

Convolutional neural networks, a model for deep learning in diagnostic imaging. A topic review

Redes neuronales convolucionales: un modelo de *Deep Learning* en imágenes diagnósticas: revisión de tema

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Summary

Advances in artificial intelligence have impacted several areas of everyday life, as well as in the area of medicine. Due to the rapid application of deep learning in biomedical data, radiological and nuclear imaging has begun to adopt this technique. Deep learning is expected to have an effect on the process of image acquisition and interpretation, as well as on decision making. This review first provides an overview of the basic concepts and operation of convolutional neural networks, as well as current insights into the medical application focused on diagnostic imaging.

Resumen

Los avances en la inteligencia artificial han repercutido en varios espacios de la vida cotidiana, así como en la medicina. En vista de la rápida aplicación del aprendizaje profundo —conocido como *Deep Learning*— en los datos biomédicos, las imágenes radiológicas han comenzado a adoptar esta técnica. En lo que respecta, se espera que el aprendizaje profundo tenga un efecto en el proceso de adquisición e interpretación de imágenes, así como en la toma de decisiones. Esta revisión ofrece en primer lugar una descripción general del funcionamiento de las redes neuronales convolucionales, los conceptos básicos de estas, y las percepciones actuales en la aplicación médica centrada en imágenes diagnósticas.

Abbreviations: artificial intelligence (AI); deep learning (DL); convolutional neural networks (CNN); ImageNet large-scale visual recognition competence (ILSVRC); computed axial tomography (CAT); reduction layer (max pooling); dense layers (fully connected). (TAC); capa de reducción (*max pooling*); capas densas (*fully connected*).

Introduction

The concept of artificial intelligence (AI) has been developing since the 1950s, although technological limitations in the early years meant low performance compared to humans. Today, with the rapid progression of algorithm design, the growth of digital data sets, and the development of computational capability, AI has the potential to outperform humans in many tasks. Consequently, its potential exploration in the last ten years has increased in the medical field, especially in diagnostic imaging.

Deep learning, known as Deep Learning (DL), is considered by many to be an integral part of the fourth revolution (1). It investigates the use of artificial neural networks with an algorithm inspired by the structure and function of the human brain, by recognizing or categorizing hierarchical images of data distributed in multiple layers composed of simple and nonlinear modules, thus performing data transformation for dis-

crimination. Convolutional Neural Networks (CNNs) are the most important DL model at present (2).

CNNs have their origins in the neocognitron proposed by Fukushima et al. (3), whose idea was based on the biology of human primary visual cortex recognition investigated by Hubel and Wiesel (4). These CNNs consist of multiple artificial neurons (Figure 1). The rise in popularity of CNNs was secondary to the victory obtained in the ImageNet large-scale visual recognition competition (ILSVRC) in 2012 (5). At this event, Krizhevsky and Hinton (5) developed a CNN called AlexNet, which outperformed other competing machine learning techniques. Today, that CNN is considered one of the leading influencers in image analysis (6, 7). Since then, many image recognition and classification models have been developed based on this DL model.

Initially, the development of DL was slow due to the fact that medical data were not well structured and

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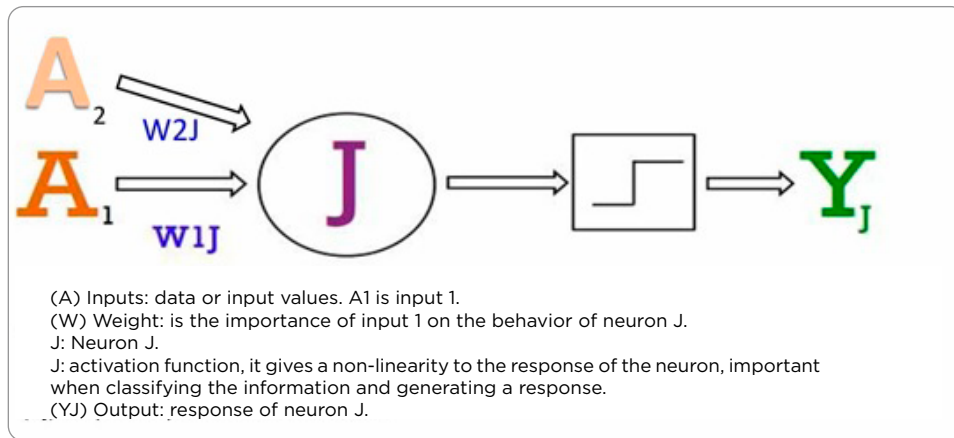


Figure 1. General scheme of an artificial neuron.

Source: own elaboration.

