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RESEARCH ARTICLE

Quantum Machine Learning Applications in the Biomedical Domain: A Systematic Review

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ABSTRACT Quantum technologies have become powerful tools for a wide range of application disciplines, which tend to range from chemistry to agriculture, natural language processing, and healthcare due to exponentially growing computational power and advancement in machine learning algorithms. Furthermore, the processing of classical data and machine learning algorithms in the quantum domain has given rise to an emerging field like quantum machine learning. Recently, quantum machine learning has become quite a challenging field in the case of healthcare applications. As a result, quantum machine learning has become a common and effective technique for data processing and classification across a wide range of domains. Consequently, quantum machine learning is the most commonly used application of quantum computing. The main objective of this work is to present a brief overview of current state-of-the-art published articles between 2013 and 2021 to identify, analyze, and classify the different QML algorithms and applications in the biomedical field. Furthermore, the approach adheres to the requirements for conducting systematic literature review techniques such as research questions and quality metrics of the articles. Initially, we discovered 3149 articles, excluded the 2847 papers, and read the 121 full papers. Therefore, this research compiled 30 articles that comply with the quantum machine learning models and quantum circuits using biomedical data. Eventually, this article provides a broad overview of quantum machine learning limitations and future prospects.

INDEX TERMS Quantum computing, quantum machine learning, biomedical and healthcare.

I. INTRODUCTION

In recent years, Quantum technologies have been growing at a rapid pace. The Noisy intermediate-scale quantum (NISQ) devices combine with quantum physics, and quantum information [1]. Quantum computers (QC) are the next big leaps in computing, and they may be just around the corner. Unlike classical computers, which use bits represented by either 0 or 1, quantum computers use qubits that can simultaneously represent both values. Quantum information is data that represents the state of a QC [2]. A QC employs quantum mechanical properties such as superposition, entanglement, and tunneling [1]. As a result, QC can swiftly solve issues beyond the capabilities of conventional devices [3]. The state of quantum systems and quantum information techniques are employed in machine learning (ML), and the interaction is referred to as Quantum Machine Learning (QML) [3], [4]. The performance and speed revolution of QML algorithms uses the Moore Law. A computational criterion based on quantum mechanics laws is called ''quantum computation.'' Quantum information and artificial intelligence (AI) are prominent subjects in the current age of informatics development [3].

The QML is widely used in almost every field of science, such as Chemistry, Industrial, healthcare, physics, and biomedical. This work focuses on biomedical applications,

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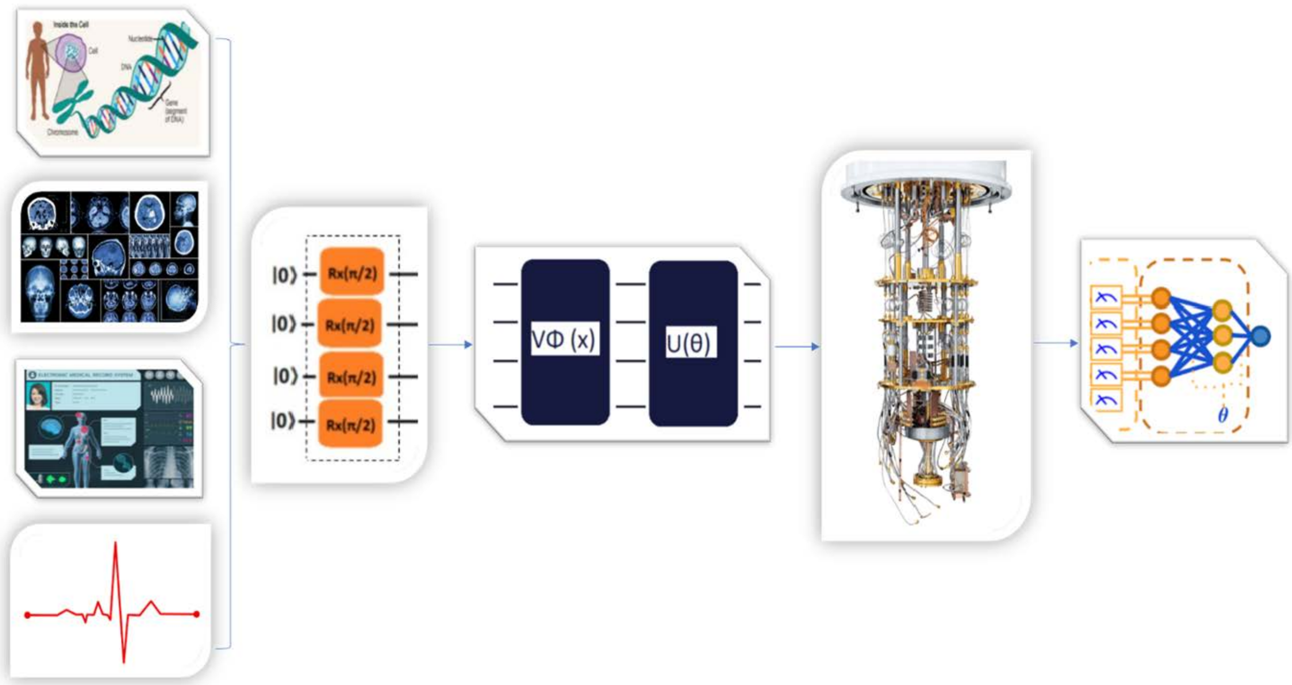

