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Elcin Nizami Huseyn
Netherlands Institute for Neuroscience
elcin.huseyn@asoiu.edu.az

APPLICATION OF DEEP LEARNING TECHNOLOGY IN DISEASE DIAGNOSIS

Summary

The rapid development of deep learning technology provides new methods and ideas for assisting physicians in high-precision disease diagnosis. This article reviews the principles and features of deep learning models commonly used in medical disease diagnosis, namely convolutional neural networks, deep belief networks, restricted Boltzmann machines, and recurrent neural network models. Based on several typical diseases, the application of deep learning technology in the field of disease diagnosis is introduced; finally, the future development direction is proposed based on the limitations of current deep learning technology in disease diagnosis.

Keywords: *Artificial Intelligence; Deep Learning; Disease Diagnosis; Neural Network*

1. Introduction

Since 1950, as a branch of artificial intelligence, machine learning has caused a historic revolution in many application engineering. With the rapid development of big data technology and the more diverse problems people are eager to solve, simple machine learning methods can no longer meet increasingly complex application scenarios, and deep learning technologies have naturally been introduced. Deep learning is a class of advanced machine learning technologies developed since 2006. It is used in the fields of computer vision, natural language processing, machine translation, medical imaging, medical information processing, robotics and control, speech recognition, audio recognition, and biological information. Great progress has been achieved [1].

With the rapid development of medical care and long-term accumulation, complicated and huge amounts of medical data are difficult to manually extract and analyze valuable information. Medical data includes basic patient data, electronic medical records, diagnosis and treatment data, medical image data and medical management data, etc. [2]. Based on these medical data, deep learning technology has penetrated into all aspects of disease diagnosis, such as radiology, pathology, and dermatology, etc. [3], it can extract valid information from medical data and make preliminary diagnosis of diseases.

2. Deep learning

Deep learning is a method for data processing using multiple layers of complex structures or multiple processing layers composed of multiple non-linear transformations [1, 4]. It combines low-level features to form more abstract structured high-level representations (attribute categories) Or features) to discover distributed feature representations of data, and demonstrate a powerful ability to learn essential features of data from a small sample set.

Today, deep learning technology has made breakthrough progress in the field of disease diagnosis. Its purpose is to build models that simulate the neural connection structure of the human brain. When dealing with practical problems, use multiple layers of complex structures or multiple processes consisting of multiple nonlinear transformations. Layer for data processing [5]. The network structure obtained by using deep learning technology is called deep neural network (DNN). DNN has multiple effective typical models [1], including convolutional neural network (CNN), and recurrent neural network (CNN). recurrent neural network (RNN), auto-encoder (AE), deep belief network (DBN), generative adversarial network (GAN), deep reinforcement learning (DRL) Among them, CNN, RNN, AE, DBN, etc. have made breakthrough progress in disease diagnosis.

2.1. CNN

In 1962, Hubel and Wiesel [6] proposed the concept of a receptive field by studying the visual cortex cells of cat brain. In 1988, Fukushima [7] first proposed a neural cognitive machine (neocognitron) model based on the concept of receptive fields. It can be regarded as the first implementation network of CNN, but it was limited by the computer hardware and neural cognitive machine model that trained the network at that time. Not widely used in various fields. In recent years, with the continuous improvement of computer hardware, CNN has gradually been successfully applied to various fields, especially the image field.

CNN mainly includes 3 kinds of network layers: convolutional layer, pooling layer and fully connected layer. Figure 1 is a brief architecture diagram of CNN. It can be seen that it contains 2 convolutional layers, 2 maximum pooling layers, and 1 fully connected layer [4].