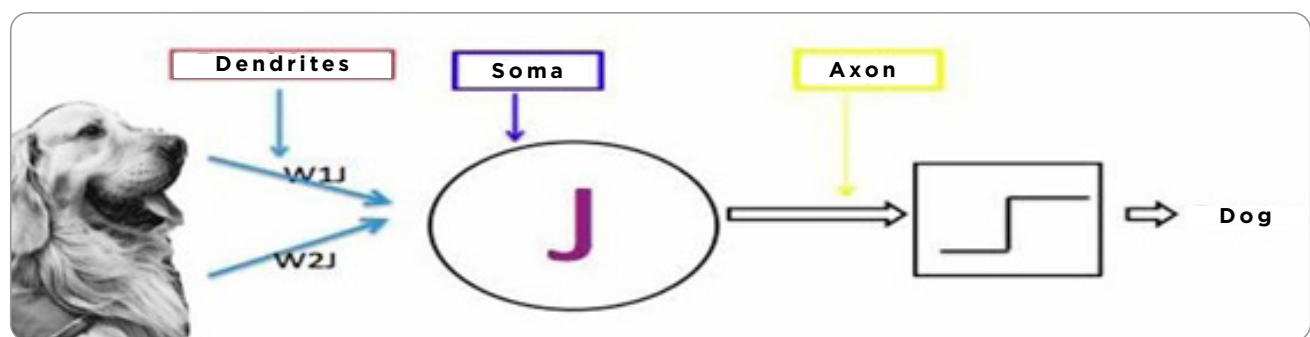


Figure 2. Artificial neuron. The basis of artificial neural networks is inspired by the biology of neurons and their connections. We can see what could be called “artificial neuron” and how it tries to follow the same architecture of a biological neuron.

Source: own elaboration.

labeled; however, the number of reports on the application of this model in clinical data has increased rapidly in recent years (8). Its current application includes the segmentation and classification of pathological processes. Medical research studies using CNN have been developed in multiple fields, such as in the detection of diabetic retinopathy (9), for the classification of skin lesions (10) or for the detection of lymph node metastases (11). In radiology, countless studies have been published with applications of CNN (6, 12) ranging from the detection of pulmonary nodules using chest X-rays (13) or computed axial tomography (CT) (14), classification of pulmonary nodules (15), detection and classification of masses in mammography (16, 17) and the application in cardiology and cardiac imaging (18).

The aim of this article is to clarify the order of the basic concepts of CNNs, in such a way that it allows an approach to the subject and can be a guide for those who wish to go deeper into the subject. A review of the literature was carried out, providing the most relevant definitions and the application of AI in the activity of the radiologist and nuclear physician in order to support clinical decisions in the near future.

1. Function of a Convolutional Neural Network

CNNs applied to diagnostic imaging seek to act in a manner very similar to the primary visual cortex of the human brain. Humans

classify and differentiate perfectly between multiple objects, given the ability to distinguish various features, such as color, edges, curves, shadows; that is, they focus on everything that allows them to distinguish or classify each object individually. For that reason, many of these systems attempt to mimic the functioning of neurons in the visual cortex (4, 19) (Figure 2).

CNNs operate on both 2D and 3D images and are typically made up of three layers: convolution layer, max pooling layer and fully connected layers (Figure 3), of which the first two carry out a feature extraction phase, while the latter two (fully connected) are in charge of performing the classification phase (20).

The first layers allow the CNN to perform a feature extraction phase, which acts in a similar way to the human brain when searching for those types of features that define an object. In the classification phase or the regression phase that is performed on the dense layers, all the features already extracted are related and a classification is obtained directly (20). For example, a CNN is created and trained to detect dogs. The first phase (convolution and max pooling) extracts the main features of a dog-the coat, the color, the shape the dog has. The second phase (fully connected) uses all the extracted features and can tell whether what is in the image is a dog or not. CNNs establish relationships between the different pixels of an image, looking for relationships in it, and that allows them to have a much more general context with spatial coherence.

