Machine-Learning Based Disease Diagnosis: A Comprehensive Review

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***Abstract*—Early diagnostic discovery of disease globally is a significant challenge due to the complexities of disease mechanisms and diverse patient symptomology. Developing tools that are capable of disease discovery earlier is difficult, but advancements in machine learning (ML), a subfield of artificial intelligence (AI), are beginning to address these issues. ML provides a framework for researchers, doctors, and patients to discover solutions to these challenges. This review discusses the applications of ML in disease diagnosis, particularly in disease detection. It begins with a bibliometric exploration of disease diagnosis in ML literature, which is tracked in 1,216 publications from databases, including Scopus and Web of Science (WOS). This analysis provides an overview of the most productive authors, countries, institutions, and the most cited articles in the literature. Second, the review will characterize the trends and recent application practices of machine learning-based disease diagnosis (MLBDD), including types of algorithms used, diseases being diagnosed, data/inputs used, applications of ML, including metrics utilized to measure the impact of ML-DBD. In conclusion, the paper will summarize the findings and provide some thoughts of prospects and opportunities in the area of ML-based disease discovery.**

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Keywords—Artificial neural networks; convolutional neural networks; COVID-19; Deep Learning Deep neural networks; diabetes; disease diagnosis; heart disease; kidney disease; machine learning

I. INTRODUCTION

Machine Learning (ML) has emerged as a strong tool across many domains, from cutting-edge technologies in smartphones, computers, and robots, to healthcare settings involving manageable problems like diagnosing patients or ensuring patient safety. It is particularly gaining traction in the healthcare sector, and already shows significant promise in optimizing how diseases are diagnosed. So far, ML-based disease diagnosis (MLBDD) has been characterized by its cost-effectiveness and time effectiveness relative to traditional diagnosis processes. While traditional diagnostic approaches are costly, time-consuming, and often very human-dependent, ML systems can operate with automation and process expansive datasets without significant human limitations, such as fatigue.ML has the potential to facilitate improvements in the accuracy of diagnosis and increase turnaround time via the use of healthcare data, such as medical images (such as X-rays or MRIs) and tabular datasets (numerical and textual patient information including basics such as age, gender, and medical history). ML is a sub-field of artificial intelligence (AI) that operates by processing data through complex mathematical functions to produce results, which could be through classification or regression. ML can perform complex and difficult tasks that humans usually cannot, such as effectively identifying malignant cells in a microscopic image. Furthermore, the accuracy of ML has improved with advancement in deep learning, which is another type of machine learning.

Machine learning (ML) can be described as a process that utilizes statistical and mathematical methods to analyze data samples that generate significant insights that in turn allow machines to learn and make decisions without explicit programming. Arthur Samuel made the first assertion about "learning" in ML in 1959, regarding games and pattern recognition, demonstrating that computers were capable of learning from experience. This was a landmark event in ML in terms of recognizing "the machine learns. "The essence of ML is to allow systems to learn from a dataset and be able to predict some outcome or make a decision based on the task. With recent advancements in technology, especially in computing ability and data storage, the training of ML models leads to considerably enhanced accuracy that benefits real-world predictions. In a wide variety of cases, tasks which at one time were incredibly time-consuming and required considerable human resources have been significantly automated and completed rapidly with little human interpretation of results. The rapid growth of ML has also benefited from greatly improved capabilities for working with large datasets and processing speed. More available data allows ML models to be accurate in predicting outcomes from learning, allowing for widespread use of the approach. Types of ML and related approaches have been investigated research, whereby numerous articles have offered new methods or enhancements.

Machine learning (ML) algorithms can generally be grouped into three primary types: supervised, unsupervised, and semi-supervised learning [10]. These classifications are based on the method by which the model is trained and how the data is applied. Supervised Learning: With supervised learning, the model is trained with labeled data, i.e., each training example is associated with a target or outcome. The algorithm learns the relationship between the input data and the output target, and it can then predict the target variable on new, unknown data samples. Common examples of supervised algorithms include Linear regression which is Used to predict continuous values. Logistic regression used when the task is a binary classification type.

