The state of the art of deep learning models in medical science and their challenges

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ONLINE FIRST

Multimedia Systems

ISSN 0942-4962

Multimedia Systems
DOI 10.1007/s00530-020-00694-1

Springer

Multimedia Systems
https://doi.org/10.1007/s00530-020-00694-1

SPECIAL ISSUE PAPER

The state of the art of deep learning models in medical science and their challenges

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Abstract
With time, AI technologies have matured well and resonated in various domains of applied sciences and engineering. The sub-domains of AI, machine learning (ML), deep learning (DL), and associated statistical tools are getting more attention. Therefore, various machine learning models are being created to take advantage of the data available and accomplish tasks, such as automatic prediction, classification, clustering, segmentation and anomaly detection, etc. Tasks like classification need labeled data used to train the models to achieve a reliable accuracy. This study shows the systematic review of promising research areas and applications of DL models in medical diagnosis and medical healthcare systems. The prevalent DL models, their architectures, and related pros, cons are discussed to clarify their prospects. Many deep learning networks have been useful in the field of medical image processing for prognosis and diagnosis of life-threatening ailments (e.g., breast cancer, lung cancer, and brain tumor, etc.), which stand as an error-prone and tedious task for doctors and specialists when performed manually. Medical images are processed using these DL methods to solve various tasks like prediction, segmentation, and classification with accuracy bypassing human abilities. However, the current DL models have some limitations that encourage the researchers to seek further improvement.

Keywords Artificial intelligence · Machine learning · Deep learning models · Medical healthcare system

1 Introduction

Since the last decades, the simulation of the human brain efficiently is considered a challenging task for everyone. However, various attempts made by different groups have enabled the possibilities of implementing such simulation that has led to the development of a variety of concepts like a virtual assistant (Alexa, Siri, Cortana), language translation Chatbot, Image colorization, facial recognition and so on using deep learning networks [1–5]. The deep learning approach is a subset of machine learning stimulated by the human brain's data processing pattern [1, 3–8, 13–16]. The Venn diagram in Fig. 1 shows the logical relationship between deep learning (DL), machine learning (ML), and artificial intelligence (AI).

The term AI was first used in 1956 but gained popularity recently due to the availability of vast amounts of data. The term AI is defined as a method that facilitates a machine to mimic human behavior and to design an operational model of the human brain that can make decisions according to its learning [9, 17, 18, 94, 95, 98–101]. Thus, AI became the center of attention and the most popular topic for researchers

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Published online: 25 September 2020

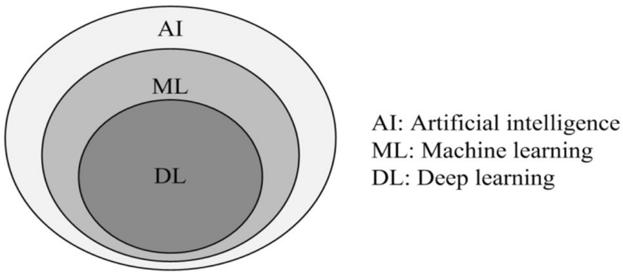


Fig. 1 Relationship between artificial intelligence, machine learning and deep learning

in the 1980s. ML is a subset of AI that uses statistical techniques to enable a machine to improve through learning and experience. It covers a broad area of research, and a lot of methods have been developed like clustering, Bayesian network, decision tree, deep learning, and so on [2, 3]. Deep learning is a particular class of machine learning that simulates the functionality of our brain cells called neurons, which led to the idea of neural networks. AI-based system development and evolution of DL is shown in Fig. 2.

Deep learning (DL) is the evolution of machine learning [1, 13–16]. ML approaches can be classified as supervised and unsupervised, playing a significant role in developing an AI-based system [4, 9, 10, 102]. In such type of ML models, the features like pixels value, texture, orientations, shape, or anything needed to be recognized by the expert and after that hand-coded by the domain expert and data analyst. The performance of the ML algorithm depends on how accurate features are identified or extracted. While in the case of DL algorithm, it tries to learn high-level features from the data [1, 4, 11, 19–21]. The working principle of a deep learning algorithm and the ML algorithm is positively given in Fig. 3.

It is worth mentioning that DL is getting too much attention as it can yield outstanding accuracy, sometimes beyond human perception [13, 21]. The relation between the performance of ML-based algorithm and DL-based algorithm concerning the amount of data is given in Fig. 4.

From Fig. 4, it has been observed that for small datasets, traditional ML-based models performed extraordinarily as compared to astronomical neural network-based algorithms. However, the outcome has been drastically changed for large amounts of data means DL-based algorithms perform outstandingly.

1.1 Application of deep learning models

After the detailed study of literature, it is observed that so many research areas have been explored by the various research communities where deep learning-based algorithms are widely applicable and getting better accuracy than ML-based techniques [10–17, 104–110]. In ML-based classification techniques, ANN [96], PNN, KNN, and SVM [97] are used widely for development of decision-making system for medical science. In these systems, texture, shape or transform domain features [102] are extracted and selected features are used for system development.

The literature also suggests that the traditional health-monitoring system's decision is entirely dependent on the experience of experts and is too time-consuming, leading to a high error rate in such a model. The overall performance of ML-based systems for a small dataset is outstanding, but ML-based models do not perform well for large datasets. So, the area of machine learning is further explored, and deep learning comes in role with outstanding outcomes for large datasets. Figure 5 shows the various research fields in which DL is playing a vital role.

