

# Machine Learning in Healthcare: A Review

**Akanksha Saini<sup>a</sup>, A J Meitei<sup>b\*</sup>, Kh. Jitenkumar Singh<sup>c</sup>**

<sup>a</sup>Department of Operational Research, University of Delhi, India, [akankshasaini.du.or@gmail.com](mailto:akankshasaini.du.or@gmail.com)

<sup>b</sup>Department of Mathematics, Maharaja Agrasen College, University of Delhi, India, [ajmeitei@yahoo.com](mailto:ajmeitei@yahoo.com)

<sup>c</sup>ICMR-National Institute of Medical Statistics, New Delhi, India, [jitensinghkh@gmail.com](mailto:jitensinghkh@gmail.com)

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Abstract:

This study attempts to introduce artificial intelligence and its significant subfields in machine learning algorithms and reviews the role of these subfields in various areas in healthcare such as bioinformatics, gene detection for cancer diagnosis, epileptic seizure, brain-computer interface. It also reviews the medical image processing through deep learning for diseases such as diabetic retinopathy, gastrointestinal disease, and tumour. And finally, this article discusses the real-world obstacles that need to be overcome to make AI techniques easier to use.

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## 1 Introduction

The self-learning process of the computer without being explicitly programmed or instructed is the art of artificial intelligence (AI). As a part of computer science that is simultaneously in the learning process through instructions and command, it has a sense of decision making and the construction of algorithms from the imputed data. We also understand AI as the ability of a computer to convert data from an external source into machine-understandable form, learn from such data, and the process continues till the learning reaches a specific task or goal through flexible adaption.

It develops artificial intelligence techniques to handle both structured and unstructured data. Structured data are those data that AI can directly use for analysis, whereas the data that require processing first before analysis using AI falls under unstructured data. One of the highly implemented tools of artificial intelligence is machine learning (ML).

ML handles the data using various algorithms such as logistic regression, linear discriminant analysis, random forest, support vector machine, k-nearest neighbour classifiers, cluster analysis, and modern deep learning, reinforcement learning, decision tree, etc. The learning methods used by ML fall into supervised or unsupervised learning. But there is another type of learning method which came into existence in recent years, called semi-supervised learning.

A vast majority of ML algorithms use supervised learning. Any new ML practitioner will begin his journey with this type of algorithms. Supervised learning, as the name suggests, teaches the machine to develop a model using the available dataset to have the desired program. In supervised learning, we divide the whole dataset into training and testing datasets. The ML models are developed using the training dataset. Testing datasets are then used for accuracy checking and adjustment of the error so that expected outputs are closer to the actual to the extent possible.

It has a wide application that includes email managing procedures such as automatic answering of incoming messages, organization mails in folders, identifying spam, and thread summarization. It is also useful in handwriting recognition, face and speech recognition, natural language processing, or computer vision,

which means the ability of the machine to understand languages and images, signature detections, etc.

Based on data received, the supervised learning techniques are further subdivided into regression and classification. Regression is a useful statistical predictive technique wherein attempts are made to discover a meaningful relationship between dependent and independent variables. The regression algorithm in ML is used to predict a continuous output, i.e., the expected output is a real number. Whereas, in classification, predicted output will be in discrete form.

While the other type of learning, unsupervised learning, is well suited for feature extraction. In unsupervised learning, we only have the input data with no corresponding expected output. Predictions here are purely based on the identification of input data patterns through our own discovering and adopting skills. The learning algorithm includes dividing the data into various groups of similar nature. We find the applications of this type of ML in astronomical data, speech detection, acoustic factor analysis for robust speaker verification and cocktail party problem, etc.

Two main algorithms that come under unsupervised learning are clustering and principal component analysis (PCA). We normally use PCA for dimension reduction. When a feature variable has many dimensions, PCA projects the data onto a few principal component directions without losing most of the information. Usually, PCA is used before the clustering of data to reduce some dimensions of the data. While the clustering method is associated with making a group of variables that show similar or common traits using no output information. The output of these algorithms is the cluster labels for the variable have maximum similarity within and between the clusters. Some well-known clustering techniques involves affinity propagation, mean shift, hierarchical clustering, k-mean clustering, Gaussian mixture clustering, and OPTICS.