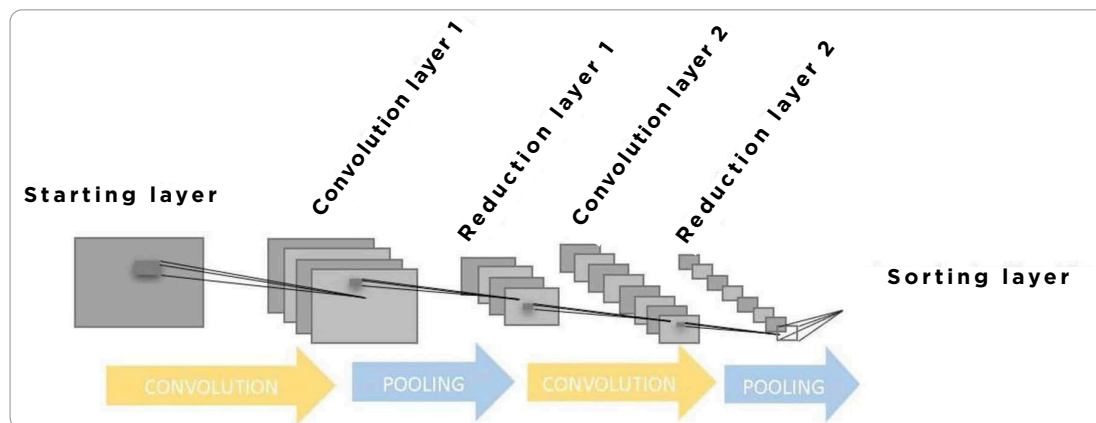


Figure 3. Architecture of a convolutional neural network. Starting layer (input image).

Source: own elaboration.

2. Key concepts of neural networks

2.1. Pixels and neural networks

Pixel: A single point or small square containing color, which can be white, black or shades of gray in the case of diagnostic images, and is part of a digital image (Figure 4) (20).

Kernel: Known as feature detector, filter or “property detector”, it is a matrix of numbers used to focus, blur, record, detect edges and image features (20).

Preprocessing: A digital image is a matrix stored in the computer where, in the case of grayscale images (radiological images), each pixel is represented by a value ranging from 0 (dark shades) to 255 (light or bright shades). The normalization of the data refers to the division of the pixel value into 255. This transformation assigns pixel values between 0 and 1 (21), which reduces the computational load and generates a better neural network with greater learning agility, which will be reflected positively in the image predictions (Figure 5).

3. Operation of the CNN

3.1. Convolution layers

What convolution does is that through a filter (kernel) that is applied to the image, it allows to extract certain features. So, if you have for an image a filter that allows to detect edges, what you will see in the convolution is an image like figure 6. The general idea of convolution is to apply a pattern to an image, in order to extract certain characteristics or patterns within that image (7).

To understand the mathematical operation (Figure 7) a simple 6×6 pixel image was drawn, on the right side you see a kernel or filter that has a vertical orientation with a size of 3×3 (Figure 7). Generally, the filter has a smaller size than the image. The idea of convolution is that this filter moves through the image and as it does so it performs a series of operations, thus generating a map with the features of greater weight or importance.

It is an iterative process, in the first iteration what the convolution does is to multiply point by point the coefficients of the filter by the portion of the image that is under that filter (corresponding pixels of the portion of the image) and then the values are added to generate the corresponding pixel in the output image. On the right side you see the output image and this first pixel resulting from multiplying the filter coefficients by the corresponding values of the image. In the second iteration, exactly the same operation is performed with the only difference that the filter moves one position to the right and here the next output pixel is obtained, and so on, successively. When it reaches the right end, the kernel moves down one position and returns to the left side and repeats the same operations until the kernel sweeps the entire image, thus obtaining the resulting image to then go to the reduction layer.

3.2. Max pooling layer or reduction layer

The reduction layer is the second layer of the CNN and is responsible for reducing the data flow obtained from the convolution layers, extracting the most important information or the most important features of the convoluted image (22) (Figure 8); this layer reduces the computational load that the CNN will have, helping the network to better train and segment which are the most important features, to remove noise from the image.

If the max pooling is exceeded, not only noise will be removed, but also important features could be eliminated, so this layer should not be abused. Ultimately, the purpose of these layers is to reduce the image size while preserving the main features (higher activations) of the convoluted image.

The resulting image after convolution and reduction will be smaller, with its main features, a cleaner image in the computational context compared to the input image. In this case, we started with a 4×4 image and obtained a 2×2 image on the right side (22, 23).