FIGURE 1. Quantum machine learning application in different healthcare domains.

which support a diverse study field including several applications, i.e., medical specializations and related diseases [5]. Some of these diseases are well-known and mastered by physicians, while others are not. Medical practitioner's technical and scientific advancements with biomedical data have become increasingly diverse, including a wide variety of clinical analyses and metrics, biological parameters, and medical imaging modalities. Biomedical data are generally asymmetrical [5]–[7], non-stationary [5], and classified by a high degree of sophistication [6] due to the volume of data and the completeness of some unusual conditions.

Extensive research in biomedical engineering has been conducted. Various researchers benefit by employing the QML techniques in the biomedical domain, such as medical imaging [8], clinical diagnostics [9], e-Healthcare Records [10], and associated diseases [11], as shown in figure 1. Physicians are familiar with some of these medical specialties and diseases. The complexity and severity of the disease can be distinguished using a wide variety of data [5]. In such an era, the QML represents a massive opportunity to assist physicians, biologists, and health practitioners in using and positively impacting extensive medical data analysis to reduce the possibility of medical errors. It also generates a better harmonization of diagnosis and prognosis protocols. The healthcare data use the QML tools for medical image analysis, classification, prediction, and diagnosis. Researchers have employed different QML algorithms in the healthcare domain in recent years. Including the very famous Quantum Support Vector Machine [12], Quantum inspired ML [13], Variational Quantum Classifier [14], Quantum Neural Network [15], Quantum Random Access Coding [16], Quantum Convolutional Neural Network [17], Quantum Deep Neural Network [18], Quantum Boltzmann Machine [19], Autonomous Perceptron Model [20], Hybrid Quantum Feature Selection Algorithm [21], and Quantum Nearest Mean Classifier [22] on publicly available UCI ML healthcare datasets [23], and some of them employed on private healthcare datasets. In this manuscript, we deep dive into analyzing the applications of QML in the healthcare sector, especially in the biomedical domain. We distributed the biomedical section on the basis of its applications, such as Omics, biomedical imaging, biosignals, and medical healthcare records. We also gave the descriptive depth of the papers. We created the paper's quality metric to analyze and evaluate the considered articles and discuss the research questions in the discussion section, which will be helpful for upcoming QML researchers.

The remaining part of the paper is divided into 7 sections. The material, methods, and systematic review procedure are discussed in Section 2. Section 3 dives into quantum computing. Section 4 is on Quantum Machine Learning and its algorithms. The biomedical applications of QML are discussed in Section 5. Then, we discussed the research questions in Section 6, and in the last section, we concluded the article in the conclusion section.

II. MATERIAL & METHODS

Material and Methods for the current systematic review have been obtained by exploring and evaluating the information presented in the previously published work, which is discussed in state of art. The desired article has been studied

