# TİBB VƏ ƏCZAÇILIQ ELMLƏRİ

# MEDICAL AND PHARMACEUTICAL SCIENCES

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## APPLICATION OF DEEP LEARNING IN MEDICAL IMAGING

### Abstract

Medical imaging technology plays an important role in the detection, diagnosis and treatment of diseases. Due to the instability of human expert experience, machine learning technology is expected to assist researchers and physicians to improve the accuracy of imaging diagnosis and reduce the imbalance of medical resources. This article systematically summarizes some methods of deep learning technology, introduces the application research of deep learning technology in medical imaging, and discusses the limitations of deep learning technology in medical imaging. There has been a long-term traditional research in computer-aided detection systems, namely automatic detection of lesions, which can improve detection accuracy or reduce reading time for human experts.

*Keywords: artificial intelligence, deep learning, medical imaging, big data, method*

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### Dərin öyrənmənin tibbi görüntülərdə tətbiqi

### Xülasə

Tibbi görüntüləmə texnologiyası xəstəliklərin aşkarlanması, diaqnozu və müalicəsində mühüm rol oynayır. İnsan mütəxəssis təcrübəsinin qeyri-sabitliyi səbəbindən maşın öyrənmə texnologiyasının tədqiqatçılara və həkimlərə görüntü diaqnozunun dəqiqliyini artırmaq və tibbi qaynaqların balanssızlığını azaltmaq üçün kömək etməsi gözlənilir. Bu məqalə sistematik olaraq bəzi dərin öyrənmə texnologiyasının metodlarını ümumiləşdirir, dərindən öyrənmə texnologiyasının tibbi görüntüləmə tətbiqetmə tədqiqatını təqdim edir və dərindən öyrənmədə dərin öyrənmə texnologiyasının məhdudiyyətlərindən bəhs edir. Kompüter dəstəkli aşkarlama sistemlərində, yəni lezyonların avtomatik aşkarlanmasında uzunmüddətli ənənəvi tədqiqat aparılmışdır ki, bu da aşkarlama dəqiqliyini yaxşılaşdıra və ya insan ekspertləri üçün oxu vaxtını azalda bilər.

*Açar sözlər: süni zəka, dərin öyrənmə, tibbi görüntüləmə, böyük məlumatlar, metod*

### Introduction

In recent decades, medical imaging technologies such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) ultrasound, X-rays, etc. Detection, diagnosis and treatment play an important role (Brody, 2013). Medical image interpretation is mainly performed by radiologists and clinicians. However, the physician's experience has great instability, so it is hoped that it can be improved through machine learning technology, so that physicians can benefit from computer assistance.

In the process of medical image analysis applying machine learning, meaningful feature extraction is the core of successful completion of the target task. Traditionally or task-related features are mostly based on human expert knowledge in the target domain. Therefore, non-experts using machine learning techniques to conduct research are challenging, and deep learning techniques can help remove this obstacle by absorbing feature engineering steps in the learning process (Schmidhuber, 2015: 85-117). That is to say, to manually extract features, if some preprocessing is required, and then input data and learning targets, deep learning technology can find solutions through self-learning (Lecun, Bengio, Hinton, 2015: 436-444). Therefore, the burden of feature

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extraction engineering has been shifted from people to computers, enabling non-machine learning experts to effectively use deep learning techniquesfor research or applications in medical imaging and other fields.