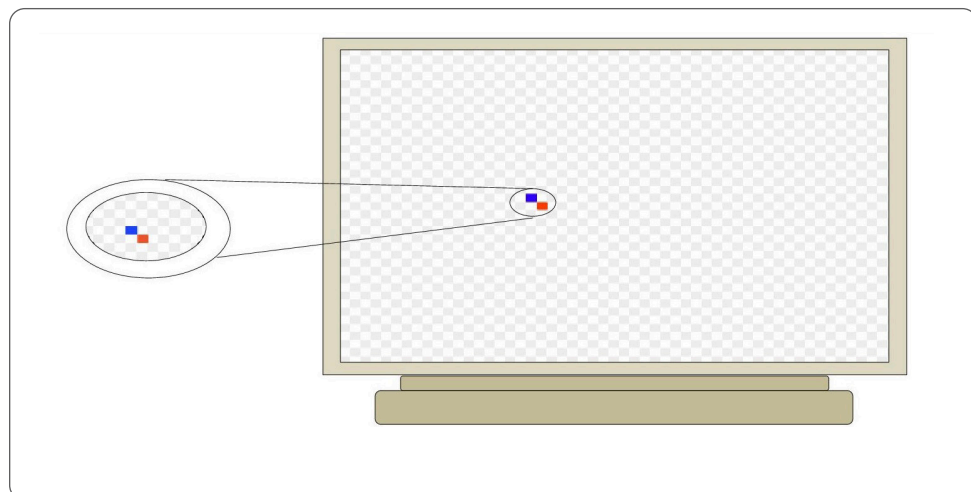


Figure 4. Diagram of a pixel.
Source: own elaboration.

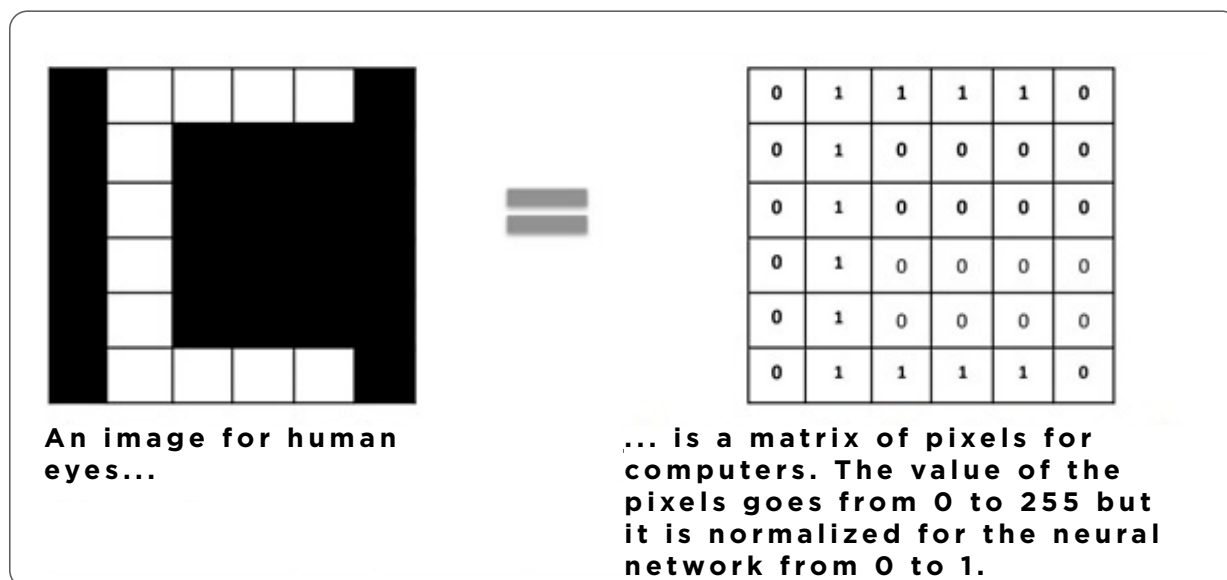


Figure 5. Preprocessing.
Source: own elaboration.



Figure 6. Convolution
Source: own elaboration.