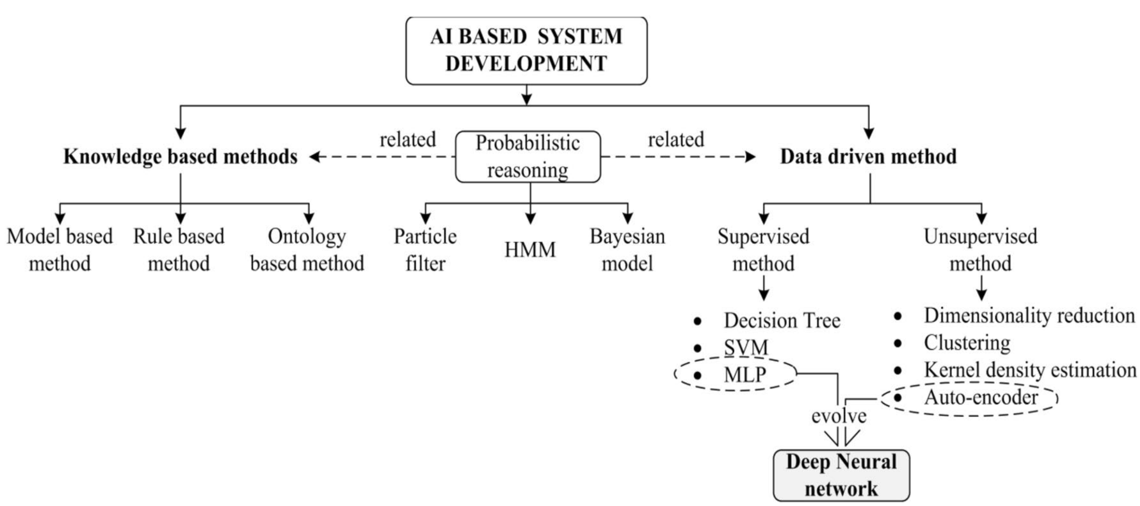


Fig. 2 Evaluation of deep learning

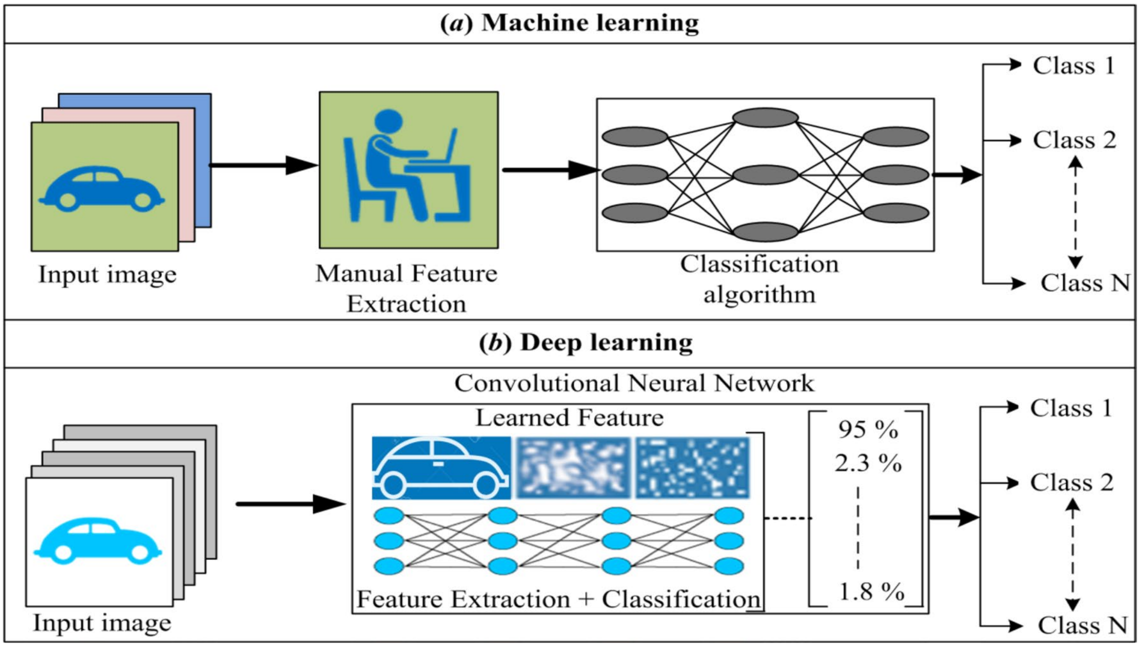
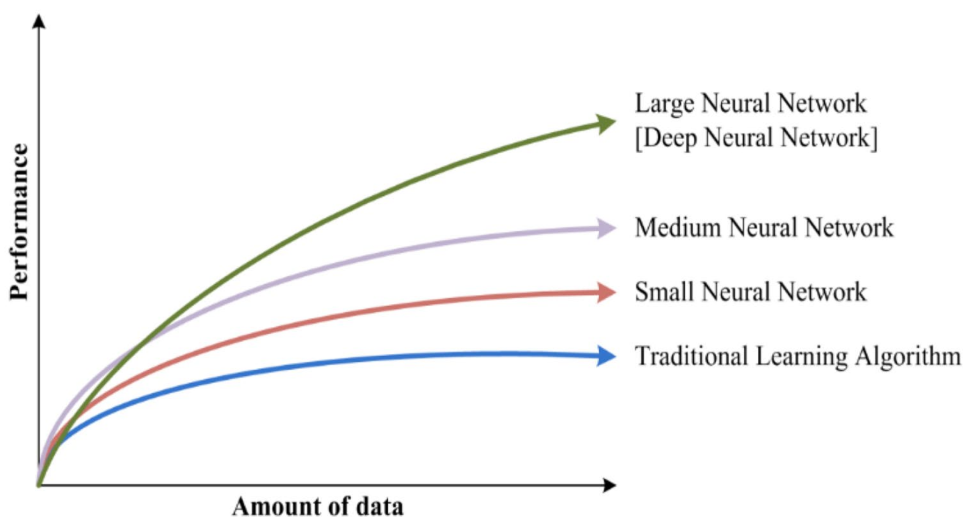