ML has a vast area of significance in social sectors such as agriculture, automotive, finance and economics, law-related professions, healthcare, cybersecurity, military, advertising, art, and many more. There is no possible way to elaborate on its overall significance. Hence, we limit our study to the healthcare area only. Healthcare is one of the critical social fields with highly prioritized functional operations and expected to give a high level of care and services regardless of cost.

ML need prior preparations before its application can be implemented in healthcare so that it can differentiate the types of data, associate among similar kind of data, learn from the data, and gives out appropriate output. This data can be in the form of clinical records, diagnosis reports, screening records, demographics, images, physical examinations, medical notes, etc.

The data recognition at the diagnosis stage is in the form of diagnostic imaging, genetic testing, and electrodiagnosis, etc. While medical notes and physical examinations are other major sources of data that can be distinguished in the form of an image.

Genetic and electrophysiological (EP) data is mainly found in unstructured form, that is, it cannot be used for analysis in its recent form. This data needs to be “filtered” before used for analysis. And by “filtering” we mean the conversion of this data into a machine-readable electronic medical record (EMR) form. Some AI applications such as clustering algorithms, works efficiently in this process.

## 2 Applications of machine learning in healthcare

### 2.1 Bioinformatics

It is termed as the interdisciplinary branch of biology and computer science applications for managing and analysing biological data. This data has increased exponentially in recent years. ML techniques help to manage this data and extract the useful knowledge to transform this data into biological knowledge. This biological data includes gene sequences, DNA sequences, gene expression, array analysis, combinatorial chemistry, etc. and developed machine algorithms provide an easily understandable scenario of Human Genomics.

In 2009, Caragea et al. demonstrated the significant role of bioinformatics which also can be termed computational biology. It can be defined as the development of algorithms and establishing the relationships among various biological systems using biological data. One can also refer to Guyon et al (2003), Sajda & Paul (2006), Tarca, Adi L., et al (2007), and Hou, Shujie et al (2011) for detailed study in computational biology. Some interesting books on bioinformatics and ML has been published of the authors like Frasconi P, Shamir R (2000), Baldi P, Brunak S. (2001), Gary B. Fogel, David W (2002), Frasconi P, Shamir R (2003), Wang JTL, Zaki MJ, Toivonen HTT, et al. (2004), Husmeier D, Dybowski R, Roberts S (2005), Seiffert U, Jain LC, Schweizer P (2005). Special issues in journal Larrañaga P, Menasalvas E, Pen'a JM, et al. (2003), Li J, Wong L, Yang Q (2005) and Ling CX, Noble WS, Yang Q (2005).

In recent years, deep learning proved to be the essential part of ML and according to Li et al. (2019), it can also handle non-linear function within the specified accuracy level and have been used to solve various computational tasks. Recently, Li et al. (2020) proposed a range of optimization techniques that made the deep neural network the most reliable and efficient technique among other competing techniques. In the field of bioinformatics, it helps to solve complex biological problems such as DNA binding prediction by Luo et al. (2019), bio-sequence analysis technique that includes analysis and predicting RNA sequence by Park et al. (2017), prediction of protein structure for amino acid sequence by Zuo et al. (2018) and enhancer-promoter interaction (EPI) identification by Hong et al. (2020).

#### 2.1.1 Understanding genomics: DNA classification

Genomics is one of the main branches of bioinformatics where ML tools and methods are used to obtain useful information. Gene finding technique is the most promising area for the applications of ML Mathe' C, Sagot M.-F, Schlex T, et al. (2002) reviews the gene prediction methods. Cho, Sung-Bae and Hong-Hee Won (2003) explain DNA classification in a detailed way through the identification of a group of individuals having similar types of genes or to what extent do these individuals have a specific gene through the color pattern of DNA microarray data using clustering algorithms of ML. This is the typical example of unsupervised learning as the algorithm does not give any prior information about the individual as to which group does it belongs. Salzberg S. (1995) searches the protein-coding area in human DNA by using the help of a classification tree. Yvan Saeys, Sven Degroeve, Dirk Aeyels, et al. (2004) applied the optimization method for feature subset selection in the problem of splice site prediction. The same technique is handled by Degroeve S, De Baets B, Van de Peer Y, et al. (2002) using different ML techniques. Degroeve S, De Baets B, Van de Peer Y, et al. (2004) and Pavlovic V, Garg A, Kasif S. (2002) make

gene prediction more interesting by including a different source of evidence in the process.