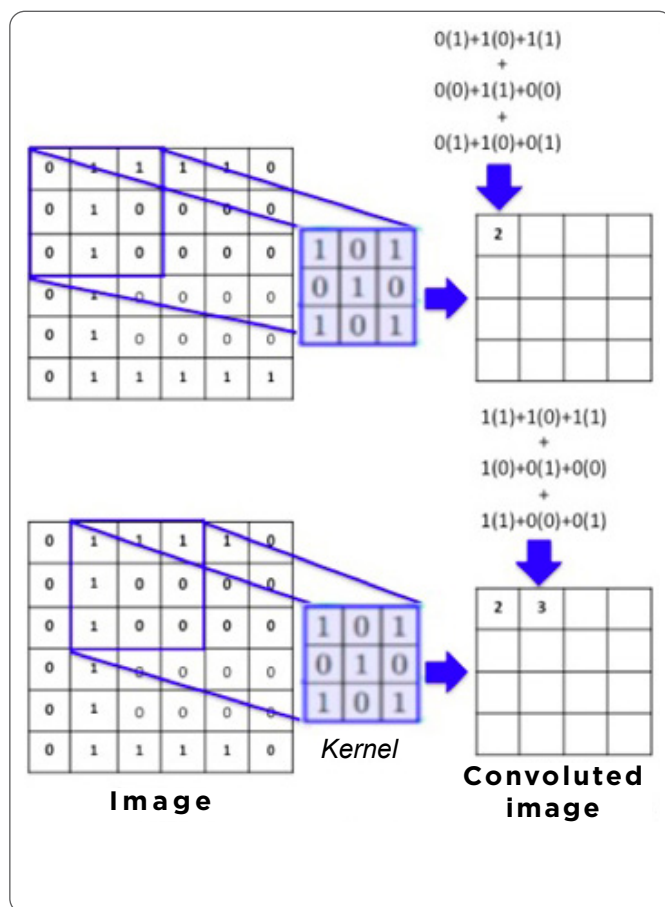


Figure 7. Kernel function: the resulting image will be smaller with features that outweigh the input image. In this case, we started with a 6x6 image and obtained a 4x4 image on the right side; the same operation is repeated until the kernel sweeps the whole image.

Source: own elaboration.

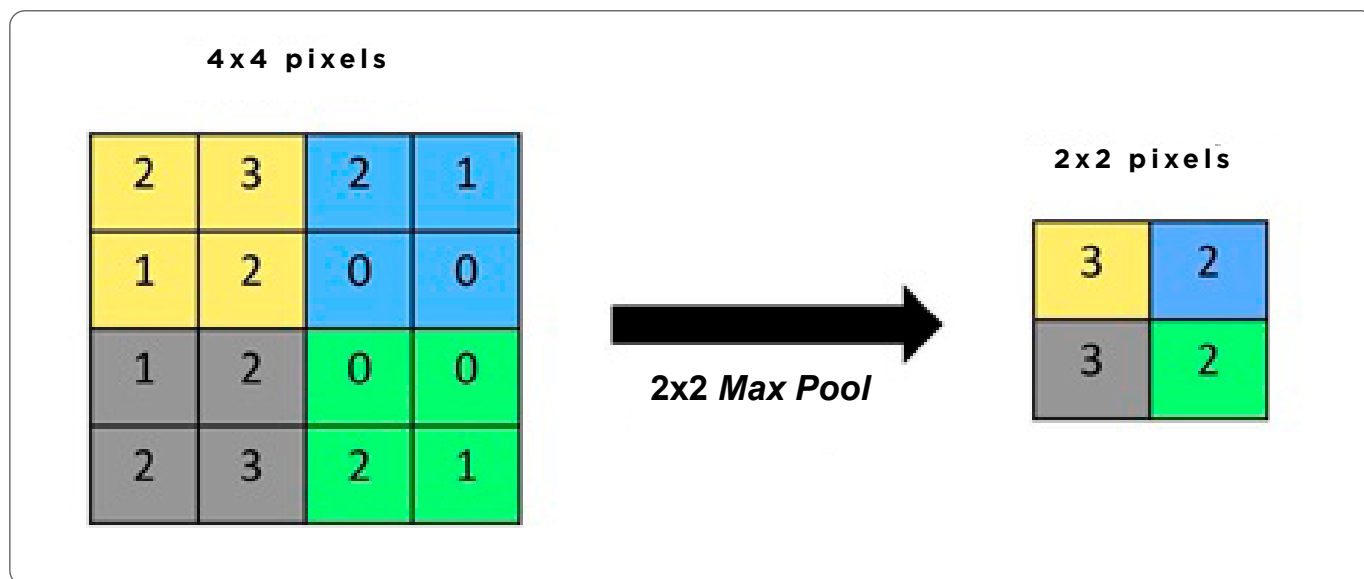


Figure 8. Convolved image of the previous example with a pool or filter size. Its size can vary in one or another neural network. In this example a size of 2x2 is imposed, which means that each of the 4x4 pixels of the convolved image is traversed from left-right, up-down, but 2x2 (2 high by 2 wide = 4 pixels) and the highest value among those 4 pixels will be preserved in the output, hence the term "Max". In this case, the resulting image is halved to obtain a 2x2 pixel image. In this way, the number of neurons needed to continue storing the most important information to detect the desired features is also decreased.

Source: own elaboration.

