Deep Learning and Neural Networks in Healthcare

Introduction to Deep Learning

1. Deep learning is a part of machine learning,
2. which is inspired by neurons in the human brain: there are tens of millions of neurons in the human brain, and there are more than 100,000 connections between them.
3. The deep learning method is called artificial neural network.
4. The neural network is composed of the input layer, hidden layer, and output layer.
5. Each layer is composed of several neurons, and the hidden layer may consist of many layers.
6. According to different task types, there are different numbers of neurons in the output layer of the neural networks. For example, there are three neurons in the

output layer in the three-classification problem, and each neuron represents the probability of belonging to a certain category.

- The training of the neural network depends on forward propagation algorithm and back-propagation algorithm.

- Forward propagation refers to the whole process of data propagation from the input layer to the output layer, where the neural network calculates intermediate variables of each neuron in turn. ● Back propagation refers to the parameter optimization process of the neural network. ● According to the intermediate variables calculated by forward propagation, the parameters of the neural network are updated by gradient descent

Fully Connected Neural Network

- As the name implies, a fully connected neural network means that the neurons in the layers of the neural networks are completely connected.
- The fully connected neural network consists of the input layer, the hidden layer, and the output layer.
- The input layer is responsible for receiving input data.

- The hidden layer is composed of many neural network layers for feature extraction. The output layer outputs the final prediction result.

Fundamentals of Deep Learning in Healthcare

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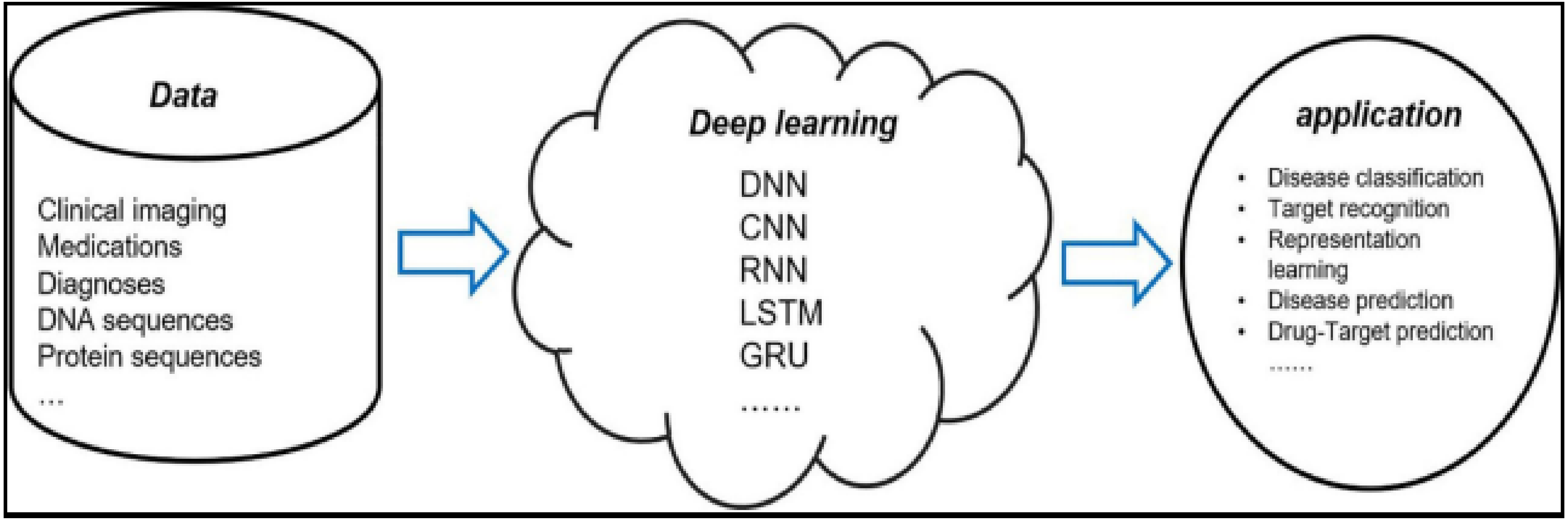


Convolutional Neural Networks (CNNs) in Healthcare

The convolutional neural network has made remarkable achievements in image recognition. The convolutional neural networks adopt the method of local connection and weight sharing, which reduces the complexity of the network and enables the network to directly use the image as input.

