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Machine Learning and Deep Learning based AI Tools for Development of Diagnostic Tools

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18.1 Introduction

Coronavirus disease-2019 (COVID-19) is a highly infectious disease caused by severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) (Zhou et al., 2020) virus and was first identified in Wuhan city located in CHINA in December 2019 (Usha et al., 2021). World Health Organization (WHO) declared this as a pandemic on March 11, 2020. At the time of writing this chapter, the world suffered from two waves of COVID-19 during which 180,844,266 confirmed cases were reported worldwide, 3,917,738 deaths, and 165,478,429 recoveries (Worldometer, "Covid-19 Coronavirus Pandemic", 2021). Various types of vaccines have been invented and 2,445,759,606 vaccinations were successfully administered. To contain the COVID-19 outbreak, WHO suggested measures such as early infection detection, rapid treatment, and isolation (Islam et al., 2021).

Intelligent systems are built using artificial intelligence (AI) (Lu & Wang, 2020; Rong et al., 2020). The medicine and healthcare system is one of the promising application areas of AI (Murphy et al., 2021), in which researchers have proposed and developed several successful systems for decision support related to health and disease diagnosis (Rong et al., 2020). Though healthcare is an emerging area of research in AI, maximum research is focused on diseases such as cardiology, cancer, and neurology. A strong AI system reveals insights from medical data to help decision support and forecasting systems. Based on the success of AI in healthcare, researchers suggest leveraging AI in fighting against COVID-19 (Usha, 2021). AI systems aid in COVID-19 infection detection, forecasting the next outbreak, unveiling the outbreak pattern, and finding treatment on COVID-19. First-generation rule-based AI system relies on the prior medical knowledge of experts

and formulation-based rules and is very complex to build, whereas modern AI leverages machine learning (ML) algorithms to find patterns, associations, and learn from data (Islam et al., 2021). Researchers believe, physicians take better and quicker decisions with significant aid from AI systems and may even eliminate the necessity of human decisions (e.g., radiology) (Dreyer & Allen, 2018), while the question still remains will AI-doctors replace human physicians? (Rubin, 2019) The increased use of digital technology in healthcare leads to a collection of a huge volume of data and requires big data analytics for the success of AI in healthcare.

The implications of AI like biological data mining and ML algorithms can be exploited in detection, diagnosis, COVID-19 classification, and vaccine development. The recent developments in AI allow implementing deep learning (DL) to train an artificial neural network (ANN) using huge labeled datasets (Jiang et al., 2017). A modern DL network, in general, contains hundreds of hidden layers in ANN.

In this chapter, the need for AI for medical diagnosis is described. Further, ML and DL-based AI tools and their implementation for diagnostic applications are discussed. Objectives of diagnostic tools to be developed and various challenges to be faced in the fight against SARS-CoV-2 are discussed and a few case studies are described.

18.2 Artificial intelligence for medical diagnosis

Artificial intelligence is an umbrella term (Islam et al., 2020), for ML and DL techniques, which demonstrates its significance in the field of medical diagnosis (Esmaeilzadeh, 2020). AI applications are extensively used in the areas of basic biomedical research, clinical research, and translation research (Yu et al., 2018). In the area of biomedical research, AI applications are used for automated experiments, automated data collection, simulation of molecular dynamics, gene function annotation, literature mining, and so on. In translational research, AI applications are used for drug discovery, drug-target prioritization, drug repurposing, genetic variant annotation, prediction of chemical toxicity, biomarker discovery, etc. Similarly, in the area of clinical practice, AI applications are used for genome interpretation, treatment selection, automated surgery, monitoring patient, disease diagnosis, and so on.

Sophisticated algorithms in AI, learn from a huge volume of healthcare data, and insights obtained are used to aid physicians in medical practice (Davenport & Kalakota, 2019). In addition, human errors can be eliminated by using an AI system and completing the diagnosis process in reduced time (Ichikawa et al., 2016; Islam et al., 2020). These AI systems are trained using available data (Li et al., 2020). Healthcare data is categorized into two types. The first one is structured data such as computed tomography (CT) scan images, genetic and electrophysiological (EP) data, etc., whereas the second one is unstructured data such as medical examination results, clinical data, medication and so on which is in textual form and help in diagnosis process (Jiang et al., 2017). In order to process the unstructured data, Natural Language Processing (NLP) techniques which are part of AI can be applied to convert data into structured format, that is, electronic medical records (EMRs). Further ML or DL techniques are applied to analyze these EMR for diagnosis (Jiang et al., 2017). The availability of abundant healthcare information and rapid

development techniques of big data analytic methods combined have paved the way to build AI applications successfully in healthcare. The use of AI systems can assist the physician in many cases, by eliminating issues associated with human fatigue and habituation; providing a rapid diagnosis in real-time. A medical specialty such as radiology (Liew, 2018), pathology, ophthalmology, and dermatology depend on image-based diagnoses (Yu et al., 2018).

In radiology, X-ray, CT, magnetic resonance imaging (MRI) scan, and positron emission tomography (PET) scan image techniques are used to diagnose disease. AI-based image analysis systems provide rapid disease diagnosis accurately to deal with huge patient demand (Pham, 2020). For example, AI-based image analysis of a CT scan requires only a few seconds whereas manual assessment can take up to 15 minutes. In ophthalmology, a noninvasive fundus photography procedure is used for capturing retina, optic disk, and macula images using retinal cameras and have a key role in detecting causes of preventable blindness and monitoring diseases like diabetic retinopathy, glaucoma, neoplasms of the retina, and age-related macular degeneration (Panwar et al., 2016). In dermatology, for diagnosing various types of skin lesions, inspection plays an important role. Automated AI diagnostic systems can be developed for classifying images of benign and malignant lesions. The final model for diagnosis may even be deployed on mobile devices with improved access to screen skin lesions. In pathology, the histopathological assessment procedure comprises processing a biopsy into tissue slides, staining with pigments, and interpreting the slides under a microscope based on visual evaluation (Rubegni et al., 2002). This process can be automated with AI systems.