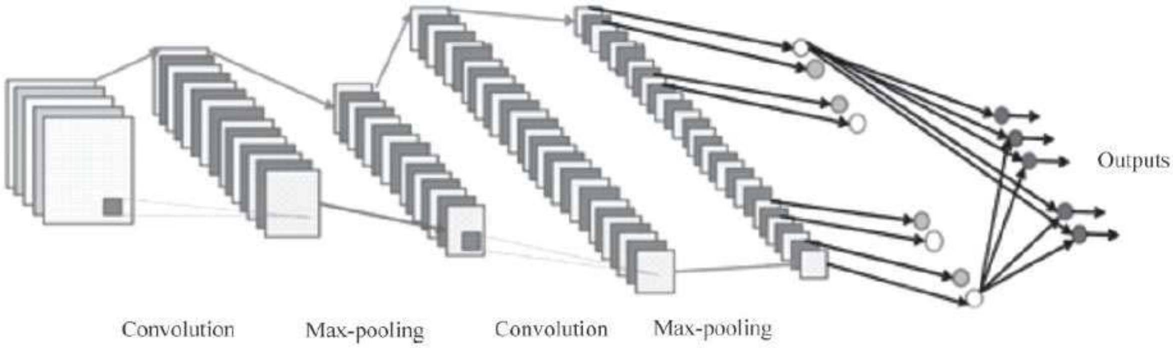

Fig.1. Architecture of convolutional neural network[4]

The key elements of CNN are multilayer stacking, local connections, weight sharing, and pooling. Multi-layer stacking is to stack single-layer convolutional layers, and use the output of the first layer as the input of the next layer, so that CNN is generated. The connection between the layers in the CNN is not a full connection, but a local connection. At the same time, the weight sharing and pooling operations are added, which reduces the complexity of the model and the number of parameters.

As shown in Figure 2A, when a full connection and a local connection are used to simultaneously process a 7 × 7 pixel image, and it is assumed that the output contains 7 × 7 = 49 hidden layer units. For a full connection, each hidden layer unit connects each pixel on the image, so there are 7 × 7 × 49 = 2 401 connections, which is 2 401 weight parameters. When using a local connection, each output node is connected to an upper-layer node at the same location with a 3 × 3 window connection, so the 49 hidden layer units have only 49 × 3 × 3 = 441 weight parameters, and their weight parameters are not yet To the original 20%. Weight sharing is to set each neuron with the same parameters and use the same convolution kernel to deconvolve the image. When a 3 × 3 convolution kernel is used, the meaning is that using this unique convolution kernel corresponds to each of the local connections A window, so that the convolution process only contains 3 × 3 = 9 weights, which can further reduce the weight parameters and prevent the model from overfitting.

Pooling is performed independently on the feature map, mainly including maximum pooling and mean pooling. When the maximum pooling is performed, a pooling window that is defined and smaller than the size of the feature map is used, and the pooling window translation step size is greater than 1 (≤ pooling window size) to calculate the maximum value within the range of the pooling window. And output it to the next stage; mean pooling is to replace the maximum value with the mean of all pixel values within the pooling window [8]. As shown in Figure 2B, the size of the feature map is 4 × 4, the pooling window is 2 × 2, and the translation step of the pooling window is 2. Then, a 2 × 2 feature map can be obtained through the pooling operation. Spatially invariant features are obtained by reducing the resolution of the feature map, which reduces the amount of data to be processed in the next layer, which indirectly reduces the number of parameters and prevents the model from overfitting.

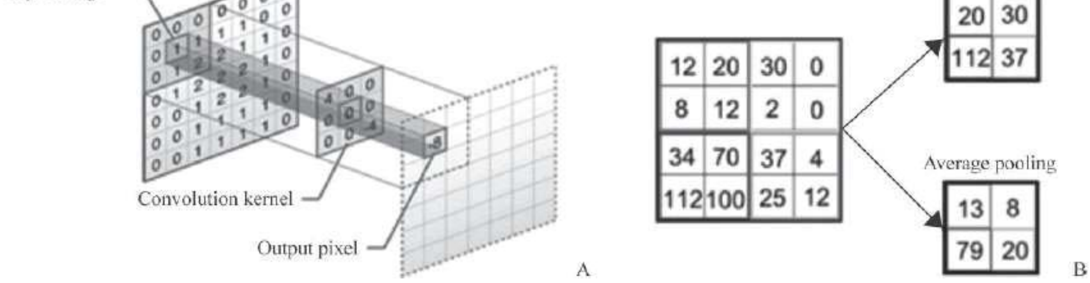

Fig.2. Convolution and pooling sampling methods in convolutional neural network[9]
A: Convolution; B: Max-pooling and average-pooling