The convolution neural network has two important characteristics:

● first, the features learned from the image are translational and non deformable; ● second, the higher the convolution layer, the more abstract and complex the features extracted.

The convolution neural network is composed of the convolution layer, the pooling layer, and the fully connected layer.

● The convolution layer is composed of filters.
● Each filter is equivalent to a small window.
● These small windows move on the image to learn features from the image. ● Then, the learned features are subsampled by pooling operation to extract more representative features and improve the robustness and accuracy of the model.
● Finally, the fully connected layer outputs the prediction result. A convolutional neural network framework for lung pattern recognition

Recurrent Neural Networks (RNNs) in Healthcare,

Another common neural network is called the recurrent neural network, which is very suitable for processing sequential data, such as time-dependent data.

In the fully connected neural networks and the convolutional neural networks, their inputs are independent.

In contrast, in the recurrent neural network, the former input and the latter input are dependent and have sequence relation.

Just like analyzing a sentence, because the current word depends on the front and back words, it means that analyzing each independent word will not produce good results.

The structure of the recurrent neural network is shown in Figure 6. At time t, the input of the neural network is xt.

The output of the neural network is yt, which is calculated from the hidden layer state st that depends not only on the input xt at the current time t, but also on the state st–1 at the time t-1, which makes the recurrent neural network have memory, and the state of the last moment can affect the effectiveness of the current time.

The fourth deep learning framework is called the autoencoder, which is often used in unsupervised learning.

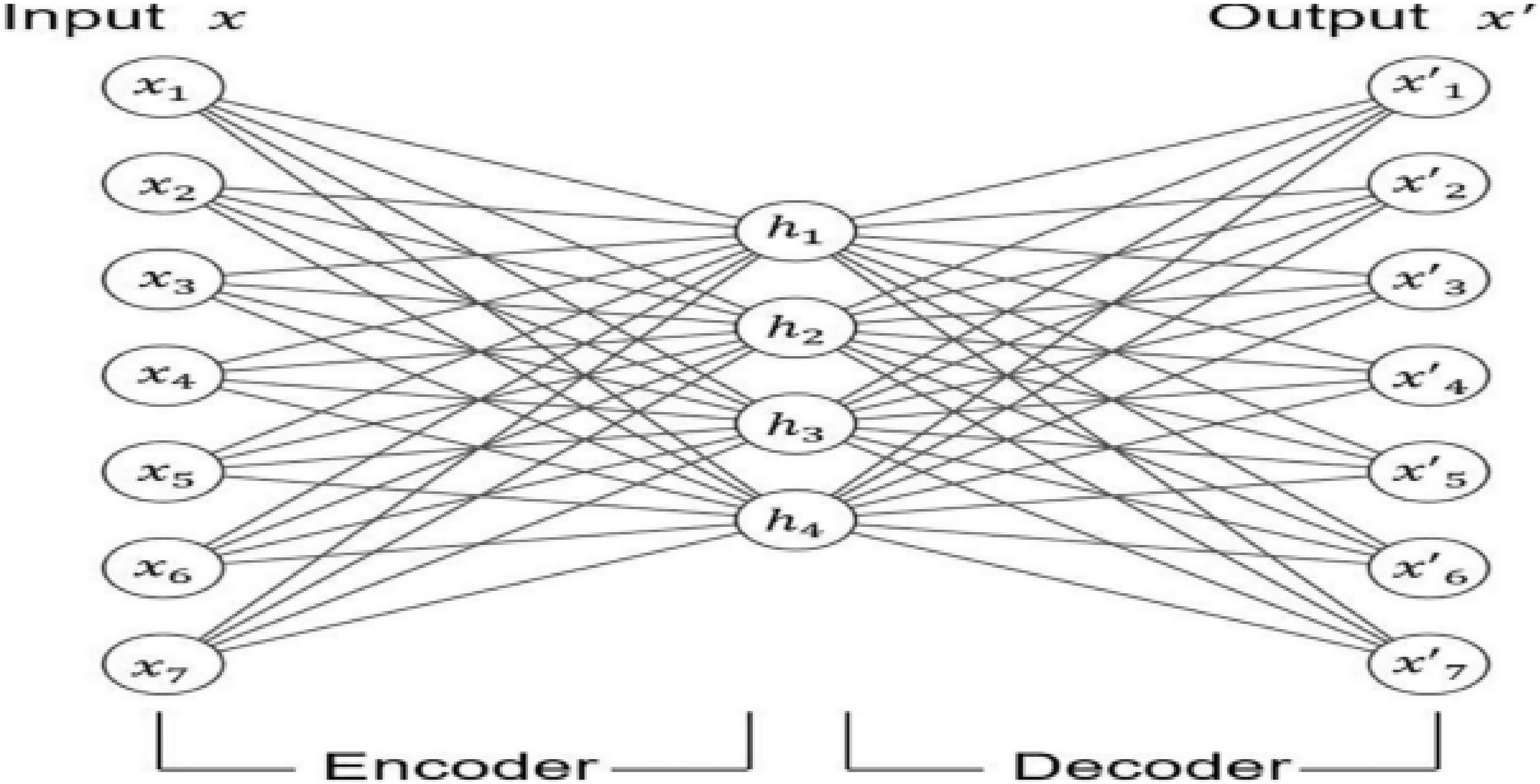
The autoencoder can be used to reduce dimension and learn feature. The structure of the autoencoder is shown in Figure.