The deep success of deep learning technology is due to the advancement of the computing power of the central processing unit (CPU) and graphics processing unit (GPU), the acquisition of large amounts of data, and the development of learning algorithms (Hinton, Salakhutdinov, 2006: 504-507). From a technical perspective, deep learning can be seen as improving traditional artificial neural networks by building more than two layers of networks. Studies have shown that hierarchical feature representations are found in deep neural networks, which can extract high- level features from low-level features Hinton, Salakhutdinov, 2006: 504-507. Due to the excellent characteristics of learning layered features from data, deep learning has achieved excellent performance in various artificial intelligence applications (Karpathy, Fei-fei, 2017: 664-676; Silver, Huang, Maddison, Guez, Sifre, Van Den, Driessche, 2016: 484-489). Especially the huge progress in the field of computer vision has inspired its application in medical image analysis, such as image segmentation (Zhang, Li, Deng, Wang, Lin, Ji, 2015: 214-224; Kleesiek, Urban, Hubert, Schwarz, Maier-Hein, Bendszus, 2016: 460-469), image registration (Wu, Kim, Wang, Munsell, Shen, 2016: 1505-1516), image fusion (Suk, Lee, Shen, 2014: 569-582), image annotation (Jiu, Sahbi, 2017), auxiliary diagnosis and prognosis (Suk, Lee, Shen, 2015: 841-859; Suk, Wee, Lee, Shen, 2016: 292-307) lesion detection (Van, Tulder, De Bruijne, 2016: 1262-1272; Dou, Chen, Yu, Zhao, Qin, Wang, 2016: 1182-1195), and microscopic imaging analysis (Cireshan, Giusti, Gambardella, Schmidhuber, 2013: 411-418). This article gives a brief overview of several deep learning methods, then introduces the related applications of deep learning techniques in medical imaging, and discusses the limitations of deep learning techniques in medical imaging.

## Overview of Deep Learning Methods

Deep learning is a type of machine learning algorithm that uses multiple cascaded non-linear processing units to perform feature extraction and transformation. Each successive layer uses the output of the previous layer as input; learning (such as classification) and / or unsupervised (such as pattern analysis) behavior in a monitored environment; learning is a multi-level representation corresponding to different levels of abstraction; concepts The formation of the hierarchical structure; back-propagation training and gradient descent. The levels of deep learning include the hidden layers of artificial neural networks and a set of propositional formulas. They may also include latent variables in deep generative models, such as nodes in deep trust networks and deep Boltzmann machines. Existing deep learning technologies include feedforward neural networks (Bebis, Georgiopoulos, 1994: 27-31), deep belief networks (Hinton, 2011: 267-269), deep Boltzmann machines (Salakhutdinov, Hinton, 2009: 1967-2006), deep convolutional neural networks (Shen, Wu. Suk, 2017: 221-248), and so on.

## Feedforward Neural Network

Feedforward neural network (Figure 1) is the simplest kind of neural network (Bebis, Georgiopoulos, 1994: 27-31). Its neurons are arranged in layers. Each neuron only receives the output of the neurons connected to the previous layer and outputs it to the next layer. There is no feedback between layers. The research of feedforward neural network started in the 1960s, and its theoretical research and practical application have reached the mature stage. For the structure design of feedforward neural network, direct training method, pruning method and growth method are generally used. The direct training method is to design a practical network. The pruning method requires starting from a sufficiently large initial network, so the entire process is complicated and long. The training of the learning network is only the steepest descent optimization process, and for a very large initial network, it cannot guarantee that it will converge to a global optimal solution or a sufficiently good local Optimal solution, therefore, pruning is not always effective. The growth method is more in line with the process of people's knowledge and accumulation of knowledge. It has the characteristics of self-organization and more development potential.
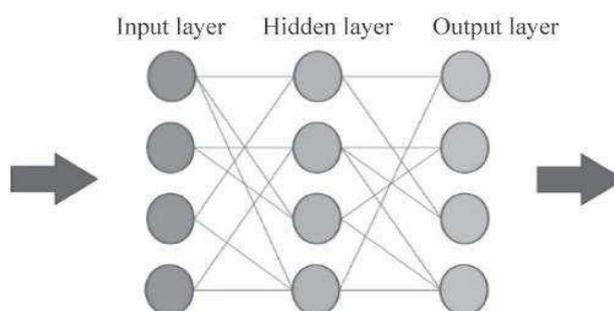


**Fig.1.** Schematic diagram of feedforward neural network structure

Feedforward neural networks have a simple structure and are widely used. They can approximate arbitrary continuous functions and square integrable functions with arbitrary precision. They can also accurately implement arbitrary limited training sample sets. From a system point of view, feedforward neural networks are a kind of static non-linear mapping, and complex non-linear processing capabilities can be obtained through composite mapping of simple non-linear processing units. From a computational point of view, most feedforward neural networks are learning networks, Its classification and pattern recognition ability is generally stronger than the feedback network.

