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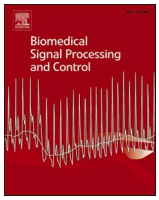

Reviewing methods of deep learning for intelligent healthcare systems in genomics and biomedicine

Imran Zafar [a,*], Shakila Anwar [b], Faheem kanwal [c], Waqas Yousaf [d], Fakhar Un Nisa [e], Tanzeela Kausar [f], Qurat ul Ain [g], Ahsanullah Unar [h], Mohammad Amjad Kamal [i,j,k,l,m], Summya Rashid [n], Khalid Ali Khan [o,p], Rohit Sharma [q,*]

[a] Department of Bioinformatics and Computational Biology, Virtual University, Pakistan
[b] Life Sciences Department, Arid University, Burewala Campus, Pakistan
[c] Institute of Molecular Biology and Biotechnology (IMBB), University of Lahore, Pakistan
[d] Institute of Molecular Biology and Biotechnology, Department of Botany, The University of Lahore, Punjab, Pakistan
[e] Depatment of Molecular Biology, Virtual University of Pakistan, Pakistan
[f] Department of Zoology, Virtual University of Pakistan, Lahore, Punjab, Pakistan
[g] Department of Chemistry, Government College Women University Faisalabad (GCWUF), Punjab, Pakistan
[h] School of Life Sciences and Medicines, University of Science and Technology China, Hefei, Anhui, China
[i] Institutes for Systems Genetics, Frontiers Science Center for Disease-related Molecular Network, West China Hospital, Sichuan University, China
[j] King Fahd Medical Research Center, King Abdulaziz University, Saudi Arabia
[k] Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Bangladesh
[l] Enzymoics, 7 Peterlee Place, Hebersham, NSW 2770, Australia
[m] Novel Global Community Educational Foundation, Australia
[n] Department of Pharmacology and Toxicology, College of Pharmacy, Prince Sattam Bin Abdulaziz University, P.O. Box 173, Al-Kharj 11942, Saudi Arabia
[o] Unit of Bee Research and Honey Production, Research Center for Advanced Materials Science (RCAMS), King Khalid University, P.O. Box 9004, Abha 61413, Saudi Arabia
[p] Applied College, King Khalid University, P. O. Box 9004, Abha 61413, Saudi Arabia
[q] Department of Rasashastra and Bhaishajya Kalpana, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

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ABSTRACT

The advancements in genomics and biomedical technologies have generated vast amounts of biological and physiological data, which present opportunities for understanding human health. Deep learning (DL) and machine learning (ML) are frontiers and interdisciplinary fields of computer science that consider comprehensive computational models and provide integral roles for disease diagnosis and therapy investigation. DL-based algorithms can discover the intrinsic hierarchies in the training data to show great promise for extracting features and learning patterns from complex datasets and performing various analytical tasks. This review comprehensively discusses the wide-ranging DL approaches for intelligent healthcare systems (IHS) in genomics and biomedicine. This paper explores advanced concepts in deep learning (DL) and discusses the workflow of utilizing role-based algorithms in genomics and biomedicine to integrate intelligent healthcare systems (IHS). The aim is to overcome biomedical obstacles like patient disease classification, core biomedical processes, and empowering patient-disease integration. The paper also highlights how DL approaches are well-suited for addressing critical challenges in these domains, offering promising solutions for improved healthcare outcomes. We also provided a concise concept of DL architectures and model optimization in genomics and bioinformatics at the molecular level to deal with biomedicine classification, genomic sequence analysis, protein structure classification, and prediction. Finally, we discussed DL's current challenges and future perspectives in genomics and biomedicine for future directions.

* Corresponding authors.
E-mail addresses: bioinfo.pk@gmail.com (I. Zafar), Shakilarana5@gmail.com (S. Anwar), kanwalf674@gmail.com (F. kanwal), fakhar_220@hotmail.com (F. Un Nisa), tanzeelaarifsoomro@gmail.com (T. Kausar), chemistquainhawk@gmail.com (Q. ul Ain), aunar@mail.ustc.edu.cn (A. Unar), rrs.usa.au@gmail.com (M.A. Kamal), s.abdulrashid@psau.edu.sa (S. Rashid), kkhan@kku.edu.sa (K.A. Khan), rohitsharma@bhu.ac.in (R. Sharma).

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1. Introduction

Bigdata Analysis of biomedical information and personalized health activities are becoming more considerable and essential in personalized medicine to treat multifunctional diseases via providing a powerful tool and techniques to introduce modern medicine [1–3]. For instance, a personalized approach to cancer therapy incorporates a range of patient data to decide on the best progression of action, including genetic variants, environmental variables, imaging genetics, existing drugs, and the patient's lifestyle [4–6]. Scientists now offer patients-centred medication due to the massive volumes of data that genetic, imaging, and life-monitoring technology have collected over the previous ten years in the context of precision medicine and digital phenotyping to improve E-health objectives [7,8]. Even with all the management revaluation and extensive data we've gathered, it's still unclear what illnesses are and how to treat them effectively [9].

Deep Neural Networks (DNN), a type of machine learning, have grown in popularity due to the complexity of the material being examined based on the role-based algorithm and solve automatically segmenting various interlinked diseases [10]. With the development of reliable data-driven ML techniques, it is essential to successfully connect several patient profile analysis categories [11,12]. An ANN known as a "DL architecture" uses two or even more buried neurons to increase prediction accuracy [13]. Compared to regular ANN, the number of veiled layers in DL is significantly more significant for manifold disease identification [14]. In a typical DNN, the nonlinear stimulation techniques like Sigmoid, Hyperbolic tangent, ReLu, softmax, Softplus, Absolute value rectification, and Maxout produce a productive output for classifying the disease using activation functions in the context of the deep dataset [15]. These deep datasets have been balanced, and their biases are addressed based on computational approximation capabilities [16]. A DNN's weights are intended to reduce the harm caused by these factors through intelligent fault diagnosis [17].

The Convolutional deep belief network (CDBN) is based on semantic interaction. It provides higher-level features for disease diagnosis using deep transfer learning architecture and efficient inspection in the context of intelligent healthcare for genetic objects of genomics and biomedicine [18–20]. DL has wide-ranging applications in the domain of intelligent health [21,22], including digital picture analysis in cross-disciplinary diseases [23],text mining in healthcare [24], monitoring of human health in the context of aura [25], integration of medicine and biology research [26], and object identification [27].

In the context of IHS, this review examines how DL tools and techniques are applied in genomics and biomedicine. Healthcare providers may considerably benefit from this prompt disease diagnosis framework; the contextual overview of the DL system in the milieu of innovative health is mentioned in Fig. 1 for enhancing the invariance of various manifold diseases. Furthermore, we explore the Overview of the DL system used in IHS and provide wide-ranging decisions and applications (Diseases Detection, Computer Vision, Drug Discovery, NLP, Object Detection, etc.) for future genomics and biomedicine details prediction. DL tools based on computational algorithms (CNN, DBN, RNN, RvNNs, ANN, and RBM) and techniques for diseases (Cancer, Heart, Brain, Diabetics, Epilepsy, etc.) detections shown in the diagram have been extensively studied for personalized IHS to classify manifold diseases for numerous digital treatment options (ST Scan, X-Ray, MRI, etc.).

Deep learning (DL) has made significant research contributions in IHS for genomics and biomedicine. DL has significant potential in medicine, particularly in analysing medical images like X-rays, MRI scans, and CT scans. DL algorithms can accurately diagnose diseases, detect risks, and identify irregularities in medical images, particularly in cancer detection. However, challenges persist, such as the lack of diversity and accuracy in datasets and insufficient data. DL models can automate and improve various aspects of healthcare, including monitoring patient vitals, predicting outcomes, and automating repetitive tasks.

DL also offers insights into brain connectivity and can impact neurotechnology. Despite the potential, deploying DL systems in biomedicine requires addressing challenges related to explaining and justifying model decisions. Researchers propose incorporating flexibility into DL algorithms to explain predictions, particularly for medical professionals

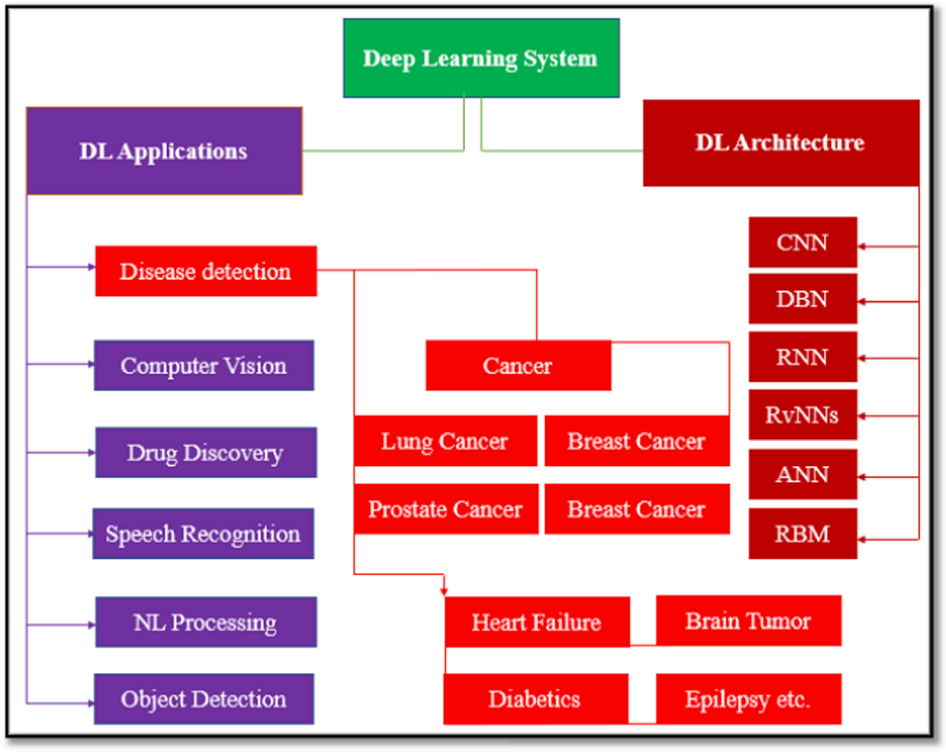

Fig. 1. Deep Learning Applications in Integrative Health Systems for Predictive Diagnosis and Treatment of Diseases.

and regulatory authorities. DL can potentially revolutionize biomedicine by addressing complex challenges and improving disease treatment. Its applications span disease detection, medical imaging, drug discovery, clinical decision support, biomarker discovery, patient risk stratification, and genomic data analysis. These contributions can potentially enhance diagnostics, treatment, and personalized care, ultimately improving healthcare outcomes.

1.1. Biological interpretation of XAI and deep learning in genomics

DL has succeeded in several disciplines, including ML and computer vision processing [28]. It revolutionizes data-driven research because of its capacity to learn complicated structures from data without the need for human interaction. Due to its widespread success, DL is becoming more popular in genomic research [29]. Genomes' data are complex and interact with reactions (e.g., disease outcomes). Unlike traditional approaches (e.g., linear regression), DL enables complex learning characteristics from genetic information, making it a vital tool for analyzing nonlinear or interaction effects in genomic data analysis, and Explainable Artificial Intelligence (XAI) provides image-based deep learning (DL) algorithms. A short overview of several DL's uses in genomics research provides an exclusive prototype for future medicine, and XAI can play a crucial role in improving controllability by providing insights into how these algorithms make decisions. DL is increasingly used to ascertain the nature and function of genomic components, including regions, regulators, and gene expression levels. In computational genetics and bioinformatics, extracting fundamentally important information from substantial omics data sets is still tricky. Supervised and unsupervised learning are subcategories of DL and ML techniques [30]. Starting with an introduction to basic ideas in supervised learning and moving on to prominent DL techniques and their applications in genomics research, we discuss the future directions of genomics research using these approaches. Several DL techniques are available, but because of space constraints, this study concentrated on conventional DL approaches, particularly those that may be used to analyze genomic data [31].

Deep neural networks (DNNs) have revolutionized pattern recognition and machine learning, especially in image identification and object detection [32]. According to Carvalho, et al. [33], DNNs have gained popularity in bioinformatics due to their ability to handle large-scale genomics and epigenomics data. They outperform traditional machine learning algorithms in tasks such as discovering sequence motifs and predicting genetic variants. However, one challenge with DNNs is their lack of interpretability, as they are often considered black boxes [34]. Despite this, their speed and accuracy make them valuable for genomic research. The focus is now on finding ways to explain and interpret DNN predictions in genomics and omics applications [35].

1.1.1. Application of XAI for genomics and biomedicine

Explainable Artificial Intelligence (XAI) offers significant benefits for genomics and biomedicine [36]. By providing interpretable models, XAI can aid in understanding complex biological processes, enhancing diagnostics, and enabling personalized medicine [37]. XAI techniques facilitate the analysis of genomic data, helping researchers identify disease-causing genetic variations, understand gene regulation mechanisms, and discover drug targets. In clinical settings, XAI can be integrated into decision support systems, providing transparent explanations for predictions and assisting healthcare professionals in making accurate diagnoses and treatment plans [38]. In drug discovery, XAI models help researchers comprehend the relationships between molecular features, pathways, and drug responses, leading to the development of safer and more effective therapeutics [39]. XAI also supports precision medicine by enabling personalized risk prediction and treatment selection with understandable rationales.

Additionally, XAI aids in interpreting biological experiments, identifying biomarkers and uncovering underlying disease mechanisms. Ethically, XAI using DL promotes transparency, fairness, and compliance with regulatory standards in genomics and biomedicine [40]. Overall, applying XAI in these fields contributes to our understanding of biology, improves healthcare decision-making, and ensures responsible AI usage.

1.1.2. XAI for improved controllability in Image-based DL algorithms

Explainable Artificial Intelligence (XAI) techniques play a vital role in improving the controllability of image-based deep learning (DL) algorithms [41]. XAI methods enable users to gain insights and understand the decision-making process of DL models by visualizing important features and regions in images. Techniques such as activation maximization and saliency mapping help reveal the specific parts of an image that contribute most to the algorithm's predictions. Additionally, attention mechanisms in DL algorithms can be visualized through XAI, allowing users to understand and control the model's focus. Rule extraction techniques provide interpretable representations of DL models, empowering users to modify and refine rules to influence the algorithm's behaviour [42].

Furthermore, XAI techniques can generate counterfactual explanations, enabling users to explore alternative scenarios and understand how changing specific image attributes affects the algorithm's output. Finally, by integrating XAI into interactive interfaces, users can actively engage with DL algorithms and have real-time controllability by adjusting parameters, modifying input images, and exploring different decision paths. Overall, XAI techniques in image-based DL algorithms enhance controllability by providing interpretability and transparency, allowing users to understand, influence, and fine-tune AI systems for improved image analysis and decision-making [43].

1.1.3. XAI decisions and predictions in healthcare sectors

XAI refers to the ability of an AI model or algorithm to provide understandable explanations for its decisions or predictions. In healthcare, XAI plays a crucial role in providing explanations for image-based deep learning (DL) algorithms used in the diagnosis of various conditions such as cancer, chronic obstructive pulmonary disease (COPD), and COVID-19, such as earlier researcher provides DL architecture DeepOCT to analyze macular edema on OCT images [44]. By using XAI techniques, clinicians can gain insights into how the DL algorithms arrive at their predictions, which is essential for verifiability. Instead of treating the AI model as a black box, XAI allows clinicians to understand the underlying features and patterns contributing to the algorithm's decision-making process, such as the researcher developing Grad-CAM to explore visual explanations from deep networks [45]. This transparency is vital for clinicians to trust and verify the algorithm's accuracy, particularly in critical healthcare scenarios.