The autoencoder is composed of an encoder and a decoder. Encoders and decoders can be any neural networks models.

In general, the number of neurons in the middle-hidden layer is less than that in the input layer and the output layer, which is useful for compressing data and learning effective features from data.

The number of neurons in the input layer and the output layer in the autoencoder is the same.

Specifically, the encoder reduces the dimension of the original data to get a new representation. Then, the decoder restores the input data through this new representation.



The deformation of autoencoder includes stacked autoencoder denoising autoencoder variational autoencoder, etc.

The stacked autoencoder is a hierarchical deep neural network structure composed of multilayer autoencoders.

It has deeper depth and stronger learning ability.

The denoising autoencoder adds random noise to the input data and then uses the data with noise to train the autoencoder.

The autoencoder trained in this way is stronger and has better antinoise ability.

Variational autoencoder adds some restrictions in the encoding process, which makes the generated vectors follow the standard normal distribution.

The encoding method makes the automatic encoder more effective.

Deep Belief Network

Deep belief network is a probability generation model based on the restricted Boltzmann machine, which establishes a joint probability distribution between data and label.

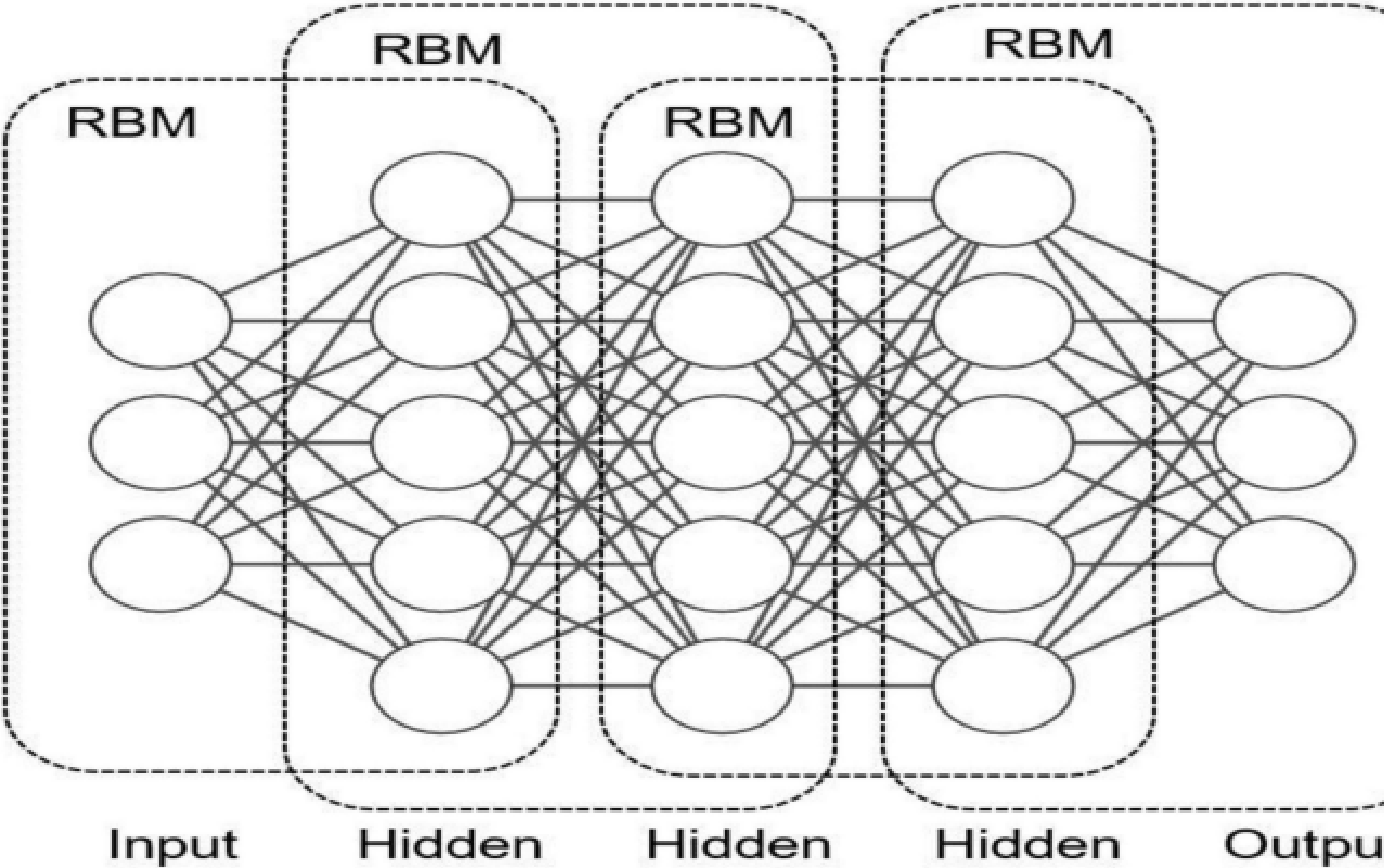
As shown in Figure , the restricted Boltzmann machine has only two layers:

- the visible layer composed of visible units
- the hidden layer composed of hidden units.

The visible layer is used for the input of training data, whereas the hidden layer is used as a feature detector. Each layer can be represented as a vector, each dimension by each neuron.

Neurons are independent of each other.
The advantage of this is that given the values of all the explicit elements, the values of each implicit element are independent of each other.

The trained restricted Boltzmann machine can extract the features of the explicit layer more accurately or restore the explicit layer according to the features represented by the implicit layer.


RBM
RBM
RBM
RBM
Input
Hidden
Hidden
Hidden
Outpu

Applications of DL and NN in Healthcare

Application of Deep Learning in Computational Medicine

Search Strategy and Selection Criteria

Specifically, for the application of deep learning in the clinical imaging, the combination of “deep learning” and “medical image” was used to search.

For the application of deep learning in the field of the electronic medical records, the combination of “deep learning” and “electronic health record” or “electronic medical record” was used to search.

For the research of deep learning in genomics, the combination of “deep learning” and “genomics” or “gene” was used to search.

For the research of deep learning in drug development, we used the combination of “deep learning” and “drug development” or “drug repositioning” or “drug repurposing.”