Fig. 3 Comparison between ML and Dl algorithm

Fig. 4 Data vs. performance



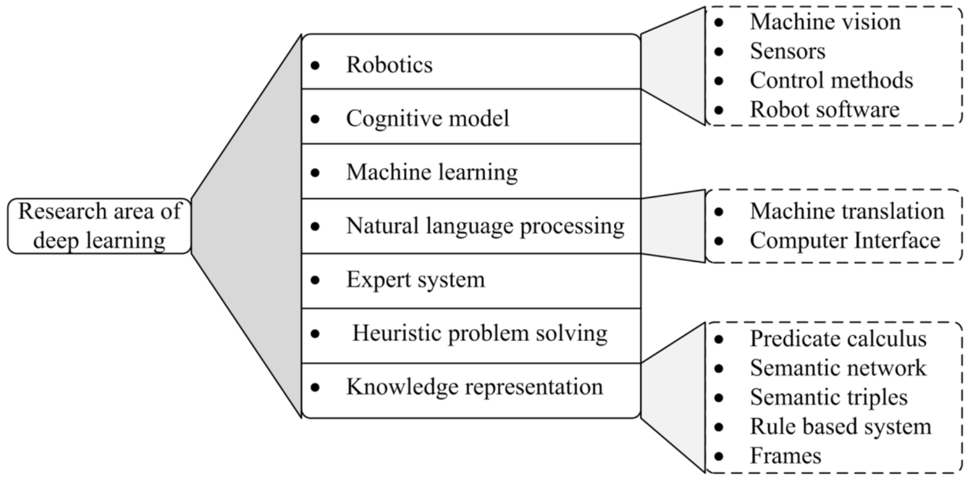
This paper explores the systematic study of published work related to deep learning-based models and their applications in medical and health monitoring. This study also highlights the recent research challenges in deep learning models so that the different research communities can overcome these challenges.

The rest of the paper is structured as deep learning models in Sect. 2. In the same section, the deep learning networks and their key features are given. In this section, the authors have also explored the available deep learning packages and their supported platforms. Section 3 contains information related to past studies in the medical field of deep learning and outcomes. In the same manner, quantitative analysis of publications related to deep learning is given in Sects. 4 and 5 describes the challenges associated with DL models.

2 Deep learning models

The architecture [3, 5, 6, 8, 9, 19–21, 77–82, 104–110], brief description and key features of DL-based model are specified in Fig. 6.

Fig. 5 Research area of deep learning



2.1 Deep learning packages

Till now, various deep learning packages like Caffe [22, 25], CNTK [90], Deeplearning4jK [91], TensorFlow [92], Torch [93], Keras [78] have been developed for operating system *i.e.*, Linux, Win, OSX, Android using the interface of C/C++, MATLAB, Python, Java, Clojure, Lua, LuaJIT, Scala. The supported models for these packages are DBN, RNN, and CNN [79–90]. Among these models, only Neon supports cloud computing features. The available deep learning libraries, supported platform, interface, and models are given in Table 1.

3 Medical healthcare system

In medical science, there are so many research areas available, where computers play a crucial role. The research areas like health monitoring, medical informatics, pervasive sensing, bioinformatics, medical imaging, etc. are the most prominent domains. In each field, the computer-assisted module is applicable for proper detection and formation of the treatment schedule. It is worth mentioning that the accuracy of a system is crucial in decision-making in medical science. Therefore, various machine learning models are being created to take advantage of the data available and accomplish tasks, such as automatic prediction, classification, clustering, segmentation and anomaly detection, etc. Tasks like classification need labeled data and, thus, used for training the models to achieve reliable accuracy. However, traditional machine learning models perform moderately in the case of image classification. This study presents aggregate information regarding previous studies and suitable deep learning models in each research area.

3.1 Application of deep learning in medical science

In the medical field, accurate prediction or detection of disease or abnormalities is a challenging task. Therefore, machine learning techniques based on automated or semi-automated computer-aided diagnosis (CAD) systems play a healthy role in predicting or detecting disease or abnormalities for medical experts to take their decision or to prepare accurate scheduling of treatment [23–33, 101, 103, 104]. With the enhancement of technology, CAD systems based on deep learning perform outstandingly, and the system's outcome is helpful for experts to make adequate decisions. The working framework of three different health-monitoring models [8, 10–12] is shown in Fig. 7.

The summary of research done in past for medical fraternity using DL-based algorithm is given in Table 2.

From the detailed study of literature, it has been analyzed that there are so many research areas in medical and health monitoring where deep learning is applicable. Table 3 shows the application area and a suitable model of deep learning techniques.

3.2 Open-access datasets for medical healthcare

From the study of related work associated with deep learning in medical science, it has been found that most of the studies were validated on a self-collected dataset. The collection of datasets from laboratories and hospitals is a time-taking process and extensive work. Therefore, the list of open-access datasets for medical study and research are presented in Table 4.