Furthermore, XAI enhances controllability by allowing clinicians to identify and validate the most responsible sections or pathologies in medical images. Clinicians can use these explanations to evaluate the reliability of the algorithm's predictions and ensure that the algorithm focuses on the relevant regions or features most indicative of a particular condition. This controllability gives clinicians greater confidence in the algorithm's output and enables them to make more informed decisions regarding patient care.

1.2. Deep learning for genomic prediction in animals and plants

DL holds significant potential for genomic prediction in animals and plants. It can enhance breeding programs by accelerating genetic gain and enabling more informed selection decisions. Continued research and advancements in deep learning techniques, coupled with the availability of large-scale genomic datasets, will further improve the accuracy and applicability of these models in genomics. Breeding animals and plants have a significant role in maintaining a stable food supply for the world's growing population [46], which some estimates anticipate will reach 9.5 billion consumers by 2050 [47]. For animal and plant breeders to keep up with the anticipated increase in food consumption, genetic

improvement rates in plant breeding must be feasible at the most astounding levels [48,49]. Utilizing new approach options is a crucial starting step for genetic selection, initially introduced by Gjedrem, et al. [49]. Still, it is widely used as one of the most commonly used breeding strategies. Estimating the unobserved values of population attributes using information from such an observable population and genome-wide DNA variation (markers) is possible. Numerous animal and plant breeding organizations have made genotyping a common practice to shorten breeding cycles due to declining genotyping costs [50].

The most famous prediction technique is genomic best linear biased prediction [51]. Applying any approach to document the link between genotypic and phenotypic data in a training dataset for genomic prediction is possible. By adjusting the genetic data to the mathematical model, we may determine how well it correlates with a predicted value. The earlier researcher developed Numerous genetic forecasting techniques [52]. As reported in her article, Van Vleck claims that GBLUP (genomic best linear unbiased prediction) is a typical additive gene impact model that necessitates estimating and resolving Henderson's process formulations and the mixed model formulations. It is common to use Bayesian techniques that use Markov Chain Monte Carlo to find the crucial variables [53]. Various DL approaches have been tested in the field of genomic prediction in recent years. AI incorporates DL as a subfield of machine learning and is limited in dealing with complex relationships between input and output since they are nonparametric models for generic medicine [54]. One of its distinctive characteristics is the model's ability to adapt to sequences of unknown value, which could not be modelled mathematically initially.

AI-Based Robust Hybrid Algorithm Design and Implementation for Real-Time Detection of Plant Diseases in Agricultural encompasses various techniques for predicting and detecting plant diseases using genomic and phenotypic data [55]. One widely recognized prediction technique is Genomic Best Linear Biased Prediction (GBLUP) [51].. In this context, the goal is to establish a connection between genotypic information and phenotypic characteristics within a training dataset, enabling accurate disease detection. The genetic data is adjusted and integrated into a mathematical model that evaluates its correlation with predicted values to achieve this. Previous researchers [52] have explored different genetic prediction techniques, with Van Vleck highlighting GBLUP as a prominent example. GBLUP relies on estimating and resolving Henderson's process formulations and mixed model formulations to account for additive gene effects. Bayesian techniques are also commonly employed, utilizing Markov Chain Monte Carlo methods to identify crucial variables [53].. These approaches contribute to developing effective predictive models for plant disease detection.

Furthermore, recent Artificial Intelligence (AI) advancements have introduced various Deep Learning (DL) approaches to genomic prediction. DL, as a subfield of machine learning, has shown promise in handling complex relationships between input and output variables. However, it is essential to note that DL models are nonparametric and may face limitations when dealing with generic medicine and other related challenges [54]. One distinguishing feature of DL models is their ability to adapt to sequences of unknown value that were initially difficult to model mathematically. This characteristic holds significance in real-time detection of plant diseases, as it allows for efficient and accurate identification of disease patterns in agricultural settings.

Numerous studies [56,57], have shown that DL effectively creates AI systems, goods, devices, and applications. In multiple domains, ranging from social scientists to the natural sciences, these objects have found use in various applications covering machine learning, computer vision, and natural language technique [58]. Many "high-tech" products, such as self-driving cars, robots, chatbots, components of speech, voice recognition, and digital assistants, are built based on digital learning [59]. Medical applications include genomics and biomedicine, detecting and classifying cancer and dermatological issues [60]. For example, Menden, et al. [61], assessed the survival of human cancer cell lines subjected to treatment using a DL technique. The specificities of DNA- and RNA-binding proteins were predicted using DL and an entirely convolutional architecture developed by Alipanahi, et al. [62]. It was found that Andrades and Recamonde-Mendoza [63] employed the DL method to identify tumour suppressor and oncogene genes. The methylation state of a single cell's DNA can also be correctly predicted using DL methods [64]. With DL, it has proven very successful in predicting DNA & RNA-binding sequence-based selectivity, methylation status, and gene expression. This is because DL uses structures directly adopted from modern machine learning and voice recognition implementations. Jiang and Li [65], thoroughly assess DL's high-throughput plant phenotyping applications.

AI-Based Robust Hybrid Algorithm Design and Implementation for Real-Time Detection of Plant Diseases in Agricultural has been demonstrated to leverage the power of Deep Learning (DL) techniques, leading to the development of effective AI systems, devices, and applications [56,5755]. DL has found applications across multiple domains, including machine learning, computer vision, and natural language processing [58]. Notably, it has contributed to the creation of advanced products such as self-driving cars, robots, chatbots, speech and voice recognition systems, and digital assistants [58].

In the medical field, DL has made significant strides in genomics and biomedicine, particularly in detecting and classifying cancer and dermatological issues [60]. For instance, Menden, et al. [61], employed DL techniques to assess the survival of human cancer cell lines under various treatments. DL models have also been used to predict the specificities of DNA- and RNA-binding proteins, as demonstrated by the work of Alipanahi, et al. [62], who developed a fully convolutional architecture for this purpose. Andrades and Recamonde-Mendoza [63] utilized DL methods to identify tumor suppressor and oncogene genes. Additionally, DL has successfully accurately predicted the methylation state of individual cells' DNA [64]. By adopting structures from modern machine learning and voice recognition implementations, DL has proven effective in predicting DNA and RNA-binding selectivity, methylation status, and gene expression. In the context of AI-Based Robust Hybrid Algorithm Design and Implementation for Real-Time Detection of Plant Diseases in Agricultural, DL techniques hold great promise [55]. These techniques can be harnessed for high-throughput plant phenotyping applications, as comprehensively assessed by Jiang and Li [65]. By leveraging DL's capabilities, this hybrid algorithmic approach enables real-time detection of plant diseases in agricultural settings, leading to more efficient disease management and improved crop health.

1.3. DL approaches for Intelligent Healthcare Systems (IHS)

In recent years, a broad range of AI and DL technologies have been used to analyze the enormous volumes of health records [66]; e.g., a model based on statistical regression was used to diagnose heart problems early and automatically [67]. DL has also been used in medical imaging to aid in detecting object characteristics [68]. DNN-based models are top-rated in screening complex datasets among the many DL models. Data is sifted through a series of layers in a process known as DL, which employs many phases of learning [69]. DNN models can outperform traditional ML models when they analyze massive amounts of data. Researchers have made significant progress in image and natural language processing (NLP) using DNN-based approaches. DL, also known as learning-based and hierarchical teaching, data is evaluated using a layered computer architecture [69]. DL techniques employ many layers to filter and analyze data, with the previous layer's output being used to direct the future ones [70]. DL models may be taught to evaluate ever-increasing volumes of data to enhance their ability to find connections and correlations [69]. An approximation of how the connections between neurons in the brains of animals provide DL. Each layer becomes active when a layer of nodes gets input from nearby neurons. Electrical impulses pass between actual cells, and data may be sent through the layers numerous times to improve and optimize the final output in ANNs, which are the Foundation for DL models [31]. AI, ML,

and DL algorithms can discover trends and address common issues because NNs mimic the activity of the human brain.

Fig. 2 explores the mathematical translation activities that transform raw input towards meaningful outcomes in the hidden layers. Weights are added once the input layer has been identified. These weights aid in determining the relative relevance of each variable, with greater weights having a more substantial influence on the result than smaller ones. The proper weight is then multiplied by each input before being added together. An activation function will then decide what the output will be once the output has passed through it. The node "fires" (or activates) whenever the output rises over a certain threshold, sending data to the network's next tier. As a result, the input of one node becomes the output of the following node. This NN is a feedforward network (FFN) as data is sent from one layer to another during the process.

The functional linear regression, feedforward function, and cost estimation for optimization are derived in formula-based equations to understand DL networks' working complexity for genomic data analysis.

$$\sum_{i=1}^{m} w_i x_i + bias = w_1 x_1 + w_2 x_2 + w_3 x_3 + w_4 x_4 + w_5 x_5 + bias \;\; \mapsto linearRegression$$

$$output = f(x) = \sum_{0if \sum w_1 x_1 + b < 0}^{1if \sum w_1 x_1 + b \geqslant 0} \mapsto feedforwardFunction$$

$$CostFunction = MSE = \frac{1}{2m} \sum_{i=1}^{n} (y_{\cdot} - y)^2$$

Linear regression is a trained DL model that determines the linear connection between the variables by determining the best-fitting linear line among them. In learning algorithms, the KNN model is frequently used for non-linear regression. KNN simply implements non-linear regression in DL. Regression analysis' supervised learning method is used to learn the relationship between the attributes and the goal. Each solution with an interval—for instance, between 1.2 and 5.6—is regarded as a linear combination since the objective parameters are continuous. Using a gradient-based technique, the backpropagation (BP) algorithm trains a feedforward architecture. The projected value is continuous rather than conditional when using linear regression as a classifier, making it susceptible to imbalance data.

In detail, DL, sometimes referred to as DNN models, have become new and exciting tools for analyzing healthcare data because of their high performance and quick methodological progress. Biomedical and healthcare data has been employed in developing DL models. Optimization features are used from fuzzy sets optimized cost, productivity, and time such as cost function, linear regression (LR), and feedforward function. Google DeepMind [71] and IBM Watson [72] are two examples of AI systems that employ computers to analyze healthcare data. Short-axis cardiac MRI and MMNet may segment the left ventricle (LV) using DL to encode the model's parameters [73]. MRI biomarker discovery using Restricted Boltzmann Machines (RBM) is another illustration of a DL model in medical imaging [74].

There are 400 billion people around the world who suffer from a rare genetic disorder. The quick & accurate identification of several disorders is a significant barrier for medical doctors as they lack the expertise to accomplish the correct task. The prediction of diseases is another challenging issue in medical sciences due to domain experts' lack of computational framework knowledge. Therefore, data mining is a crucial tool for predicting diseases with already developed models, as mentioned in Table 1.

The new strategy offers a broad disease diagnostic strategy with 100 % accuracy using patient symptomatology by utilizing DL algorithms like CNN for automatic feature extraction and disease prediction and KNN for computation to identify the exact match in the data set for proper prognostication about illness consequence. The training dataset has previously been identified with a collection of wide-ranging cases and information as mentioned in Table 1 diseases category. A misdiagnosis might have a substantial negative influence on the patient's life. Therefore, there is a critical need to increase knowledge of rare diseases in medical sciences. The NLP and DL approaches may be able to extract valuable information about rare diseases to make identifying and treating them simpler.

1.4. Deep learning multiplayer models for genomic selection

DL is revolutionizing how AI systems are created such as; until 2015; humans were better than artificial machines at solving a variety of computer vision problems related to object localization and recognition using photographs [91]; however, in more recent years, earlier researchers [92,93], the abilities of artificial machines have surpassed those of humans in this particular endeavour. Here we explore an example of how the application of DL models has exceeded the performance of other machine-learning algorithms and human abilities. As a result, DL models have been applied to genomic selection since the volume of data produced during the breeding of plants and animals keeps growing; DL approaches have also been used to predict the outcomes of genomic and biomedical research [94]. The outcomes for datasets with a limited sample size are usually erratic and underperform the -possibly exaggerated- expectations. In this step, we provide a meta-picture that outperforms traditional genomic estimation models in predictive accuracy. To effectively use DL approaches, it is essential to comprehend the basic concepts of DL and its needs for knowledge, computer resources, and data amount and diversity [95].

We also explored literature from earlier research [96]. We examined

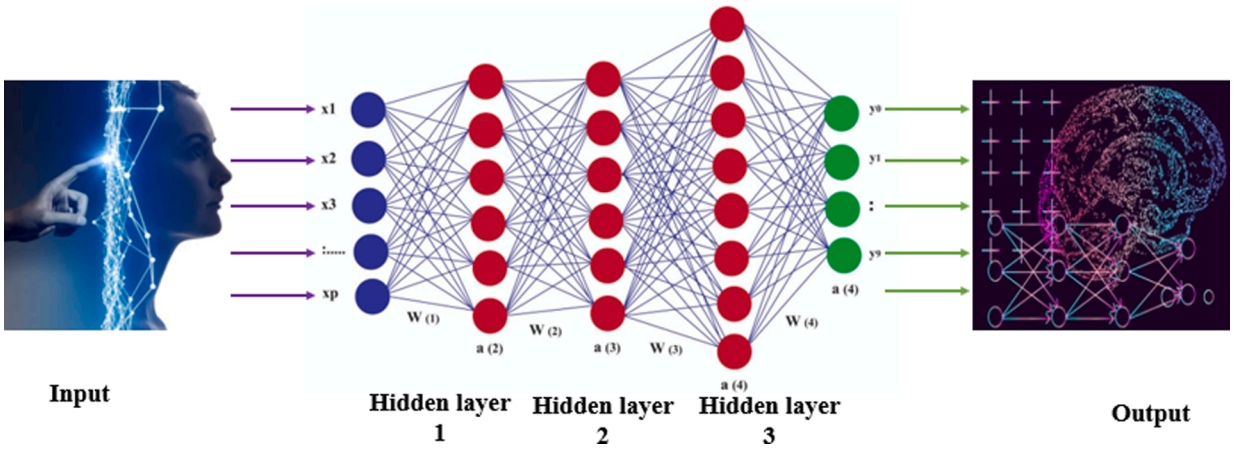

Fig. 2. The working mechanism of a feedforward neural network (FFN) in deep learning to explore the optimized output.

Table 1
Deep Learning Approaches for Predictive Disease Diagnosis: A Review of Multi-Dataset Methods.