Bockhorst J, Craven M, Page D, et al. (2003), Stein Aerts, Peter Van Loo, Yves Moreau, et al. (2004) and Won K.-J, Prugel-Bennet A, Krogh (2004) proposed some useful ML techniques that are used to identify regulatory elements and non-coding RNA gene. While Carter RJ, Dubchak I, Holbrook SR. (2001) used the classification paradigm. Another application of this technique is found in Bao L, Cui Y. (2005) where the prediction of phenotypic effects of non-synonymous single nucleotide polymorphism has been made by comparing support vector machine and random forest techniques.

To make multiple alignment problems less complex, several optimization approaches have been proposed. These approaches include simulated annealing by Kim J, Cole JR, Pramanik S. (1996), parallel simulated annealing by Ishikawa M, Toya T, Hoshida M, et al. (1993), the iterative method by Hirosawa M, Totoki Y, Hoshida M, et al. (1995), relaxation algorithm by Thomas D. Schneider, David N. Mastronarde (1996), Monte Carlo optimization by Neuwald AF, Liu JS. (2004) and tabu search method by Tariq Riaz, Yi Wang, Kuo-Bin Li (2004).

One of the latest contributions on the use of deep learning techniques for DNA-Binding proteins (DBP) identification can be found in the work by Shadman Shadab et al. (2020). A similar type of work was also done by Riccardo Rizzo et al. (2016).

#### 2.1.2 Analysis of gene expression data: Cancer diagnosis

Cancer can be defined as any unusual growth of cells in the body. There are over approximately 100 types of cancer found in medical research today. Early detection of cancer can help to prevent declining patient's health and save many lives. Hwang et. al. (2002) in their paper and Luca Silvestrin in his book focuses on cancer detection through the classification of patient samples. And with the help of ML algorithm such as Bayesian network, Neural trees and Radial basis function (RBF) network, this study can be done through analysis of gene expression to classify the cancer type. Wag Yu, et al. (2005) in their paper effectively use the process of gene selection for diagnosing cancer. We can also refer to Zararsiz, Gokmen, et. al. (2012) for leukemia classification.

#### 2.1.3 Detection of Epileptic Seizures

Epilepsy is a kind of nervous system disorder in which patients suffer from unanticipated recurrent seizures that occur without any warning signs. Consequently, temporary loss of concentration, judgment or memory, and whole-body convulsions. Frequent seizures may lower the chances of sustaining physical injuries and even may cause death. ML techniques, in this case, can construct detectors according to the patient medical condition that is capable of detecting seizure onset quickly and with high accuracy with the help of an Electroencephalogram (EEG), a non-invasive measure of the brain's activity.

Hosseini et al. (2017) analyse epileptogenicity localization using a convolutional neural network with the help of the data available on EEG and rs-fMRI measurements from the ECoG dataset and proposed the conclusion as normal p-value 1.85e-14 and p-Seizure value 4.64e-27. Acharya et al. (2017) trained CNN for the analysis of seizure detection using Freiburg EEG DB with an accuracy rate of 88.67%. Mirowski et al. (2008) predicts epileptic seizure using Freiburg EEG DP using CNN and observed zero-false-alarm seizures prediction on 20 patients out of 21.

#### 2.1.4 Evolving signal processing for brain computer interface (BCI)

Brain computer interface is a collaboration between the brain and a device or machine that reads the electrical signals from the brain and uses them to guide some external activities like moving the

cursor or a prosthetic limb. It plays a major role to support people with disabilities, multimedia, virtual reality, video games, etc. The muscle-controlling commands are issued at specific locations of the motor cortex, a relatively well-understood region of the cortex. Even the brain of many paralyzed patients is fully capable of generating these commands; unfortunately, the information fails to reach the muscles. In this case, brain computer interface comes in existence by Makeig et al. in (2012).