Support Vector Machine (SVM) Uses classification or regression type algorithms to find a hyperplane that separates classes of data. In unsupervised learning, the model is given the data without labels. The objective is to find patterns or class rations in the data without a target. Unsupervised learning is more commonly used for clustering and dimensionality reduction tasks. Common unsupervised algorithms include K-means clustering: Commonly used when the goal is to cluster data points that are similar to each other. Principal Components Analysis (PCA): Used to reduce the dimensionality of the dataset while explaining as much of the variance as possible.

II. MACHINE LEARNIG ALGORITHMS

This section provides a comprehensive review of the most frequently used machine learning algorithms in disease diagnosis.

A. Decision Tree

The decision tree (DT) algorithm is grounded in divide-and-conquer principles. In DT models, the attribute can have several values, so they are known as classification trees; leaves indicate separate classes, while branches indicate the combination of characteristics associated with that class label. Decision trees can also, however, take continuous variables, called regression trees. C4.5 and EC4.5 are the two most well-known and widely used DT algorithms [12]. DT is widely used by the following reference literature. Support vector machine (SVM) is a widely used machine learning approach for classification and regression-type problems.

B. Support Vector Machine

SVM was first introduced by Vapnik in the late 20th century [17]. SVMs are also used in a variety of areas apart from disease diagnosis such as facial expression, protein fold, distant homology detection, speech recognition, and text classification. For unlabeled data, supervised ML algorithms cannot work. Using a hyperplane to find the clustering of the data, SVM can classify unlabeled data. In addition, the SVM output is not nonlinearly separable. Selecting a suitable kernel and parameters are two major factors when using SVM in data analysis [11].

C. K-Nearest Neighbor

The K-nearest neighbor (KNN) classification is a nonparametric classification method that was first introduced in 1951 by Evelyn Fix and Joseph Hodges. KNN can be used for classification and regression analysis. The result of KNN classification is class membership. A voting mechanism classifies an item. The Euclidean distance methods are used to find the distance between two samples of data. The predicted value of KNN in the case of regression analysis is the mean of the KNN [18].

D. Naïve Bayes

The naïve Bayes (NB) classifier represents a probabilistic classifier that is Bayesian-based. It predicts membership probability for each class based on the input record or data point. The class with the highest probability is the predicted class. The NB classifier predicts likelihoods rather than predictions [11].

E. Logistic regression

Logistic regression (LR) is a machine learning (ML) technique for classification problems. The LR model is considered probabilistic and predicts output values between 0 and 1. Examples of LR approaches in ML are spam identification in emails, online fraud transactions, and detection of malignant tumors. LR uses a cost function also known as the sigmoid function, which takes every real number such that the output is in the range of 0 and 1 [19].

F. Adaptive Boosting

Adaptive Boosting, also known as AdaBoost, was developed by Yoav Freund and Robert Schapire. AdaBoost is essentially a classifier combining different weak classifiers into a single classifier. AdaBoost works by increasing the weight placed on samples that are difficult to classify while decreasing weight on those samples that have been well classified. It can be used for classification and regression analysis [20]

III. DEEP LEARNING OVERVIEW

Deep Learning (DL) is a branch of machine learning (ML) that aims to extract higher and lower- level information from input (i.e., images, numerical value, categorical values) using multiple layers. Most modern DL models are based on artificial neural networks (ANN), specifically convolutional neural networks (CNN), and may be combined with other DL models such as generative models, deep belief networks, and the Boltzmann machine. DL can be categorized as supervised, semi supervised, or unsupervised. Some well-known architectures for DL are deep neural networks (DNN), reinforcement learning, and recurrent neural networks (RNN) [21].At each level in DL, it learns to transform its input data to the next layers while learning different characteristics of the data. For example, when processing images, raw input could be a pixel matrix, where the first layers may learn to detect the image's edges. The second layer then will construct and encode the nose, eyes, etc. The third layer may detect the face after incorporating all the information captured by the previous two layers [6].DL has tremendous potential to impact medical fields. DL has been heavily used in the fields of radiology and pathology for disease diagnosis.