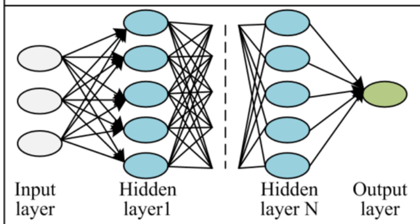
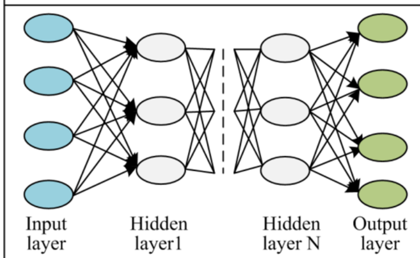
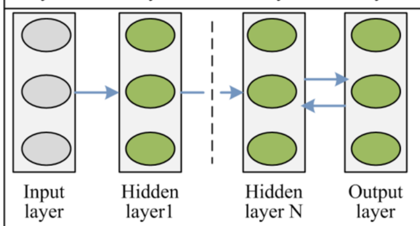
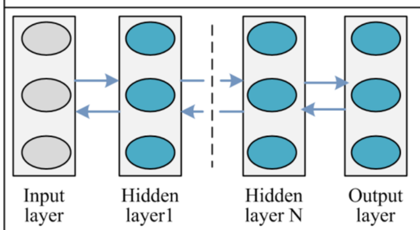
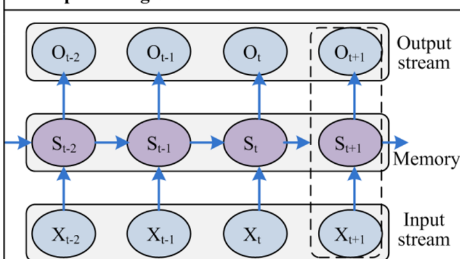
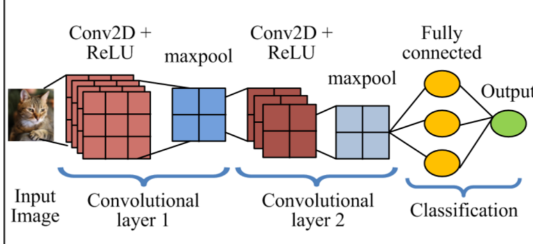
Deep learning based model architecture	**Brief description**	**Key features**
	**Deep Neural Network** • Generalized frame work of deep learning model. • Widely applicable for classification and regression model. • Consisting of more than 2-hidden layer.	**Pros:** • Widely used with high success rate in different area. **Cons:** • Learning process is very slow.
	**Deep Auto-encoder** • Mainly used for feature extraction and space dimensionality reduction. • It has same number of input and output nodes. • Type of unsupervised learning.	**Pros:** • No need of labeled data. • So many modified versions of auto-encoders are designed according to need. **Cons:** • Training can be suffered from errors.
	**Deep Belief Network** • Combination of restricted Boltzmann machine (RBM). • Hidden layer of each network is visible to the next layer. • It allows supervised and unsupervised learning.	**Pros:** • Used greedy learning approach to initialize the network. • Maximizing the likelihood inferences directly. **Cons:** • Training can be expensive due to initialization and sampling process.
	**Deep Boltzmann Machine** • Another proposed model of Boltzmann Machine family. • Possess conditionally independent connection between layers of network. • It uses stochastic MAX likelihood method to maximize the lower bound of likelihood..	**Pros:** • Integrate top-down feedback for robust inferences for indefinite inputs. **Cons:** • Higher time complexity for inference with respect to DBN. • Optimization of parameters is tedious for large dataset.
Deep learning based model architecture	**Brief description**	**Key features**
	**Recurrent Neural Network (RNN)** • A neural network having capability of analyzing data stream • Share the same weight for each step. • Widely useful where output depends on previous results.	**Pros:** • Can memorize sequential events. • Good response in NLP area. **Cons:** • Learning issues due to gradient problem.
	**Convolutional Neural Network (CNN)** • This model is suitable for 2D data. • Designed by the functionality of human neuron's behavior. • Every hidden layer filter transform its input to 3D output volume for neuron activation..	**Pros:** • Few neuron connections required with respect to a typical NN. • So many variants have been proposed like AlexNet, GoogleNet etc. **Cons:** • It requires large labeled dataset.

Fig. 6 Architecture, brief description and key features of DL-based model

Table 1 Available deep learning packages

Name	Supported platform	Interface	Supported models			Clouding computing
			DBN	RNN	CNN	
Caffe	Linux, Android, Win, OSX	C++, MATLAB, Python	X	✓	✓	X
CNTK	Linux, Win	Command-Line	X	✓	✓	X
Deeplearning4jK	Linux, Android, Win, OSX	Java, Scala, clojure	✓	✓	✓	X
TensorFlow	Linux, OSX	Python	✓	✓	✓	X
Torch	Linux, Android, Win, OSX, Ios	C, Lua, LuaJIT	✓	✓	✓	X
Keras	Linux, Win, OSX	Python	✓	✓	✓	X
Neon	OSX, Linux	Python	✓	✓	✓	✓