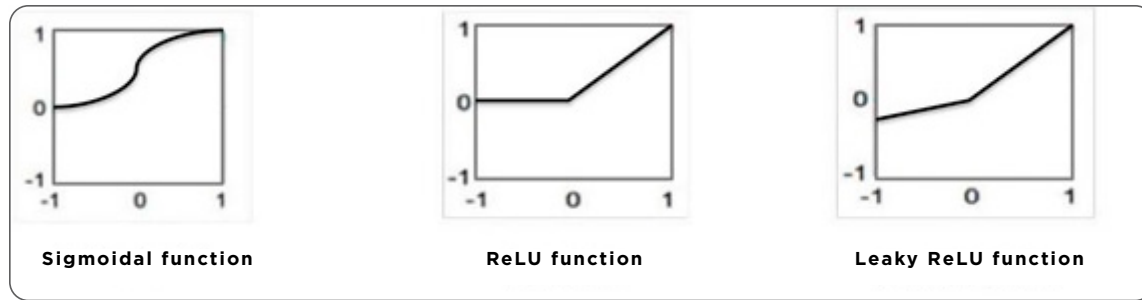


Figure 9. Representation of the activation function.
Source: own elaboration.

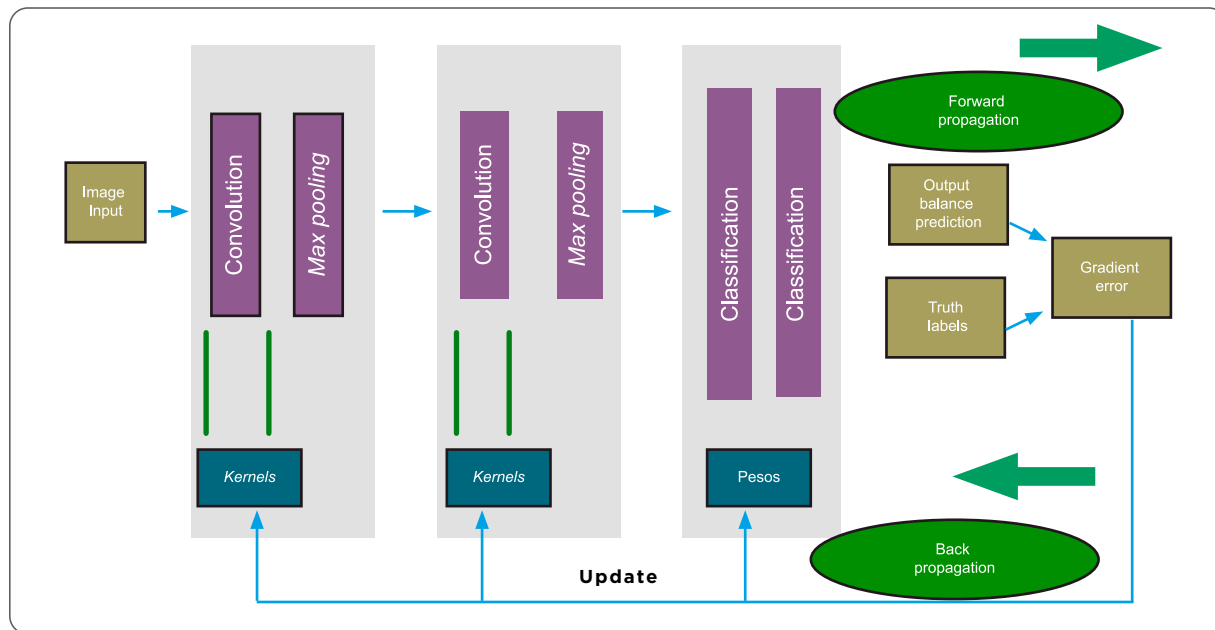


Figure 10. Training scheme of a convolutional neural network.
Source: own elaboration.

3.3 Dense layers or classification layers (multilayer or fully connected neural network):

These layers calculate the score of each class of features extracted from the convolution and max pooling layers, relating all the features or all the data that have been extracted prior to training the neural network to obtain a final classification (24). There are no rules regarding the number of fully connected neuron layers to be used in this final block of the CNN; however, the literature describes the use of 2 to 4 layers; such is the case of LeNet (25), VGG Net (26) and AlexNet which is the most influential (5).

Each neuron in the fully connected layer contains a nonlinear function and the choice of this will depend on the type of task to be performed by the CNN. However, because the classification layers are so computationally heavy, other approaches have been proposed in recent years. These include the global average pooling layer and the average pooling layer, which help to significantly reduce the computational load (27).

3.3.1. Activation function

It is important to add that activation functions are present in the convolution layers and in the fully connected layers. In other words, these activation functions are part of the structure of each artificial neuron that makes up the aforementioned layers, and are structurally very similar to the artificial neuron schematized in Figure 1; thanks to this activation function, the neuron - as a functional unit - classifies the data collected to obtain a final response (27).

There are several types of activation functions. On the one hand, there is the sigmoidal function used in binary classification, as shown in Figure 9, which varies between 0 and 1, where 0 is a negative response and 1 is a positive response, given in terms of probability (28). The sigmoidal operation is understood as follows: if a CNN model is used to identify dogs, when the image of a dog is entered into the neural network it yields a result of 0.9, very close to 1, therefore, it has a probability that the image entered is a dog; otherwise, if the image of a cat is entered, the neural network yields a result of 0.2, which is close to zero, which would mean that it is not a dog.