In healthcare, maximum research in AI has been focused on diseases such as cancer, neurology, and cardiology. The IBM Watson is an AI system, that pioneered in this field with promising advancements in oncology. Recommendations made by IBM Watson in cancer treatment are comprehensible with the physician's decisions (Jiang et al., 2017). Biomedical signals recorded by modern wearable devices using embedded sensors include heart rate, voice, tremor and limb movement, etc. These biological signals are possibly useful for disease detection and inferring health conditions. Using heart rate and skin temperature data recorded by wearable devices, infectious disease signs, and inflammatory responses can be detected in the early stage (Li et al., 2017). The data collected from photoplethysmography sensors inserted in wearable devices allows monitoring cardiovascular diseases, pulmonary diseases, anemia, and sleep apnea (Majumder et al., 2017; Yu et al., 2018). Sensors embedded in wearable devices also help in detecting symptoms of Parkinson's disease patients such as tremors and lessened hand movement, gait, posture, and speech patterns that help in early treatment (Yu et al., 2018).

AI has been successfully implemented in the various fields of medical diagnosis (Ichikawa et al., 2016). Hence, AI techniques can be helpful in fighting against COVID-19 disease. Diagnostic tools can be developed and implemented for early detection of COVID-19 disease thus containing the disease and reducing the burden on the healthcare system.

As per the analysis done by the Verified Market Research team, the global market share of AI-based medical diagnostic tools was valued at approximately US\$1000 million in 2019 and is projected to achieve a market share of approximately US\$6,000,000,000 by 2027, with a growth rate of 26% approximately from 2020 to 2027 (Verified Market Research, 2021).

18.3 Machine learning and deep learning-based artificial intelligence tools

In computer science, AI being an emerging field mimics human behavior by making machines think, learn, perform human-like actions and take decisions. AI, an umbrella term, covers various ML and DL techniques. AI has numerous applications in society, as complex problems can be solved efficiently in the fields of healthcare, education, entertainment, finance, manufacturing, etc. The association of AI, ML, and DL (Kumar & Pradhan, 2019) are shown in Fig. 18.1.

In this section, ML and DL techniques have been discussed for developing diagnostic tools. The success of the developed model mainly depends on the data used to train the model. The use of balanced dataset, that is, the dataset that has an equal representation of all classes in the data gives a perfect/accurate model. For an unbalanced (or imbalanced) dataset, there is no equal representation of all the classes inside the dataset, then the developed model may not be perfect, and predictions may be biased. Hence, to deal with unbalanced dataset bootstrapping techniques with *upsampling* or *downsampling* can be used.

- **Upsampling:** Replicate the minority class instances/observations and increase the dataset size with redundant data. A statistical technique, sampling with replacement, also called oversampling is used.
- **Downsampling:** The majority of class instances/observations are eliminated from the dataset to bring the balance.
- **Data augmentation:** These are applied to image datasets to increase the size of the dataset artificially which helps to generate a model with better accuracy. Rotation of image, flipping the image, introducing the noise, increasing or decreasing the resolution are common techniques used for data augmentation.

18.3.1 Machine learning

Machine learning uses algorithms and data to develop models by learning without intervention and extracts useful patterns and insights from data that help in decision-making (Jordan & Mitchell, 2015). The success of the model built depends upon the features selected to develop the model (Usha, 2021). Traditional ML-based systems rely upon experts to take a decision on feature selection. Hence, user intervention is required. These models perform better on small to medium (< 1 million but vary based on type data)

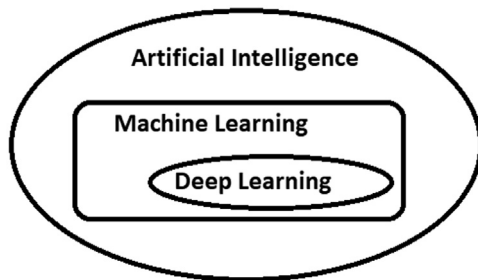


FIGURE 18.1 Association of artificial intelligence, machine learning, and deep learning.



FIGURE 18.2 Traditional machine learning process.

sized datasets. In developing ML models user intervention is required at the input level, in feature selection, and to verify output, whereas feature engineering and learning are taken care of by the algorithms. These algorithms can be executed on low-power machines, whereas the use of graphical processing units (GPUs) speed up the execution. Machine learning algorithms can be implemented as shown in Fig. 18.2.

Based on the learning technology and data, ML algorithms are classified broadly into the following categories (Kumar & Pradhan, 2019):

1. Supervised learning algorithms need the knowledge of feature/input variables and the outcome variable. A few examples are linear and logistic regression, discriminant analysis, decision tree, random forest (RF), k-nearest neighbor, support vector machine (SVM) and neural network, and so on.
2. Unsupervised learning algorithms require the knowledge of feature/input variables, but they do not have knowledge of outcome variables. For example, clustering algorithms, principal component analysis (PCA), etc.
3. Reinforcement learning algorithms use datasets where there could be uncertainty with respect to both feature/input variables and output variables. For example, Markov chain and Markov decision process, etc.
4. Evolutionary learning algorithms imitate the natural evolution problem-solving techniques. For example, genetic algorithms and ant colony optimization, etc.

18.3.1.1 Framework for developing ML model

The general framework for ML model development can be divided into several integrated stages as shown in Fig. 18.3. Various stages include problem identification, Extracting features, preprocessing, ML model building, and model deployment (Kumar & Pradhan, 2019).

