G. H. Patel college of Engineering & Technology (GSET), Vallabh Vidhyanagar, Gujarat, India.
- ii. "Diagnosis of Breast Cancer by using Support Vector Machine", at the second International Conference on Frontiers in Industrial and Applied Mathematics (FIAM-2019), held on December 21-22, 2019, organized by department of Applied Sciences (Mathematics), Galgotias College of Engineering & Technology, Greater Noida, U.P., India.
- "Regularized Deep Neural Network in Identification of Breast Cancer", at 2nd International conference (Digital) On research and Innovations In Science, Engineering & Technology, ICRISET-2020, held on September 4-5, 2020, held at Birla

Vishvakarma Mahavidyalaya Engineering College, Vallabh Vidyanagar, Gujarat, India.

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