In the case of a multi-class classification, where there is more than one possible output, the soft max function was created, which allows obtaining a normalized probability and is an extension of the sigmoidal function. Returning to the previous example, if you want to obtain the breed of the dog, a neural network model is trained to differentiate four possible classes of dogs (Labrador, terrier, bulldog and pincher); the output of the neural network will be a probability for each of these dog breeds and the sum of all these possibilities will be 1 (29). Therefore, the image of a terrier in a trained neural network could give as an answer: terrier 0.9, labrador 0.05, bulldog 0.03, pincher 0.02, the sum of the answer is equal to 1. If the neural network gives the highest value, in this case 0.9, there is a probability that the dog is a terrier breed.

On the other hand, it has been demonstrated the high efficiency and effectiveness of the Rectifier Linear Unit (ReLU) function to develop much deeper networks (Figure 9). It is able to eliminate gradient fading (which refers to the learning error in which the network stops learning) (5).

There are several improved versions of ReLU with high performance for making a CNN. The best known is the leaky ReLU, which adds a small gradient in that negative area, to prevent all negative activations from being taken to zero and allow the network to continue learning, to a lesser extent, but without pausing training; in this way, the CNN will daily be able to learn and will become more weighted over time. These are the two most commonly used activation functions in CNNs today (30).

4. Training a CNN

The training of a network is a process of kernel search in convolution layers and weights in classification layers that minimize the differences between the output predictions, which are the responses of the CNN being trained, and the truth labels, which refer to the correct responses that the CNN is being trained with. In the case of radiology, it corresponds to the correct diagnoses of the images with which the CNN is being trained. Learning a CNN is an iterative process of going back and forth between the layers of neurons. Forward propagation is called forward propagation, and refers to the mathematical processes performed in the CNN when passing information through each layer of the neural network to generate an output response or prediction; this is then compared with the truth label and through mathematical processes generates what is known as the error gradient, which could be said to correspond mathematically to the adjustment made in the kernels of the convolution layers and the weights of the classification layers. This retrograde and feedback process that makes adjustments in each layer of the neural network is known as back propagation. In this way, if the response of the neural network is wrong, the respective correction will be made in the CNN (29) (Figure 10).

Forward propagation and back propagation are carried out with all the data, through successive iterations through the database, in this way, if there were 10,000 data, multiple iterations would have to be carried out to cover all the training data.

Once the corresponding modifications are made and enough iterations have been generated to cover all the databases, an epoch (epochs) will culminate (20). Normally, these trainings are performed

over several epochs, i.e. they do not see the database data only once, but they see it as many times as necessary.

5. DL applications in radiology

5.1. Lesion detection

Several studies have evaluated the use of CNNs in the identification of lesions in chest radiography (X-ray) with very significant results. Thus, for tuberculosis detection, the area under the curve (ABC) found was 0.99 (31); for pleural effusion, 0.96; for pulmonary edema, 0.87; for consolidations, 0.85; cardiomegaly, 0.88 and pneumothorax, 0.86, (32, 33). Breast ultrasound-based CNN models have also been described for early detection of breast cancer with ABCs between 0.79-0.87 (34, 35).

CT-based CNN models have been proposed for the detection of critical findings in non-contrast CT of the skull. One study demonstrated a model for the detection of hemorrhage, mass effect or hydrocephalus with a sensitivity of 90 %, specificity of 85 % and an ABC of 0.91 (36). On the other hand, Nakao et al. developed a method for aneurysm detection in MRI with a sensitivity of 70 % (37).

5.2. Segmentation of lesions

Accurate segmentation is the key to effective planning of radiotherapy in head and neck cancer. Ibragimov and Xing developed a CNN model for fast and consistent segmentation of these structures (38). It is also the case of Men et al. who proposed an automatic segmentation using DL in rectal cancer radiotherapy planning, demonstrating high efficacy in terms of accuracy and speed (39).

5.3. Patient prognosis

Advances in computing, artificial intelligence and especially in medical image analysis have made it possible to extract quantitative data that allow a better oncological approach. This concept was described in 2012 as radiomics (40, 41), and refers to the extraction of large amounts of quantitative features from different medical images correlating them with each other to generate an optimal diagnosis, prognosis and treatment of cancer (42). This is the case of a DL model based on MRI radiomics for predicting survival in glioblastoma multiforme (43) and of a CNN based on chest CT to predict mortality in patients with chronic obstructive pulmonary disease in chronic smokers (44).