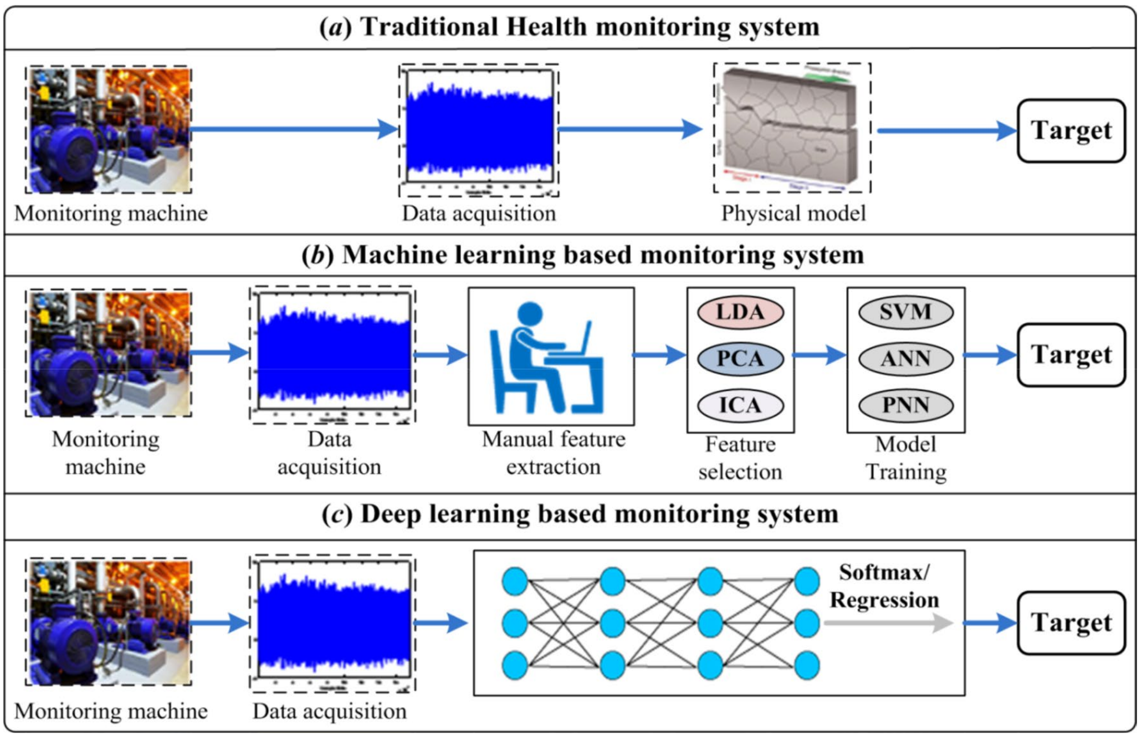


Fig. 7 Working framework of health-monitoring models

4 Quantitative analysis of publication related to deep learning models

The line graph of published manuscripts that make use of the concept of deep learning approach in subareas of medical health informatics is shown in Fig. 8. This indicates that the use of deep learning methods is exponentially growing in the medical field since 2014. All the statistics are collected from Google Scholar for the keyword "Deep learning in the medical field."

The analysis of deep learning-based publications from reputed libraries or journals like ScienceDirect database, Springer database, and IEEE digital library, including conference proceedings and journal publications for the duration of 2006–2019, is shown in Figs. 9 and 10.

The statistical analysis of published articles in medical science using deep learning shows the popularity of deep learning models. Initially, the implementation of deep learning models was pricey, so the growth rate is slow for all publications. In contrast, after GPU development, it gained attention and growth because of promising results and a high response rate. Therefore, the application of deep learning models in medical science has bright future research scope.

Table 2 Summary of literature review

References	Objective of the work	Used DL model	Dataset/no. of images	Accuracy (%)
Khan et al. [34]	Breast cancer classification	CNN GoogleNet VGGNet ResNet	8000	97.5 93.5 94.1 94.3
Zhang et al. [35]	Medical image classification	SDL	CLEF-15: 6776	78.2
			CLEF-16: 10942	87.9
			ISIC-16: 1279	86.2
			ISIC-17: 2750	91.3
		ResNet-50^{n}	CLEF-15: 6776	76.6
			CLEF-16: 10942	87.3
			ISIC-16: 1279	85.5
			ISIC-17: 2750	90.2
Mahbod et al. [36]	Skin lesion classification	CNN + SVM	2037	97.5
Xu et al. [37]	Prediction of lung cancer	CNN + RNN	759	74.0
Nagpal et al. [38]	Improving performance of Gleason scoring in prostate cancer	CNN + Gleason pattern	TCGA, 331 slides	70.0
Asuntha et al. [39]	Lung cancer diagnosis	FPSOCNN	Aarthi scan hospital, 1000 images	94.9
			LIDC Dataset	95.6
Ardila et al. [40]	Screening on chest computed tomography	3D-CNN	42.290	94.0.4
Benhammou et al. [41]	Breast cancer automatic diagnosis	MIM approach + CNN	BreakHis, 7909	88.9
Xie et al. [42]	Pulmonary nodule automatic detection	R-CNN, 2D CNN	LUNA-16	86.4
Morgan et al. [43]	Tuberculosis on chest radiographs	CNN	1007	99.0
	classifying interstitial lung diseases	CNN	1007	85.5
	occurrence of an Endotracheal-tube on chest radiograph	5-layer CNN	1007	99.0
Janssens et al. [44]	Infrared thermal image based machine health monitoring	CNN	60	95.0
Rajkomar et al. [45]	Predictive models for EHR data	TANN	216,221	95.0
Oh et al. [46]	Parkinson's disease detection	13-layer CNN	20	88.5
Coudray et al. [47]	Lung cancer histopathology images	Inception V3	1634	85.6
Mohamed et al. [48]	Breast density classification	CNN	22,000	94.2
Nguyen et al. [49]	Microscopic image classification	CNN	1779	92.6
Xu et al. [50]	4-Class breast density classification	RNN	410	92.6
	2-Class breast density classification	RNN	410	96.8
Rehman et al. [51]	ALL classification	AlexNet	230	97.7
Mohsen et al. [52]	Brain tumors classification	CNN	66	96.6
Chaudhary et al. [53]	Hepatocellular carcinoma detection	Auto-encoder	360	92.0
Rajpurohit et al. [23]	ALL identification	CNN	243	98.3
		FNN	239	95.4
		SVM	249	91.4
		KNN	239	93.4
Saffari et al. [54]	Breast density segmentation	Cgan	410	95.0
Soriano et al. [55]	Breast lesion classification	CNN	1070	85.0
Acharya et al. [56]	Diagnosis of seizure using EEG signals	13-Layer CNN	700	88.6
Lakhani et al. [57]	Tuberculosis on chest radiographs	AlexNet and GoogLeNet	1007	99.0
Hassan et al. [58]	Diagnosis of focal liver diseases	SSAE	110	97.2
Gardezi et al. [59]	Mammogram classification	VGG-16	2795	99.8
Kooi et al. [60]	Mammographic lesion detection	CNN	45,000	92.9