- **Problem identification:** In this stage with the help of domain experts, the model developers identify the context of the problem.
- **Extracting features:** It is a process of extracting features from different sources and identifying the relevant features for building models.
- **Preprocessing:** Raw data cannot be used as it is in the given form, as there will be missing values or impurities. Hence, preprocessing is an important step in which data cleaning, transformation, and feature engineering techniques can be applied to prepare the data in a usable format.
- **ML model building:** To build a model, a data split is created with 70%/80% training data and 30%/20% test data. ML model is constructed with training data and accuracy is tested with the test data. It is an iterative process to develop various models and finally, a suitable model for the problem context is selected.

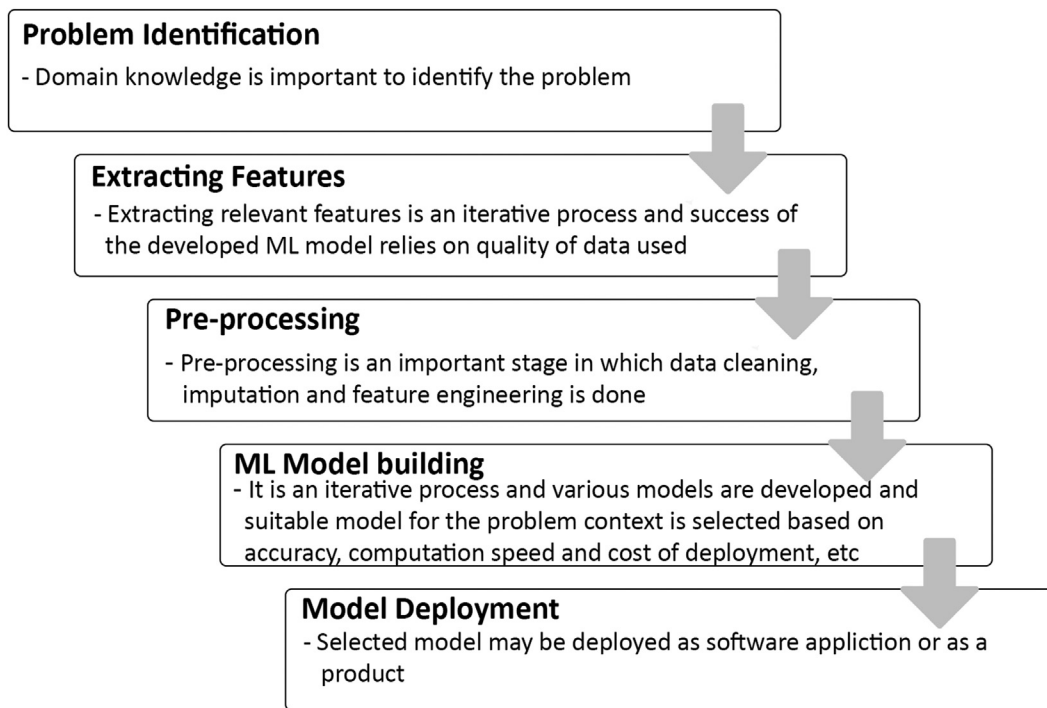


FIGURE 18.3 Framework for machine learning model development.

- **Model deployment:** The model selected will be deployed based on various criteria like accuracy, computation speed, deployment cost, and so on. During model deployment activity in the last stage, strategy for deployment can be decided in the form of software application, product, robots, chatbots, real-time actions, and so on.

The developed ML model's success depends on the activities such as extracting suitable features, feature engineering, model building, and model deployment. Extracting suitable features from different sources is called feature extraction. For example, for disease diagnosis features that can be extracted from clinical reports, demographic data such as age, gender, and physical examination data may be used. Feature engineering is an important phase in ML in which data from independent variables are not much significant by themselves, then use the data from the derived new feature. For example, if X_1 and X_2 are two extracted features from the medical records then new features can be derived by taking ratio (X_1/X_2), product ($X_1 * X_2$), or other innovative technique binning, centering the data, and so on. Feature engineering is a key technique for the success of the ML model.

The objective of model building is to identify the suitable model for the specified problem context. The accurate model may require more computation time and expensive infrastructure; hence, the selected model may not be accurate. The final model will be selected with multiple criteria such as accuracy, computation speed, deployment cost, etc., for deployment. During this stage, feature selection can be done by identifying a significant

relationship with the outcome. During model deployment activity in the last stage, strategy for deployment can be decided in the form of software application, product, robots, chatbots, real-time actions, and so on.

ML techniques for problem-solving that we intend to use, depending on the type of the task (Deo, 2015), fall into roughly two broad categories: Supervised learning and unsupervised learning. In this chapter, we limit our discussion to supervised learning algorithms and unsupervised learning algorithms.

In unsupervised learning, the training data collected will have only features/inputs but there are no associated output labels to predict. Instead of classifying to known output labels, a natural pattern or group will be generated within the data. Indeed, it is a more challenging task to judge the value of generated pattern or group. Often the performance of such groups generated by unsupervised learning is evaluated by supervised learning tasks in the subsequent stage. The common applications of unsupervised algorithms are data exploration, which helps to understand data in a better way and as a preprocessing step to supervised algorithms.

Frequently used unsupervised algorithms are k-means clustering, hierarchical clustering, PCA, *t*-distributed stochastic neighborhood embedding (*t*-SNE), etc. Clustering techniques are used to discover new knowledge, unknown patterns or reoccurring patterns, and so on. Clustering algorithms generate subgroups by maximizing or minimizing the similarity between the instances in the dataset, that is, instances with similar traits are formed as a cluster. For example, for the given COVID-19 suspect dataset, for a number of infected individuals, viral infection anosmia may be present in the absence of other symptoms. Hence, along with other symptomatic features, anosmia can be considered for similarity, and clusters can be formed to generate probable COVID-19 positive or negative individuals.