Sr #	Disease Category	Article	Data	DL Methods
1	Breast Cancer	[68]	INbreast	CNN + DBN
2		[75]	DDSM	CNN
3			MIAS	
4		[76]	DM, SFM-UM	DCNN
5			DM, SFM-USF	
6		[77]	MITOS12	CNN
7			TUPAC16	
8		[78]	227 SWE Images	DBN(PGBM)
9	Gastric Cancer	[79]	AUC	CNN
10	Lung Cancer	[80]	LIDC/IDRI	CNN + DBN + SDAE
11	Brain Cancer	[80]	BRATS	FCNN + CRF-RNN
12		[81]	Dataset III from BCI	CNN + SAE
13			Competition II	
14			Dataset 2b from BCI	
16			Competition IV	
17	Cancer	[82]	RNA-seq (LUAD + STAD + BRCA)	DNN
18	Multiple	[83]	Myelin and T1w	CNN
19	sclerosis		Images	
20		[83]	Myelin and T1w	DBN
21			Images	
22	Parkinson	[84]	PPMI	CNN
23			SNUH	
24	Heart Failure	[85]	Sutter-PAMF	RNN adopted by GRU
25		[86]	MIT-BIH	DNN + DAE
26			INCART	
27			SVDB	
28	Epilepsy and Seizure	[87]	EEG signals	CNN
29	Diabetic	[88]	E-ophtha	CNN + HCF
30	Retinopathy		DIARETDB1	
31			MESSIDOR	
32	Mental Workload	[89]	–	SDAE
33	Multiple Disease	[90]	–	SDN
34		[88]	Everyone Healthy	SCDP
35			WebMD	
36			MedlinePlus	

Table 2
Comparing Deep Learning Approaches for Accurate Analysis of Genetically Modified Crops and Animal Breeds.

Crop& Animals breeds	Topology	Comparison with different approaches	References
Human traits	*MLP&CNN*	*BayesB*, *BRR*	[97]
Pig data and TLMAS2010 data	*MLP*	*GBLUP*, *BL*	[98]
Six species	*MLP*	*rrBLUP*, *BRR*, *BA*, *BB*, *BL*, *SVM*, *GTB*	[99]
Holstein bulls	*MLP&CNN*	*GBLUP*, *BayesBandRF*	[100]
Wheat and Jerseycows	*MLP*	*BayesianRidgeregression*(*BRR*	[101]
Holstein-Friesian and German Fleckvihcattle	*MLP*	*GBLUP*	[102]
Arabidopsis, maizeand wheat	*MLP*	*OLS*, *RR*, *LR*, *ER*, *BRR*	[102]
Maize and wheat	*MLP*	*PNN*	[103]
		GBLUP	[104]
		BMTME	[105]
		BayesianOPLM	[106]
Wheat	*MLP*	*BL*, *BayesA*, *BayesB*, *BRR*, *RKHS*	[107]
		RR −*BLUP*, *GBLUP*	[108]
		SVM, *TGBLUP*	[109]
		GBLUP	[109]
Soybean	*CNN*	*rrBLUP*, *BRR*, *BayesA*, *BL*	[110,111]
Strawberry andblueberry	*MLP&CNN*	*RKHS*, *BRR*, *BL*	[112]
Arabidopsis	*MLP&CNN*	*GBLUP*, *EGBLUP*, *BayesA*	[113]

See

RF	*RandomForest*.	*ER*	*ClassicElasticNetRegression*
OLS	*OrdinalLeastSquare*	*BL*	*BayesianLasso*
RR	*ClassicalRidgeRegression*	*DBN*	*DeepBeliefNetworks*.
LR	*ClassicalLassoRegression*	*GTB*	*GradientTreeBoosting*
GP	*GeneralizedPoissonRegression*	*EGBLUP*	*ExtendedGBLUP*

how effectively DL can handle challenging prediction problems and how combining genomic and biomedical datasets and DL algorithms can hasten the shift in breeding practices that the genomic section technique has already begun. Based on a literature review, we also discuss a few DL approach trends and point out certain instances in which the DL methodology can be successfully used in genomic and biomedical research. In addition, we recognize that further research is required before we can adapt and enhance DL methods that consider the unique characteristics of breeders' inputs and biomedical investigation rather than relying on the current DL tools and techniques. The benefits, drawbacks, and potential applications of DL in the future are also examined by comparing different methods in Table 2.

As methods are mentioned in Table 2, Analyses of genetically modified crops and animal breed variants have been transformed by technological innovations, resulting in the frequent creation of massive, complicated data sets. As a result, we find the literature and pursue data where the conclusion is done because there are now more attempts being made by computational exports to combine different data sets in the context of DL and interpret these metrics to check the accuracy of outputs. Meanwhile, DL has developed quickly and is now used in many research fields, including crops and animal breed sequencing & identification in particular to study more attentional outputs. In the same way, we investigate whether DL is used in conservation biology, genetically modified crops, and animal breed variants. We concentrate on genetic-based assessments based on review and literature at several morphological stages via applying DL methods and topologies, ranging from biological investigation and their productivity, and explore how genetics relate to them based on highly proficient topology-based approaches.

1.4.1. Meta-analysis of deep learning techniques for genomic selection

Multilayer Perceptron (MLPs) were shown to be better than the Bayesian linear model (BLM) in prediction accuracy for genomic prediction in multiple species [97,114]. The projected Pearson's correlation (PPC) for comparing wheat to bottleneck bandwidth and round-trip time (BRR) ranged from 0.48, 0.03, 0.54, 0.56, 0.6 *and* 0.7 and from 0.59 *to* 0.02 points, depending on the MLP correlation. These findings demonstrate a fundamental contrast between shallow (BRR) and DL (MLP). MLP surpassed BRR by 11.2, 14.3, 15.8, and 18.6 percent in measures of Pearson's correlation between the first, second, third, and fourth neurons. On the other hand, Gianola, et al. [101]found that for Jersey cow data, A six-neuron application of MLP surpassed the BRR in fatty production (52 %), milk production (33 %), and protein production (82 %), both with pedigree or markers.

According to Panda and Panda [115], Models based on radial basis functions and Bayesian regularized neural networks surpassed linear models in terms of effectiveness when generating predictions. According to the authors [115], nonlinear models (including neural networks and kernel models) surpassed regression analysis specifications when applied to grain datasets for forecasting purposes. The MLP, RKHS (reproducing kernel hilbert space), and BL regressions were tested on 300 tropical inbred lines of maize with 21 combinations of environment-

trait. This model's average trait-environment correlation (0.553), fared better than RBFNN (0.557) and the linear model (0.554 to 0.551). Regarding trait-environment combination, 0.542 and total accuracy of prediction, RKHS, and RBFNN (radial basis function neural network) outperformed an additive Bayesian LASSO (least absolute selection and shrinkage operator) model.

1.5. Multiplayer functions of deep learning incorporating biological structure in biomedicine

The current state of the art for various tasks in patient and disease classification, basic biological research, genomics, and therapeutic research, where DL-based approaches meet or surpass the prior state of the art [116]. Given this continuous evolution, how do we investigate human illness using deep learning? We conclude that deep learning has not yet fully realized its significance or generated a strategic inflexion point, even though the proper response mostly depends on the particular domain and challenge. DL has not entirely "fixed" these issues, despite outperforming rival network constructivist approaches in many of the areas discussed below and showing measurable gains in prediction performance [60].

Medical images, electroencephalograms, genomic and protein sequences, and other physiological and biological data are created at an ever-increasing rate due to developments in biology and medical technology [117]. These details aid in our understanding of human health and illness. ANN-based DL techniques have a lot of potential for sorting through complex data and spotting pattern traits. The development of high-throughput technology has resulted in an explosion of biomedical data during the last several decades, including genetic sequences, protein structures, and medical imaging. We'll need robust and efficient computing tools to store, analyze, and understand this big biological data. Algorithmic frameworks based on DL provide insight into these complex issues. This review also examines DL methods and modern medical applications for bioinformaticians and informaticians.

1.5.1. Current updates of deep learning for predicting biomedicine properties

Due to advancements in biological and medical technology, we now have access to enormous volumes of physiologically based data, such as clinical images, electroencephalograms, genetic data, and meta-proteomics. Evaluating human health & pathology is made more accessible by using this data for learning [118]. DL-based algorithms, created from artificial neural networks, have significant potential for identifying trends and characteristics in large amounts of complex data [119]. This Perspective investigates the use of machine learning to enhance diagnosis and therapy. We show how computer vision might improve three critical areas of biological systems as we face various diseases and the natural ageing process: healthcare diagnostics, precision medications, and health monitoring. There are successful applications of computer vision and potential concerns in every industry. When these issues are addressed using computer vision, a future of rigorous medical results is possible, with detection, diagnostic, and treatment methods that are constantly adjusted to personal and environmental differences.

DL necessitates technology breakthroughs in conjunction with balancing concerns, the large amount of data required, and labelling for biological data [68]. In contrast to other varieties, minor medical imaging changes may reveal the condition's existence. As a result, high-resolution inputs, quick training, and many memories are necessary for image analysis. Developing a consistent evaluation tool for classifying or predicting biological data is difficult. Except for prior systems, we can tolerate some false positives and reject few, if any, false negatives in disease diagnosis. When working with different data sets, examining the model correctly and fine-tuning it based on the data's characteristics is critical. Fortunately, deeper networks with inception modules are faster and more accurate in biological imaging analysis. An alternative strategy that has started to pave the way for collecting annotations, which may become a powerful instrument in the coming years, is crowdsourcing. DL in biomedicine might benefit from including these bidirectional drivers [60].

To accomplish its long-term goals, precision medicine research has to actively learn from all available biological, biomedical, and health data [8]. In addition to medical gear and equipment, wearable sensors from smartphones and other devices produce health data. DL has a lot of potential to interpret this data for disease detection, diagnosis, prognosis, and treatment [60]. We anticipate that more DL applications are also available for disease prevention, epidemic prediction, and clinical decision-making. The fundamental objective of DL, AI, is being achieved, and details of deep learning-based architectures for predicting biomedicine properties using different computational languages are mentioned in Table 3. The DL's cutting-edge image retrieval capability allows for various applications. Numerous DL architectures, including popular ones like Torch, Caffe, Theano, MXNet, DMTK, and TensorFlow, are open-source platforms. Some frameworks, like Keras, Lasagne, and Blocks, are meant to be high-level wrappers that are simple to use.

2. The fundamentals of deep learning models

Before being employed in patient diagnosis and treatment, DL requires high-quality databases that have been painstakingly developed [93]. Use high-quality datasets to improve ML algorithms' capacity to foresee and minimize the data needed for training and the complexity of learned representations. ImageNet, a database of annotated and ontologically linked images, makes it feasible to use advanced DL algorithms for image recognition [120]. Computer science can be applied to various tasks in biomedicine, and similar efforts are necessary [121]. To be extensively employed in clinical settings, high-quality data sets for ML in diagnosis and therapy must overcome technological, governmental, and financial challenges. Combining data from many compartmentalized systems using federated learning is theoretically feasible since no correct data transmission is required, and personal data may be retained [117]. At the pre-processing stage, DL may gather information from unstructured sources like health records and publications using wearables and other home appliances. The standardization and interchange of medical data must be desirable to biomedical organizations and individuals. Insurance providers, drug manufacturers, and groups that fund biological research must be prepared to invest in data administration, infrastructure, and collection.

2.1. Deep learning algorithms and architectures

Artificial neural networks (ANNs) are a crucial component of DL and are critically embedded with ML algorithms to perform multiple tasks to detect brain function [122]. Complex algorithms in ANNs imitate the brain's capacity to perceive patterns, such as machine perceiving, labelling and natural grouping input are used to interpret the sensory

Table 3
Deep Learning Approaches for Predicting Biomedicine Properties through Computational Languages.

Python	C++	MATLAB	JAVA	Julia	Lua
Chainer	ConvNet	DLToolBox	DL4J	Mocha	Torch
Hebel	TensorFlow	MetConvNet	ConvNetJS	–	–
Theano	Caffe	–	–	–	–
DeepNet	Cuda-Convnet	–	–	–	–
Blocks	MShadow	–	–	–	–
Neon	DMTK	–	–	–	–
Pyleam2	MXNet	–	–	–	–
Karas	IntelDLfreamwork	–	–	–	–
Genrism	–	–	–	–	–
Lasagne	–	–	–	–	–
Cxxnet	–	–	–	–	–

data [123]. This data must be translated into numerical vectors to identify the patterns they seek in the real world.

Almost all of us are exploiting the advantages of the careful DL models wrapped around smartphones' covers daily. It goes with a basic auto-correction to requesting Alexa by Ram, et al. [124] for the news report or score to the chatbot aiding us with daily support issues and if Facebook encourages us to tag our people based on recognizing the photographs. These are rudimentary uses of DL models, but there are many more complex implementations of DL [125]. Not forget driverless as well as autonomous autos! All of them function utilizing the foundations of neural networks. NNs are not just a new age phenomenon; they have existed for over 70 years. The researcher [126] created the first NN that constructed "computer simulations for NN models based on threshold logic methods.

In Table 4, we show the complete detail and mechanical phenomena of DL approaches data flow towards contextual architecture in basic models, where NNs are forwarded in Training Feed-Forward Neural Networks (FFNNs) and then forwarded to Convolutional Neural Networks (CNNs) for addressing the wide-ranging challenges associated with different diseases and make scientific purposes for non-domain experts in medical science includes innovative healthcare system, biomedicine, and genomic sections.

AI-NNs, also known as NNs for DL domains, are crucial instruments in medical science. Their extensive utilization previously was constrained by antiquated technology, but as vast and complicated networks could be taught, their popularity began to rise starting in the early 2000 s. DL is frequently employed in biomedicine, from machine vision to diagnostics. This also covers more complicated subjects like criminology. We show how the most recent networks flow with FFNNs and how they work relying on features of review-based NNs, with an attention on the interpretation of biological data. Table 3 shows a variety of technological aspects, including training algorithms and paradigms proposed for addressing different disorders, that we review from the literature. To give a fundamental understanding of the use of NNs transformation, the number of journals published each year to identify the usage in various scientific disciplines, we also present data analysis of publications regarding neural networks to conventional details about different datasets.

In Table 5a, We collect the data from the review and literature to identify the different Models for Sequence Analysis in genomics and biomedicine and also provide the details about how they can be used in the future for the transformation of DL to predict computational results with maximum accuracy.

Table 4
Deep Learning in Computational Medical Sciences: Neural Network Architectures and Data Flow.

Sr #	The NNs	Training FFNNs	CNNs
1	Building Intelligent Machines	The Fast-Food Problem	Neurons in Human Vision
2	Restrictions Placed on Modern Computer Systems	Gradient Descent	Shortcomings of Feature Selection
3	Mechanics of Machine Learning	Learning Rates and the Delta Rule	Intuitive Deep Neural Networks Cannot Scale
4	Neuron	Gradient Descent with Sigmoidal Neurons	An Image Preprocessing Pipeline Allows for More Resilient Models.
5	Expressing Linear Perceptron's as Neurons	The Backpropagation Algorithm	Visualizing Learning in Convolutional Networks
6	Neural Networks with Feed-Forward Information	Stochastic and Minibatch Gradient Descent	Building a Convolutional Network for CIFAR-10
7	Linear Neurons and Their Limitations	Oversampling, Validity Sets, as well as Testing Set	Using Convolutional Networks to Close the MNIST Loop
8	Sigmoid, Tanh, and ReLU Neurons	Keeping Deep Neural Networks from Overfitting	Accelerating Training with Batch Normalization
9	Softmax Output Layers	Multi-Class Neural Networks	Feature Spaces and Filter
10	ConvNets	Capture the low-level features	Convolutional Level Detailed Explanation
11	Gatys's Neural Algorithm of Artistic Style	VGG16 models pre-trained	Replicating Artistic Styles using Convolutional Filters

2.1.1. Feedforward networks (FFNs) in genomics and biomedicine

An artificial deep neural network (ADNNs)has a single path of information flow: from the input neurons to the output layer. Only neurons in layers $X_1 and X_n$ are linked, and the weights at the ends of those connections might vary Wkj, W_{Ik}, W_{ml} $and W_{tm}$. It is not feasible to have interconnections inside the same layer (no intralayer), nor can information be sent from a higher layer to a bottom level (Fig. 3). It is the easiest way to train ANNs. It may be used for various applications in genomics and biomedicine if the input data are presumed unrelated.