Table 2 (continued)

References	Objective of the work	Used DL model	Dataset/no. of images	Accuracy (%)
Mohanty et al. [61]	Plant disease detection	CNN	54,306	99.3
Gulshan et al. [62]	Detection of diabetic retinopathy	–	9963	99.1
			1748	99.0
Sirinukunwattana et al. [63]	Classification of nuclei for colon cancer	SC-CNN	29,756	91.7
Wang et al. [64]	Microcalcifications detection	Auto-encoder	1204	89.7
Lévy et al. [65]	Breast mass classification	AlexNet	1820	89.0
		GoogleNet	1820	92.4
Cheng et al. [66]	Breast lesions at ultrasound	Auto-encoder	520	82.4
	Pulmonary nodules detection by CT scans	Auto-encoder	1400	94.4
Wang et al. [67]	Metastatic breast cancer detection	GoogLeNet	400	98.4
		AlexNet	400	92.1
		VGG16	400	97.9
		FaceNet	400	96.8
Kallenberg et al. [68]	Breast density segmentation	CNN	48,000	61.0
John Arevalo, 2015 [69]	Mammographic lesion classification	CNN	736	86.0
Dhungel et al. [70]	Mass detection using mammographic images	R-CNN	410	96.3
Bar et al. [71]	Chest pathology detection	CNN	433	94.0
Xu et al. [72]	Histopathology imaging	DNN	132	95.4
Heung et al. [73]	AD/NC	DBM	194	95.3
	MCI/NC	DBM	305	85.6
	MCIC/MCINC	DBM	204	74.5
Liao et al. [74]	Automatic prostate segmentation	ISA + DL	30	–
Prasoon et al. [75]	Knee segmentation	CNN	114	–
Heung et al. [76]	AD/MCI classification	Auto-encoder + SVM	207	85.5
Bellotti et al. [77]	CAD system for mass detection	2-layer FNN	3369	78.3

SVM support vector machine, *DBM* deep Boltzmann machine, *CNN* convolutional neural network, *NC* healthy normal control, *MCIC* MCI converter, *MCINC* MCI not converter, *MCI* mild cognitive impairment, ISA independent subspace analysis, *cGAN* conditional generative adversarial networks, *AD* Alzheimer's disease, *SC-CNN* spatially constrained convolutional neural network, *FNN* feed forward neural network, *DNN* deep neural network, *ALL* acute lymphoblastic leukemia, *SSAE* stacked sparse auto-encoders

5 Developments and challenges in deep learning for medical science

After the systematic review of past studies, it has been observed that deep learning provides promising results for different medical applications like image classification, tissue classification, cancerous cell characterization, detection, and segmentation. Some essential facts have also been observed regarding the request of auto-encoder and DBN. Two most prominently used models CNN and RNN have much complex architecture; thus, the implementation of these models is a little bit difficult [8, 37, 105, 108]. And despite the fruitful conclusion from the systematic review of past studies, there are many open challenges.

5.1 Proper selection of deep learning model

From the study of literature, it has been found that most of the DL models are application- or equipment-dependent. Most of the authors did not mention the reason for the selection of DL models like how and why CNN or RNN [37, 105].

5.2 Selection criteria for acceptable solution

It should be recognized from the literature review that there are no selection criteria of the optimal solution as one problem has multiple solutions using heuristic problem-solving techniques. Among these solutions, which is

Table 3 Research, Application area and suitable model of deep learning

Area	Application	Base model
Health monitoring	Predicting lifestyle disease Air pollutant prediction Infectious disease detection Demographic information prediction	DBN Deep neural network CNN Deep auto-encoder
Medical informatics	Data mining Human behavior monitoring Disease prediction	Deep auto-encoder DBN CNN RNN Deep neural network
Pervasive sensing	Anomaly detection Biological parameter monitoring	DBN
	Human activity recognition using videos	CNN DBN Deep neural network
	Hand gesture recognition Obstacle detection	CNN DBN
Bioinformatics	Gene selection Gene classification Gene variants detection/prediction Cancer diagnosis	Deep auto-encoder DBN Deep neural network
	Drug design or development	Deep neural network
	RNA binding DNA methylation Compound protein interaction	DBN Deep neural network
Medical imaging	Neural cell classification Brain tissue classification AD/MCI classification	CNN DBN Deep neural network
	Tissue classification Cell clustering Hemorrhage detection Organ segmentation Tumor detection	DBN CNN Deep neural network Deep auto-encoder

the optimal solution, needs to be selected according to some parameters. But in the case of machine learning techniques, there are so many parameters and framework tuning for choosing an optimal solution [8]. Due to that limitation, the selection of DL model solutions is a challenging task for beginners.