2.2. Restricted Boltzmann machine (RBM)

RBM is a random stochastic neural network rooted in statistical mechanics proposed by Hinton and Sejnowski in 1986 [9]. The neurons in this network are random neurons, and their output has only two states (inactive and active). The value of the state is determined by the probability method. The network has 1 visible layer and 1 hidden layer, and there is no connection in the layer, as shown in Figure 3A. In addition, Roux and Bengio [10] theoretically proved that as long as there are enough hidden units, RBM can represent an arbitrary discrete distribution. Figure 3B illustrates the dimensionality reduction or feature extraction applied by RBM in image processing. Currently, RBM has been widely used in machine learning, such as classification, dimensionality reduction, high-dimensional time series modeling, regression, collaborative filtering, and image feature extraction.

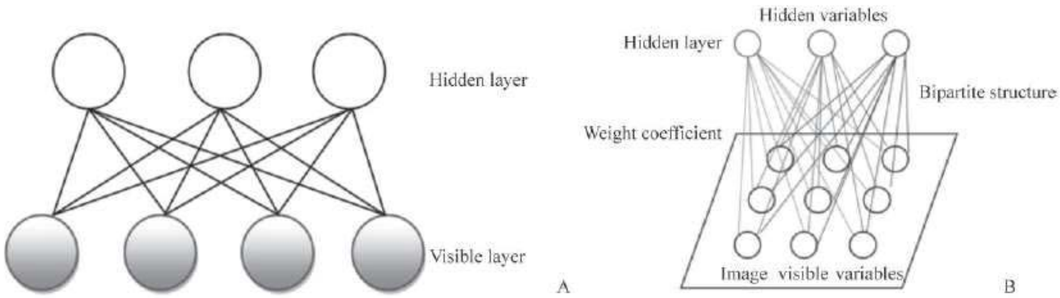

Fig.3. Basic structure of restricted Boltzmann machine

A: Network structure of Boltzmann machine;
B: Application of Boltzmann machine in dimensionality reduction or feature extraction in image processing

2.3. DBN

In 2006, Hinton et al. [11] proposed DBN, which can be interpreted as a Bayesian probability generation model. By training the weights between neurons, the entire neural network can generate training data according to the maximum probability. DBN can be used to identify features, classify data, or generate data.

The DBN consists of multiple layers of random hidden variables, which can be divided into two parts. The upper two layers have undirected symmetrical connections. The lower layers get top-down directed connections from the previous layer. The state of the lowest unit is visible input Data vector. A DBN consists of a stack of several structural units, which are generally RBMs. Its training process is to use unsupervised greedy layer-by-layer pre-training to obtain weights. First, fully train the first RBM, then fix the weight and offset of the first RBM, and use the state of its hidden neurons as the second The input vector of RBM, after fully training the second RBM, stack it on top of the first RBM, repeat the above steps to train to the top layer, and add labeled neurons to the top layer. For each training data, the corresponding labeled nerve Yuan is turned on and set to 1 while others are turned off and set to 0.

2.4. RNN

RNN is a specialized for speech, writing and other temporal data relating to artificial neural network, wherein the connection unit forms a one-way nerve loop [12], i.e. the internal state of the RNN creates a network, so that it can display dynamic time behavior. Unlike a typical neural network with a feedforward network structure, RNNs can use the network's time memory to significantly improve performance in natural language processing, gesture recognition, speech recognition, and generation tasks.

RNN network structure shown in Figure 4, and an output connected to the input ***X*** in the ***h*** block A, which has a cycle time of the permission information is transmitted to the network the next time. At present, the combination of RNN and CNN makes deep learning technology more convenient and fast in disease diagnosis.