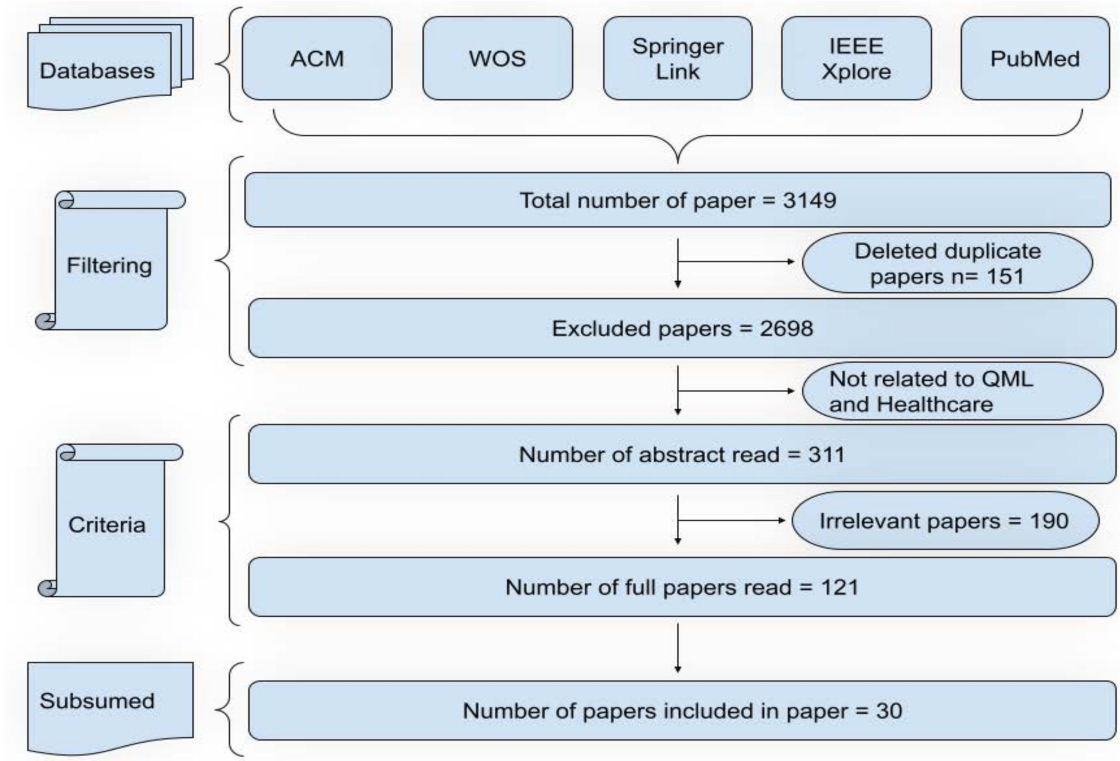

FIGURE 2. **Flow graph of paper selection.**

and defined based on the techniques used and achieved performance. This section is further divided into 3 subsections.

A. DATA COLLECTION

In this subsection, we discussed data collection techniques, such as the Search databases, search terms, inclusion criteria, and exclusion criteria.

1) SEARCH DATABASES

State of the art was explored and employed via various resources, including the Web of Science, SpringerLink, IEEE Xplore, Science Direct, Wiley Online Library, ACM, and PubMed, as shown in Figure 2.

2) SEARCH TERMS

Different keywords and terminology were used to search for articles on QC and QML in biomedical applications, and some were merged into the exact search. The authors, for example, included the phrases "Quantum Computing", "Machine Learning", "Biomedical", "Quantum Machine Learning", "Quantum Neural Network", "Cancer", "Oncology", "Tumor", "Diabetes", "Pancreas", "cardiovascular disease", "Stroke", "Epilepsy", "Alzheimer", "Omics" and "Genomics", among others.

3) INCLUSION CRITERIA

The titles and abstracts served as the primary anthology stage for understanding the papers and their fundamental ifoundation, where duplicates articles were deleted. The corresponding papers were analyzed and retrieved using the Mendeley application.

4) EXCLUSION CRITERIA

Those papers that did not cooperate, particularly with QML methods and healthcare data, were excluded from the manuscript.

B. DATA ANALYSIS

After selecting papers deemed appropriate for the review, 30 papers satisfied the requisite criteria, and the associated full texts were examined. As a result, the following data were extracted:

- *Year and Country:* As shown in figure 3, the review article has attracted the attention of scholars in the previous decade. As a result, knowing the year of the publication and the different geographical locations has increased topic interest. Figure 4 depicts the diffusion of QML in healthcare research studies by countries like India that have made the most contributions in this domain.

- *The Type of the Publication:* Figure 5 depicts the ratio of articles merged in this manuscript. Type "J" includes international journals, and Type "C" includes international conferences and symposiums. Only 90% of the publications evaluated journal articles, and the remaining 10% of articles were conference papers.

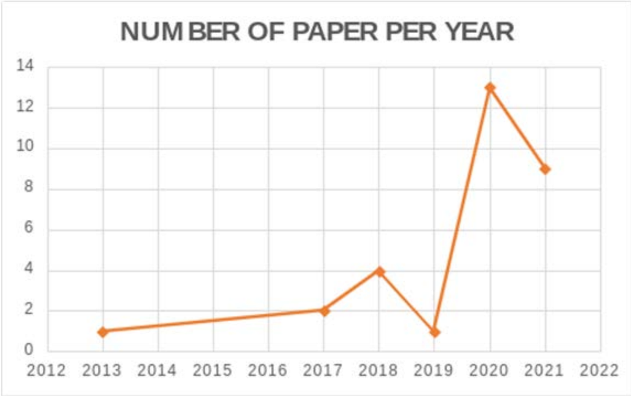

FIGURE 3. Published research articles in QML and healthcare domain.

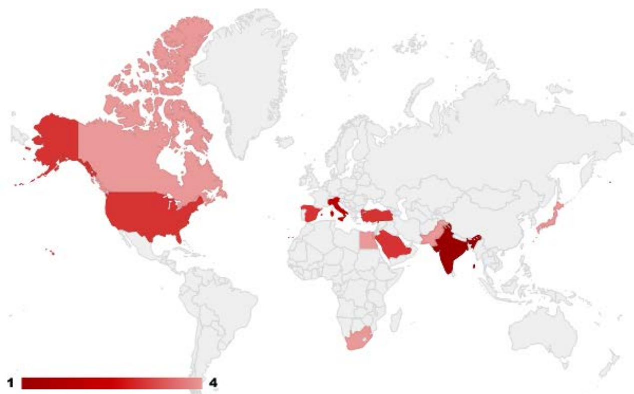

FIGURE 4. Mapped the published article in quantum machine learning and health-care domain as per country-wise.

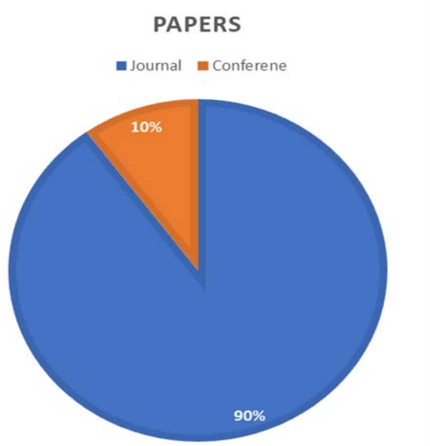

FIGURE 5. Published journal and conference articles.