2.1.2. Convolutional neural networks (CNNs)

Visual recognition tasks may benefit significantly from CNNs' ability to capture the temporal and spatial connections of the input data [140]. The data's grid layout allows CNN to use pictures as input by connecting a tiny number of neurons in the information, and parameter sharing increases the efficiency of the fitting process [141]. Fewer parameters need to be calculated as a consequence, which improves CNN's performance. In contrast to the FFNs, which only employ fully connected layers, CNN contains convolutional layers, which commonly integrate all three techniques: convolutional, nonlinear transformations, and pooling. Statistical linear convolution process in which two matrices are conjoined to generate an output matrix called the feature map, which may be understood as a filtering version from one of the matrices. There are fewer parameters and computations in a system when they are pooled. Each feature map is treated separately by the pooling layer. Down sampling is used in the most systematic pooling method, max pooling, so no new parameters are introduced; max pooling conducts dimensional reduction and de-noising by summarizing the input as that of the maximum in the vicinity of a rectangular neighborhood [141,142]. The pooling method reduces the initial 4-by-4 matrix to a 3-by-3-dimensional array with all features of input to output in the context of activation, optimization, and cost reduction to make desired results, as mentioned in the formula.

Table 5a
Computational Models for Sequence Analysis in Medical Domains.

Sr. no	Models	Models working details	References
1	ANN	Analyzing Inputs of varying length	[127]
2	Neural N-Grams	Using Neural N-Grams for seq2seq	[128]
3	NNs	Making a Part-of-Speech Tagger Work	[129]
4	ANNs	Parsing of dependencies and Syntax Net	[130]
5	NNs	Infrared Search and Normalization for the Whole World	[131]
6	ANNs	DL Models that Are Stateful	[132]
7	NNs	Neural networks that use recurrence	[133]
8	CNN	Problems Associated with Disappearing Gradients	[134]
9	LSTM	Long-Term Memory Retention (LSTM)	[135]
10	RNN	RNN Modeling with TensorFlow Primitives	[136]
11	RNNs	How to Put Sentiment Analysis into Practice	[137]
12	RNNs	Seq2seq problems can be solved using Recurrent Neural Networks.	[138]
13	RNs	Adding Attention to Recurrent Networks	[138]
14	NNs-RNs	Anatomy of a Neuronal Translation System	[139]

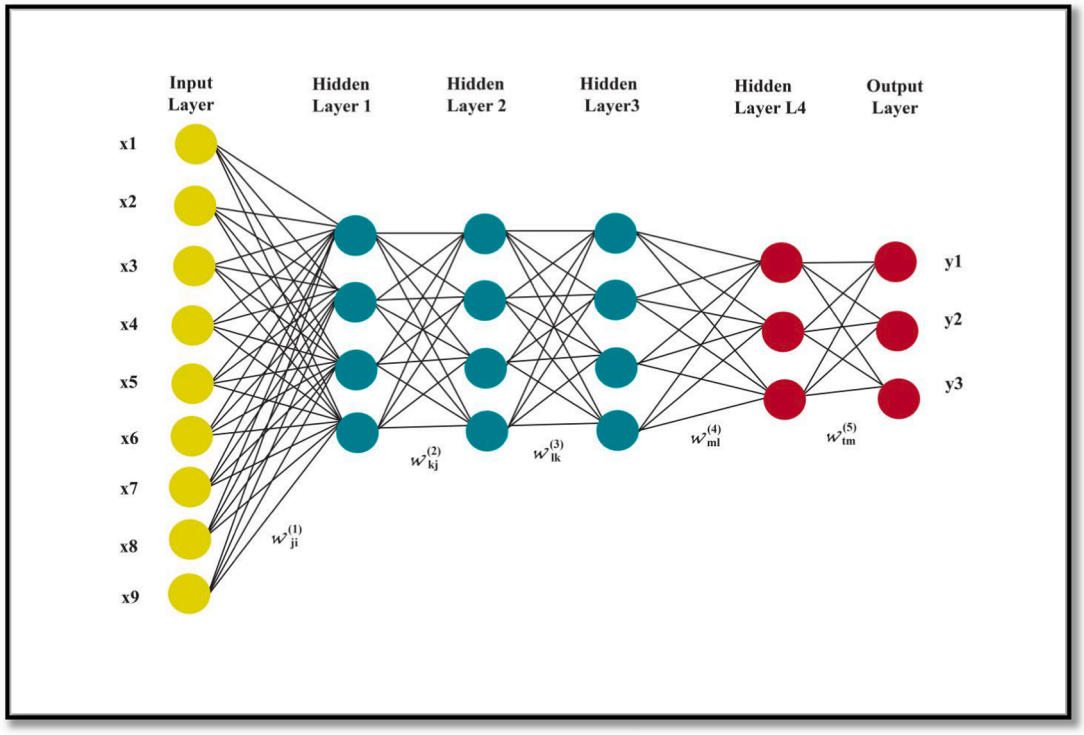

Fig. 3. Four hidden layers Wkj, W_{lk}, W_{ml} $andW_{tm}$ and an output layer y_1, y_2, y_3 follow the input layer $X_1 andX_n$ in a convolutional DL model with nine layers. Twelve neurons, four in the first four hidden units and three inside the fourth are utilized to predict a subject's qualities.

$$\textbf{\textit{Input}}: nXn = n_h\ Xn_w\ Xn_c$$
$$\textbf{\textit{Filtersize}}: fXf$$
$$\textbf{\textit{Output}}: (n-f+1)X(n-f+1) = [\{(n_h\ - -f)/s+1\}X\{(n_w\ - -f)/s+1\}Xn_c]$$
$$Explanation$$
$$z^{[1]}\ = w^{[1]} * a^{[0]}\ + b^{[1]} a^{[1]}\ = g(z^{[1]})$$
$$a^{[l+2]}\ = g(z^{[l+2]}\ + a^{[l]}) a^{[l+2]}\ = g(w^{[l+2]}\ * a^{[l+1]}\ + b^{[l+2]}\ + a^{[l]})$$
$$a^{[l+2]}\ = g(a^{[l]})$$
$$J(G) = a^* J_{Content}(C,G) + \beta^* J_{Style}(S,G)$$
$$a_{i,j,k}\ = activationsat(i,j,k)$$

Due to the formula we explore, a convolutional layer is shown in further depth in Fig. 4. After a nonlinear modification like Linear or ReLU, the input becomes convolutional (hyperbolic tangent& any activation function). Convolutional layers allow us to reduce the input data while maintaining all critical information dramatically. Each image is processed via several convolutional layers to decrease the original representation (input) without omitting important information. The edges of a picture are captured in the first convolution layer. A deep FFNs requires at least half of the variables to be established during the learning process for CNNs (Fig. 3). As a byproduct of decreasing the parameters, training times are also reduced. As shown in Fig. 4, the amount of convolution layer may be increased to capture more outstanding features at lower levels of complexity depending on the input (pictures). A feedback mechanism fallows these convolutional layers (flattening layer), and the variables of interest may be predicted using the high-level qualities gleaned from pictures as input (Fig. 4).

2.1.2.1. CNNs in biomedical domains. Convolutional Neural Networks (CNNs) have gained significant popularity and success in various

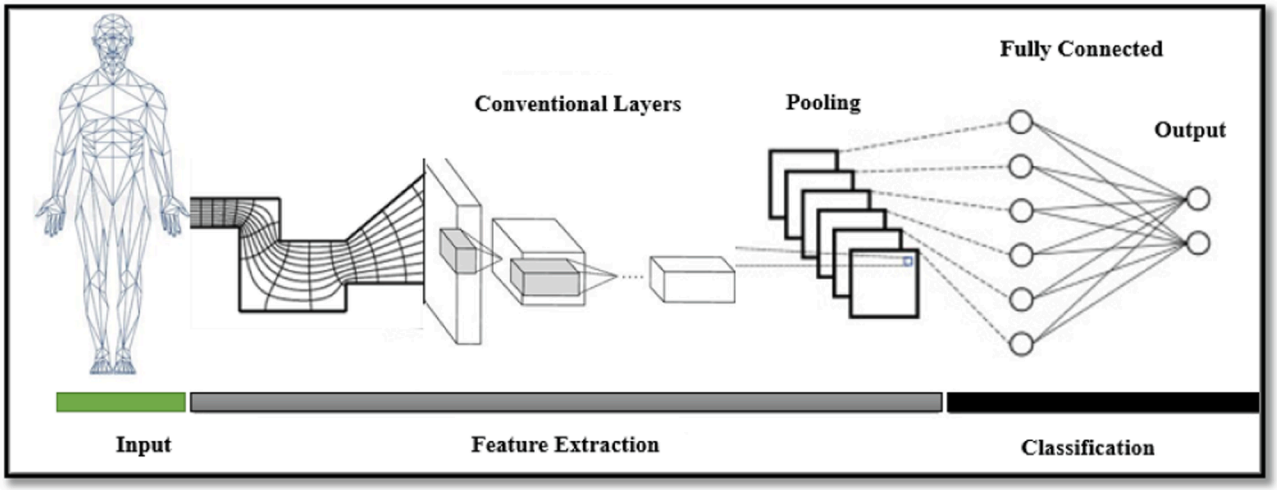

Fig. 4. Deep Learning for Predicting Biomedicine Properties using Conventional Layers and Pooling Methods with Fully Connected Networks.

biomedical domains [143]. CNNs excel in extracting meaningful features from high-dimensional and complex biomedical data, such as medical images, genomic sequences, and physiological signals. In medical imaging, CNNs have revolutionized the field by achieving state-of-the-art results in tasks such as image classification, object detection, segmentation, and disease diagnosis. CNNs have also shown promise in genomics and bioinformatics, where they can analyze DNA sequences, predict protein structures, and classify gene expression patterns [144]. The ability of CNNs to automatically learn hierarchical representations of data, capture spatial dependencies, and generalize well to new samples makes them a powerful tool in biomedical research and healthcare. Their impact in these domains is expected to grow, facilitating early disease detection, personalized medicine, and improved patient care.

Altan and NARLI [145] study focuses on enhancing transfer learning in COVID-19 detection by incorporating Contrast Limited Adaptive Histogram Equalization (CLAHE)-based enhancement techniques. By improving the contrast and details in chest X-ray images, the proposed approach enhances the feature extraction capabilities of CNNs, resulting in higher accuracy, sensitivity, and specificity in COVID-19 diagnosis. Earlier researcher [146] investigates the potential of DBNs in breast cancer diagnosis using Region of Interest (ROI) images. By training DBNs to learn high-level representations of cancerous and non-cancerous regions, accurate classification of breast cancer is achieved. DL architecture for mammogram classification in breast cancer automatically learns discriminative features using CNN from mammographic images, enabling accurate classification of mammograms as either benign or malignant [147]. Altan [148], proposed DL architecture for identifying breast cancer on mammography by learning diverse representations of cancerous masses. The model utilizes deep learning techniques to extract relevant features and patterns, leading to accurate identification of breast cancer.

2.1.3. Recurrent neural networks (RNNs)

In Recurrent Neural Networks (RNNs), information can leak back into a lower layer due to synaptic connections, guaranteeing that it does not always travel in one direction [149]. In this classification, neural networks with one or more layers may be connected. The system's neurons are all connected by neural pathways, which use repeated connections to convey information from one layer of neurons to another. Incoming impulses link every neuron in the layer before, and neuronal connections continue into the following layer and link among individual neurons [150]. RNNs differ from feedforward neural networks in that they have at least one feedback loop because transmission happens both ways. RRNs are favoured for time series prediction because short attention spans or delays significantly increase their strength. However, the computational resources required to train these networks are substantial. In Fig. 5, we explored the recurrent two-layer NN; each neuron's output is delayed before being distributed to the other neurons in the network. Here, the feedback control flow is computed, the input units get a single input variable, and the outputs are sent via auxiliary inputs. Another set of unit activation will be generated as a result, and so on. Once the activations have subsided, the final output signals can be used to forecast future behaviour.

2.1.4. The beep belief networks (DBNs)

DBNs were developed as an alternative to address several issues encountered with traditional neural networks, such as slow learning, insufficient parameterization, and the need for large datasets. These limitations prompted the creation of a new class of neural networks known as DBNs. They were introduced as an alternative to regular neural networks due to their ability to overcome the challenges identified by Larochelle, et al. [151], including their lack of discrimination. DBNs offer a more efficient and effective approach by leveraging deep hierarchical structures to capture complex patterns and relationships in data. These networks have gained popularity as they exhibit improved learning capabilities, better parameterization, and can use smaller datasets.

Deep Belief Networks (DBNs) have emerged as a promising approach for the computerized analysis of Chronic Obstructive Pulmonary Disease (COPD). DBNs are deep learning models consisting of multiple layers of hidden units, which are trained unsupervised using Restricted Boltzmann Machines (RBMs). These networks can effectively extract relevant features from various types of input data, including clinical data and imaging modalities like CT scans or X-rays. The pretraining phase with RBMs enables the DBN to learn complex data representations. Subsequently, a fine-tuning phase using labelled data optimizes the network for specific COPD analysis tasks such as disease diagnosis, severity classification, and progression prediction [152]. By leveraging the deep hierarchical structure of DBNs, they can capture intricate patterns and relationships in the input data, leading to improved accuracy and automation in COPD analysis.