## Deep Belief Network

Deep belief networks (Figure 2) can be used both for unsupervised learning, similar to autoencoders, and for supervised learning, that is, as classifiers. When used for unsupervised learning, the goal is to preserve the characteristics of the original features as much as possible while reducing the dimensionality of the features (Hinton, 2011: 267-269). When used for supervised learning, the goal is to minimize the classification error rate. The neuron component of a deep belief network is a restricted Boltzmann machine. Several restricted Boltzmann machines are connected in series to form a deep belief network. The hidden layer of the previous restricted

Boltzmann machine is the visible layer of the next restricted Boltzmann machine. The output of one restricted Boltzmann machine is the input of the next restricted Boltzmann machine. During the training process, the restricted Boltzmann machine of the previous layer needs to be fully trained before the restricted Boltzmann machine of the current layer can be trained until the last layer.
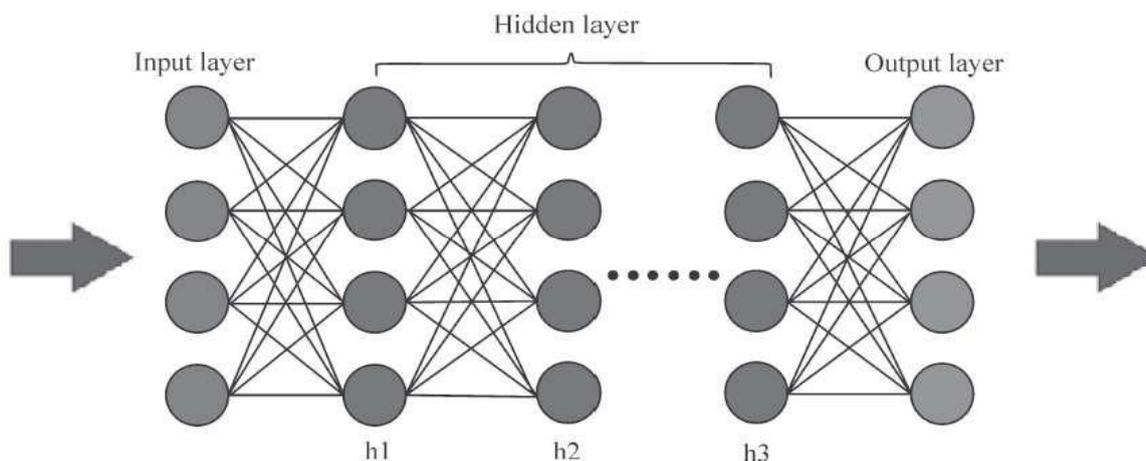


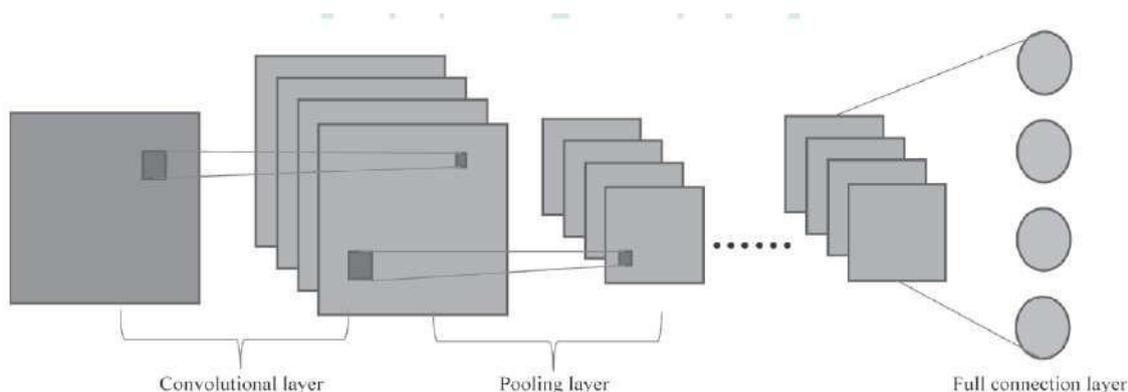**Fig.2.** Schematic diagram of deep confidence network structure