QC and ML have been widely used in related biomedical applications. Research carried out in the field of QML in the biomedical domain has been published exponentially, as shown in figure 4.

There are three aspects to using machine learning in biomedical applications. First, with the help of computer aid, diagnosis assists the physician ineffective, early diagnosis and less conflict. Second, one-on-one therapies overburden medical patient's care. Third, improve human well-being by examining the scalation of diseases and social behaviors associated with environmental factors [5].

TABLE 1. Research questionnaire.

Question	Purpose
Q1: Do the scientific papers provide a strong foundation for implementing QML algorithms on healthcare data? and its novelty.	To know the objectives of the QML system and its novelty in healthcare data, in order to analyze the ultimate the strategy of the QML study for general purpose with its framework in this reference.
Q2: What role does QML play in the analysis of healthcare data?	To compare various QML frameworks, which are stated in the context of reference, to how QML plays a role in evaluating healthcare data.
Q3: What kind of QML architectures are employed? What particular adoption in this frame of reference?	To compare with various QML frameworks stated in the context of reference, which QML techniques are implemented and evaluated in the healthcare domain. In the application scenario, it is neither necessary/ desirable to perform further the effort to improve the general-purpose approach.
Q4: Can QML be used with publicly available/open-access healthcare data. What are the quantum computing systems utilized to evaluate healthcare data?	To identify a significant amount of research is accessible in open access data to train and analyze health care data in QML, and various QC stimulators or QPUs are employed.
Q5: Does the majority of researchers follow the dependability and validity principle?	To evaluate the research studies, evaluate the author's training and validation processes, and determine if they were equipped with the necessary data and information to reproduce the research and contrast their system to others.

C. METHODS

In this subsection, we have focused on finding a couple of research questions from various articles considered. The desired articles are deeply reviewed, analyzed, and evaluated to form quality matrices. Research questions and paper quality metrics are given in Tables 1 and 2.

III. QUANTUM COMPUTING

The foundation of quantum computing (QC) explores the difficulty of storing, processing, and analyzing data [24]. Quantum mechanical systems are created by converting information; the type of information is invariably referred to as quantum information. Quantum information is data representing the state of a Quantum system [25].

The basic concept of quantum information is the state of any quantum system with two degrees of freedom recognizable by the participant; the logical values 0 and 1 are called a Qubit [4]. A QC has the counter-intuition of quantum physics phenomena like superposition, entanglement, and tunneling [1], as shown in 6 (a,b) and 7. Therefore, a QC can quickly solve problems beyond classical machines limits.

TABLE 2. Designed point based quality metrics for evaluation of considered articles.

Matric Type	No	Illustration	Merit	Points
	1	It gives an informed and comprehensive overview of the original problem background, what was accomplished, and what has been discovered in the abstract.	0 to 1	1
	2	Acknowledged the overview of the system and described the evaluation process.	0 to 1	1
	3	The execution of various QML classifiers are considered, which helps enhance the diagnosis of different problems to healthcare.	0 to 2	2
	4	Provides a brief overview of the limitation, challenges, detailed literature review, and simplifies the results.	0 to 1	1
Content of paper (6 points)	5	Provides the accuracy, precises, and constraints of the research along with impartial discussion.	0 to 1	1
	6	Research is based on open access or private datasets.	0 to 1	1
	7	Provided the availability of the code publicly.	0 to 0.5	0.5
	8	Novelty of research	0 to 0.5	0.5
	9	Determination of system in terms of accuracy, loss function, and error.	By considering the same dataset or the implementation that depends on the other work's maximum and average results. Depending on the percentage quality of results, which obtain the following score, i.e., between (60 to 70) percent (0.5), amongst (71 to 85) percent (1.0) and in between 86 percent onwards (1.5). The rest of the accuracies below 60 percent are considered to be 0.	1.5
Additional Quality Measures (4 points)	10	No of Citation	0 to 0.5	0.5

QC relies on the difference between binary digital computers based on the transistor [7].

Quantum technology has three fields: QC, Quantum Information, and Quantum Cryptography. The strength of QC stems from the vast permutations that allow QC's to have twice the memory capacity and the addition of each qubit. We require N bits of binary integers to define the classical N-bit system. We know in quantum systems that the two possible definite states are $|0\rangle$ and $|1\rangle$. The bipartite quantum system's general state can be represented as $\phi = \alpha|00\rangle + \beta|01\rangle + \gamma|10\rangle + \sigma|11\rangle$, as shown in figure 8. Four classical bits of information can be easily generated by a two-qubit quantum system $(\alpha, \beta, \gamma, \sigma)$. Similarly, we can get 2^N bits of classical information from an N-qubit quantum system [26].

$$\mathrm{H}|0\rangle = \frac{|0\rangle + |1\rangle}{\sqrt{2}}; \quad \mathrm{H}|1\rangle = \frac{|0\rangle - |1\rangle}{\sqrt{2}} \tag{1}$$

QC are general-purpose of the Turing machine, a mathematical formula of computing that theoretically specifies the characteristics of a machine and is essential to the performance of symbols on a strip of tape using a detailed list of norms. Quantum physics enables quantum state superposition, leading to quantum parallelism, which may be used to perform stochastic processes faster than any conventional method.