For the literature found, we also conducted manual screening to check whether the content of the article is about the application of deep learning in computational medicine

Medical Image

The medical image plays a key role in medical diagnosis and treatment providing an important basis for understanding a patient's disease and helping physicians make decisions.

As medical devices become more advanced, and the career of medical health is rapidly growing, more and more medical image data are generated, such as magnetic resonance imaging, computed tomography (CT), and so on.

Huge amounts of medical imaging data require much more time if experts analyzed the data alone. And the analysis of medical image data may produce erroneous or biased results due to varying degrees of experience, knowledge, and other factors that the experts themselves have.

Machine learning algorithms are, to some extent, able to assist specialists in automated analysis, but may not have the ability to process and achieve high accuracy when faced with such vast data and complex problems.

Deep learning has been successful in the field of image processing:

it carries out tasks such as image classification, target recognition, and target segmentation by analyzing images.

Therefore, the application of deep learning in the task of medical image analysis has become a trend in medical research in recent years.

Researchers used the artificial intelligence methods to help physicians make accurate diagnoses and decisions.

Many aspects are involved in these tasks, such as detecting retinopathy, bone age, skin cancer identification, etc.

Deep learning achieves expert level in these tasks.

The convolutional neural network is a powerful deep learning method.

The convolutional neural networks follow the principle of translational invariance and parameter sharing, which is very suitable for automatically extracting image features from the original image.
Figure shows a convolutional neural network structure for detecting pneumonia with chest X-ray images.

The convolution neural network is composed of the convolution layer, the pooling layer, and the fully connected layer.

First, the filtering window in a convolution layer will move step by step in the image to learn local features from the image.

Second, the pooling layer will sample the learned features to reduce the parameters and overfitting to improve the performance of the network. Finally, these features will output the final results through the fully connected layer.

In a convolution neural network, there are usually multiple convolution layers such that the convolution layer at the bottom can learn the local features in the image, and the high-level convolution layer can integrate these local features and learn the overall features.

Usually, for the same symptom, the location and shape of lesions or tumors are different in different pictures, making it very difficult to analyze.

The advantage of the convolutional neural network is that it can automatically learn local features from images and integrate them into global features.

Therefore, the convolutional neural network is very suitable for clinical image processing. Although the effect of deep learning on medical imaging is better than that of machine learning, and deep learning achieves human-level performance, there are still some limitations:

It is difficult to collect sufficient labeled data. Training a convolutional neural network with good performance requires a large number of parameters and samples. Sometimes it is difficult to collect sufficient and labeled training data. In addition to the differences in features, patterns, colors, values, and shapes in real medical image data, it is difficult to train a suitable network.

There are two ways to deal with the problem.

The first way is the strategy of data augmentation, which is a very powerful technology to reduce overfitting. It generates a new image through a series of transformations (such as translation, flipping, changing contrast) of the original images to expand the dataset, so that the model has better generalization ability.

The other is to use transfer learning, which uses a model trained in other training data in advance and then transfers the model to the medical image data to fine-tune the model, so as to get a model with strong generalization ability.

Convolution neural networks cannot explain the hierarchical and positional relationship between features extracted from images.

For example, neurons can capture the dataset feature, but neurons cannot well capture the spatial relationship between these features.

For this reason, the Capsules Network came in to existence. In this structure, the input and output of the capsules are not a scalar, but a vector instead of a traditional neuron.

The length of the vector means the probability of the existence of instances, while the value of the vector can represent the relationship between features.

At present, there are few types of research on the Capsules Network in medical imaging. The experimental results showed that Capsules Network could be trained with fewer data to obtain the same or better performance, and it was more robust for unbalanced class distribution. This result undoubtedly brought new ideas and directions to the application of deep learning in medical imaging.

Convolutional neural networks are suitable for processing two-dimensional image data, but the images produced by magnetic resonance imaging or CT image have the inherent three-dimensional structure.

If the convolutional neural network is used to process these medical images, key information will be lost.