Convolutional neural networks (CNNs) are a subcategory of artificial neural networks (ANNs) that have found various applications in image processing. CNNs have been used significantly for facial recognition, textual analysis, human organ position identification, and biological image detection and recognition [24]. After CNN was introduced in 1989, a different type of CNN's architecture has been developed over 30 years which has been effective in disease diagnosis. A CNN architecture has three components: the input layer, hidden layer, and output layer. Any feedforward network with intermediate levels are referred to as hidden layers and the number of hidden layers depends on the specific architecture type. The first layers that perform convolutions are hidden layers that consist of dot products of convolution kernel with an input matrix, and each convolutional layer generates feature maps that offer inputs to the next layers. Following the hidden layers, there are additional layers, including pooling layers and fully connected layers [21].

Fig. Some of the most well-known CNN models, along with their development time frames.

In general, it may be considered that ML and DL have grown substantially throughout the years. The increased computational capability of computers and the enormous amount of data available inspire academics and practitioners to employ ML/DL more efficiently. A schematic overview of machine learning and deep learning algorithms and their development chronology is shown in Figure 3, which may be a helpful resource for future researchers and practitioners.

IV. PERFORMANCE EVALUATION

This part discusses the evaluation metrics used in the reference literature. Evaluation metrics used in disease diagnosis are accuracy, precision, recall, and f1 score. Lung cancer, for instance, can be classified as TP or TN if diagnosed correctly, or FP or FN, if diagnosed incorrectly. Below are the most widely used metrics [10].

Accuracy (Acc) : Accuracy represents the total correctly identified instances out of all of the instances. Accuracy can be calculated using following equations.

$$ACC = \frac{Tp + TN}{Tp + TN + Fp + FN} \quad (1)$$

Precision (Pn): Precision is measured as the proportion of precisely predicted to all expected positive observations.

$$Pn = \frac{Tp}{Tp + Fp} \quad (2)$$

Recall (Rc): The proportion of overall relevant results that the algorithm properly recognizes is referred to as recall.

$$R = \frac{Tp}{T_n + Fp} \quad (3)$$

Sensitivity (Sn): Sensitivity denotes only true positive measure considering total instances and can be measured as follows:

$$S_n = \frac{Tp}{T_n + Fp} \quad (4)$$

Specificity (Sp): It identifies how many true negatives are appropriately identified and calculated as follows:

$$S_p = \frac{Tp}{T_n + Fp} \quad (4)$$

F-measure: The F1 score is the mean of accuracy and recall in a harmonic manner. The highest F score is 1, indicating perfect precision and recall score.

$$F - Measure = 2 \times \frac{Precision \times Recall}{Precision + Recall} \quad (5)$$

Area under curve (AUC): The area under the curve represents the models' behaviors in different situations. The AUC can be calculated as follows:

$$AUC = \frac{\sum Ri(Ip) - Ip((Ip + 1)/2)}{Ip + In} \quad (6)$$

where lp and ln denotes positive and negative data samples and Ri is the rating of the ith positive samples.

V. ARTICLE SELECTION

A. Identification

The databases Scopus and Web of Science (WOS) are being used to find original research publications. Because of their high quality and peer review index for papers, Scopus and WOS are significant databases when searching for articles, as many students and scholars have used Scopus and WOS for systematic review [25,26]. Using keywords in combination with Boolean operators, the title search was performed in the following way:“disease” AND (“diagnosis” OR “Support vector machine” OR “SVM” OR “KNN” OR“K-nearest neighbor” OR “logistic regression” OR “K-means clustering” OR “random forest” OR “RF” OR “adaboost” OR “XGBoost” , “decision tree” OR “neural network” OR “NN” OR “artificial neural network” OR “ANN" OR “convolutional neural network” OR “CNN” OR “deep neural network” OR “DNN” OR “machine learning" or “adversarial network” or “GAN”).The search started with a total of 16,209 from Scopus, and 2129 from Web of Science (WOS).

B. Screening

Once the search period was narrowed to 2012–2021 and only peer-reviewed English papers were evaluated, the total number of articles decreased to 9117 for Scopus and 1803 for WOS, respectively.

C. Eligibility and Inclusion

These articles were chosen for further exploration if they are open access and in the journal form. Overall, there were 1216 full-text articles (724 from Scopus database and 492 from WOS). Bibliographic analysis was carried out on all 1216 included articles. One investigator (Z.S.) imported information from 1216 articles as excel CSV data for future analysis. We then used the excel duplication functions to identify and remove duplicate articles. Two independent reviewers (M.A. and Z.S.) reviewed the titles and abstracts of 1192 articles. Disagreements were resolved through discussion. We removed articles that did not pertain to machine learning but the disease diagnosis did or vice-versa. After examining the titles and abstracts, we then reviewed the full texts of 102 total papers, with all 102 papers meeting all inclusion criteria.