5.3 Expensive system

DL-based models mainly depend upon the system's feature representation and data acquiring for every problem that can lead to a system more expensive. For a sound system's feature representation, proper labeling of data is compulsory [108]. The labeling process requires expert knowledge, which is generally a time-killing process. It indicates that the implementation of the DL method-based systems is expensive. So, the cost factor is still an open challenge for different groups, and so much research is going on to reduce the cost of developed systems.

5.4 Minimize the computation complexity

In deep learning-based models, too many computations are involved, which increase the complexity of the system. The previously done studies did not find any work which is looking to minimize the complexity [105]. So, according to the author, complexity is again an open area of research.

6 Conclusion

The deep learning model is a simple multiple hidden layer neural network trained using back-propagation and gradient descent method where the weights are revised for each layer using derivatives of the prior layer. This article has examined the research area of deep learning in health monitoring and health management. Initially, the development of a deep learning-based CAD system was not promising for clinical practice. Still, after the construction of GPU, it gained attention and growth because of promising results and a high

Table 4 List of open access datasets for medical study and research

Organization/dataset	Description	Source link
EPILEPSIAE database	Data sets from more than 200 patients with epilepsy	https://www.epilepsy.uni-freiburg.de/database
Cancer data set	7909 breast microscopic images of 82 patients	https://www.web.inf.ufpr.br/vri/breast-cancer-database/
Image CLEF 2017	CT images and biomedical images	https://www.imageclef.org/2017
ISIC2017	Skin disease dataset contain more than 24k images	https://www.isic-archive.com/#!/topWithHeader/onlyHeaderTop/gallery
Mini-MIAS database	3369 mammograms of 967 patients. It is classified on the basis of lesion type, morphology, breast tissue and pathology type	https://www.mammoimage.org/databases/ https://www.peipa.essex.ac.uk/info/mias.html
DDSM-BCRP	2620 scanned film contain normal, benign and malignant cases with verified pathology information	https://www.eng.usf.edu/cvprg/Mammography/DDSM/BCRP/bcrp_mass_01.html
INbreast	115 cases with 410 images, 90 cases are from women with both breast and 25 cases from mastectomy patients	https://www.medicalresearch.inescporto.pt/breastresearch/index.php/Get_INbreast_Database
ADNI	ADNI dataset contain data of Alzheimer's disease patient	https://www.adni.loni.usc.edu/data-samples/access-data/
LIDC	Lung image database consortium. CT scan images of lung for detection of lung cancer	https://www.wiki.cancerimagingarchive.net/display/Public/LIDC-IDRI#
DRIVE	Digital Retinal images for extraction. It contains 40 images of retina	https://www.isi.uu.nl/Research/Databases/DRIVE/download.php
ALL-IDB	It is a new and pubic dataset of microscopic images of blood samples	https://www.homes.di.unimi.it/scotti/all/
LUNA	888 CT images are in this dataset	https://www.luna16grand-challenge.org/data/
LIDC	Lung images database Consortium contains lung screening thoracic CT scan	https://www.wiki.cancerimagingarchive.net/display/Public/LIDC-IDRI
NLST	It has SCT screening images and lung cancer progression dataset	https://www.biometry.nci.nih.gov/cdas/learn/nlst/images/
TCGA	The cancer genome atlas, it has genomic, transcriptomic, epigenomic and proteomic data	https://www.portal.gdc.cancer.gov/

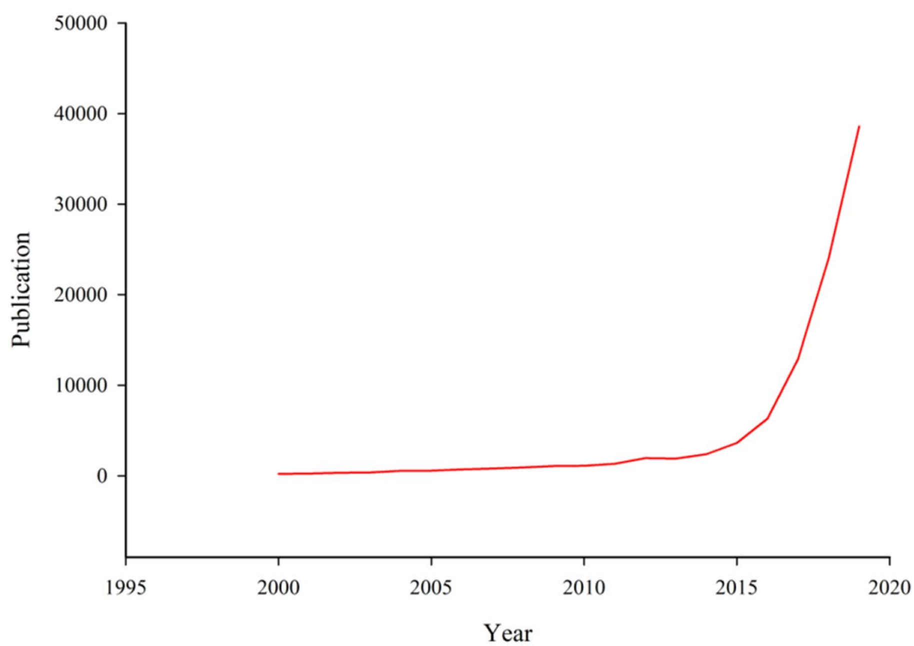


Fig. 8 Line graph of published manuscript that uses the deep learning approach in subareas of medical health informatics

response rate. Therefore, the application of deep learning models in medical science has bright future research scope. The use of deep learning networks is not restricted to only earlier mentioned. It is further extended to research areas like agriculture, weather prediction, gaming, physiological signals analysis, computer security, and key management in