Electronic Health Record

One-dimensional convolutional neural network, recurrent neural network, LSTM, GRU, and other neural networks in deep learning have been widely used in the natural language processing community and have achieved great success.

These networks are very suitable for processing sequence-related data, such as sentence, voice, time series, and so on. Similarly, natural language processing technology is also used in the field of computational medicine, which uses these neural networks to process electronic medical records.

Traditionally, machine learning is used to analyze electronic health record data. Usually, we need to extract the features manually and then input them into the model.

This feature extraction method often depends on the professional domain knowledge of the extractor, and it may be difficult to find the hidden relationship in the data.

Therefore, the quality of the model prediction results is affected by the quality of the manually extracted features. Moreover, this method causes huge human and time loss and affects the research efficiency.

Deep learning overcomes the disadvantage of traditional machine learning, which needs manual feature extraction.

However, because of the particularity and complexity of electronic health record data, there are some problems when using deep learning method to deal with them.

There are many clinical concepts in the electronic health records, which contain rich information.

These concepts are recorded in the form of coding, such as diagnostic coding, disease coding, drug coding, etc. Different medical ontologies formulate the rules of coding and the meanings they represent. At the same time, doctors record these clinical concepts in chronological order.

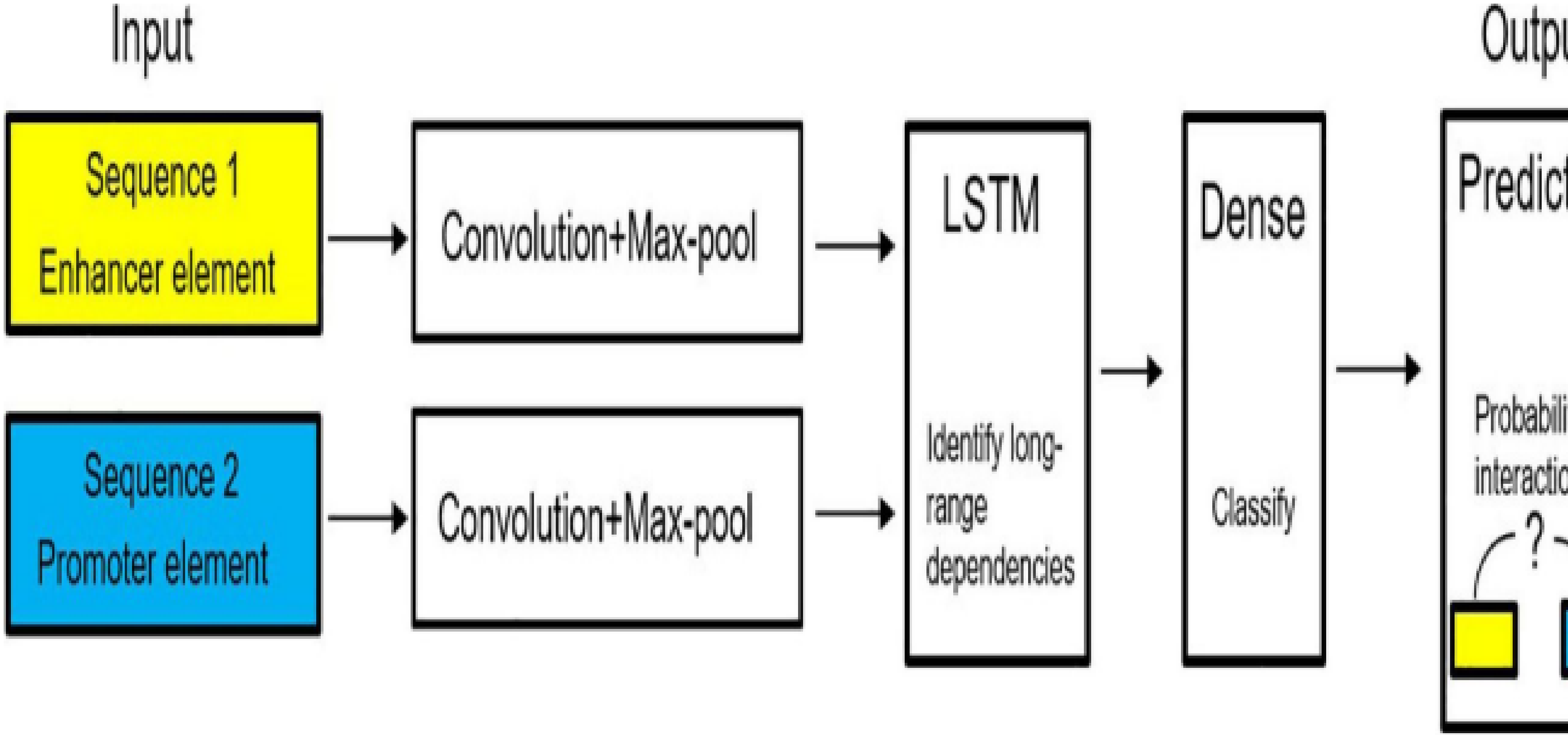
However, it is difficult to find and explore the relationship between these concepts simply by coding the patient's condition.

