REVIEW

Deep learning in ophthalmology: a review

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Deep learning is an emerging technology with numerous potential applications in Ophthalmology. Deep learning tools have been applied to different diagnostic modalities including digital photographs, optical coherence tomography, and visual fields. These tools have demonstrated utility in assessment of various disease processes including cataracts, glaucoma, age-related macular degeneration, and diabetic retinopathy. Deep learning techniques are evolving rapidly, and will become more integrated into ophthalmic care. This article reviews the current evidence for deep learning in ophthalmology, and discusses future applications, as well as potential drawbacks.

Introduction

Ophthalmology is on the cusp of a revolution in the screening, diagnosis, and management of eye disease. This revolution is being led by computer-based deep learning (DL) technology that has the potential to change the practice of ophthalmology. DL is the newest and fastest growing component in the field of machine learning. It is a process by which vast databases are analyzed, and then compared to known ground-truths. Such DL technology is behind self-driving cars and the improvement in the success of computers to win at board games such as go and chess.[1,2] This technology is incorporated into social media and photo software to identify searchable components of a video or image.[3] In due time, DL may even allow the development of true artificial intelligence.

Ophthalmologists rely on pattern recognition via direct or indirect visualization of the eye and its surrounding structures to diagnose disease. Ophthalmology-related diagnostic technology provides further information to the clinician via digital representation of these same structures. This dependence on imaging makes the field of ophthalmology perfectly suited to benefit from DL algorithms. Incorporation of DL algorithms into the practice of ophthalmology has begun and could potentially change the fundamental type of work performed by ophthalmologists. Computer led intelligence will likely play an important role in screening and diagnosis of eye disease in the coming years. Such technological advancements may lead to human resources being left to focus on direct clinician-patient interactions such as a discussion of the diagnosis, prognosis, and treatment options. We believe that giving of consent and any medical or surgical intervention will remain the responsibility of a human clinician for the near future. Inclusion of DL algorithms into ophthalmology decision making is likely to take place faster than many may expect.[4]

Technical Aspects of Deep Learning

There are a few terms commonly associated with computer methods that deal with analysis and decision-making scenarios, including medical image assessment. Computer-aided diagnosis refers to approaches in which specific clinical features that are associated with the disease are extracted via specifically designed image-processing filters/tools.[5] The term "machine learning" generally refers to any pattern-classification method that requires a training scheme, whether supervised or unsupervised, to learn what may delineate the underlying patterns.[6] DL, for the most part, refers to machine-learning schemes that employ convolutional based neural networks (CNNs). Such networks utilize a bank of image-processing filters to extract various types of image features that the network deems indicative of pathological signs, as learned from the training set, which is an integral part of pattern classification methods.[7] DL can be viewed as a brute-force approach in determining the most appropriate image-processing filters/tools, which can quantify various biomarkers of the disease. Finally, the term artificial intelligence (AI), in a very general sense, refers to any system, mainly machine-learning based, that is capable of learning new patterns and features in an unsupervised manner, where intervention from a third party, usually humans, is not required. It is debatable whether a true AI system already exists or not.

Initially, the main drawback in real-world application of CNNs was simply lack of computational power. The rise of graphical processing units (GPUs), that have far surpassed the computational capabilities of central

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processing units (CPUs), has made running CNNs of farther depths (deep learners) much more time efficient and powerful. These deep neural networks are now commonly referred to as DL solutions and include networks such as GoogLeNet,[8] VGG,[9] and SegNet.[10] Such solutions have shown a lot of promise in generalizing overall content of an image, as well as in industrial applications such as different suggestive algorithms similar to Netflix's recommendation system. In the recent years, there have been many attempts to assess such systems for medical applications, including biomedical-image analysis.

DL-solutions for biomedical-image analysis fall into two main categories:

1 Supplying the DL network with only images and their associated conditions (diagnoses/labels/stages), commonly referred to as image-classification methods; and
2 Supplying the network with images and their associated ground-truth masks (black and white images), in which the pathological conditions that are associated with the disease are manually delineated, commonly referred to as semantic-segmentation methods.

Figure 1 illustrates a general flow-chart representation of a typical CNN that provides a two-class classification.