Such example the factorization of huge integers employing Shor's method [27]. Furthermore, if conventional and quantum computers are used for the same objective, there may be instances when quantum algorithms are shown to be even more convenient. These techniques are classified as BQP complexity (Bounded-error Quantum Polynomial time) [28].

Another complicated task in the traditional computation framework is to solve Pell's equation effectively using the QC paradigm [28]. Furthermore, QC has made significant advances in optimization and simulation. It entails determining partition module characteristics, approximation optimization, and simulating various quantum systems. Quantum simulations also have relevance in quantum optics and condensed matter physics [29].

A. COMPARISON BETWEEN CLASSICAL AND QUANTUM COMPUTING

There are several distinctions between conventional and QC. The classical computer is known as a multi-targeted computer on a broad scale. It is also dependent on the bit's voltage or charge. It only relates to two values: 0 and 1. Logic gates such as AND, OR, NOT, NAND, and NOR are employed. It is based on classical physics and employs the use of Boolean algebra. It is used to describe discrete values. QC, on the other

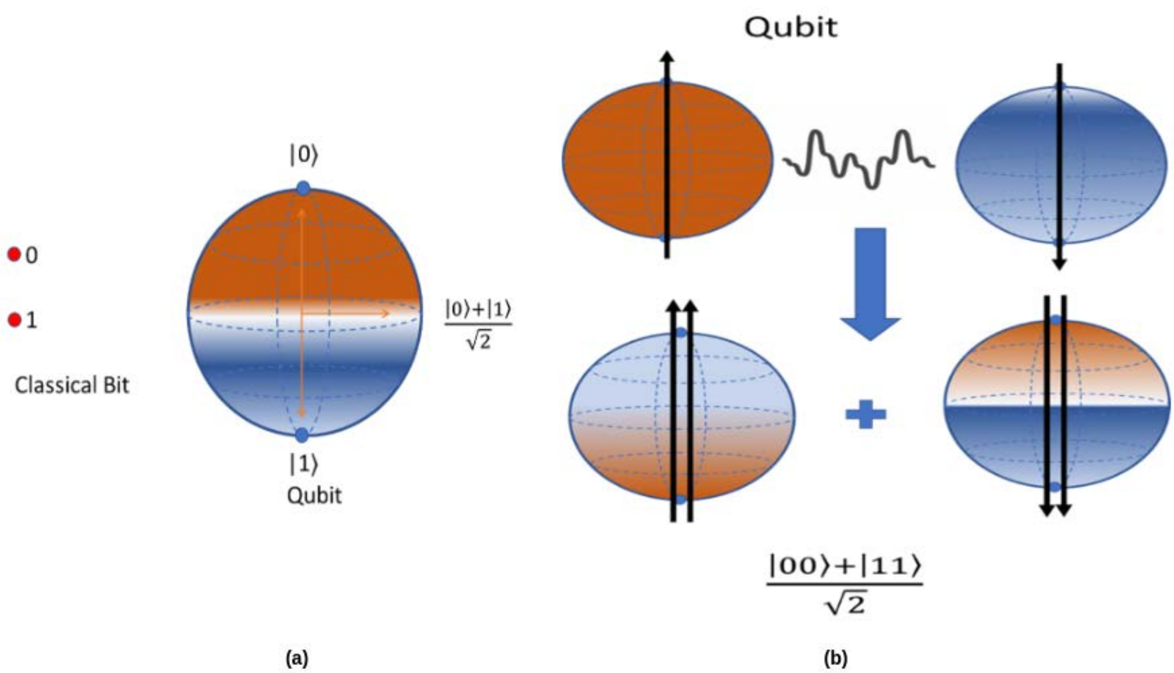

FIGURE 6. (a) Classical and quantum state (b) Quantum superposition and entanglement [8].

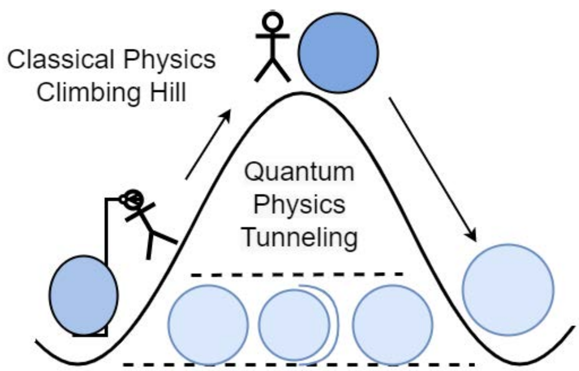

FIGURE 7. Quantum tunneling [9].

hand, refers to high-speed parallel computing using quantum devices. In QC, storage is based on quantum bits [qubits] that rely on the spin electron. It can convert not only 0 and 1 readings but also more complex data and even negative values.