### 1.1. Deep Boltzmann Machine

The deep model formed by all restricted Boltzmann machines is the deep Boltzmann machine (Salakhutdinov, Hinton, 2009: 1967-2006). If the part near the input layer is replaced with a Bayesian confidence network, that is, a directed graph model, and the part far from the input layer still uses a restricted Boltzmann machine, a deep confidence network is formed.

### 1.2. Deep Convolutional Neural Networks

Convolutional neural network is a kind of feed-forward neural network. The neurons formed by the convolution kernel can respond to the surrounding cells in a part of the coverage and have excellent performance for image processing (Krizhevsky, Sutskever, Hinton, 2012: 1097-1105). It includes a convolution layer and a pooling layer. The basic structure of a general convolutional neural network includes two layers: (1) a feature extraction layer, each neuron's input is connected to the local area of the previous layer, and the local feature is extracted. The positional relationship between features is also determined; (2) feature map layer, each calculation layer of the network is composed of multiple feature maps, each feature map is a plane, and all neurons on the plane are equally weighted. The feature map structure uses a function with a small influence function kernel (such as sigmod) as the activation function of the convolutional neural network to make the feature map displacement-invariant. In addition, the shared weights of all neurons on a mapping surface reduce the number of free parameters of the network. Each convolutional layer in the convolutional neural network is followed by a calculation layer for local averaging and secondary extraction. This unique secondary feature extraction structure

reduces the feature resolution. A multi-layer convolutional neural network is used as a hidden layer to form a deep convolutional neural network (Figure 3).



**Fig.3.** Schematic diagram of deep convolutional neural network structure

## 2. Application of deep learning technology in medical imaging

### 2.1. Classification

Image or detection classification is one of the first application areas of deep learning, which has made a significant contribution to medical image analysis. In classification tests, one or more images (tests) are often used as inputs, and diagnostic variables (such as the presence or absence of disease) are used as outputs. Each diagnostic test in this environment is an example. The data set is usually smaller than the size of computer vision (such as hundreds of samples), which has strongly promoted the popularity of migration learning for this application.

The essence of transfer learning is to use a pre-trained network (usually in natural images) to try to focus on the needs of large data sets (perception) trained on large networks. Two migrations of learning strategies, namely using a pre-trained network as a feature extractor and pre-adjusting or fine-tuning through a medical data network have been widely used. Extensive research uses architecture to take advantage of the unique attributes of medical data. Hosseini-Asl et al. (Hosseini-Asl, Ghazal, Mahmoud, Aslantas, Shalaby, Casanova, 2018: 584-596) used three-dimensional convolutional neural networks instead of two-dimensional convolutional neural networks to classify patients with Alzheimer's disease; Kawahara et al. (Hosseini-Asl, Ghazal, Mahmoud, Aslantas, Shalaby, Casanova, 2018: 1038-1049) applied to brain connection diagrams for diffusion tensor imaging of magnetic resonance Similar to the classification of convolutional neural network structure, they developed several new layers to form a unique network structure, and then used this network structure to predict the development of the brain. The results show that the new network structure is superior to the evaluation of cognitive and athletic performance. Existing methods.

### 2.2. Detection

Detection of objects or lesions of interest in the image is a key part of the diagnosis and one of the most intensive tasks for clinicians. General tasks include the location and recognition of small lesions in the complete image space. There has been a long-term traditional research in computer-aided detection systems, namely automatic detection of lesions, which can improve detection accuracy or reduce reading time for human experts.