Similarly, deep learning techniques combined with 3D second-order

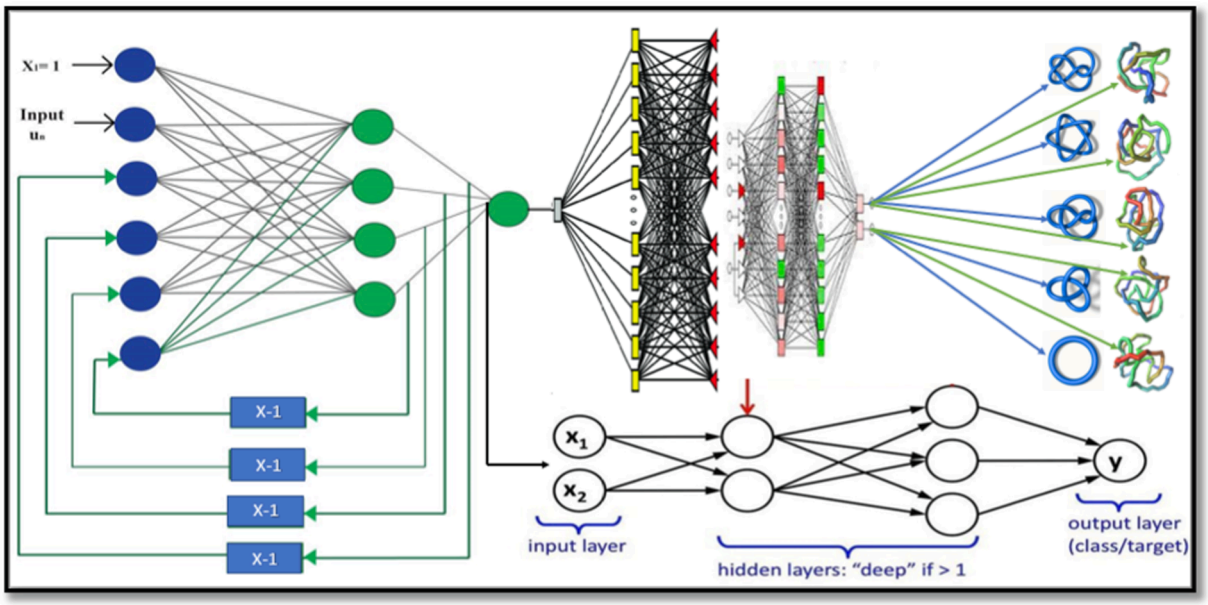

Fig. 5. Recurrent Two-Layer Neural Network for Time-Series Prediction.

difference plot analysis have been utilized to analyse respiratory sounds [153]. By constructing a three-dimensional representation of the spectro-temporal patterns in respiratory sounds, deep learning models, such as convolutional neural networks (CNNs) or recurrent neural networks (RNNs), can extract relevant features and patterns. This enables accurate classification, abnormalities detection, and disease progression tracking. Training these models on large datasets of labelled respiratory sound recordings allows them to generalize and make predictions on new, unseen data, thereby aiding in respiratory disease diagnosis, monitoring, and treatment.

Generic models offer a combined probabilistic model over input data and labels, making it more straightforward to estimate $P(x|y)$ and $P(y|x)$, in contrast to discriminative models, which only use $P(y|x)$. DBNs comprise numerous layers of neural nets, or "Boltzmann Machines,". In Fig. 6, we show the phenomena of a visible layer catches the data as an input, as well as a hidden layer processing data in the mode of health care already provided rule-based algorithms to handle big data (OMICS), computational data flow, and transparency; at the end, the top-level units show the output based on node 1 to node two and provide many available options for each of these characters to solve the problem with very efficient way.

2.1.5. Deep autoencoder

A deep autoencoder is a feedforward neural network (FNN) type comprising multiple hidden layers to transfer input data to output neurons. The key components of the autoencoder architecture are the encoder and decoder functions, which play a crucial role in reconstructing the data. The structure of a deep autoencoder typically includes input, hidden, and output layers, enabling the network to learn and represent complex patterns in the data [154,155]. The DL model can be used to analyze the severity of Chronic Obstructive Pulmonary Disease (COPD) using multi-channel lung sounds [152]. By compressing the lung sound recordings into a lower-dimensional latent space and reconstructing them, deep autoencoders can extract meaningful features related to COPD severity [152]. The model is trained on labelled datasets of lung sounds to learn patterns associated with different severity levels. This approach can potentially enhance COPD diagnosis, monitoring, and personalized treatment.

The Deep Auto Encoder Architecture is one of the most popular applications in the context of DL algorithms used for data reconstruction and dimensionality reduction [155]. To solve these problems, sparse, denoising and sub-complete autoencoders are used. Some applications for deep autoencoders include compression, recommendation systems, feature extraction, and image reduction are engaging in the domain of smart healthcare systems (SHS). Here in Fig. 7, we explore that input has rough and fuzzy data as input, and after that, an encoder encodes input data by using latent and bottleneck layers to provide an apparent image as output, as mentioned in diagram graphics to view excellent dots resolutions and celerity of blurriness.

2.1.6. Deconvolutional methods

In a seismology experiment, a person is given drugs; the computational methods compute the source shock wave and the absorption process. The use of logical-mathematical equations for augmentation and attenuation of the seismic background subtraction problem is used to tackle this problem. Reconstructing undetected basal and pulse-like secretory contributions while accounting for random sampling error is the goal when dealing with pulse-like hormone-concentration patterns.

When fluorescence from out-of-focus structures is included in an image, deconvolution is a treatment process that can be employed to remove the blurring [156]. The most popular use is wide-field fluorescence, although it may also enhance phase-based images and conventional image stacks. If a wide-field picture is deconvolved, noise is removed or reassigned to the originating planes, whereas fluorescence microscopy uses a pinhole to eliminate unwanted information [157].

2.1.7. Performance metrics for intelligent healthcare systems

Performance metrics play a crucial role in evaluating the effectiveness and efficiency of IHS. IHS aim to optimize these performance metrics to enhance accuracy, sensitivity, specificity, and precision and reduce false positive and false negative rates. IHS can improve diagnostic accuracy, patient outcomes, and overall healthcare efficiency by achieving high performance in these metrics, as mentioned in Table 5b.

In terms of performance, CNNs outperform Feedforward Networks. CNNs achieve an accuracy of 95.7 %, which is higher than the accuracy of 92.3 % achieved by Feedforward Networks. CNNs also exhibit a higher sensitivity of 91.2 % and a specificity of 96.5 %, indicating their ability to identify both positive and negative instances correctly. The precision of CNNs is 94.8 %, indicating a low rate of false positives, and the F1 score is 92.7 %, indicating a good balance between precision and

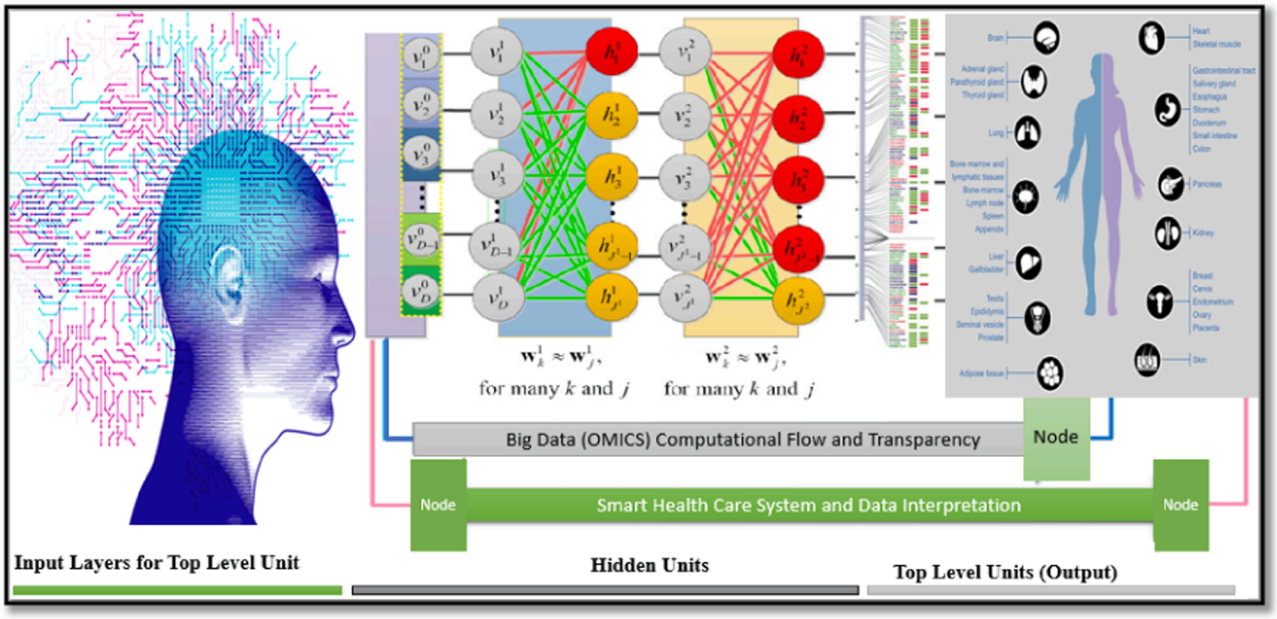

Fig. 6. Efficient Data Processing in Healthcare Using OMICS, Computational Flow, and Transparent Algorithms.

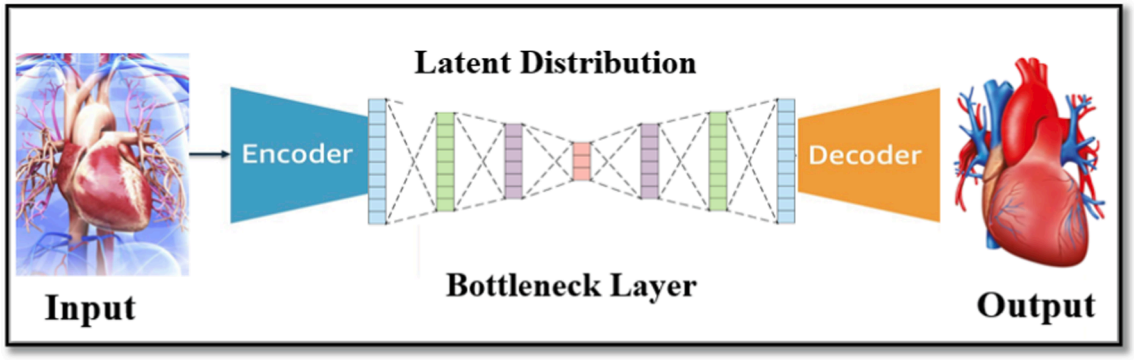

Fig. 7. Encoding Rough and Fuzzy Data for Improved Image Output using Latent and Bottleneck Layers.

Table 5b
Performance Metrics of different Networks for IHS.

Network Type	Accuracy (%)	Sensitivity (%)	Specificity (%)	Precision (%)	F1 Score (%)	Response Time (ms)	False Positive Rate (%)	False Negative Rate (%)
Feedforward Networks	92.3	87.6	95.4	91.2	89.3	50	4.6	12.4
Convolutional Neural Networks (CNNs)	95.7	91.2	96.5	94.8	92.7	100	3.2	8.8
CNNs in Biomedical Domains	93.5	89.7	94.8	92.1	90.4	80	5.2	10.3
Recurrent Neural Networks	89.1	85.2	91.5	87.9	86.3	150	8.5	14.8
Bayesian Belief Networks	86.7	82.4	88.9	85.2	83.6	200	11.1	17.6
Deep Autoencoders	91.8	87.9	94.2	90.6	88.9	70	5.8	12.1
Deconvolutional Methods	94.2	90.5	95.8	93.6	91.9	120	4.2	9.5

recall. However, CNNs have a slightly higher response time of 100 ms compared to 50 ms for Feedforward Networks. The false positive rate for CNNs is 3.2 %, and the false negative rate is 8.8 %, indicating a relatively low rate of misclassifying positive and negative instances. It is important to note that another variant of CNNs is designed explicitly for biomedical domains. This specialized variant achieves an accuracy of 93.5 %, a sensitivity of 89.7 %, and a specificity of 94.8 %. The precision is 92.1 %, and the F1 score is 90.4 %. The response time for this variant is 80 ms, with a false positive rate of 5.2 % and a false negative rate of 10.3 %. This indicates that CNNs can be optimized for specific domains to improve their performance in specialized applications.

RNNs achieve slightly lower performance compared to both Feedforward Networks and CNNs. RNNs demonstrate an accuracy of 89.1 %, sensitivity of 85.2 %, and specificity of 91.5 %. The precision is 87.9 %, and the F1 score is 86.3 %. However, RNNs have a higher response time of 150 ms and relatively higher false positive and false negative rates of 8.5 % and 14.8 %, respectively. Bayesian Belief Networks, another type of neural network model, achieve an accuracy of 86.7 %, sensitivity of 82.4 %, and specificity of 88.9 %. The precision is 85.2 %, and the F1 score is 83.6 %. However, they have a higher response time of 200 ms and relatively higher false positive and false negative rates of 11.1 % and 17.6 %, respectively.

Deep autoencoders achieve an accuracy of 91.8 %, sensitivity of 87.9 %, and specificity of 94.2 %. The precision is 90.6 %, and the F1 score is 88.9 %. The response time is 70 ms, with a false positive rate of 5.8 % and a false negative rate of 12.1 %. Deconvolutional Methods achieve an accuracy of 94.2 %, sensitivity of 90.5 %, and specificity of 95.8 %. They demonstrate good precision at 93.6 % and an F1 score of 91.9 %. The response time is 120 ms, with a low false positive rate of 4.2 % and a false negative rate of 9.5 %. Finally, the CNNs generally outperform other types of neural network models in terms of accuracy, sensitivity, specificity, precision, and F1 score. However, the choice of the neural network model depends on the specific requirements of the task at hand and the trade-offs between performance metrics such as response time and false positive/negative rates.

3. Key deep learning tools and techniques for disease diagnosis

Doctors have used the traditional approaches for decades to diagnose the disease: they look at the symptoms, conduct lab tests, and consult medical diagnostic standards. A new generation of AI and computer vision& DL advancements have enabled computers to identify and detect diseases accurately. In this blog article, data scientists may utilize ML and DL approaches to train models for disease diagnosis.

A few years ago, discovering and developing new medicines was primarily the responsibility of a small team of researchers and scientists who worked in a laboratory. Having one medicine authorized for use based on a single sickness connection would require significant time and cost investment in screening, validation, and synthesis procedures. The development of several bioinformatics, pharmacoinformatic, and automated analysis tools of DL with various model combinations has sped up the process of identifying novel medications to treat various diseases and their effects. Therefore, the combinational tools of DL, as mentioned in Table 4, were made possible by technological advances in computational techniques mixed with an increase in multi-omics datasets shown in Table 5c. However, developing AI, ML, and DL combinations has further streamlined the traditional clinical research method. ML/DL-based methodologies can precisely identify patterns and algorithms that can be used to recognize potent therapeutic substances with a significantly lower asset in terms of time, workforce, and money via applying extensive biological data in the form of big data in numerous databases worldwide. The combinational perspective of DL with a conditional perspective provides a detailed mechanism where DL-based methods can be used to identify multiple diseases and address computational challenges (Table 6).

3.1. Deep learning approaches in intelligent healthcare systems (IHS)

Healthcare study has been increasing in recent years to provide improved health care. The healthcare industry offers various basic and specialized services depending on the patient's needs. An absence of specialists, a lack of health services in rural places, traffic jams that

Table 5c
Conditional working of DL-based tools and techniques for targeting wide-ranging diseases.