QC is based on continuous number of possible states or infinite numbers. It based on quantum logic according to information processing parallel. Mostly, The quantum results [30] are based on the probabilities and the meaningful information because the overlapping and entanglement for the varied possible results. Quantum mechanics is the responsible for circuit behavior versus the classical type based on classical physics. In this type, there are several restrictions on copying or measuring signals. The circuit [31] must use microscopic technologies that are slow, fragile, and not yet scalable, such as NMR (Nuclear magnetic resonance).

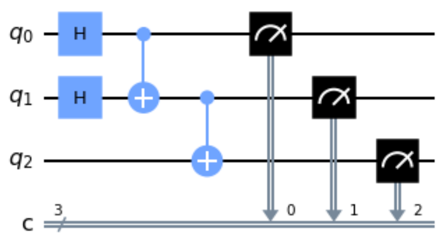

FIGURE 8. Basic quantum computing circuit.

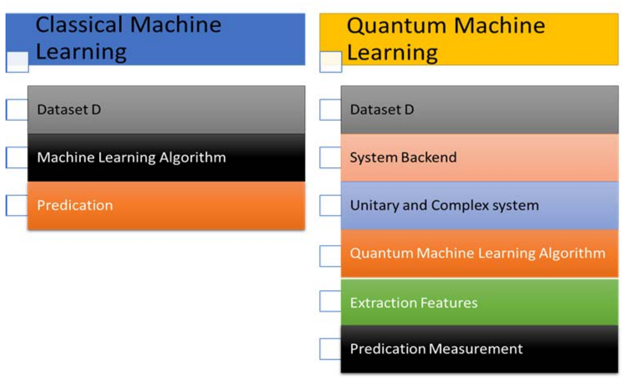

FIGURE 9. Comparison between machine learning and quantum machine learning.

IV. QUANTUM MACHINE LEARNING

Quantum Machine Learning (QML) [3], [4] is a new multidisciplinary research domain that combines quantum physics with ML. In the current state of quantum systems, quantum

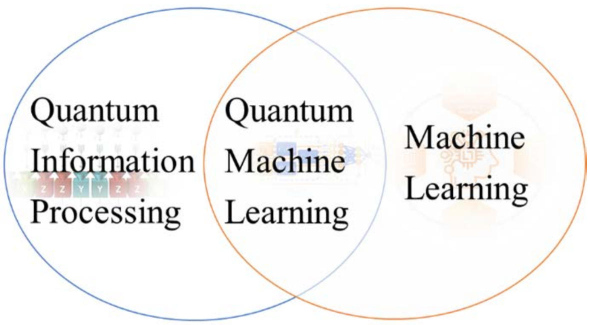

FIGURE 10. Intersection of machine learning and quantum information processing [4].

Quantum Logic	Qubits	Atoms, Ions & Photons
	Quantum Computation	Quantum Theory
	Quantum Circuits	Quantum Gates
	Quantum Algorithms	Model of Quantum Computation
	Quantum Information Processing	Qubits, Quantum Gates, Quantum Algorithms, Entanglement & Bloch sphere

FIGURE 11. Quantum logic includes the quantum parts for the technology.

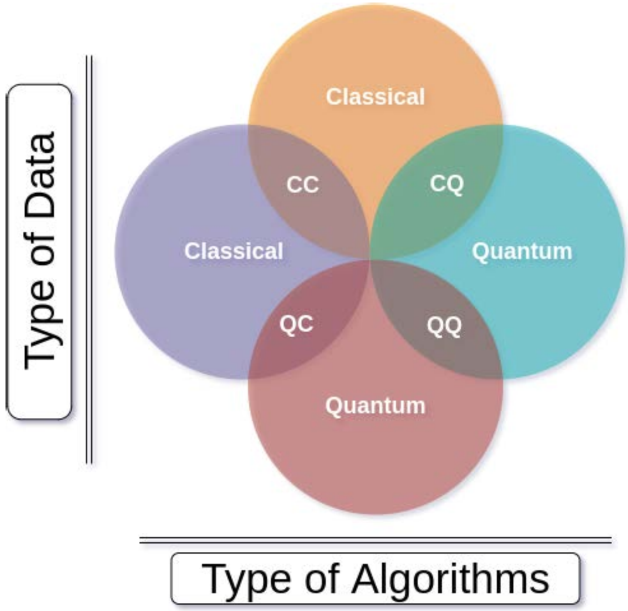

FIGURE 12. Matrix of classical and quantum system [35].

information techniques are employed in machine learning, and artificial intelligence [4]. The interaction between ML and QC is known as Quantum Machine Learning [3], shown in figure 10. The use of QML has resulted in a significant improvement in the performance and computational speed [32]. The term "QC" refers to a computational paradigm based on quantum mechanics rules. Quantum information technologies and intelligent learning applications are hot topics and recently released informatics technologies [33]. Quantum algorithms need to encode and decode conventional data into a QC to be used for quantum information processing [34], as depicted in figure 11.

Quantum processing of data is frequently used for QC outcomes. The conclusion is deduced via a quantum system assessment [35]. For example, the outcome of a qubit measurement may reveal the outcome of a binary classification task. Some QML algorithms, on the other hand, have been implemented on specialized quantum devices or NISQ devices. The most important promise of QC is the continual utilization of many computer units based on processing power.