Kiral-Kornel et al. (2017) used CNN for analysing BCI using 6 subjects up to 1000 individual's hand squeeze and proposed power comparisons of various processing platforms. Schirrmeister et al. (2017) used BCI competitive IV dataset 2a and measurement data for analysing EEG decoding and visualization using CNN and comes up with an accuracy rate up to 89.8%. Nurse et al. (2016) used 1 subject and 30 min of data for BCI and conclude with the accuracy rate of 81%. Lu et al. (2017) analysed motor imagery classification with the help of BCI competitive IV data set 2b and improved the accuracy by about 5% as compared with other methods.

### 3 Deep learning

Deep learning is a subset of ML that has a network that is capable of unsupervised learning from unstructured data, also known as deep neural learning and the network called a deep neural network (DNN). It is the function of artificial intelligence that has a structure much like a human brain and mimics the working pattern of the brain in processing data for use in detecting objects, recognising speech, translating languages and making decisions. It can learn without human help or supervision from both types of data, structured and unstructured. It can help to detect fraud or money laundering among other functions.

The evolution of deep learning begins with the evolution of digital information in almost all the forms all over the world, which is called big data in a customary manner. Major sources of big data include searching engines, e-commerce sites, social media, apps and many more among other sources that we can use on the internet.

Deep learning unravels the huge amount of unstructured data that would normally take human decades to grasp fully and extract relevant information. The traditional ML techniques have linear ways to build analysis with data. Whereas, deep learning uses hierarchical levels of artificial neural network which are structurally and conceptually inspired by human biological nervous system. Consequently, deep learning systems process the data in a non-linear way as well.

One of the earliest forms of a neural network, named perceptron based on the human brain. This algorithm was invented at Cornell Aeronautical laboratory in 1958 by Frank Rosenblatt funded by the United States Office of Naval Research. It is a ML algorithm for supervised learning for binary classifiers. It contains an input layer that is connected to the output layer in a direct manner and enables to classify linearly separable patterns. As the complexity of data increased, neural network was introduced that has layered architecture that includes an input layer, an output layer and one or more than one hidden layer. These hidden layers have the capacity to tackle the complexity in the data as it contains non-linear relationships. This neural network is connected through the neurons that takes input data process the data and the output generated from processing is further forwarded to the next layer.

Each neuron sums up the input data and applies functions that activate the data which has been already summed up and provide output to the next layer, which can be either the final output or the output that needs to be processed at the next layer. Thus, deep learning network contains multiple layers of neurons build up in a hierarchical manner which is now extended over more than 1000 forming feature representation hierarchically. This level of modelling capacity allows the deep learning to commit to the memory containing all possible mappings. But it needs to do

successful training with a huge database and make intelligent decision predictions at an initial stage.

Various types of deep learning algorithms are now used in healthcare research areas such as convolutional neural network (CNN), recurrent neural network (RNN), deep neural network (DNN), multilayer perceptron (MLP), deep belief network (DBN), autoencoder, deep Boltzmann machine (DBM), deep belief network (DBN), deep conventional extreme ML (DC-ELM) and many more.

#### 3.1 Deep learning in healthcare

Deep learning has the ability to construct new features, i.e., it is not only able to identify and extract relevant features but also construct new ones. In healthcare sector, it is used to diagnose the disease as well as predict the model with a specific target for treatment to help the physicians. Deep learning algorithms like CNN, recurrent neural network (RNN), radial basis function network (RBFN) long short-term memory (LSTM), autoencoder, extreme learning model (ELM), self-organising maps (SOM), generative adversarial network (GAN), etc. can work on raw data, automatic feature learner and consumes less processing time. Most of the deep learning algorithms show efficient performance in various domains like a virtual assistant, entertainment, healthcare, robotics, image colouring, etc [122-126].

Applications of deep learning cover a broad range of problems ranging from disease detection to personalized treatment. There are some particular areas that are responsible for revolutionising deep learning algorithm in ophthalmology, pathology, cancer detection, radiology. Ophthalmology is the first to revolutionise deep learning but pathology and cancer detection receive more attention and have applications that are quite accurate.