PCA is used as a preprocessing step for supervised algorithms on high dimensional linear data, that is when there are a greater number of features given in the dataset. To build an accurate model, all features need not be used but relevant important features to be considered. For example, given various features of a patient data, all features need not be used to diagnose the disease, but few important features are used. PCA can be used for dimensionality reduction or feature extraction in the preprocessing step. PCA transforms data into a lower-dimensional space by retaining as much data variation as possible. Hence, it is used for dimensionality reduction in preprocessing step. Another technique *t*-SNE is used for dimensionality reduction of high dimensional nonlinear data. It embeds data points from high dimensions to low dimensions while preserving the neighborhood.

The goal of supervised algorithms is either to classify or predict, a known output or unknown parameter. Supervised ML approaches collect numerous “training” data containing features/inputs and the desired output labels. The algorithm analyses the existing patterns from labeled input/output pairs of training data, “learns” and produces the correct prediction for a given unseen new data as input (Yu et al., 2018). Few classic ML tools for supervised algorithms such as logistic regression, discriminant analysis, naïve Bayes, nearest neighbor, decision tree, RF, SVM, and unsupervised algorithms such as clustering, principal component analysis are extensively used in the development of diagnostic tools (Tanwani et al., 2009). In the following section, various ML classification algorithms that are used for developing medical diagnostic tools are discussed.

For the situations, when the complexity in the data increases or unstructured data is used for training and testing, or a huge volume of structured data is used, classic ML algorithms may not perform better for the required accuracy. In such cases, advanced ML algorithms need to be used, which are also known as DL algorithms, which use neural networks with multiple hidden layers.

18.3.2 Deep learning

DL (Lecun et al., 2015) is a subfield of ML, which is fundamentally a neural network that simulates the functionality human brain with three or more layers. These neural networks are trained to learn from large amounts of data. A neural network with a single layer can make approximate predictions, where to optimize and refine the accuracy of the model additional hidden layers can help. In the DL process user intervention is limited to input and output stages, and entire processing such as feature engineering, feature selection, etc., is taken care of by the DL algorithm. Multilayer nonlinear structure of deep neural network uses a black-box approach with nontransparent processing and their predictions are not traceable by humans. The DL process is shown in Fig. 18.4.

Deep neural networks contain multiple nonlinear layers with interconnected nodes. Either forward propagation or backpropagation algorithms are used for prediction or classification.

In *forward propagation algorithms*, each layer is built over the previous layer and is used to improve and optimize predictions. The input layer and output layer of a deep neural network are called *visible* layers whereas the intermediate layers are called hidden layers. The input data given at the input layer of the DL model moves forward after processing and the output layer makes the final prediction or classification.

In *backpropagation algorithms*, for example, gradient descent moves from output to hidden to input layers, and in that process, it updates the weights and biases to reduce the error, in an effort to train the model and minimize the *loss function*. *Loss function* means the variance of the generated output and actual output. The accuracy of the neural network prediction depends on its weights and biases. Training neural network is the process of improving the accuracy of the model. Forward and backpropagation together allow a neural network for making predictions and correcting any errors accordingly.

DL algorithms are used to analyze complex data, hence may require more computation power. graphical processing units (GPUs) are recommended to train the algorithms for speeding up the process. DL neural networks include ANNs, convolution neural network (CNN), and recurrent neural network (RNN). ANN works with structured data, a recommendation engine, autoencoders for anomaly detection, and so on. CNN is predominantly used for image data for image classification and segmentation. ANNs are also used for two-dimensional image and three-dimensional object detection. RNN is predominantly used for forecasting techniques on time series data, sentiment analysis, video analysis, and speech analysis.

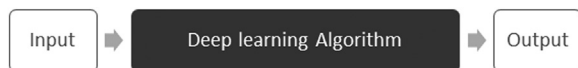


FIGURE 18.4 Deep learning process.

18.3.3 Performance evaluation of classification models

The performance of the ML model developed can be estimated using a few statistical measures. Let us discuss classification model evaluation using statistical measures such as accuracy, sensitivity, specificity, precision, F-score, and the area under the receiver operating characteristic curve (AUC).

In classification models, confusion or contingency matrix can be used as a base for computing the performance of the model using statistical measures. It shows correctly classified and incorrectly classified predictions.

Let us assume that, the ML model has two classes namely positive and negative. Let P be the total number of instances/predictions in the dataset that belong to a positive class, whereas N be the total number of instances/predictions in the dataset that belong to the negative class. Let, TP be correctly classified instances as positive, whereas FN is the incorrectly classified instances as negative, which were supposed to be positive. Let TN be the correctly classified instances as negative, whereas FP be the incorrectly classified instances as positive.

A total number of instances/predictions is the sum of total positive instances and negative instances, that is, $P + N$.

Accuracy: It is a percentage of correctly classified predictions

$$Accuracy = \frac{(TP + TN)}{(P + N)} \times 100 \quad (18.1)$$

Sensitivity/Recall: It is the percentage of predictions that are correctly classified as positive class. It is also called recall

$$Sensitivity = \frac{(TP)}{P} * 100 \quad (18.2)$$

Specificity: It is the percentage of predictions that are correctly classified as negative class

$$Specificity = \frac{(TN)}{N} * 100 \quad (18.3)$$

Precision: It is the ratio of correctly classified predictions to total predictions classified as positive

$$Precision = \frac{(TP)}{(TP + FP)} \quad (18.4)$$

F-score: It is the harmonic mean of precision and recall/sensitivity, that balances precision and recall/sensitivity

$$F - Score = \frac{(2TP)}{(2TP + FP + FN)} \quad (18.5)$$

(or)

$$F - Score = \frac{(2 \times Recall \times Precision)}{(Recall + Precision)} \quad (18.6)$$

ROC: Receiver operating characteristic is a probability curve plotted for the true positive rate (TPR = sensitivity) against the false positive rate (FPR = 1—specificity) at various threshold settings.