Conclusion

Medical decisions are made based on the comprehensive interpretation of relevant patient data, such as signs, symptoms, laboratory tests and diagnostic images. DL allows the automatic extraction of discriminative features from high-dimensional data, therefore, it makes a great impact in the medical field and in particular in quantitative analysis (Figure 11).

There is skepticism about its accuracy and the challenges it faces, as well as fear that it will replace radiological or nuclear physicians; however, AI enables faster and more reproducible practice. Adequate involvement of the medical community ensures optimal technological development for improved quality of work life and better health care.

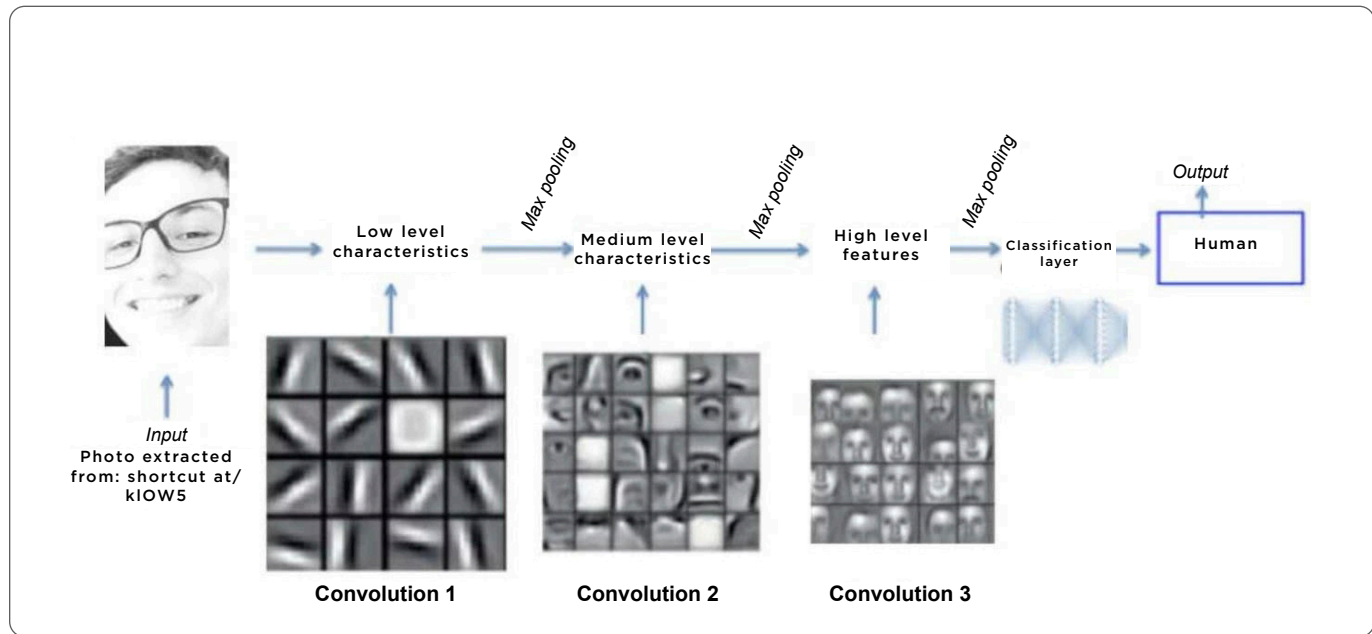


Figure 11. General and summarized scheme of the operation of a CNN model with three convolutional layers, three max pooling layers and three classification layers to identify faces. Convolution 1: Going through the first convolutional layer, the network looks for simple relationships in the image, such as lines or shadows; these are very simple filters. Convolution 2: Once it passes to the second convolutional layer, it has at the input an image already filtered by the filters of the first convolutional layer and reduced, because it passed through the max pooling layer, preserving its characteristics; Therefore, what it produces is abstraction in the sense that the filtering of the second layer will be on the output of the first filtering, looking for more complex and concrete relationships; in this second layer, for example, we look for typical curves of the face, the shape they may have, the oval shape of the eyes, the shape of the nose and the shape of the eyebrows. Convolution 3: After the third convolutional layer, again the outputs are obtained, after applying the first two filters, once again increasing the complexity and specificity of the filters. The filters now look for aspects as complex as the relationship of the shape and location of the eyes and other structures with respect to the others, such as the nose, lips, mustache, eyebrows, etc., characteristics of the face that differentiate it from other faces. In other words, as one moves towards deeper layers, the level of abstraction of the content of the image to which they are sensitive increases, as can be seen in the images.

Source: own elaboration.

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