Quantum data processing is consistent, and it may be handled using QC to yield consistent outputs. However, ML improves solutions rapidly on QC and analyzes data considerably more quickly [4]. Recently, QC has emerged as a popular field of study, particularly in creating ML algorithms. This field of study, dubbed "QML," is gaining traction quickly. Current quantum algorithms (QA) researchers are working on building blocks and ML approaches. However, the problems highlight the mix of hardware and software challenges. 1) QC executes ML algorithms to solve problems apart from the capacity of classical computers, such as big data quantum techniques, adiabatic optimization [36], and Gibbs sampling [37]. 2) Quantum theory techniques, such as tensor and Bayesian networks, can be used to improve learning algorithms [37]. QML is considered one of the future research areas like ML and deep learning (DL). The ML and DL algorithms could be eased by being implemented in QC. The DL has become a familiar ML technique that depends on ANN. On the other hand, the QML and AI algorithms are optimized with the help of QC.

QML algorithms speed up the quantum systems, like Bayesian Interface Online [38]–[40], Perceptron Least Square Fitting [41], Quantum Boltzmann Machine [32], [42], Quantum PCA [43], Quantum Support Vector Machine [12], [44], Quantum Reinforcement Learning [45], [46]. QML focuses on the divergent methods of QC and data mining to enhance both fields. As a result, it is feasible to differentiate four perspectives on QML, each deriving from the behavior of the dataset that conceals the research and computation devices used, shown in Table 3 and figure 12.

There are four different approaches to Classical-Classical (CC), Classical-Quantum (CQ), Quantum-Classical (QC), and Quantum-Quantum (QQ). As shown in figure 12, in classical-classical (CC), ML algorithms are motivated by the conformity of quantum mechanics. Therefore, the dataset includes algorithms that can run on classical systems [19], [47]–[52]. The Classical-Quantum (CQ) algorithms depend on quantum computation and can speed up conventional ML techniques [53]–[59]. Quantum-Classical (QC.)

TABLE 3. Speedup technique for quantum machine learning [3].

Method	Speedup
Bayesian Inference	$O(\sqrt{N})$
Online Perceptron	$O(\sqrt{N})$
Least-squares fitting	$O(logN)$
Classical Boltzmann Machine	$O(\sqrt{N})$
Quantum Boltzmann Machine	$O(logN)$
Quantum PCA	$O(logN)$
Quantum Support Vector Machine	$O(logN)$
Quantum Reinforcement learning	$O(\sqrt{N})$

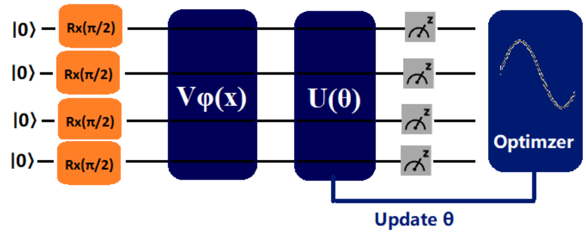

FIGURE 13. Schematic circuit of variational quantum circuit.

ML methods are implemented and evaluated on QC [61]–[66], [90]. Finally, a Quantum-Quantum (QQ) study was carried out on the quantum using algorithms and quantum systems [2], [67], [68].

The advantages of using QML models are simplicity, high calculation, fast application of algorithms, query complexity, and facilities for several new algorithms.

A. THE USAGE OF QUANTUM MACHINE LEARNING

Quantum learning theory aims to improve classical learning models and possible performance increases by employing a mathematical examination of quantum applications. Any proposed framework targets enhancing a classical computational learning theory that must include a quantum information device and quantum information processing. Whether using classical data or quantum data, it can also be used in simulations and searches as discussed follows.

1) QUANTUM SIMULATION

Simulation is a new trend to support various research areas such as nanotechnology. The simulation in the chemistry field depends on meaningful quantum systems. Quantum simulation is utilized efficiently to simulate atoms and particles behaviors during exceptional events [24].

2) QUANTUM SEARCH

The search process with quantum systems can provide discrete logarithms and QA. It will lead to a more significant polynomial speed rate than traditional approaches' algorithms. For different tasks and conditions [25], such as encapsulating physical-chemical processes, quantum, and solid-state physics, Jones polynomial parataxis [27], and making a solution to Pell's equation [27].

B. QUANTUM DEEP LEARNING

The DL has drawn attention and streamed significant scientific discoveries in the last decade. Quantum Deep Learning (QDL) is the combination of deep learning and quantum computing. In recent years, positive development in the field of QC. With the recent breakthroughs of variational quantum circuits (VQC), QC, which has long been acknowledged mainly for its promise, has opened up a new age of vast potential. Furthermore, the astonishing aspects of the different QA were demonstrated by addressing numerous sequential optimization issues and the inherent energy problems of molecules, which were impossible to solve using traditional methods. Future expansions are being studied to create ML algorithms utilizing QC amongst all; QDL domains are expanding at a rapid pace, absorbing the accomplishments of previous deep learning research [32]. As a result, multiple significant accomplishments in QDL have been reported, and recent research studies are given below.