AUC/AUROC: It is the area under the plotted ROC curve. It represents the performance of the classifier. AUC's value ranges from 0.5 to 1. That is, $0.5 < \text{AUC} < 1$, in which $\text{AUC} = 1$ indicates perfect classifier. Hence, the higher the AUC value, the better the performance of the model.

While comparing multiple models for a problem, AUC can be used as a comparison metric, that is, the model that gives the highest AUC is considered as a better model.

18.3.4 Popular learning frameworks for machine learning and deep learning

AI has provided a way to process data and develop models. With the growth of AI, numerous learning frameworks and tools have evolved, that can be leveraged to implement ML and DL. Few popular frameworks and tools are as follows: MxNet, TensorFlow, PyTorch, Gluon, Keras, Scikit Learn, Theano, Caffe, CNTK, Auto ML, Google ML Kit, and many more.

18.4 Machine learning for diagnostic applications

In general, ML models developed for diagnostic application will fall under classification problems. These models predict binary (two outcomes) or multiple outcomes or classes. A classification model with binary predictions is called binary classification and multiple predictions are called multinomial classification. Various classic ML supervised algorithms such as logistic regression, decision trees, RF, ensemble, neural networks, and SVM can be leveraged for classification problems.

18.4.1 Logistic regression

A statistical model, logistic regression is used for classification to predict a discrete value as outcome whereas features/input variables can be either continuous value or discrete. If the prediction results in two values, then it is called the binary logistic regression model. For example, classify an individual with COVID-19 positive and COVID-19 negative. While developing a model, if several categorical features/input variables are found in the dataset then, the One Hot Encoding (OHE) technique can be used for encoding using dummy variables.

The developed logistic model can be validated before using for practical applications. The Chi-square test can be used to check the statistical significance of selected feature variables. Similarly, a likelihood ratio test can be used for checking the statistical significance of the overall model and pseudo R^2 can be used for the goodness of the model.

The performance of the model can be checked using various statistical measures such as sensitivity, specificity, f -score, AUC, etc. AUC gives the overall performance of the

model and for practical application of the model, an AUC of at least 0.7 is required and a model with AUC higher than 0.9 is considered as an outstanding model.

18.4.2 Decision tree

The decision tree learning model develops a tree-like structure using the divide and conquers technique, to predict the outcome class. It starts at the root node and splits the data into multiple child nodes by dividing the dataset into subsets. To split the node, that is, feature selection it uses Gini impurity index or entropy measures. The decision tree model works well with both numerical and categorical data. To use categorical data, we need not normalize data or create dummy variables. IT helps to generate simple interpretable rules that can help to make a decision.

18.4.3 Random forest

RF classification model is an ensemble of decision trees, where each decision tree is built from bootstrap samples, using a statistical method sampling with replacement, and features/input variables are randomly selected without replacement. To increase the model accuracy the number of decision tree models can be tuned. The hyperparameters in the RF model are a number of decision trees, a selected number of features and sampled instances per model, and the depth of the decision trees and search criteria. Gini impurity index or entropy can be used for feature selection and splitting criteria. The hyperparameters are used to control the learning process of the model.

18.4.4 Ensemble

Ensemble methods use a set of classification models for predicting new data using a majority voting strategy. The majority voting means, simply counting the vote from each classifier/model or weightage could be given based on their individual accuracy measure. As an ensemble contains multiple classification models, we require multiple datasets. Hence, bootstrapped strategy is used to generate multiple datasets for all classification models in the ensemble.

18.4.5 Support vector machine

SVM classifies the instances into two or more classes. SVM can be used for both linear and nonlinear dataset. SVM algorithm aims to generate a model by creating the best line/boundary so that, data can be segregated into multiple classes, and during prediction new data can be easily classified to a particular class.

In SVM, the goal is to create the best line/decision boundary, also called a hyperplane, to segregate n -dimensional space into classes so that, a new data point can be correctly classified in the future. Then SVM finds the closest points of the boundary line called support vectors and distance from support vectors to hyperplane is computed which is called margin. The optimal hyperplane is the one that has the maximum margin. Hence, the goal

is to maximize the margin. To handle nonlinear data, SVM adds one additional dimension and computes the hyperplane. SVM is extensively used in the development of medical diagnostics.

ML-based AI models have been extensively developed and implemented in the healthcare system for diagnostic applications (Doupe et al., 2019). These diagnostic applications use various types of structured data and unstructured data. In the recent past, researchers proposed and developed various diagnostic models to fight COVID-19 as well. Various ML diagnostic tools are available, hence a few frequently used ML algorithms are summarized in Table 18.1. For Example, A model for predicting treatment outcomes based on physiological parameters after stroke was built with linear structured data and real-time tracking to predict potential positive COVID-19 with symptomatic data using a logistic regression algorithm (Menni et al., 2020; Zhang et al., 2013). A model to diagnose COVID-19 based on symptomatic data was built using the decision tree algorithm (Zoabi et al., 2021). Another diagnostic model for evaluating cerebral edema following hemispheric infarction was built using a Random forest algorithm with CT scan image data (Chen et al., 2016). Support vector machine algorithm was used with image data for building a diagnostic tool for diagnosis of cancer (Sweilam et al., 2010), Alzheimer's disease detection with MRI scan image data (Khedher et al., 2015), and a diagnostic model for predicting stroke mortality at discharge with Image data (Ho et al., 2014). Similarly, a diagnostic model for heterogeneity in prostate cancer was built using DNA methylation data using an ensemble algorithm (Babalyan et al., 2018).

TABLE 18.1 Machine learning tools an overview of machine learning tools for diagnostic applications.