Fig. 9 Publication analysis in ScienceDirect digital library

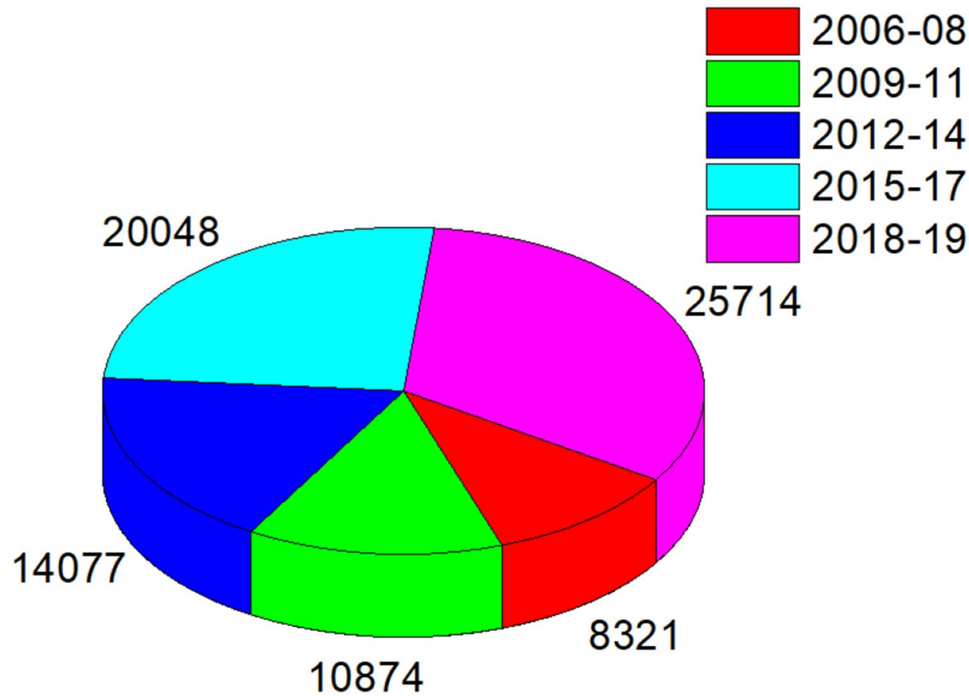
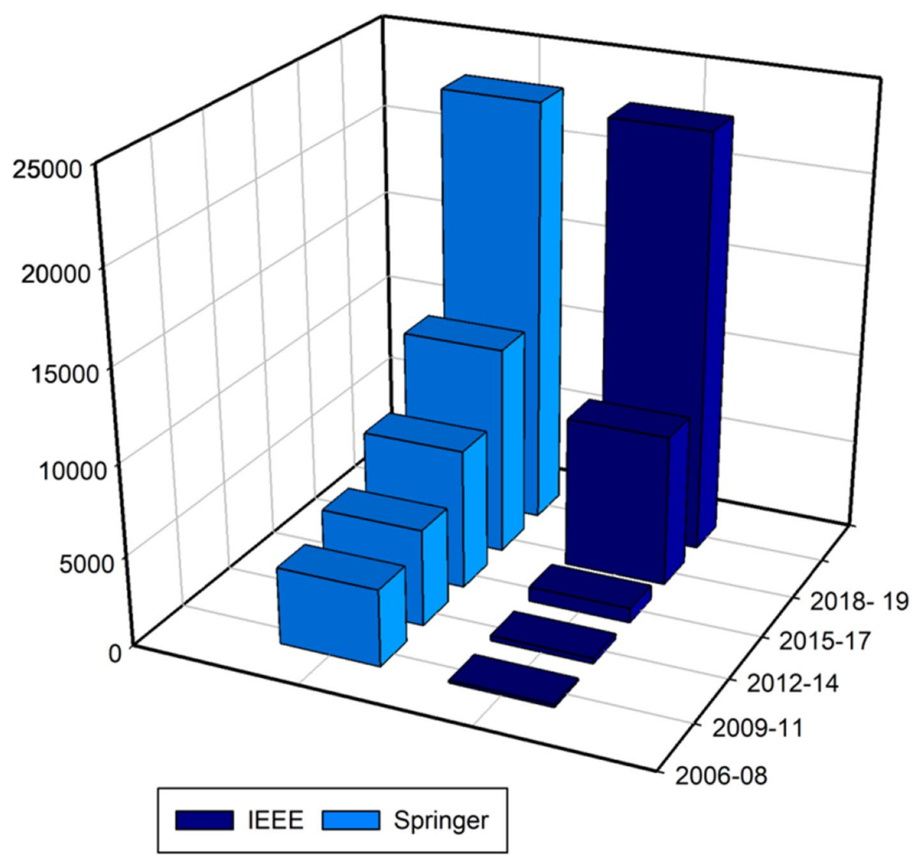


Fig. 10 Publication analysis in Springer database and IEEE digital library



cloud computing and yields outstanding performance. And despite the fruitful conclusion from the systematic review of past studies, there are a lot of open challenges for future work.

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