Sr. #	Targeted diseases	Conditional working of DL-based tools and techniques	References
1	Prognosis and Early Identification of Cancer	ML algorithms may be used to identify a wide range of malignancies. DL and CNN may be used to identify melanoma from images of skin lesions and provide the opportunity for image analysis, segmentation, and implementation of other role-based algorithms. Combining different role-based methods is very feasible to predict the presence of cancer tumors at an early stage. DNN is also applied to provide a detailed study for automatically detecting different diseases using X-ray and mammography pictures.	[158]
2	Heart Diseases	Data scientists can use computer vision techniques to detect cardiac disease. In the vascular system that delivers oxygen-rich blood back to the heart & brain, for instance, coronary arterial disease (CAD) is a disorder where plaque accumulates. Data analysts can train a DNN to diagnose illness on pictures taken from health scans, including CT or MRI machines, to visualize CAD.	[159]
3	Liver Diseases	Liver illness has been diagnosed using AI-related approaches, including ML/DL and computer vision algorithms. Researchers have employed DNN to detect fatty liver disease or steatosis in ultrasound images using disease indicators such as liver texture and echogenicity.	[160]
4	Lung's Diseases	The output of DL methods and classification of images in the context of lung details study can be used by data scientists to detect numerous diseases like tuberculosis, pulmonary nodules, and lung masses. For example, DL researchers have done substantial work on illness detection using characteristics derived from CT-scanned x-ray images.	[161]
5	Autistic Disorder	Neuroimaging & DL can be used to diagnose autism spectrum disorder. An autistic child's eyes can be tracked using computational techniques like DL methods, computer vision, face detection, face image analysis, and eye tracking.	[162]
6	Diabetic Retinopathy Disease Diagnosis	High blood sugar can damage the retina's tiny blood vessels, which is one example of this condition. Computer vision techniques such as segmentation, illness classification, and other forms of DL may be used to diagnose this disease using ML approaches deep - learning - based (e.g., convolutional neural networks).	[163]
7	Psoriasis Disease Diagnosis	A deep-learning model may be used to create algorithms for diagnosing psoriasis using images of lesions.	[164]
8	Alzheimer's Disease	DNNs or support vector machines (SVM), as well as characteristics collected from natural speech, may be used to help in the diagnosis of Alzheimer's disease through machine learning techniques (MLTs).	[165,166]
9	Parkinson's Disease	Detecting Parkinson's disease (PD) has been made possible via deep learning algorithms (DLAs) that use movement-related characteristics of the body as input. CNNs may be used to predict disease progression and monitor signs of stress and despair, which are common side effects of PD.	[167]

prevent patients from getting to a hospital on time, and patients who don't like to see a doctor can all be addressed via a mobile or remote healthcare application. A shortage of geriatric specialists has been exacerbated by the rise in elderly persons seeking medical care. Wearable sensors monitor a patient's physiological signals, which are then sent to a computer, smartphone, or the cloud for analysis. DL approaches eliminate the need for a patient to attend the clinic in either case; consequently, healthcare apps enable effective treatments in real-time [180].

Medical research has benefited from technological advancements [116]. New healthcare applications may be created because of new technologies like the Internet of Things (IoT), wireless connection, ML techniques, and AI [181,182]. Diabetes, obesity, psychological health, cardiac illness, and chronic disease have all been successfully treated with mobile applications for preventative healthcare. For rehabilitation and aged care, real-time monitoring of human activities is used. As a result, falls and odd behaviours can be prevented by keeping track of daily activities. Mobile sensors and wearable gadgets are employed to monitor daily routines (ADL). The wearables (e.g., inertial sensors and smartphones) are placed on the body (e.g., in various body regions) (e.g., chest, head, waist, wrist, hand). A wireless network of sensors is used to gather and transmit data on body posture. Early cancer diagnosis in several organs, such as the breast, lungs, brain, and liver, is another critical use. This earlier discovery was made possible by advances in image processing technologies.

Additionally, image processing can be used to analyze neurodegenerative disorders like Alzheimer's, and picture biomarkers can be employed in clinical practice to diagnose these diseases. Since AI and IoT enable better patient diagnosis decisions, healthcare services are improved due to their implementation [183]. As in Fig. 8, we mentioned e conversion of Basic biomedical data as input to translate it using multiple DL tools and techniques based on role-based algorithms to create an efficient output in favour of humanity applications and the internal structure of whole individuals for providing multidomain biomedical benefits.

3.2. Deep learning potentials to target power of intelligent healthcare systems (IHS)

The traditional medical system depends on the knowledge of medical specialists to recognize and foresee health issues [184]. Experts can ignore the data in various formats and feature space definitions. DL and ML may automatically predict and retrieve these patterns and feature spaces [116]. The proliferation of digital health records has spurred researchers in medical data analysis. For large datasets, these strategies are powerful & execute well in feature extraction and pattern detection. Fig. 9 shows how DL is applied in healthcare applications. NN is used to forecast, diagnose, treat, or follow it inside the health service by feeding it with multimedia data. Learning has been used in visual extracting features, language recognition, and textual analysis. Mobile applications or medical institutions may get information from wearable devices and

Table 6
List of advanced DL methods and their uses for targeting multifunctional diseases.

Sr. no.	DL Methods	
1	Convolutional Neural Networks (CNNs)	A diagnostic technique application in multifunctional diseases uses DL, such as ANNS has at least three layers: convolutional, pooling, & fully linked. A disease-specific extracting features model built with CNN can be used to diagnose disease. Medical depictions can also be used for prediction, diagnosis, and medicine discovery (MD). Disease categorization, illness segmentation, and disease identification are some disorders that can be diagnosed using CNN. Imagery aids in diagnosing diseases, as CNN can treat skin cancer, prostate cancer, heart disease, etc. [168].
2	Fully Convolutional Networks (FCNs)	DL algorithms may diagnose sickness from text data, such as patient medical records (PMRs) stored in healthcare information systems (HCIS) and CNN, used to explore wide-ranging disease diagnoses [169].
3	Recurrent Neural Network (RNN) / LSTM	Machine translation models, for example, frequently employ deep reinforcement learning in their work. This system has at least one or two stacks of neural network recurrent cells called LSTM [170]. A disease-specific language model, such as disease symptoms or medical information, may be created using an RNN to help in disease diagnosis of different diseases such as Alzheimer's, Parkinson's, and Crohn's disease [85].
4	Dilated Convolutions (DLs)	A disease diagnostic technique uses DLs for weight matrixes in DNNs that can be adjusted in size (dilation). Numerous DL applications exist, including object detection and segmentation in image processing or computer vision systems such as disease classification & disease segmentation challenges [171].
5	Generative Adversarial Networks (GANs)	Detection and prediction of illness onsets using a DL algorithm such as GANs; there are two networks: a sample generator and an assessment network [172]. Patients' medical records (PMRs) can be loaded into GAN to identify illnesses. GAN uses clinical symptoms & medical information to develop a model of disease onset [173]. Leukaemia & myocardial infarction are among the conditions for which GAN may be utilized to build disease prediction models (heart disease).
6	Classifier GANs with auxiliary GAN (AC-GAN)	DL is a technique for disease diagnosis, and this adversarial network comprises the generating & discriminatory networks. AC-GAN is more accurate than GAN as it combines information from both models utilizing disease-specific extraction characteristics, illness images, symptoms, or medical data. Based on supervised learning, AC-GAN may be used to create multiple models for disease classification and detection [174,175].
7	Generative Adversarial Network with Convolutional Auxiliary Classifiers	DL algorithms may enhance classification tasks like illness diagnosis and prediction. When a disease image, symptom, or medical information is merged with a classifier network to help diagnose, the result is known as a CAC-GAN [176].
8	Neural networks with attention-based features (Attentional NNs)	DL is a method for generating medical diagnoses, and a specific type of NN may take context into account while creating predictions about its output using a learning algorithm, making it well-suited for demanding tasks like identifying diseases and formulating treatment plans [177]
9	Adversarial autoencoders (AAE)	The DL approach known as Adversarial Autoencoders (AAE) may be used to construct feature extraction models. Two parts make up this system: an encoder and a decoder. An image or symptom encodes a disease-relevant trait and is decoded to provide a disease-relevant characteristic [178].
10	Auxiliary output GANs (GAN-AO)	DL is a technique for determining if a patient is ill, and a GAN-AO is used to distinguish between malignant and benign tumours and those that are healthy or ill in diabetic patients. It resembles a discriminatory adversarial network [179].

telephones. A DL model can provide unique and efficient solutions to complex and noisy healthcare data [185]. To do this, DL uses multilayer neural networks, which can represent input data features effectively. As in Fig. 9, we explore that DL technologieDL technologieDL technologieDL technologieDL technologies have influenced Medical applications. These tools allow for the handling of multi-dimensional input data (e.g., OMICS-Big data), the learning of correlations between data in the context of data transparency (e.g., images, text, information, real vitalization, sound, and voices), the extraction of prediction models (e.g., model and systems), and the analysis of real-time data trends (e.g., predication, diagnosis, and treatments). After monitoring, the patient's clinical data can be examined to determine the prognosis; for instance, DL can find patterns in clinical data to forecast patient health or, more precisely, diagnose disorders (e.g., healthcare system outputs).

DNN, information from the unstructured text (input data) can be used to locate clinical triage textual data [186]. Healthcare costs and lives rate can be improved using DNNs and advanced Internet of Things (IoT) applications to identify & diagnose disease early and provide preventative therapy [182]. Due to the massive development of DL applications in medical sciences, there is a substantial branch of big data originating from healthcare tenders, and healthcare research approaches are in great demand [187]. The medical data source is patient-taken sensors, records, pictures, and videos. Traditional diagnosis relies on the medical professionals' practical experience and is based on symptoms, antecedents, and consultation information.

Nevertheless, adopting this diagnostic method could result in a mistake due to human error. It's also possible that patients or medical professionals won't use the information collected well. Medical imaging has become increasingly dependent on images and videos during the past decade. As a result, improvements in extensive data analysis have simplified the diagnosis and treatment of ailments, and the purpose of contemporary healthcare techniques is to build a system that can be used to examine the association between conditions and illnesses or investigate therapies, disease patterns, and risk factors [188].

3.3. Computational methods of deep learning in biomedical research

DL approaches have profoundly impacted bioinformatics, making it a hugely successful field. In the DL community, we've tackled most of the main computational methods biologists use. Despite this, the third

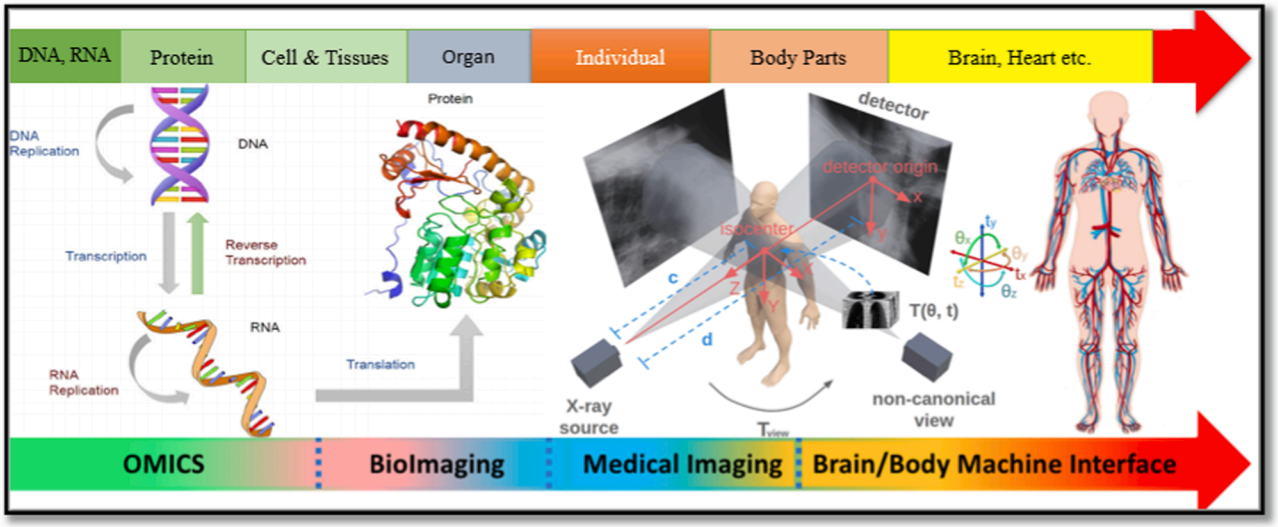

Fig. 8. Translating Basic Biomedical Data using Deep Learning Tools and Techniques for Multidomain Biomedical Benefits.

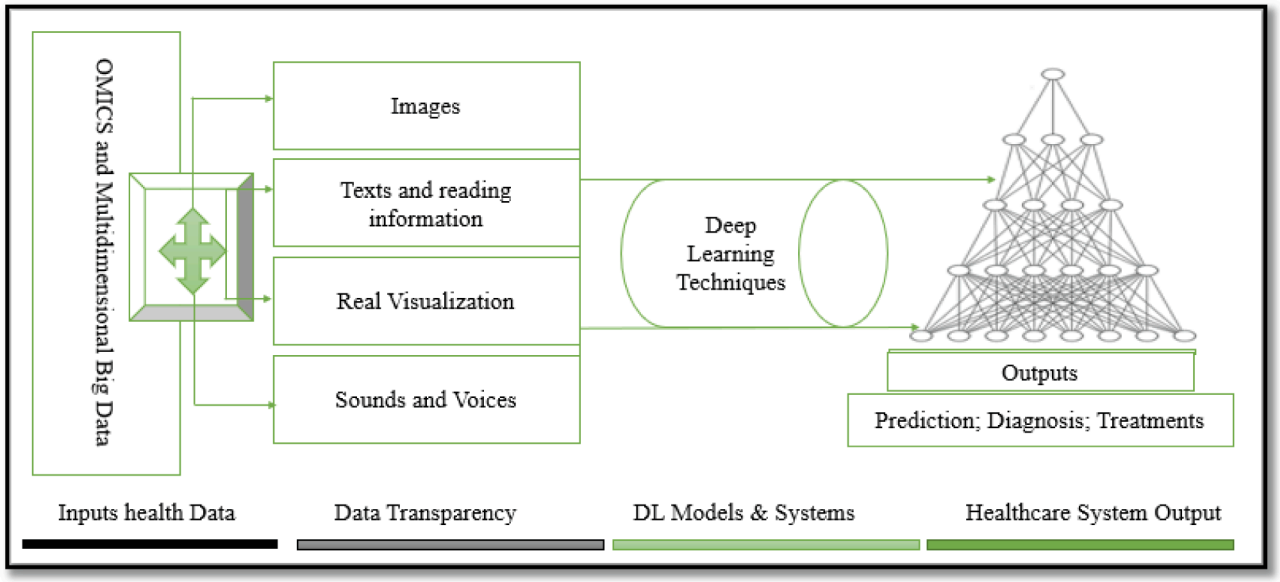

Fig. 9. Influence of Deep Learning on Medical Applications for Improved Clinical Data Analysis and Forecasting.

type period has brought new chances and challenges for the DL community to work together. The DL categories of classification, clustering, & regression may be used to handle biomedical research issues such as gene signatures, genetic analyses, gene-phenotype linkages, and gene interactions.

3.4. Deep learning and genomics data analysis

Numerous disease groups were categorized and stratified using machine learning techniques that have been suggested and put to the test. (For example, treatment response, the likelihood of severe adverse effects, or the probability of a favourable result.) Classes may be discovered, groups of comparable feature space may be found, and instances may be classified using the Least one occasion et al. approach for categorizing cases and mixed data. These techniques have been used for multi-level genomic classification, particularly in the investigation of cancer.

Precision medicine techniques that use genetic and clinical data and the power of DL in prognostic prediction are found in the literature. Post-genomic findings have made it possible to create multi-scale genetic profiles that can be utilized to develop personalized treatment plans in precision oncology (multi-omics). Rapid advances in genetics and technology have resulted in enormous data being created in the -omics study area. Examples include next-generation sequence (NGS) based technologies, high-throughput platforms, and related genomic sequence affiliation studies like GWAS, which generate quantifiable gene expression profiles and identify many genetic variations. These platforms measure the expression of thousands or even tens of hundreds of genes (e.g., RNA-seq technology).