Algorithm	Type of dataset	Medical diagnostic tool
Logistic regression	Linear data, structured data	A model for predicting treatment outcome based on physiological parameters after stroke (Zhang et al., 2013)
	Symptomatic data	Real-time tracking to predict potential positive COVID-19 based on symptoms (Menni et al., 2020)
Decision tree	Symptomatic data	ML model to diagnose COVID-19 based on Symptoms (Zoabi et al., 2021)
Random forest	CT scan image data	For evaluating cerebral edema following hemispheric infarction (Chen et al., 2016)
Support vector machine	Image data	Diagnosis of cancer (Sweilam et al., 2010)
	MRI scans image data	Alzheimer's disease detection (Khedher et al., 2015)
	Image data	Stroke Mortality Predicting at discharge (Ho et al., 2014)
Ensemble	DNA methylation data	Diagnostic model for heterogeneity in prostate cancer (Babalyan et al., 2018)

18.5 Deep learning in diagnostic applications

DL is an emerging subset of ML, which is basically a neural network that simulates human brain behavior with more than three layers.

18.5.1 Neural network

In a densely connected neural network, neurons/nodes are organized into multiple layers such as input, hidden, and output layers. The goal of the neural network is to transform input into output. A node/neuron is also called a *perceptron*, processes the input by performing a dot product of inputs and their weights thereby adding the bias and applying nonlinearity using activation function and giving the output value. The activation function is a mathematical function, that adds nonlinearity to neuron/node so that complex data can be handled. The few common activation functions used are sigmoid, Tanh, and ReLU. The nonlinear function sigmoid inside the neuron converts the output to a value between 0 and 1, the Tanh function converts the output to a value between -1 and 1 , whereas the ReLU function converts the input x to output as $\max(0, x)$.

A neural network with more than three layers is known as a deep neural network. The “*deep*” in the deep neural networks represent a greater number of hidden/invisible layers in the network. In this section, DL networks ANN, CNN, RNN, and transfer learning are discussed.

18.5.2 Artificial neural network

ANN will have more than one hidden layer and is known as deep neural networks. ANNs mimic the working of the human brain. They are made of multiple nodes/neurons imitating the human brain’s biological neurons. The nodes in ANN that represent neurons are interconnected by links. The input data is processed by these interconnected nodes. The output of each node is passed to other nodes/neurons which are called activation or node value. Artificial neurons connected to other neurons have an associated weight and a threshold value or bias. The output generated by each node/neuron is above the threshold value, then that node/neuron is activated and sends data to the next layer in the network. Activation functions such as the sigmoid function can be used. ANN is also known as multilayer perceptron (MLP). Implementation steps of ANN are shown in [Fig. 18.5](#). ANNs work with structured data, a recommendation engine, autoencoders for anomaly detection, and so on.

18.5.3 Convolution neural network

Convolution neural network predominantly works on image data for image classification, image segmentation, detection of object and face recognition, etc. In CNN, feature extraction is done using a kernel/filter/convolution. Feature engineering is done automatically; hence predefined filters are not required. These filters learn automatically and are passed through the image to extract features. These filters capture spatial information

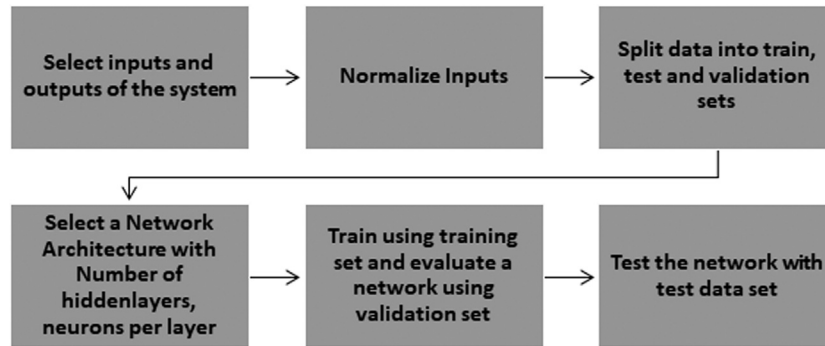


FIGURE 18.5 Implementation steps in artificial neural network.

which is in the form of an arrangement of pixels. This spatial information represents the relationship between the pixels in the image. CNN contains three layers known as convolutional, pooling, and fully connected layer. Extracting *feature maps* is done by convolutional layer then the pooling layer performs dimensionality reduction and extracts dominant features using *Max Pooling* technique and finally, the fully connected layer performs classification using techniques such as *SoftMax*.

18.5.4 Recurrent neural network

RNN is predominantly used for forecasting techniques on time series data, sentiment analysis, video analysis, and speech analysis. These networks capture sequential information in the input. The RNN illustrates to have a memory inside the neurons/nodes as prior inputs are used to influence the current input and output. Activation functions such as sigmoid, Tanh, or ReLU will be used that determine whether the neuron should be activated or not. Based on the architecture, different variations of RNN are available, such as long–short-term memory (LSTM), bidirectional RNN, gated recurrent units (GRUs), and so on. LSTM is frequently used RNN, which enables memorization of the inputs for an extended period, hence responsible for memory extension.

18.5.5 Transfer learning

A neural network, pretrained on a large-scale image dataset, such as Imagenet, can be used as it is, or by applying transfer learning to customize the network for the given new task (Lu et al., 2015). A few examples of pretrained neural networks are VGGNet, ResNet, LeNet, AlexNet, ZF Net, GoogLeNet, etc.

DL models are extensively developed and implemented in the healthcare system for diagnostic applications. These diagnostic applications use various types of structured data and unstructured data. In the recent past, researchers proposed and developed various diagnostic models to fight COVID-19 (Ghaderzadeh et al., 2021) as well. For example, a diagnostic model for early detection of dengue was built with structured patient data using an artificial neural network (Gambhir et al., 2017). With the help of image data, a

TABLE 18.2 Deep learning (DL) tools an overview of DL tools for diagnostic applications.