VI. MACHINE LEARNING TECHNIQUES

Machine learning (ML) techniques have been employed in disease diagnosis by many authors and professionals. This section describes a range of types of machine learning-based disease diagnosis (MLBDD) that have received a lot of attention because of their significance and severity. For instance, due to COVID-19 being of global significance, many studies have focused on COVID-19 disease detection using ML during the period from 2020 onwards, this also have received higher precedence in our study. Serious diseases like heart disease, kidney disease, breast cancer, diabetes, Parkinson’s, Alzheimer’s and COVID-19 are discussed in brief, while other diseases are addressed in brief with the “other disease” tag.

Most researchers and practitioners use machine learning (ML) approaches to identify cardiac disease [37,38]. Ansari et al. (2011), for example, offered an automated coronary heart disease diagnosis system based on neurofuzzy integrated systems that yield around 89% accuracy [37]. One of the study’s significant weaknesses is the lack of a clear explanation for how their proposed technique would work in various scenarios such as multiclass classification, big data analysis, and unbalanced class distribution. Furthermore, there is no explanation about the credibility of the model’s accuracy, which has lately been highly encouraged in medical domains, particularly to assist users who are not from the medical domains in understanding the approach.

Rubin et al. (2017) uses deep-convolutional-neural-network-based approaches to detect irregular cardiac sounds. The authors of this study adjusted the loss function to improve the training dataset’s sensitivity and specificity. Their suggested model was tested in the 2016 PhysioNet computing competition. They finished second in the competition,with a final prediction of 0.95 specificity and 0.73 sensitivity [39].

Aside from that, deep-learning (DL)-based algorithms have lately received attention in detecting cardiac disease. Miao and Miao et al. (2018), for example, offered a DL-based technique to diagnosing cardiotocographic fetal health based on a multiclass morphologic pattern. The created model is used to differentiate and categorize the morphologic pattern of individuals suffering from pregnancy complications. Their preliminary computational findings include accuracy of 88.02%, a precision of 85.01%, and an F-score of 0.85 [40]. During that study, they employed multiple dropout strategies to address overfitting problems, which finally increased training time, which they acknowledged as a tradeoff for higher accuracy.

Although ML applications have been widely employed in heart disease diagnosis, no research has been conducted that addressed the issues associated with unbalanced data with multiclass classification. Furthermore, the model’s explainability during final prediction is lacking in most cases. Table 3 summarizes some of the cited publications that employed ML and DL approaches in the diagnosis of cardiac disease. However, further information about machine-learning-based cardiac disease diagnosis can be found in [5].

Renal disease, commonly referred to as kidney disease, indicates nephropathy or kidney injury. Individuals suffering from renal disease have reduced kidney functional activity, and without timely treatment, this will lead to kidney failure. As stated by the National Kidney Foundation 10% of the world's population has chronic kidney disease (CKD); millions of people die annually due to a lack of management related to CKD [49]. The emergence of ML- and DL-based kidney disease diagnosis and management could deliver hope to those countries who are unable to manage the diagnosing-related tests for kidney disease [49]. For instance, Charleonnan et al. (2016) focused on four various ML algorithms: K-nearest neighbors (KNN), support vector machine (SVM), logistic regression (LR), as well as decision tree classifiers using publicly available datasets and presented an accuracy of 98.1%, 98.3%, 96.55%, and 94.8%, respectively [50]. Aljaaf et al. (2018) undertook a similar study, with the authors testing different ML algorithms including RPART, SVM, LOGR, and MLP using a similar dataset CKD, as the dataset used by [50] and produced an accuracy of MLP at 98.1% in detecting chronic kidney disease [51]. To detect chronic kidney disease Ma et al. (2020) used a collection of datasets which contained data gathered from many data sources [52]. Their heterogeneous modified artificial neural network (HMANN) model achieved the accuracy of 87 - 99%.