Genome analysis may experience a fundamental transformation as a result of the promising technology that applies DL to genomic data, which is increasing exponentially because a large number of biological data sets that are now available and the application of cutting-edge successes in DL domains like computer vision or NLPs, deep genomics, or the integration of DL to genomic sequences is actively changing computational biology. The conventional genetic effect model allows participants to adapt to complex interactions between data and output with the potential to respond to highly complex structures, as described

in Table 7. The variable features are modelled through a mixed simulation setting. According to literature reviews, several standard genomic Bayesian estimate methods have also been identified. The success of the most recent, realistic models presented in the section on DL tools, algorithms, and processes in genomics shows that DL is an effective technique in functional genomics. Here, we focus on deep learning (DL) techniques often utilized in genomic settings, such as CNNs, GANs, FNN, ANN, NLP, RNNs, LSTMs, AE, BLSTMs, and GRU, which are mentioned in Table 7.

3.5. Practical approaches of deep learning in genetics and healthcare

It is interesting to see how DL may be applied to genomic datasets, and this field is poised to transform genome analysis shortly. We are excited about the promise machine learning holds to help us better understand genome biology, & we also hope this interest will spread to other areas of genomics study [207]. Biological sciences are being transformed into "big data" disciplines due to recent advances in high-throughput genomic & biomedical data. Advances in deep neural networks are transforming both image recognition & natural language processing at the same time [208]. Speech recognition and picture classification are two recent examples of widely used DL. Complex regression and categorization tasks, where the high-dimensional data's detailed structure is challenging to detect using traditional ML methods, have considerably improved DL performance. Predicting the functioning and structure of genomic regions like promoters, enhancers, or gene expression levels using DL techniques is becoming increasingly popular in biology [209].

More than three billion base pairs make up the human genome. Recent technological developments have greatly improved the mechanical comprehension of genomic biology. DNA and chromatin's complexity and vast information remain obstacles to a thorough understanding of the genome's activities and interactions [210]. New insights can be gained by utilizing genomic data from large numbers of individuals in genotype-phenotype correlation, regulatory function prediction, and mutation classification. New and imaginative techniques in genomic research are needed to increase our understanding of fundamental physiology and its relationship to illness. Computer vision that employs ML can extract features and attributes from input data is an exciting and promising technology in genomics [211]. DL has proven particularly effective when dealing with enormous amounts of data, especially in image identification and robotics (e.g., self-driving automobiles). In this regard, using ML as a genomics technique is appropriate [212]. DL has several applications in genomics, from cancer diagnosis and treatment to agricultural development, epidemiology and public health, genetics, population genetics, and evolutionary or phylogenetic analyses [213].

The most incredible significant breakthrough in functional genetic analyses has been accomplished via ML. Thanks to the wealth of training datasets, it is now feasible to create effective forecast models for gene expression and genome regulation or variation interpretation (For example, methylation, chromatin accessibility, histone modifications, and chromosomal connections)[214].

Splice-site prediction and detecting long non-coding RNAs are two more features that can be examined [215]. Improved genetic traits and functions may be predicted when more data is available, making it feasible to train more robust models. Genome research may benefit from DL, but caution and attention are required when using it [216]. It is recommended that DL can be used on biological datasets with a substantial number of samples, often in the tens of thousands. Because of their inherent "black box" nature, DNNs cannot be fully understood or transparent [217]. There might be significant effects from little changes in the input data, so it is essential to remember these when analyzing the results. The increased complexity supplied by DL must be compared with simpler computer models with lower dimensionality to confirm that the information has not been overfitted. As with any new technology, DL can be beneficial or detrimental depending on how the data is evaluated and the questions being answered [218].

According to statistics, supervised learning consists of three essential parts [219]. The first is a device that produces random numbers at random times $P_{(x)}$, the second is a supervisory (or a teacher) who offers Y for every $P(y|x)$, and the third is a class of machine language $P_{(x)}$[220]: Vapnik first proposed this idea in 1998 [221]. $X_1, Y_1, ..., (X_n, Y_n)$ are known as that of the training data. The task is how to choose from $f_{(x,y)}$: an f that best predicts the supervisor's reaction Y in the "best" feasible way from the joint probability $P_{(x,y)} = P(y|x)$ When Y it is a continuous variable, the challenge of learning is known as a prediction model to minimize the quadratic loss function; we look for the optimal parameter.

$$[03B8] \wedge 1 = \text{argmin}[03B8] \in \Theta 1n \sum ni = 1(Yi - f(Xi, [03B8]))2.$$

In this case, the learning issue is a categorization or pattern-recognition problem. Y is dichotomous. The cross-entropy function is a widespread loss function in classification problems.

$$[03B8] \wedge 2 = argmin[03B8] \in \Theta 1n \sum i = 1n[-Yilogf(Xi, [03B8]) - (1 - Yi)log(1 - f(Xi, [03B8]))].$$

When $f(x, [03B8]) = xT\theta, \theta \wedge 1$ becomes the classical least squares estimator in linear regression. Similarly, $\theta 2$ is the estimator for coefficients in a logistic regression if $f(x, [03B8]) = (1 + e - xT[03B8]) - 1$.

Activation function functions can be employed in the output layer when solving regression issues [222]. But in hidden layers, nonlinear activation functions must be used. Neuronal networks can now record nonlinear interactions between input and output data thanks to the introduction of nonlinear activation functions [223]. Instead, a neural

Table 7
List of DL models used in genomics via targeting OMICS data to resolve complexes problems.

DL model	OMICS data	Purpose / Prediction	References
RNN	miRNA-mRNA pairing	Target prediction	[189]
LSTM	positive pre-miRNA and non-miRNA	miRNA target	[190]
ANN	RNA-Seq	Control-Cases	[191]
AE	Time-series gene expression	Pre-Processing Step for Clustering	[192]
AE	cDNA microarrays	Predict the Organization of Transcriptomic Machinery	[193]
AE	gene expression	Identification/ Reconstruction of Biological Signals	[194]
RNN	expression of landmark genes	Gene Expression Inference	[195]
CNN	histone modifications	Classify Gene Expression	[196]
LSTM	histone modifications	Classify Gene Expression	[197]
DBN	gene expression, DNA methylation, and miRNA expression	Identification of Key Genes and miRNAs	[198]
CNN	whole-genome sequence	Variant Caller	[199]
ANN	cell-line with drug response	Predict Drug Response	[200]
CNN	whole-genome sequence	Predict Quantitative Epigenetic Variation	[201]
Multiple AEs	mRNA and miRNA	Normal or Disease State and Cancer Type	[202]
CNN	Single-cell methylation	Predicts Missing Methylation States and Detects Sequence Motifs	[203]
CNN and RNN	DNA-seq	Predicting the Function of DNA Directly from Sequence Alone	[204,205]
GANs	DNA-seq	Optimize the Synthetic Gene Sequences	[206]

net collapse to a regression analysis or a logistic regression when activation functions are applied in hidden layers. The hidden layer separates a perceptron from a neural net with only one hidden layer. Nonlinear activation functions applied to a weighted sum of weights & inputs generate the hidden units in the hidden layer in the same way as that of the processors in a perceptron [224].

3.6. Deep learning in genomics and biomedicine for drug development

Artificial intelligence-based medication development has lately gained attention due to its ability to cut the time and money required to produce new drugs. Various DL-based techniques emerge at every stage of the drug development process as DL increases technical and drug-related data. It has been a challenge for pharmaceutical researchers to choose and design prospective medications for preclinical testing of a target of interest. The two most demanding tasks are drug interaction prediction and the creation of novel molecules suited for the desired target [225].

Even drug discovery has been transformed by DL, which has altered many fields of science and technology. As pathogens evolve and re-emerge, traditional drug-discovery strategies cannot keep up with their fast development and re-emergence. NN and Naive Bayesian algorithms are some of the most modern tools for drug development [226]; because of the larger data sets provided by high throughput screenings, these alternative drug discovery approaches can better anticipate the targets' bioactivities and chemical features. The versatility of NN design distinguishes DL from other ML techniques used for drug development [29,227]. Due to the high costs and long lead times associated with traditional drug development, deep understanding holds great promise for speeding up the process [228]. For identifying the most promising medications against certain diseases, DL can analyze large-scale chemical libraries for biological, chemical, or topological features [5]. A wide range of DL approaches has been created during the past few years, although their use in drug development has not yet achieved its promise. The time and resources needed to collect significant volumes of data are a major roadblock for researchers who want to construct their DL models for drug detection [229]. Due to recent advances with mixed methods of DL-ML algorithms drug predictor candidates have been prioritized using open databases based on computational screenings recently to get many flexible adjustments for drug development and optimization.

3.6.1. Recent drug-driven methods in deep learning

The traditional medication design process is time-consuming, expensive, and riddled with failure; researchers test billions of molecules, but only a handful make it to developmental or clinical trials [230]. The average new medication initial investment in the pharmaceutical sector is approximately $2.6 billion, with success rates frequently falling below 10 %. High-throughput screening is one of the first phases of drug development for a given target, and DL has the potential to dramatically shorten the drug development lifecycle by doing a virtual screening of large datasets of putative therapeutic compounds against a particular target (e.g., a protein) associated with some known illness [90]. DL demonstrates the capacity, particularly with computerized technology, to reduce the complexity of pharmacological development and avoid the enormous expense and time required to bring a medicine to market [29].

Before a few decades ago, the process of developing a medicine was restricted to a group of therapeutic applications functioning in a lab that required extensive testing, verifications, and synthesizing protocols, all of which added to the time and money required to get a single drug into the clinics [29]. The development of numerous databases and pharmacoinformatic and bioinformatic tools have aided in accelerating the drug discovery process due to technological advances in computational approaches mixed with an explosion of multi-omics data [231]. But the traditional drug discovery method has also been streamlined with AI, ML, and DL creation [232]. The framework for ML/DL-based strategies is large-scale biological data in the form of big data, which is present in many global databases. This data helps select patterns and models that can be applied to recognize pharmaceutically active compounds with much less time, workforce, and capital investments. The general concepts in the drug research pipelines in this study are introduced by an overview of the drug discovery and development domains where ML/DL may be employed [227].

Schormann developed an advanced computational DL method to simulate three-dimensional protein surfaces and chemical diagrams for the ligands. The two modes were then combined to forecast a molecular docking score. Researchers then evaluated the abovementioned strategy against several baseline techniques and achieved excellent results. Researchers Richards [233] digitally screened billions of ligands as part of the worldwide Grand Challenge, and several substances will be experimentally verified in the lab for potential COVID-19 pharmaceutical therapies.

DrugBank and ZINC datasets were searched using the MT-DTI model to identify 1,400 authorized medicines with a high affinity for the host tissue targets critical for viral infection [181,234]. This method led to the discovery of therapeutic candidates with a high binding affinity (100 nM) for the ACE2 receptor and transmembrane serine two proteases. SARS-CoV-2 may be prevented from infecting human cells by Enalaprilat's affinity for ACE2 [235]. Two of the pharmaceutical possibilities revealed, Daclatasvir and Ombitasvir, are both proven HCV inhibitors and may be able to treat HCV and SARS-CoV-2 together [236]. DL-based knowledge graphs were used by MacLean [237], to identify promising SARSCoV2 therapeutics.

DL tools and techniques combine data from more than 20 million Journal entries with the DrugBank database and fifteen million edges spanning 39 kinds of connections between expression profiles, genes, pathways, drugs, and disorders for Insilco research and investigation. Researchers have used a combination of DL and molecular simulations to choose potential treatments for RdRp (RNA-dependent RNA polymerase). Pralatrexate & Azithromycin, two available commercial drug options, were shown to limit SARS-CoV-2 multiplication in vitro. Before and after SARS-CoV-2 penetrated host cells, Azithromycin was more effective than Pralatrexate.

The earlier researcher [238], combining a DL model with a traditional algorithm has resulted in an algorithm that can find drugs that interact with 3D regions of protein targets such as MolAICal'sDL model, the PDB-bind database and the ZINC database of drug-like compounds. The cell membrane glucagon receptor (GCGR) and SARSCoV2 main protease were used to demonstrate MolAICal's drug discovery and development capabilities (MP2). Using QSAR models, an ML platform performs Deep Docking to explore the ZINC database for potential drug candidates. DL and molecular docking approaches were used to identify natural medicines against SARS-CoV-2 [181]. The ChEMBL database has more than 8,200 possible anti-SARS-CoV-2 drug options [239]. Since so few are available, DL algorithms and other computer technologies are used to find potential SARS-CoV-2 drugs [240]. Furthermore, the compounds undergoing clinical testing will be identified using DL.

3.7. Deep learning opportunities and challenges in genomics and biomedicine

Due to the complexity of large datasets, DL models are ideal for capturing non-additive effects and complex interrelationships without additional variables in the predictors [105,112]. Even though DL models have only a few implementations in genomics and biomedicine [52], the following characteristics make them appealing and promising tools without requiring feature wet trials [241]; therefore, DL models can assess vast volumes of data as well as raw data like biomedical targets [242]. As a result, DL models more efficiently incorporate massive amounts of omics data into a single model, which is impossible with most machine and statistical learning techniques like Metabolite and

microbiome, phenome, proteome, transcriptome, etc. [243]. A variety of activation functions, such as RELU [244], leakyRELU [245], and sigmoid function [246], are used for the optimization of different latent objects in the context of genomics and biomedicine to provide support for finding reprogrammable logics to get better results based on maximal proximity (fuzzy sets). Still, in this situation, more expertise is needed to draw the conclusion of applied algorithms for the perfection of complexity and accuracy; therefore, this type of drawback leads to many challenges [247]. These DL frameworks represent these latent objects in various ways [116]. The DL models using CNN-style topologies can efficiently grab the connection (particular structure) among adjacent input variables [248]; there is much experimental proof that the achievement of DL models improves with the size of the dataset, opening up many possibilities for the design of specific topologies (DCNNs) to handle with any data more smartly than previous genomics and biomedicine models [218,249].

In large-scale deep methods, It is possible to significantly reduce the number of variables that must be estimated and computed by using a topology like CNN, which allows parameters to be shared and data compression to be accomplished without requiring the estimation of new parameters for fast optimization [250]. In complex adoptive systems, utilizing DL's modelling frameworks, which are more similar to complex systems, produce observable phenotypic values to introduce intelligent output for the prediction of parental combinations, which is essential in F1-hybrid breeding operations to choose superior combinational homozygous parental lines, is followed by a few examples of how digital libraries (DLs) might be used to improve traditional breeding practices [251]. For example, DL was used to categories Cinnamomum (Lauraceae) using deep convolutional neural networks (DCNNs) and perform the genome-wide investigation to discriminate between morphologically similar species for genetic diversity & genotype categorization [252].

In genomics and biomedicine, object pictures are considered a manifold of output without knowing an object's conditional and environmental circumstances; in this contrast, DL has gained general acceptance [253]. In light of these limitations, DL is not a broadly applicable solution for all types of problems and challenges, especially in biological datasets; unlike many prediction approaches, its features (weights) cannot be read for generating realistic results, rendering it worthless for point estimation of results interpretation and correlation analysis for object reflection and decision making [254].