Algorithm	Type of dataset	Medical diagnostic tool
ANN	Structured patient data	Diagnostic model for the early detection of dengue (Gambhir et al., 2017)
CNN	Image data	Lesion segmentation using multimodel brain MRI (Kamnitsas et al., 2017)
CNN	Image data	Diagnostic tool for congenital cataract disease using ocular images (Long et al., 2017)
CNN	Fundus image data	To detect DR through the retinal fundus photographs (Gulshan et al., 2016)
CNN-VGG16	Fundus image data	Diagnosis of dry and neovascular age-related macular degeneration (Heo et al., 2020).
RNN- NLP, ML	Image data, text data	IBM Watson system—cancer diagnosis (Jiang et al., 2017)
RNN	Multivariate clinical data	Predicting medications from billing codes (Liu et al., 2020)

diagnostic model for lesion segmentation using multimodel brain MRI ([Kamnitsas et al., 2017](#)) and a diagnostic model for congenital cataract disease using ocular images ([Long et al., 2017](#)) was built using CNN. Similarly, with the help of Fundus image data, a diagnostic model was built to detect diabetic retinopathy (DR) through the retinal fundus photographs using CNN ([Gulshan et al., 2016](#)), and a model for diagnosis of dry and neovascular age-related macular degeneration was built with Fundus image data using a pre-trained CNN-VGG16 ([Heo et al., 2020](#)). IBM Watson system ([Jiang et al., 2017](#)) for cancer diagnosis was built with image data and text data using RNN and NLP. Similarly, a diagnostic model for predicting medications from billing codes was built using RNN with multivariate clinical data ([Liu et al., 2020](#)). There are numerous DL diagnostic tools available, out of which few diagnostic tools are summarized in [Table 18.2](#).

18.6 Objectives and challenges of severe acute respiratory syndrome-Coronavirus-2 diagnostic tools

COVID-19 was declared as a pandemic by WHO in March 2020 as it is a highly infectious disease caused by the SARS-CoV-2 virus ([Usha et al., 2021](#)). Healthcare professionals faced many challenges to contain COVID-19 and serve the world and many healthcare workers themselves got infected. Due to this pandemic, healthcare systems worldwide faced challenges in numerous ways that include a steep increase in demand for beds, oxygen supply, and healthcare workers and critical shortages in medical equipment. In developing countries, Governments and regulatory bodies faced many problems to bring awareness about the pandemic to the public and also set up the capacity and usage of healthcare resources for immediate clinical decisions. During the initial stages of the pandemic, reverse transcriptase-polymerase chain reaction (RT-PCR) kits were in shortage,

which is the utmost validated test for COVID-19 diagnosis. This contributed to an increase in infection rates, mortality rates, and delays in preventive measures (Chen et al., 2016).

In this scenario, diagnostic tools based on AI may be leveraged for early diagnosis and treatment to contain the disease, as many diagnostic tools based on AI are implemented effectively in the medical diagnosis in the past. The main objectives of the diagnostic tools in containing SARS-CoV-2 are disease detection, disease diagnostics, epidemic forecasting, sustainable development, performance comparison, patient management and monitoring, and so on. Apart from developing AI-based diagnostic tools, various other models based on AI can be developed to fight against COVID-19 that help in literature mining for COVID-19, tools that change the public perspective to handle COVID-19 pandemic and bring awareness in public to contain the COVID-19 pandemic.

AI-based models, such as ML and DL, are built using data and algorithms based on past experiences. Researchers and health professionals faced many challenges in the initial stages of COVID-19 due to a lack of historical data and up-to-date information. Intelligent systems cannot be developed successfully unless they learn with enough reliable data. To construct these models' various kinds of global data are required. AI-based tool for COVID-19 forecasting requires a huge time series of data of clinically tested patients for positive. Similarly, for developing AI tools for sustainable development, environmental, geographical, and demographical data related to COVID-19 is required. For developing disease diagnosis AI tools, data in various forms such as medical data, CT scan images, chest X-ray images, time-series data, and full blood count data may be required.

AI models can also be developed, to manage intensive care unit (ICU) surges during the COVID-19 crisis, to predict which patients have a higher likelihood of being critical cases based on symptoms and medical history. This helps healthcare professionals to classify patients who can be treated at home, patients who require ICU support, prevent patients from premature departure from ICUs, and early release of some patients. Worldwide researchers have currently been working with the help of healthcare professionals on developing new treatment options, medications, and vaccines for COVID-19.

18.7 Diagnostic tools for severe acute respiratory syndrome-Coronavirus-2— case study

Early diagnosis of COVID-19 disease, treatment can lessen the burden of medical professionals in containing the disease for which quick and effective screening techniques should be adopted. Considering limited healthcare resources, with the hope of assisting medical staff globally, diagnostic models were developed to evaluate the infection risk. Features such as clinical symptoms, laboratory tests, X-ray images, CT scan images, and integration of these features are used in developing AI models. Ever since the COVID-19 pandemic is identified, researchers came up with various diagnostic tools using AI models in the form of mobile applications, products, wearable devices, robots or AI integrated with internet of things (IoT) and drones to contain the COVID-19 disease. These tools help the healthcare system in diagnosing and treating COVID-19 affected populations. In this section, various case studies are discussed.

18.7.1 ML model to diagnose Coronavirus disease-2019 based on symptoms

During the initial period of the pandemic, acute scarcity of medical resources was faced in developing countries. This model will help in the initial diagnosis of the patient and predicts the positive rate on the RT-PCR test. [Zoabi et al. \(2021\)](#) developed an ML model using publicly available nationwide data published by the Ministry of Health, Israel. The ML model was trained on weekly data collected from around 50,000 plus tested individuals (out of whom 4700 confirmed COVID-19 positive individuals approximately). The subsequent week's data was used as test data. This dataset contained only eight binary features. Demographical data of the suspect individual, initial clinical symptoms, and other information such as known contact with COVID-19 positive individuals are collected.