Genomics

Genomics studies the function, structure, editing, and performance of genes. Because of its powerful ability to process data and automatic feature extraction, many researchers have applied it to the field of genomics to discover deeper patterns.

Compared with traditional machine learning methods, the deep learning methods can extract the higher dimensional features, richer information, and more complex structure from biological data.

In recent years, deep learning has been widely used in genomics, such as gene expression, gene slicing, RNA measurement, and other tasks. Deep learning brings new methods to bioinformatics and helps to understand the principles of human diseases further.



Although deep learning has made impressive achievements in genomics, some problems still exist. The problems of deep learning in genomics are as follows:

(1) Deep learning training usually requires a large number of datasets, and the quality of these datasets is required to be high so that the deep learning model can learn distinguishing features and patterns from the data. However, data insufficiency still exists in genomics, so the model cannot learn from sufficient data and cannot provide key information for researchers or doctors.
(2) Biomedical data are complex and need professional domain knowledge to analyze. Unlike other fields, in genomics, the structure and function of the genome are a very complex model, which puts forward higher requirements for the interpretability of the deep learning model.

In recent years, the multimodal learning has become an attempt to improve the interpretability and accuracy of the model.

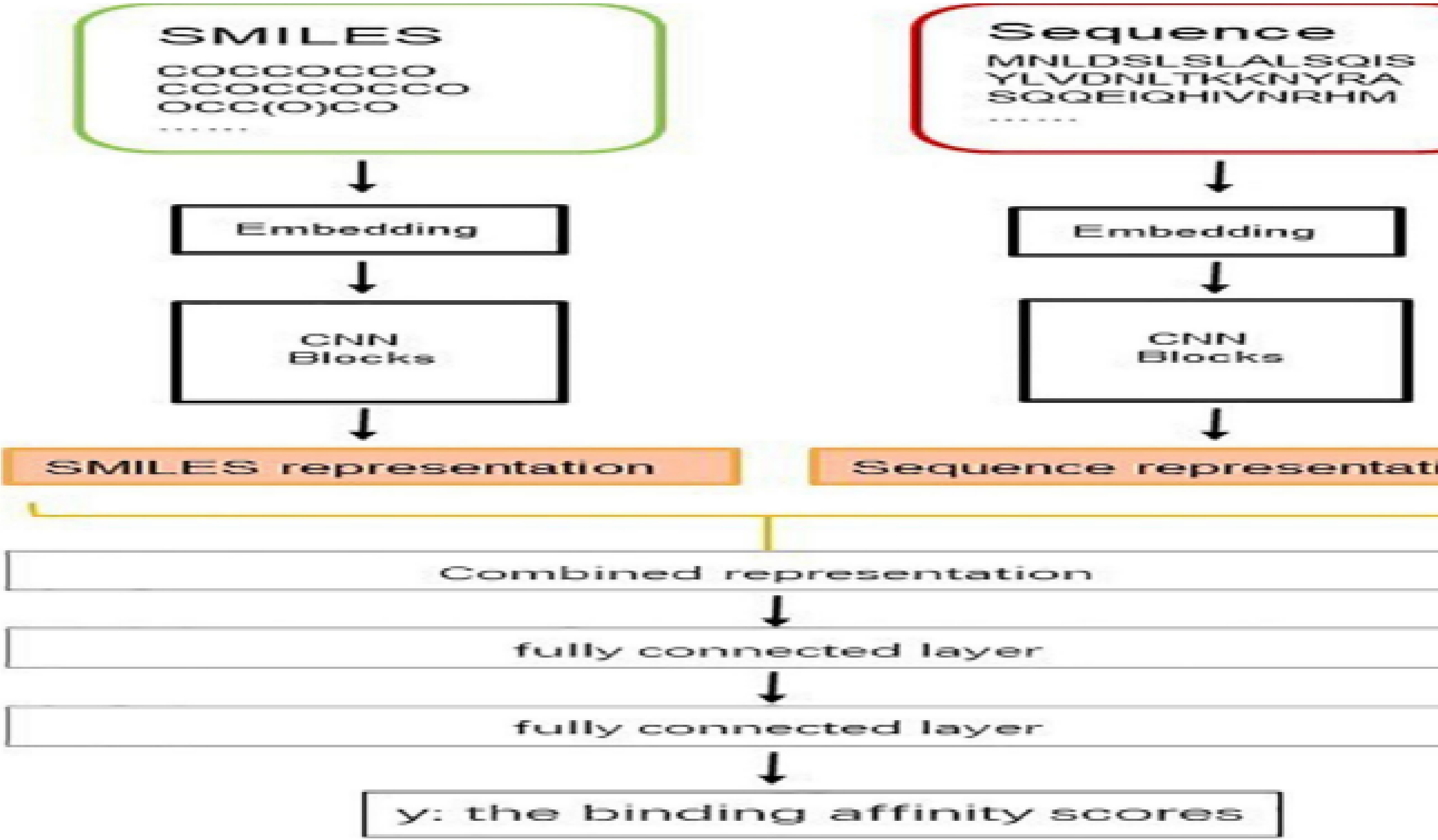
The so-called multimodal learning refers to the combination of data from different input sources and the establishment of different types of deep learning models for different types of data to make full use of the relationship and characteristics of different types of data, so the model can make a more comprehensive and accurate prediction.