Numerous academics in medicine have put forward utilizing machine-learning (ML)-based breast cancer analysis as a possible answer to this early-stage diagnosis question. Miranda and Felipe (2015), for example, proposed fuzzy-logic-based computer-aided diagnosis systems to perform breast cancer categorization. With fuzzy logic, one advantage is the potential to lessen computational difficulty, while effectively simulating the expert radiologist's reasoning and mode of action. If there are specified parameters in, such as contour, form and density, another method for categorizing cancer again is provided by the algorithm based on that person's individual method [57]. The accuracy was achieved at roughly 83.34%, following Miranda and Felipe (2015)'s suggested model. It should be noted that all images used for the experiment were made up in approximately equal ratios which led to greater accuracy and no biases in the results. Note that since the authors did not weight their interpretation of their results in an explainable manner, it could be difficult to conclude that all accuracy in general denotes true accuracy for both conditions of benign or malignant. Additionally, no confusion matrix is included to evaluate the models' actual prediction for each class.One of the pieces of work (Zheng et al. 2014) included hybrid strategies for diagnosing breast cancer disease utilizing k-means clustering (KMC) and SVM strategies as a model. The accuracy achieved was certainly improved, and the dimensional issues reduced considerably.

As reported by the International Diabetes Federation (IDF), there are now over 382 million people worldwide with the disease, and this is projected to worsen to 629 million by 2045 [71]. Many studies also widely presented ML-based systems to identify diabetes patients. For example, Kandhasamy and Balamurali (2015) compared ML classifiers (J48 DT, KNN, RF, and SVM) on diabetes mellitus patient identification. The study used the UCI Diabetes dataset, and found that KNN (K = 1) and RF classifiers had near-complete success [72]. However, a downside of this research was predicated on a simplified dataset, consisting of only eight parameters, which were binary classified about Diabetes. Therefore, having an accuracy at 100% from a less difficult dataset is certainly not surprising. Furthermore, there is no conversation about how the algorithms relate to the final prediction nor how to look at the result from the nontechnical side of the experiment.Yahyaoui et al. (2019) presented a Clinical Decision Support Systems (CDSS) to assist physicians or practitioners in diagnosing Diabetes. To carry out this goal, the researchers used a variety of ML methods such as SVM, RF, and deep convolutional neural network (CNN). In their calculations, RF outperformed all other methods with an accuracy of 83.67%, while DL and SVM had accuracies of 76.81% and 65.38%, respectively [73]

The new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic COVID-19 has become humankind's greatest challenge faced in recent times. Although the vaccine had been expedited in the distribution because of the global crisis, the majority of the world did not have access to
 it for most of the pandemic [88]. Adding to the stress and strain is the fact that the new COVID-19 Omicron strain is highly transmissible and has elements of resistance related to the vaccine. The new gold standard for identifying COVID-19 infection is Real-Time Reverse Transcription-Polymerase Chain Reaction analysis (RT-PCR) [89,90]. During the pandemic, the researcher suggested potential technologies such as chest X-rays and Computed Tomography (CT) including Machine Learning and Artificial Intelligence to assist with identifying individuals who could be potentially infected. For example, Chen et al. (2020) proposed a UNet model of CT images for 51 COVID-19 patients and 82 non-COVID-19 patients, which resulted in an accuracy of 98.5% [91]. Ardakani et al. (2020) evaluated 10 different DL models using a small dataset of 108 patients with COVID-19 and 86 non-COVID-19 patients, resulting in an accuracy of 99% overall [92]. Wang et al. (2020) produced an inception-based model, using a large dataset of 453 CT scan images, with an accuracy of 73.1%. Nevertheless, the model's network