A widely used gradient-boosting ML model with decision-tree base-learners was developed. Missing values were handled by the algorithm inherently. This model was predicted with 0.90 AUC for the test set. This ML model was developed to predict a positive in an RT-PCR test for SARS-CoV-2 infection by asking basic questions. Thus, this tool can be used for screening suspects and prioritizing testing for the virus. This model can be implemented globally when testing resources are limited for COVID-19 screening.

18.7.2 Multiclass diagnostic model

In the initial days of the pandemic, due to the scarcity of RT-PCR test kits, X-rays and CT scan reports were used for diagnosis. This helped in the early detection of COVID-19, enabled in time treatment for suspected patients, and contain the spread of the COVID-19. [Jin et al., 2020](#)) developed an AI system for the detection of COVID-19 disease and also conducted a statistical analysis of CTs of COVID-19 patients. This model was developed and assessed on a huge dataset of CT scan images from COVID-19, nonviral CAP, influenza-A/B, and nonpneumonia patients. This being a complex multiclass diagnosis task, the AI model was developed using CNN and achieved an AUC of around 97.81% on the test cohort. They also used two datasets CC-CCII and MosMedData which are publicly available datasets and achieved AUC of 92.99% and 93.25%, respectively.

18.7.3 Pretrained convolution neural network on computed tomography images

CT scan images were used for rapid diagnosis of COVID-19 and found to be useful. CT scan images reveal various signs caused by the viral infection. Radiologists take a long time to recognize these visual features as they are difficult to recognize. Authors ([Pham, 2020](#)) used 16 pretrained CNNs for diagnosis using CT image data. A publicly available large database of CT images of COVID-19 patients and the non-COVID-19 population was used. The performance achieved by these CNNs was very high for classification by using only six epochs for training. Transfer learning was implemented with and without data augmentation. Out of the 16 CNNs, the performance of DenseNet-201 was best in terms of accuracy, F1 score, AUC. DenseNet-21 is the deepest net available among 16 pretrained CNNs. A transfer learning implemented without data augmentation resulted in a better classification rate than using data augmentation.

18.7.4 Real-time monitoring

In the early COVID-19 pandemic stage, AI-based facial-recognition software and cameras were leveraged by countries like China and Russia to monitor the individuals defaulting mandated self-isolation or quarantine (Reuters, 2020; Dixon, 2020; Syrowatka et al., 2021). This technology progressed in identifying individuals accurately for wearing a mask in public places. This technology was also proposed for contact-less employee verification at work. Many AI solutions based on computer vision were developed to monitor public health recommendations such as social distancing, mask usage, and sanitizing hands. Neural networks were used to analyze the videos monitored by closed-circuit surveillance. These systems will generate alerts in real-time to aid individuals to improve compliance to public health recommendations (Reuters, 2020; Dixon, 2020; Syrowatka et al., 2021). These real-time monitoring systems can have additional features for tracking the capacity of the store and prioritizing areas for timely sanitation.

18.7.5 Wearable device

Our ring is a wearable AI device (WVU Medicine, 2020) that collects data from patient-related symptoms such as fever, cough, breathing difficulties, fatigue, etc. The Rockefeller Neuroscience Institute (RNI) platform using the RNI app with the Oura Ring and AI models was able to forecast COVID-19 related symptoms and was able to detect subclinical signs three days in advance to the onset of classic symptoms with 90% accuracy. This technology helps to contain the spread of the virus and serves as a crucial decision-making tool.

18.8 Summary

AI is an umbrella term, used for various ML and DL techniques, and has shown a significant impact on medical diagnosis in the healthcare system. The healthcare industry is one of the key areas where AI brought a paradigm shift. AI applications are extensively used in the areas of basic biomedical research, clinical research, and translation research as well. In the past, rule-based expert systems were developed for diagnosis, which are very complex systems to build and train. Later using ML and DL algorithms are used to develop diagnostic models, that learn by using training dataset and to make predictions to support healthcare workers to serve humanity in a better way. Hence, AI-based ML and DL diagnostic tools can be leveraged to fight against COVID-19 disease. COVID-19 caused by SARS-CoV-2 is an infectious disease and was declared a pandemic by WHO in March 2020. The successful application of AI-based ML and DL tools in the medical diagnostic field in the past encouraged researchers to develop new ML and DL diagnostic tools for containing the COVID-19 disease. Early detection and treatment are imperative to contain the COVID-19 pandemic. Hence, diagnostic tools are required to speed up the process and mitigate the spread of the virus.

In this chapter, we discussed various ML and DL-based AI tools, that can be leveraged to build diagnostic models. Classic ML algorithms such as SVM, decision tree, RF,

ensemble, logistic regression, etc., can be used successfully. These algorithms work better on structured data. When the dataset size increases or unstructured data such as image data is used, we need to use advanced ML algorithms, that is, DL algorithms such as ANN, CNN, RNN, and so on. EMRs of patients are in the form of structured data, unstructured physical examination data, and unstructured image data, that are used to develop diagnostic models in this field. In the recent past, few researchers proposed and developed models for COVID-19 based on symptoms to identify potential positive patients in the RT-PCR test and prioritize the test process. Image data such as chest X-ray or chest CT scans were used for diagnosis, hence DL models were developed using deep neural networks, that will analyze the images and classify the positivity in COVID-19 diagnosis. Various mobile-based applications were developed for contact tracing, monitoring public health guidelines adherence, surveillance, etc., using AI-based algorithms. Wearable devices also can be leveraged for primary detection of COVID-19 disease. AI-based ROBOTS and drones are in progress to minimize the risk by avoiding direct contact between health workers and infected patients. Hence, ML and DL-based AI diagnostic tools are capable of being successfully leveraged in the fight against the COVID-19 pandemic and any pandemic in the future.

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