Most deep learning object detection systems still use neural networks to classify pixels and obtain candidates in some form of post-processing. For example, Teramoto et al. (Teramoto, Fujita, Yamamuro, Tamaki, 2016: 2821-2827) used multi-stream convolutional neural network detection to integrate CT and PET data. Dou et al. (Dou, Chen, Yu, Qin, Heng, 2017: 1558-1568) used a three-dimensional convolutional neural network to detect microbleeds in MRI images.

The difference between target detection and target classification is obvious, because each pixel is classified, and the class balance has a large bias for non-object classes in the training settings. In addition, most non-physical samples are vulnerable to discrimination, preventing the concentration of deep learning methods in challenging samples. Van Grinsven et al. (Van Grinsven, Van Ginneken, Hoyng, Theelen, Sanchez, 2016: 1273-1284) proposed selective data sampling, in which misclassified samples are often fed back to the network to focus on challenging areas in the retinal image; then, sliding-window approach is used to perform result-level redundant calculations for each pixel Command classification. The study of Wolterink et al. (Wolterink, Leiner, De Vos, Van Hamersvel, Viergever, Isgum, 2016: 123-136) is also an important aspect of object detection methods.

### 2.3. Segmentation

Segmentation of organs and other substructures in medical images is the basis for quantitative analysis of clinical parameters related to volume and shape, which is an important first step in computer-aided detection. Segmentation tasks are usually defined as determining a set of pixels that form the outline or interior of an object of interest. Segmentation is the most common topic of in-depth research in medical imaging and the most widely used method, including the application of deep learning methods.

Dan et al. (Cireshan, Giusti, Gambardella, Schmidhuber, 2012: 2852-2860) first used deep learning algorithms for medical image segmentation. They used pixel-by-pixel segmentation in electron microscope images to segment images in sliding windows.

The U-net method published by Ronneberger et al. (Ronneberger, Fischer, Brox, 2015: 234-241) is one of the most famous segmentation methods. The characteristics of the two main structures of U-net are the combination of equal upsampling and downsampling layers, while the network combines the so-called jump relative convolution and deconvolution.

From the training perspective, the entire image can be processed forward. Thereby directly mapped in the segmentation. This method allows us to utilize block-based cellular neural networks while taking into account the integrity of the image. Research by Çiçek et al. (Cicek, Abdulkadir, Lienkamp, Brox, Ronneberger, 2016) showed that U-net can be used for 3D segmentation. In addition, there are other U-net-based segmentation studies, such as Milletari et al. (Milletari, Navab, Ahmadi, 2016) improved V-net based on U-net; Drozdzal et al. (Drozdzal, Vorontsov, Chartrand, Kadoury, Pal, 2016) studied the short-range residual network to modify the long-range U-net structure. These specific segmentation methods help to obtaingood segmentation results and train neural networks.

### 2.4. Registration

Medical image registration (ie, spatial alignment) is a common image analysis task in which coordinate transformations are calculated from one image to another. This is usually an optimized iterative framework where a particular type of (non) parametric transformation assumptions and RICs (such as the L2 norm) are predefined. The currently widely used strategy is a deep regression network using two image-driven iterative optimization strategies for deep learning networks for similarity measures and direct regression parameters.