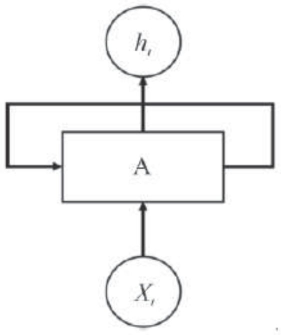

Fig.4. Basic structure of recurrent neural network
Block A is connected with input ***X*** and output ***h***

3. Deep learning and disease diagnosis

In recent years, thanks to the rapid development of hardware facilities, the Internet, and big data, the application of artificial intelligence technology has shown explosive growth [13]. The application of deep learning technology in disease diagnosis has also reached unprecedented height and scale. At present, the application of deep learning technology in disease diagnosis mainly focuses on lesion detection, image segmentation and shape modeling, and disease prediction [14].

3.1. Lung cancer

Lung cancer is one of the fastest growing morbidity and mortality rates and one of the most dangerous to the health and life of the population, and its early diagnosis and treatment are vital. Deep learning technology has made great progress in the early diagnosis of lung cancer.

Deep learning technology-based diagnosis of lung cancer is mainly based on the processing and analysis of lung image data, including the medical image data preprocessing, lung parenchyma segmentation, lung node detection and segmentation, and lesion diagnosis. Sun et al. [15] tested the feasibility of deep learning algorithms in the diagnosis of lung cancer using data from the Lung Image Database Consortium (LIDC) database in 2016; the data used in the tests were based on markers provided by radiologists After segmentation and amplification through sampling, rotation, etc., 174,414 samples were obtained, each sample was 52 × 52 pixels in size and corresponded to 1 label. They designed and implemented three deep learning algorithms: CNN, DBN, and stacked denoising autoencoder (SDAE). They used these three algorithms to perform regional detection on lung cancer data, and then used the support vector machine algorithm to The 28 features extracted manually are used for logical classification. The classification accuracy of CNN, DBN, and SDAE is 0.787 6, 0.811 9 and 0.792 9 respectively, all surpassing the performance of traditional computer-aided diagnosis systems. Anthimopoulos et al. [16] worked to find the detection mode of interstitial lung disease from two-dimensional images of chest CT scans. They trained a CNN using 19 public datasets, and then divided the 32 × 32 pixel size patches into 1 of 7 categories. Compared with the manual extraction method used previously, the CNN report is more accurate. . Coudray et al. [17] trained a CNN in 2017 using lung cell histopathology images obtained from The Cancer Genome Atlas (TCGA), and the network can accurately classify lung cell histopathological images as Adenocarcinoma, squamous cell carcinoma, and normal lung tissue; the area under curve (AUC) predicted by this model reached 0.97, which is slightly better than human pathologists. In addition, Coudray et al. [18] also trained a neural network to predict 10 common mutant genes in lung cancer and adenocarcinoma, and the accuracy of predicting mutant gene models was 0.733 to 0.856. In order to accurately describe the tumor and propose appropriate treatment methods, they further used deep learning technology to classify the pathological images of lung cancer tissues and predict the mutation status of frequently mutated genes. More than 1,600 lung histopathological images were obtained through TCGA. The image is divided into a training set, a validation set, and a test set, and then the image is segmented and sampled into an image of 512 × 512 pixel size and the Inception_v3 model is trained according to manual annotation. After training, the model can distinguish between cancer and normal areas, and once the cancer area is determined, the model can automatically identify adenocarcinoma and squamous cell carcinoma, predicting the mutation status of the most frequently mutated genes in lung adenocarcinoma; the final model distinguishes between tumor sections and normal The AUC of the slice was as high as 0.99, the AUC for recognizing adenocarcinoma and squamous cell carcinoma was 0.95, and serinethreonine kinase 11 (STK11) and epithelial growth factor receptor (EGFR) mutations were predicted. The AUCs of the genes were 0.82 and 0.86, indicating that mutations in these two genes may have specific macroscopic characteristics, and these characteristics can also be identified by training CNNs.