VII. ALOGITHM AND DATASET ANALYSIS

Most studies acknowledged multiple algorithms in MLBDD strategies. In this context, we use the term multiple algorithms to describe hybrid strategies. For example, Sun et al. (2021) utilized hybrid approaches in predicting coronary healthcare disease using Gaussian Naïve Bayes, Bernoulli Naïve Bayes and Random Forest (RF) algorithms. Bemando et al. (2021) used CNN and SVM in the automation of the diagnosis of Alzheimer's disease and mild cognitive impairment. Saxena et al. (2019) used KNN and Decision Tree (DT) for diagnosing Heart disease; and Elsalamony (2018) used Neural Networks (NN) and SVM to detect Anaemia disease in human red blood cells. The main advantage of using hybrid strategies is the high level of accuracy compared to using a singular ML model.The literature indicates that the most common individual algorithms for MLBDD models using ML techniques are CNN, SVM, and LR. Specifically, Kalaiselvi et al. (2020) used a CNN based approach for detecting Brain tumors, Dai et al. (2019) developed a device inference application for Skin cancer detection using CNN, Fathi et al. (2020) classified liver disease using SVM, Sing et al. (2019) used SVM to classify Heart disease symptomology , and Basheer et al. (2019) detected Heart disease using Logistic Regression. Figure 10 below represents the most common

This study's annotated literature has reinforced the growing importance of machine learning (ML) and deep learning (DL) in disease diagnosis over the past ten years. The review started with particular research questions and used the reference literature to try and answer them. According to extensive research, CNN is one of the newest algorithms and outperforms all other machine learning algorithms because it performs well with both tabular and image data [94,123,128,137]. Because transfer learning outperforms conventional ML techniques and does not necessitate creating a CNN model from scratch, it is also gaining popularity [47,91]. According to the reference literature, SVM, RF, and DT are among the most often used algorithms in MLBDD, aside from CNN.

From staff onboarding to customer support automation to decision-making, it finds applications in everything. It lets staff members retrieve business insights conversally and helps leaders to make data-based decisions free from reliance on BI teams. Apart from access control and logging, the assistant's flexible interaction with tools like Slack and Teams mixed with reasonably priced and scalable solutions helps to improve productivity, training efficiency, compliance, and knowledge accessibility all around the company.

VIII. CONCLUSION

This study took a close look at papers published from 2012 to 2021 that delve into Machine Learning-based Disease Diagnosis (MLBDD). Researchers have shown a keen interest in several diseases, including heart disease, breast cancer, kidney disease, diabetes, Alzheimer's, and Parkinson's, all of which are examined through the lens of machine learning and deep learning techniques. The study also touches on various other ML-based approaches to disease diagnosis. Before diving into the specifics, a bibliometric analysis was conducted, considering factors like subject area, publication year, journal, and country, while also pinpointing the leading contributors in the MLBDD arena. Our bibliometric findings reveal that the use of machine learning in disease diagnosis has surged dramatically since 2017. When it comes to the sheer number of publications over the years, the top three journals are IEEE Access, Scientific Reports, and the International Journal of Advanced Computer Science and Applications. The most-cited works in MLBDD are by Motwani et al. (2017), Gray et al. (2013), and Mohan et al. (2019). In terms of overall output, China, the United States, and India lead the pack as the most productive countries. Notably, Kim J stands out as the most influential author, with around 20 publications between 2012 and 2021, followed closely by Wang Y and Li J in second and third place, respectively. Approximately 40% of the publications hail from computer science, while around 31% come from engineering, showcasing their dominance in the MLBDD field. In the end, we meticulously selected 102 papers for a deeper analysis, with our key findings highlighted in the discussion sections. Our main takeaway is that deep learning has emerged as the go-to method for researchers, thanks to its impressive ability to build robust models. However, it's worth noting that while deep learning is widely used in MLBDD, many studies fall short in providing clear explanations for their final predictions.

IX. FUTURE DIRECTIONS

The challenges discussed in the previous section could pave the way for future researchers and practitioners. We've highlighted some potential algorithms and applications that could help tackle the current issues in MLBDD.

I. GAN-based approach: Generative Adversarial Networks (GANs) have become a go-to method in the deep learning arena. This technique allows us to create synthetic data that closely resembles real data, making it a solid choice for addressing data scarcity. Plus, it lessens our reliance on actual data and supports compliance with data privacy regulations.

II. Explainable AI: This is a hot topic right now, as it focuses on making the behavior of algorithms clear during both training and prediction phases. While there are still hurdles to overcome in the realm of explainable AI, enhancing interpretability and transparency is crucial for deploying machine learning models effectively in real-world scenarios.

III. Ensemble-based approach: Thanks to advancements in technology, we can now capture high-resolution and multidimensional data. Traditional machine learning methods may struggle with such high-quality data, but combining multiple machine learning models can be a fantastic strategy for managing this complex, high-dimensional information.

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