DL provides novel methods in evolutionary biology for comparative analysis. These methods also preclude biological testing hypotheses using parameter estimations because some feature selection layers and relevance are unclear, such as likelihood-based tests for metaheuristics [255]. In the context of Multivariate Patterns, establishing a global optimum analysis of the genotype-phenotype relationship using in silico methods are very first growth with multiple constrains [256]; logistic regression may have local minima and maxima for predicting medical outcomes [257]. Although there is some evidence that these problems can be solved using a Bayesian approach [258], there are two issues that must be addressed before these models can be implemented using the Bayesian paradigm, the problem of overfitting in DL models when the inputs are significant [259], and the problem of overfitting in conventional statistical models when the inputs are small [260].

In the context of goal-driven scientific modeling, implementing successful DL models and evaluating the biological meaning of the results need significant knowledge [261],which is a severe obstacle due to the exceptionally challenging tuning procedure dependent on several hyper-parameters [26]. Even though a role-based algorithm known as Keras [262] in DL for genomics and biomedicine provides mining opportunities, implementing DL for high performance requires substantial effort, knowledge, and computer resources for transdisciplinary challenges in biomedical datasets. It is difficult to deploy DL models for HIS in genomics and biomedicine [263] because genomic data generally contains more discrete elements and conceptual understanding for accelerating challenging tasks; another disadvantage of DL is the time required to train the different networks [264].

3.8. Future trends of DL applications

DL Trends transfer learning techniques like DBNs, RNNs, CNNs, deep auto-encoders, and deep generative networks are covered by methodologies like algorithms, applications, and systems. These techniques have become effective computational models in genomics and biomedicine to handle innovative health. Unsupervised learning, a potential new DL approach, trains a system to identify biomedical data by utilizing actual learned data rather than training it using labelled data. DL system learns to categorize original information rather than needing tagged data to train it. Unsupervised learning techniques may produce simulations resembling social actions with time and training possibilities, which appears to clash between consumer privacy regulations and the demands for large amounts of customer data in biomedical research.

DL for source code modelling and data-driven procedures provide a semantics approaches to handle intelligent health bigdata [265]; by 2025, all software platforms will be able to apply DL due to the inclusion of more straightforward frameworks in DL tools that speed up and simplify coding [266]. As digital asset management (DAM) systems grow increasingly automated [267], users may not understand what is happening in the background of programs.

In medical sciences, wide-ranging algorithms are used based on intelligent learning environments. Unsupervised learning techniques will eventually be able to compete with supervised learning systems in terms of accuracy and efficacy [268]. The discovery of data-driven techniques is anticipated to drastically lower the cost of adopting DL approaches [269], which now rely on massive amounts of labelled data in wide-ranging domains like bioinformatics and biomedicines [270].

Autonomous navigation framework and robot navigation in large-scale biomedical domains is a new DL approach that enables functional testing hypotheses with parametric estimation and is suitable for inference and expendability, such as algorithmic techniques beneficial for anticipating and explaining the event in medical domains. In the coming years, DL and ML models should become more fully automated that can automatically identify strong hypotheses from data and explain what they found [271]; these suggestions should be tested by the models, which should be able to make accurate predictions as well as reveal how the same complex biological systems that cause an event under study can be possible to predict excellent results.

3.9. Discussion

DL has emerged as a powerful tool in genomics and biomedicine, revolutionizing the healthcare field. By leveraging large-scale datasets and complex algorithms, DL techniques can extract valuable insights from genomics data and aid in disease diagnosis, treatment selection, and personalized medicine. In this discussion, we will explore the applications of deep learning in genomics and biomedicine, highlighting fundamental studies and providing relevant references. DL has been extensively employed for genomic sequence analysis tasks such as DNA sequence classification, variant calling, and regulatory element prediction. For example, the study by Alipanahi, et al. [62], introduced DeepBind, a deep learning model for predicting DNA- and RNA-binding proteins. The model outperformed existing methods and successfully identified novel binding motifs. DL models have demonstrated exceptional performance in cancer diagnosis, prognosis, and treatment response prediction using genomic and clinical data. A notable study by Coudray, et al. [272] developed a deep learning model, DeepSurv, for predicting patient survival based on histopathology images. The model outperformed traditional prognostic methods and provided valuable insights for personalized treatment decisions.

DL techniques have been applied to accelerate drug discovery and repurposing efforts. For instance, the study by Ma, et al. [273] proposed

a deep learning model, DeepDTA, for predicting the binding affinity between drug compounds and target proteins. The model achieved state-of-the-art performance and provided insights into drug-target interactions. DL models have been employed in clinical decision support systems to aid healthcare professionals in diagnosing diseases and selecting appropriate treatment strategies. A notable example is the study by Esteva, et al. [207], where a deep learning model was developed to classify skin cancer using images. The model achieved accuracy comparable to dermatologists and demonstrated the potential for improving diagnostic accuracy in healthcare.

HIS is receiving a lot of interest as a prediction tool in genomics and biomedicine due to its capacity to choose individual health interests at a very early stage by evaluating just genome-wide data in the test dataset, and morpho-physiological data in the training sets [274,275]. As a result, many biomedical experts have resorted to health informatics data using DL predictive technology for improving healthcare Systems [276]. Compared to conventional healthcare techniques, IHS can complete the drug selection process considerably faster with optimization of accuracy, time and cost [277]. By 2050, we can make more HIS via improving the quality trends of medicine and diet among worldwide individuals. DL systems can help optimise wide-ranging genetic algorithms as mentioned in Table 8; these tools and techniques are more critical for enhancing genetic growth [278].

A large amount of data from pharmaceutical companies, healthcare providers, and researchers is projected to increase productivity and the ability to make particular decisions for healthcare, where DL systems can provide intelligent inspection [279]. Intelligent healthcare researchers are presently adopting a wide variety of DL analytical methodologies in the context of computer vision, learning techniques, and artificial intelligence to assist with analysis and decision-making prospective to influence the performance of genomics and biomedicine prediction [280]. The relationship between testing and training sets is also essential; when we use it effectively, DL may be a valuable tool for overcoming long-standing prediction efficiency difficulties in HIS [281]. These tool and techniques based on role-based algorithms are used to understand better the link between genomic medicine and all inputs markers, enduring omics data, fictitious data, geospatial and environmental data, etc.

Table 8
The performance metrics of each deep learning algorithm.

Deep Learning Algorithm	Proposed Applications	Value in Genomics and Biomedicine	Performance Metrics
Convolutional Neural Networks (CNN)	Medical image analysis, tumor detection, histopathology analysis	Efficiently extracts features from medical images for accurate diagnosis	High accuracy, F1-score, precision, recall
Recurrent Neural Networks (RNN)	Gene expression analysis, protein structure prediction, clinical time-series analysis	Captures dependencies in sequential data for accurate predictions	High accuracy, F1-score, precision, recall
Long Short-Term Memory (LSTM) Networks	DNA sequence classification, disease prediction, drug response modeling	Captures long-term dependencies in sequential data	High accuracy, F1-score, precision, recall
Generative Adversarial Networks (GAN)	Synthetic medical image generation, data augmentation	Generates realistic synthetic data to address data scarcity and privacy concerns	–
Autoencoders	Dimensionality reduction, anomaly detection, missing value imputation	Captures latent representations and aids in data exploration and preprocessing	–
Transfer Learning	Disease classification, drug discovery, personalized medicine	Utilizes pre-trained models for efficient training and improved performance	High accuracy, F1-score, pre

According to our findings based on a detailed literature review, DL can be a cost-efficient approach for drug discovery and target validation in potential medicine in the context of HIS [282,283]. However, the mining of physiological data and visions, as well as the development of meaningful evaluations in situations that differ from the training data, have not been proved to be beneficial. DL might be beneficial in synthetic biology since it can be used to learn to create DNA sequences and proteins separately, each with the suitable characteristics to provide multiple targeted validation approaches for targeting novel drugs [228]. However, we must create improved trial methodologies for DL in the genetic analysis that will require more collaborative testing and iterative methods to evaluate the precision of genomic predictions in biomedical environments as close to actual drug discovery programs as practical [284].

We must promote cross-disciplinary collaboration among drug designers, biometricians, software developers, and others to automatically acquire more data at a cost [285]. The selection of novel drugs must then be improved using this data to develop efficient DL model topologies [228]. A single DL model may be created from several inputs, reducing the feature engineering requirement [286]. All issues require the adjustment of challenging, drawn-out feature engineering methods. To put it another way, feature engineering is an expensive activity that cannot be generalized, relies substantially on data, and requires professional competence [287]. This iterative process, including trial and error, is crucial because it requires the knowledge and experience of all network members, including bioinformaticians, genomics experts and microbiologists, etc. [288]. Previously, it was thought that robots would never be able to match human categorization abilities, such as picture classification and tackling other computer vision problems. Still, in the current situation, DL learning provides all flexible interactions with multiple genomics and biomedicine problems for innovative health care.

We found little significant differences in prediction accuracy between DL and standard genome-based models since DL was the best model mentioned in Tables 1 & 2. In the context of different disease-environment, multiple interactions were mapped where DL models are very competent with multiple optimizable models to treat different illnesses, as mentioned in Table 3. Although this is partly due to not every dataset containing nonlinear patterns or enough data for a successful learning process, it is also possible that the training pictures were not created effectively, for example, shallow layers and a small number of neurons [289]. It was discovered that most publications in which DL models outperformed regular health informatics models used various variants of CNN. Many researchers [16,199,290] have demonstrated that CNNs are among the best tools for prediction outcomes in genomics and biomedical domains when given raw images as inputs. Artificial neural networks with more than one hidden layer are called “DL” systems [257]. Many experts [68,90] feel this design is essential to the success of numerous DL deployments in wide-ranging sectors.

CNNs are better than MLPs at understanding the spatial structural patterns present in image inputs [291]. CNNs are intensely utilized in several biomedical science applications such as defining abiotic and biotic stress factors on genomics, predicting novel drugs, detecting multiple genes and proteins based on genome-wide analysis and identification in different species, classifying images based on supervised learning, identifying multiple OMICS characteristics for future integration with various diseases and targeted medicines [292]. Numerous examples support the concept that DL is an essential technique for enhancing genome-wide analysis and the precision of genetic predictions. These examples show how DL is hastening advances in predicting accuracy. We are nearing a new era in which we can predict almost everything given sufficient inputs, even if DL does not consistently outperform older regression algorithms [293].

4. Conclusion

Genomic and biomedical discoveries have provided exponential quantities of physiological and biological statistics, allowing us to understand population welfare completely. DL and ML, two cutting-edge, interdisciplinary topics in computational biology, are critical to the study of disease diagnosis and therapy. DL-based algorithms, which have tremendous potential for learning patterns and feature extraction from massive datasets and performing various technical fields, are used to find the internal structures in the dataset. Data-driven and complex DL algorithms are now used to complete a wide-ranging task quickly based on advancements in GPU technology. The intelligent algorithms of DLs are potent paradigms for scientific research. They are generally applicable in multiple disciplines, such as bioinformatics, genomics, genetics, biomedicine, and healthcare, to provide remarkable output. An imperative style of DL methodologies exploration is the ease with multiple DL open-source frameworks like Keras, TensorFlow, and PyTorch used to boost the tasks via multidomain construction strategies to find the right balance among manifold diseases (See Table 1). DL algorithms can be easily operated by scientists who don't know the conceptual and fundamental sophistication concepts of algorithmic exploration and statistical interpretations. These well-developed platforms allow researchers to focus more on applying DL data-driven methods to their subject fields for desired results (see Table 3 and Section 3.1). In this review, we prepared a detailed remark of the most recent DL advances and intellectual achievements (see Tables 4, 5 and Section 4) in broad-ranging research areas like genomics, biomedical, and health informatics to target high objective outcomes form complex data and from many integrated diseases datasets (see Table 3).

The extensive DL techniques for IHS in genetics and biomedicine are covered in detail in this study and provide detailed performance metrics (see Table 8). We discussed the cutting-edge DL concepts, followed by an explanation of the workflow for integrating IHS with role-based algorithms in genomics and biomedicine to resolve potential biomedical barriers like patient disease classification, fundamental biomedical processes, empowering patients-disease integration, and providing an explanation of where DL approaches are appropriate for significant challenges. Additionally, we explained DL architectures and model optimization in genomics and bioinformatics at the molecular level to deal with categorising biomedicine, analysing genomic sequences, and classifying and predicting protein structures. Finally, we discussed the difficulties facing DL in genomics and biomedicine and its prospects for the future. Predictive analytics of novel hybridization of ANN is a significant improvement in Genome-wide association (GWA) performance over traditional statistical techniques (See Table 2); the DL subject area faces several serious obstacles in data-driven methods to address complex tasks among biomedical domains. Another difficulty with DL is that it is challenging to grasp interpretation methods for future interpretable ML outcomes and trial protocols in medical sciences to provide a clear guideline to biologists for data integration and data validation in computational frameworks.

4.1. Future perspectives

Genetic association analysis in metagenome-based disease prediction is critical to identify and evaluate disease-associated genetic markers; herein, DL data-driven tools and techniques can validate the relationship of disease–genes using open-source knowledge of disease symptoms and protein sequences. DL has long been thought to be mysterious, but genetic association research has found it challenging to apply. The genetic association compliment challenge is addressed in theory by Horel and Giesecke [294], but implementing the theories in real-world data implementations remains a significant challenge. We also explore many powerful tools of DL which are used for neural solid image classification and provide contextual modelling. Deep-LIFT is a functional string that compares individual neuron activation functions based on reference activation and labelled contribution scores as per the central functional gap. Based on theoretical improvements and addressing computational obstacles, DeepLIFT is also a landmark tool or unified approach to interpreting model predictions to computer faster results and classifying different objects to provide outstanding robust empirical image annotation in the medical diagnosis of different diseases [295], such as knee osteoarthritis, cancers, chronic kidney disease, SNPs interactions, etc.

DL, a game-changing new technology looking into the future, has a great deal to offer data-driven analytics for healthcare providers in the context of biobanks, genome sequencing, genome-era pathology, genomics, proteomics, precision diagnostics, and biomedical. It is vital to have access to high-quality and comprehensive training data, which is the most challenging task for conforming reliability and validity of medical outputs. We observed no evidence that DL is demonstrably superior to typical genomic prediction models in predictive capabilities, but we also found no evidence that it is considerably worse. Using DL techniques, for example, data from several sources may be merged without feature extraction. These approaches detect deviations from the norm faster than traditional genomic prediction algorithms. It is also possible to improve anticipated performance in genomics and biomedical applications using DL algorithms to develop a unique topology for the acquired data. Innovative health must adopt and improve this cutting-edge technology to reap its benefits. However, due to the inadequate training–testing data sets, DL models cannot be blindly applied to genomes and biology.

CRediT authorship contribution statement

Imran Zafar: Conceptualization, Writing – original draft, Editing, Supervision. **Shakila Anwar:** Conceptualization, Writing – original draft. **Faheem kanwal:** Conceptualization, Writing – original draft. **Waqas Yousaf:** Writing – review & editing. **Fakhar Un Nisa:** Writing – review & editing. **Tanzeela Kausar:** Writing – review & editing. **Qurat ul Ain:** Writing – review & editing. **Ahsanullah Unar:** Writing – review & editing. **Mohammad Amjad Kamal:** Writing – review & editing. **Summya Rashid:** Writing – review & editing. **Khalid Ali Khan:** Writing – review & editing. **Rohit Sharma:** Editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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