There have been some attempts to optimize the registration algorithm through deep learning techniques (Wu, Kim, Wang, Gao, Liao, Shen, 2013: 649-656; 35). Cheng et al. (Cheng, Zhang, Zheng, 2016) used two stacked autoencoders to evaluate the local similarity between CT and MRI images of the head. This autoencoder uses vectorization of CT and MRI images to repair and reconstruct through 4 layers. After pre-training the unsupervised patch reconstruction network, they are fine- tuned using 2 prediction layers and stacked on the 3rd level of the SAE. These prediction layers are used to determine whether the two patches are similar (type 1) or dissimilar (type 2). Simonovsky et al. (Simonovsky, Gutierrez-Becker, Mateus, Navab, Komodakis, 2017) used a similar strategy to estimate the similarity between two images in different ways; at the same time, they also proposed a method that directly uses the derivative of this measure to optimize the conversion parameters, which are derived from the network Separated by itself. Miao et al. (Miao, Wang, Liao, 2016: 1352-1363) used a convolutional neural network to evaluate the position of the implant through a three-dimensional model of two-dimensional X-ray registration, and found that the registration success rate is higher than that of traditional registration methods based on pure intensity. Yang et al. (Yang, Kwitt, Niethammer, 2016: 48-57) used the oasis dataset of current / current registration in brain MRI images. They are based on large deformation differential homeomorphic mapping (LDDMM) registration method.

Unlike the research on classification and segmentation, the academic community does not seem to have determined the best way to integrate deep learning technology in the registration method. There are not many related studies and the existing research methods are not the same. Therefore, suggesting what is the most promising method seems not appropriate, and further research on medical image registration is needed in the future.

The field of medical image analysis has begun to pay attention to the development of deep learning technology on these key issues. However, the transition from a human-based system to a system that learns features from data is gradual. Shen et al. (Shen, Wu., Suk, 2017: 221-228) reviewed the application of deep learning in medical image analysis. Although they have done a lot of work, it seems flawed to understand from a computer perspective only. In recent years, new developments in deep learning technology have provided new ideas for medical image analysis. It only allows the discovery of morphology and / or texture patterns in images from data. Although deep learning technology appears to have reached state-of-the-art performance in many medical applications research, few results show that it can surpass traditional methods. At the same time, the current research in deep learning in the field of medical image analysis is still based on technology, and the evaluation indicators used are also evaluation indicators in the computer field. For any medical application, we would like to see the evaluation of related technologies in

accordance with medical rules, such as multi- center, randomized, controlled research methods to prove that this technology has more significant advantages than previous technologies. In addition, an important challenge in medical image training is that the number of training samples for most deep models is related to the number of learning parameters.

Therefore, how to reduce overfitting has always been a problem. When the training results of deep learning are sent to a new central application, the model needs transfer learning to maintain performance. This limitation undoubtedly leads to low reproducibility in clinical applications.

The stability and repeatability are the basic prerequisites for the technology to be widely used in clinical practice. Therefore, researchers in the field of deep learning should pay attention to how to ensure the repeatability of the algorithm in prospective samples.

In addition, the quality of the data used for training is another cause of catastrophic results. The problem of random noise is easier to solve, and it can improve performance through certain parameter settings (technically referred to as smooth or soft labels for labels). Structural noise is different, it adds a really different signal and will really affect model learning. Rolnick et al. (Rolnick, Veit, Belongie, Shavit, 2017) proved that the structure noise of the label will cause the performance of training results to be severely degraded. The problem is more serious when the noise comes from the same source as the actual data, because the model will confuse the class, and the black box problem of current deep learning methods will be infinitely amplified.

In addition to these technical issues, the theoretical obstacles seem more troublesome. Current deep learning methods do not have causal logic, they are only correlation calculations. These methods may have inherent limitations on the cognitive tasks they can perform (Pearl, 2017). The value of resources required to achieve our desired performance goals must also be carefully evaluated to avoid falling into the trap of non- polynomial time issues.

## Conclusion

In summary, deep learning technology brings new methods to the most important feature extraction of machine learning. If deep learning technology can perform well on all problems, it will bring great help to medical image analysis and processing.

However, deep learning technology is not the ultimate algorithm, it is just a representative of the connected school in several schools of artificial intelligence, and its performance limit needs to be reasonably evaluated. Deep learning relies too much on high-quality big data, and its economic effects may not be appropriate for medical images. It is necessary to be very careful about the application of deep learning technology to the expansion of the application field, and relevant technologies should be adopted in appropriate use scenarios to avoid falling into the trap.

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