Zhai et al. (2017) used CNN for neuroproteins control using the data from NinaPro Database (DB) 2&3 with an accuracy rate of 83%. Park et al. (2016) trained CNN for movement intention decoding with the help of kinematic and EMG data NinaPro DB and conclude the output with more than 90% accuracy rate. Xia et al. (2017) estimate limb movements estimation with the help of RNN using the measurements from eight healthy subjects and proposed that the RNN outperform other methods for estimating a 3D trajectory. Allrad et al. (2016) apply CNN in robotic arm guidance using 18 subjects performing 7 gesture with the accuracy approximately 97.9%. Fraiwan et al. (2017) analyse sleep state identification using autoencoder and comes up with the accuracy of 80.4%. Huve et al. (2017) track down the neural dynamic by comparison of CNN and DNN taking 1 subject 180 trials and conclude that DNN outperform CNN. Jirayucharoenak et al. (2014) and An et al. (2014) analyse based emotion recognition using deep learning network by taking different dataset and comes up with the result of valence accuracy 49.52% and arousal accuracy 46.03% level.

#### 3.2 Deep learning and medical imaging

The basic purpose of any image diagnosis task requires identification of abnormality and measure its intensity or quantify the abnormality. Automated image analysis tools that are use ML algorithms have the capacity to improve image analysis quality, thus, its interpretations. In this domain, there are many sources that pile up huge amount of data at the physician disposal. This data includes radiological imaging i.e., X-rays, CT scan and MRI scan, pathological imaging and genomic sequencing. Though, deep learning techniques able to process a significant amount of data but still there exist a shortage of tools to convert the whole data.

##### 3.2.1 Diabetic Retinopathy (DR)

Diabetes Mellitus (DM) is a metabolic disorder that can result high blood sugar [121]. It has two major causes- improper production of insulin by the pancreas (Type-I diabetes) and the improper response of body tissues toward the insulin produced

(Type-II diabetes). Eye disease caused by diabetes termed diabetic retinopathy (DR) and long termed DR may cause complete blindness to the patient. It is curable only if it is detected at the early stages through retinal screening. Automated detection of DR through deep learning model are far better than manual process of detecting of DR and gives optimized and better accuracy.

Gulshan et al. (2016) analysed eye picture archive communication system (Eye PACS-I) that consists of 10,000 retinal images with the help of deep CNN (DCNN) and conclude the sensitivity of 97.5% and 93.4% specificity. Harry Pratt (2016) also used DCNN for classification and detection of moderate and worse using the dataset Messidor-2 that contain 1700 images collected from 874 patients to claim the sensitivity and specificity of 96% and 93.4% respectively. Kathrivel (2016) used the dataset Kaggle fundus, DRIVE and STARE that are publicly available for classification of the fundus with DCNN with dropout layer and conclude the accuracy up to 94% - 96%.

Haloi (2015) detect early-stage DR on Retinopathy online challenge (ROC) by training a 5-layered connection mechanism using Messidor dataset and conclude upto 97% sensitivity, 96% specificity, 96% accuracy and 0.988 area under the curve (AUC) he also claims up to 0.98 AUC on ROC dataset. Alban (2017) diagnosed five class severities and de-noised the Eye PACS images of angiography for detection of DR. he applied CNN and comes up with 79% AUC and 45% accuracy. Lim et al. (2014) used the methods mentioned by Gilbert et al. (2012) for extracting features from identified region then classify these features by implementing deep convolutional neural network and realised the model on SiDRP and DIARETBD1 datasets.

Pratt et al. (2016) employed the NVIDIA CUDA DCNN library on Kaggle dataset consisting of above 80,000 digital fundus images. They also validated the network on 5,000 images. The images resized into 512x512 pixels and then sharpened. Finally, the features vector fed to Cu-DCNN. They classified the images into 5 classes using features like exudates, haemorrhages and micro-aneurysms and achieve upto 95% specificity, 30% sensitivity and 75% accuracy.