3.2. Breast Cancer

Breast cancer is one of the highest mortality cancers in the world, especially for women, and its early diagnosis can greatly increase the success rate of treatment. Therefore, it is necessary to analyze its histological image. In the diagnosis process, experts evaluate the whole and local breast tissues through full-slide images and microscope images. The complexity of a large amount of data and images makes this task time-consuming, and it is urgent to develop automatic detection and diagnostic tools. Recently, many scholars have achieved good results in the diagnosis of breast cancer using deep learning algorithms.

X-ray breast density is one of the predictors of breast cancer risk. Radiologists generally use four qualitative breast imaging and reporting data system (BI-RADS) breast density categories to assess breast density. However, it is difficult to accurately distinguish the breast density category of BI-RADS. Mohamed et al. [19] constructed and trained a CNN model based on the mammography images collected by their institution to accurately and quickly classify breast density, thereby clarifying the risk of breast cancer. Finally, the AUC of this model classification reached 0.988 2. The CAMELYON Series Challenges held in 2016 and 2017 are dedicated to evaluating new methods and existing algorithms for automatic detection and classification of breast cancer metastases in full slide images. Using the data provided by the organizer, Wang et al. [20] constructed and evaluated the performance of four mainstream deep learning models of GoogLeNet, AlexNet, VGG16, and FaceNet to detect and classify breast cancer metastasis, and used the test images to detect the trained model It was found that the AUC of the final models all reached 0.995, indicating that the application of deep learning technology can significantly improve the accuracy of pathological diagnosis. At the 2018 International Conference on Image Analysis and Recognition (ICIAR) BACH (ICIAR 2018 Grand Challenge on Breast Cancer Histology images) challenge, based on the 400 official fluorescence images (normal tissue provided by the contest) , Benign tumors, carcinoma in situ and invasive cancer each with 100 pictures), Golatkar et al. [21] put the Inception-v3 model into CNN to conduct a classification evaluation of breast cancer to evaluate the potential of deep learning to replace artificial detection of breast cancer, In the classification of 4 levels (normal, benign tumor, primary cancer, and invasive cancer), the accuracy of the deep learning algorithm reached 0.85, and in the classification of 2 levels (non-cancer and cancer), the accuracy reached 0.93. And the accuracy is excellent.

3.3. Diabetic retinopathy

Diabetic retinopathy is a major blinding disease that affects most patients with a history of more than 20 years of diabetes. Studies have shown that proper prevention and treatment can effectively reduce the incidence of diabetic retinopathy [22]. For young patients, early detection of the disease and active treatment are necessary.

Gargeya et al. [23] used deep learning to train and analyze 7 137 public fundus pictures obtained from diabetic patients to detect the presence or absence of diabetic retinopathy. It was found that the AUC detected by this deep learning model can reach 0.97, and the sensitivity and The specificity is 94% and 98% respectively; in order to test the robustness of the model, the research team conducted recognition predictions in the Messidor-2 and E-Ophtha public databases and found that the AUC of the model was 0.94 and 0.95, respectively, and The accuracy is high. Weng Ming et al. [24] studied and evaluated the feasibility of deep learning in diabetic retinopathy. They recruited a total of 186 diabetic patients (372 pictures) from January to July 2017, and manually labeled the collected data. The data included 42 normal pictures, 330 abnormal pictures (62 mildly non-proliferative) Diabetic retinopathy pictures, 55 moderate non-proliferative diabetic retinopathy pictures, 155 severe non-proliferative diabetic retinopathy pictures, 58 proliferative diabetic retinopathy pictures), the sensitivity and specificity of the final deep learning model diagnosis were 89% And 91%, significantly better than human experts.