Many researchers have begun to combine different types of data, such as gene sequences with other types of data such as electronic health records and medical imaging, to expand the field of knowledge and provide more insights for doctors.

Drug Development

In recent years, with the rapid growth of biomedical data, deep learning technology has become a new method in drug development. The application of deep learning in the field of drug development can help researchers effectively carry out drug development and disease treatment research and greatly promote the development of precision medicine.

Drug development is a complex process. Traditionally, it takes at least 10 years from the development of a new drug to its marketing, which is a very long and resource-consuming process. Traditional drug development is divided into two methods: one is the experimental method, which not only consumes time and efficiency but also causes huge cost; the other is the computational method, which can save time and reduce loss.



Deep learning has broad prospects in drug development, limitations still exist:

(1) It is known that deep learning requires a lot of labeled data. But in the field of drug development, the labeled data are limited. At present, many researchers use semi supervised learning or unsupervised learning to find key information from unlabeled biomedical data. However, even if semi supervised learning or unsupervised learning is used, it is difficult to find useful information in these unlabeled data.

(2) For deep learning, it is difficult to scientifically explain the reasons for making predictions because the occurrence and process of disease are a very complex biomedical field. Deep learning is considered as a "black box" method. If deep learning cannot provide a good explanation, it will be difficult for doctors to believe the prediction results given by deep learning, so they cannot make decisions. It is possible to integrate other types of data and information into drug development to solve the problem of model interpretability.

References:

https://www.frontiersin.org/articles/10.3389/fgene.2021.607471/full