Deep Learning in Ophthalmology

DL research in ophthalmology has progressed rapidly, and has the potential to become a part of daily clinical practice in the relatively near future.[4] In the same way that an electrocardiogram machine can provide a relatively accurate reading of the electric function of the heart, DL algorithms are now offered by a number of private companies that focus on screening for retinal disease including diabetic retinopathy and macular degeneration.[11–13] In due time, DL algorithms may become incorporated into many digital ophthalmic diagnostic tools.

Cataract

Anterior segment research has demonstrated the ability of DL to grade nuclear cataracts from cross-sectional slit lamp images on the Wisconsin grading system as compared to professional graders. The mean absolute error was 0.304 and the integral grading error ≤ 1.0 was 99%, which outperformed other published automated cataract grading methods.[14] DL has also been applied to slit lamp images of pediatric cataracts. A CNN algorithm had high sensitivity and specificity for grading, density, and location of pediatrics cataracts when compared with Pediatric Ophthalmologists.[15]

Glaucoma

Glaucoma research has investigated the application of DL for different testing modalities including optic nerve images, optical coherence tomography (OCT), and visual fields. Clinical optic nerve assessment includes cup-to-disk ratio, focal changes in the neuroretinal rim, and peripapillary nerve fiber layer, disc hemorrhages, and vessel changes. CNN has been used to develop an algorithm to diagnose a glaucomatous optic nerve as defined by clinical assessment with area under the curve (AUC) of receiver operative characteristic curve of 0.831 and 0.887 on 2 separate databases.[16] Modern day glaucoma assessment relies on OCT imaging of the optic nerve. A hybrid DL method using single wide-field OCT has successfully classified healthy glaucoma suspects from early glaucoma by creating a probability map that was 93.1% accurate when compared with a glaucoma expert diagnosis, outperforming current OCT parameters.[17] Other research has

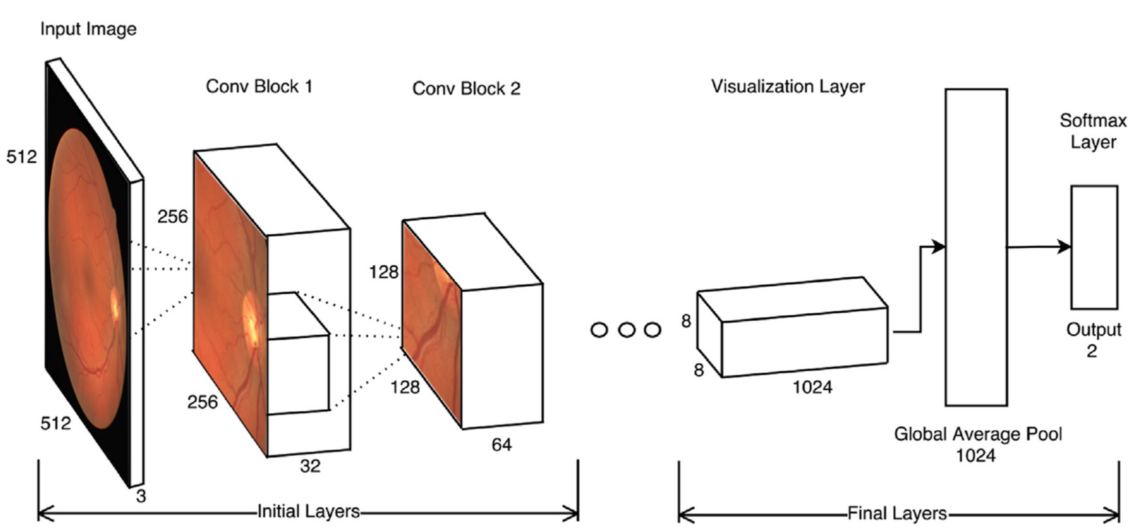

Fig. 1—A typical flow-chart representation of a deep learning network that provides classification of the image into two groups. Note that the size of the images and the convolutional blocks may vary in different applications. The convolutional layers attempt to extract relevant image features while reducing the dimensionality of them. The Softmax layer is responsible for the decision-making aspect of the network.

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