3.4. Alzheimer disease (AD)

AD is a progressive, progressive, degenerative neurological disease with a common clinical symptom that patients fall into dementia in their later years. Due to the increasing cost of nursing care for AD, early accurate diagnosis is very important, and deep learning methods have made great contributions to the diagnosis of AD. Early AD diagnosis is based on artificially extracted brain image features for classification. These characteristics require that the main AD-related variants of the brain must be accurately acquired, such as brain volume, hippocampus, ventricular size, and cortical thickness, etc .; their acquisition methods are mainly medical imaging tools such as structural magnetic resonance imaging (sMRI), Functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). Hosseini-Asl et al. [25] proposed a three-dimensional convolutional neural network, which learns and automatically extracts and identifies AD features through 3D computeraided engineering (3D-CAE), obtains changes caused by AD, and further converts 3D -CAE pre-trained CNN for another dataset. The maximum pooling method is used to down-sample the feature map of each layer to reduce the size of the feature map and improve the model training efficiency. The constructed model is applied to the AD neuroimaging (Alzheimer disease neuroimaging initiative) data set. The model can achieve excellent results in two- and three-class assessments of AD, mild cognitive impairment, and healthy control groups. Performance, its accuracy rate reached 94.8% to 100.0%, achieved a high diagnostic accuracy rate, verified the feasibility of artificial intelligence technology in AD diagnosis, and promoted the development of artificial intelligence technology in the medical field. Since then, Sarraf and Tofighi [26] trained on AD's fMRI and sMRI data using the well-known LeNet-5 framework in CNN, and obtained 98.84% and 96.85% diagnostic accuracy rates, respectively. This is the first time that fMRI data has been used for Train a deep learning-based network model.

3.5. Other diseases

In addition to the diseases mentioned above, scholars have also begun to use various deep learning methods to diagnose other types of diseases. For example, Esteva et al. [27] built a deep learning model that can autonomously detect and classify skin cancer; Han et al. [28] The clinical image data set of a variety of skin diseases evaluates the deep learning algorithm. The algorithm model has a good diagnosis effect on basal cell carcinoma, squamous cell carcinoma, epithelial cell carcinoma and melanoma; Camps et al. [29] in 2017 Proposed the use of waist-wearable measurement units and deep learning algorithms to predict Parkinson's disease; Tsehay et al. [30] proposed the use of deep learning-based CNN architecture to identify prostate cancer. With the development of artificial intelligence technology and the active participation of physicians, disease diagnosis technology based on deep learning technology will certainly develop rapidly.

4. Summary and outlook

Deep learning has achieved good results in the field of disease diagnosis. Compared to traditional machine learning, the biggest advancement in deep learning is to use automatic feature extraction instead of manual feature extraction. Not only can it improve efficiency, but it can also be more easily obtained by automatic extraction. The high-level abstract mapping makes classification more accurate. However, deep learning also has the following limitations: (1) The current deep learning architectures or model methods used in disease diagnosis are similar. Most of them use CNN, RNN or other commonly used deep learning algorithms, or use several algorithms to integrate them. Training and diagnosing diseases; (2) The application of deep learning technology in disease diagnosis is still at the theoretical stage. There is still a long way to go before it can be used clinically. Develop a depth that can adapt to most imaging equipment in the market. Learning algorithms are the prerequisite for artificial intelligence medical treatment to enter the clinic; (3) Deep learning technology is a data-driven technology that is limited to the requirements of data volume. This method is mainly focused on the research of diseases with a relatively high incidence. In some rare cases Less research in the condition. At present, deep learning technology is in a period of rapid development. In the field of disease diagnosis, the advancement of hardware technology and the improvement of medical imaging technology will promote the continuous breakthrough of deep learning technology so that it can better serve the society.

In summary, with the continuous breakthrough of science and technology, artificial intelligence technology is expected to assist or replace humans in diagnosing diseases, but it is used as a collaborative means to reduce physicians' repeated and monotonous task burden and interference instead of replacing physicians. For the clinical application of deep learning technology, the most important thing is to develop a suitable workflow. With the innovation of artificial intelligence technology, the promotion of artificial intelligence technology in the field of disease diagnosis requires a large and complete labeled database, which is essential for training and evaluating deep learning networks, and also requires the active participation of physicians. In addition, in order to solve the problem of small amount of disease data, adversarial generative networks and reinforcement learning will also play a key role in the field of medical imaging.

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