### 3.2.2 Gastrointestinal (GI) Disease Detection

Gastrointestinal diseases are the diseases that occur within the gastrointestinal tract (either upper GI tract or lower GI tract). Organs such as oesophagus, stomach, large and small intestine and rectum are the parts of GI tract.

The digestion process may be affected by various ailments and diseases like inflammation, bleeding, infection and cancer. It may also cause by diverticulitis due to bleeding from colon, there may be some small intestinal disease termed as arteriovenous malformation (angiodysplasias or Anglo-ectasias).

Image processing and ML plays a critical role in diagnosis of these kind of disease with the advancement in computer aided diagnosis system. Recently, many imaging tests that takes the help of ML algorithms are in practise, such tests are wireless capsule endoscopy, and Interoscope, colonoscopy or sigmoidoscopy radiopaque dyes and X-rays studies, deep small bowel enteroscopy, intra operative enteroscopy, computed tomography, and Magmatic Resonance Imaging (MRI).

Jia et al. (2016) apply DCNN and analyse 10,000 wireless capsule endoscopy images as data. Rongshen et al. (2015) detect GI lesion by using a popular technique for automatic extraction of features from endoscopic images using CNN. He further classifies these features by support vector machine and report the accuracy of 80%.

Syed Hamad Shirazi (2015) conducted an experiment with 337 a noted inflammatory and 599 non-inflammatory images of the gastrointestinal tract of KID. In 2016, they using CNN

architecture and passed the extracted features to SVM for gastrointestinal disease in WCE videos.

### 3.2.3 Tumour detection

An unusual growth of cells in any part of the body that make a mess is termed as tumour or neoplasm. A tumour may or may not cause cancer. Thus, we categorise the tumour into cancerous and non-cancerous tumour called malignant and benign tumour respectively. Benign tumour is much less dangerous as compared to malignant as it does not spread in other parts of the body. While malignant may spread in other parts of the body and become difficult to cure.

Wang et al. (2016) analysed 482 images of patients between the age of 32-70 years, out of which 246 women detect with tumour. The analysed images initially de-noised and then segment the breast tumour using modified wavelet transformation, morphological operations and region growth. Then morphological and textured features passed to extreme learning machine and SVM for classification and detection of breast tumour. As the output, the total error rate was 84 using ELM and 96 using SVM. In 2015, Jeimer et al. used limited data of malignant mass and benign solitary cyst in his paper “automatic coronary calcium scoring in cardiac angiography using CNN” and as the result CNN reported area under the curve upto 87%. Further, Weildi et al. (2016), Rongshen Zhu (2015) and Yixuan Yuan (2017) used CNN and report their output with area under the curve between 80%-85%.

## 4 Conclusion

Human mind is always curious about new innovations and developments and what is beyond that. Artificial intelligence is one such example as it is the result of this curiosity of learning ability of machines similar to human to learn from experience. Development of such type of intelligence is biggest achievement in itself as such learning behaviour of machines allow user to handle a big amount of data that not possible for human mind to store. This type of computer application will surely save lots of efforts of data handling but implementation of this technology is not a simple task. AI needs to be trained from past data in continuous manner. And once it is trained, the continuous data supply is also crucial for further development and improvement. In this study, we reviewed the motivation of using ML in healthcare. We also discuss the major category of ML, that is, ML. We focused on deep learning, its architecture and discuss various healthcare data that deep learning has been analysed and surveyed. Though, ML technologies have some attracting substantial attention in medical research. The real time implementation still facing problems. One such problem, is regulations. Recent regulations lack the standards of safety, assess and efficiency of the ML system. To overcome this difficulty, the US FDA provide guidance for assessing ML systems that insures to maintain the safety and efficiency. Another constraint is that current healthcare environment does not provide incentive for sharing data on the system. Consequently, training of ML before implementation has been compromised. The healthcare revolution is under ways to stimulate data sharing among many countries.

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### Conflict of interest

We declare that no competing interests exist.

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**Authors' contributions**

AJM conceptualized and designed the study. AS and KJS reviewed the literature for relevant data and documentation. AS and AJM prepared the primary draft of the manuscript. AJM and

KJS edited and critically revised the manuscript. All authors read and approved the final manuscript.

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