1) VARIATIONAL QUANTUM CIRCUIT

A variational quantum circuit (VQC) [14] is a quantum circuit that uses rotation function gates with random initialization to carry out a variety of computational tasks like approximation, optimization, and classification. An approach that uses a variational quantum circuit is known as a variational quantum algorithm (VQA. A traditional computer frequently conducts the VQC model parameters optimization because of its universal parameterization characteristic. There are several algorithms devised to address diverse numerical problems.

This cycle resulted in various VQA applications in ML and replaced the present model's artificial neural network (ANN) with VQC. VQC is comparable to artificial neural networks in that it closely resembles functions through parameter learning, but it differs owing to many QC properties. For example, quantum circuits with multilayer topologies employ entanglement layers rather than activation functions because all quantum gate operations are reversible linear operations [69], as shown in figure 13. These VQCs are referred to as quantum neural networks, and this research will classify them based on their structure and characteristics.

2) QUANTUM NEURAL NETWORK

The neural network (NN) model is based on quantum mechanics concepts [70]. Therefore, Quantum Neural Network (QNN) [15] research is divided into two approaches: one that significantly uses quantum processing to improve neural network models and another that explores potential quantum phenomena in the brain. Table 4 depicts the fundamental ideas of quantum physics and NN [70].

First, the input data is encoded into the appropriate number of qubits equals qubits state. The qubit state is then converted through several layers of parameterized rotation gates and entangling gates, as depicted in figure 14. The transformed qubit state is then quantified by calculating the anticipated

TABLE 4. Main concepts of quantum mechanics and neural networks.

Quantum Mechanics	Neural networks
Wave function	Neurons
Superposition (Coherence)	Interconnections (weights)
Measurement (De-coherence)	Evolution to attractor
Entanglement	Learning rule
Unitary transformation	Gain function

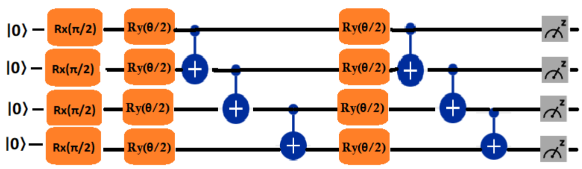

FIGURE 14. Schematic circuit of neural network quantum circuit.

outcome of a Hamiltonian operator, including Pauli gates. Next, these measurements are decoded and converted into usable expected output. Finally, an optimization technique, such as Adam [71], COBYLA [72], or SPSA [73] optimizer, is used to update the parameters. A neural network built in that manner of a VQC fulfills the various tasks in several contexts, which will be explored as quantum neural networks.

3) QUANTUM CONVOLUTIONAL NEURAL NETWORK

The quantum convolutional neural network (QCNN) [17] was proposed in 2013, with the convolution layer and pooling layer implemented on quantum circuits. On the basis of previous research findings, the QCNN [17] circuit computation is carried out. Much like in any QNN architecture, the initial step is to encode input data into a qubit state using rotation operator gates. Next, the convolution layer filters the input data into a feature map using the quasi-local unitary gates. Using controlled rotation operations, the convolution layers minimize the feature map. Repeating the following steps, the adequately connected layer operates on the qubit state in the same way traditional convolutional neural network (CNN) models [74] do. Finally, the qubit state measurement is decoded into the system output of the required dimensions, and after each measurement, the circuit parameters are modified using a gradient descent-based optimizer as shown in figure 15. However, it is also believed that relatively large quantum operations are feasible in the forthcoming QC ecosystem, and the QCNN will be able to obtain considerable computational benefits over its conventional counterparts [75].

C. QUANTUM MACHINE LEARNING ALGORITHMS

The combination of DL and ML methods refers to the successful result and powerful quantum, but these results are confusing and complex to use in different areas. Several types of research try to improve ML works by quantum linear algebra subroutines to make it faster. Quantum classifiers contain SVM Support vector machine and KLS kernel least squares. However, the implementation of QC [60] is cumbersome and

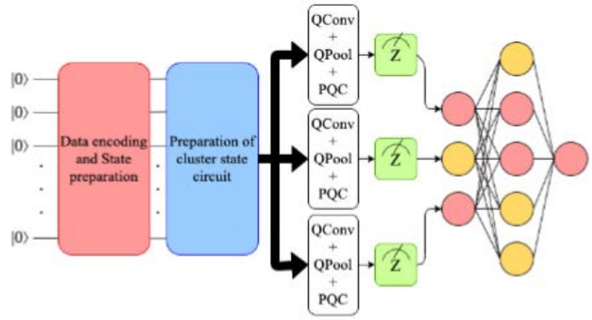

FIGURE 15. Schematic circuit of quantum convolutional neural network circuit [75].

TABLE 5. Quantum machine learning algorithms.

Quantum Machine Learning Algorithms	Application ML	References
Quantum annealing	Regression	[2] [76]
Quantum adiabatic algorithm	Classification	[77]–[80]
Quantum neural network	Regression or Classification	[81]–[84]
Quantum process tomography	Regression	[85]
Quantum support vector Machine	Classification	[86]–[90]
Quantum Convolutional Neural Network	Regression or Classification	[71], [76] [91]–[93]
Variational Quantum Classifier	Classification	[16], [75] [88], [92] [95]–[97]
Quantum Boltzmann Machine	Regression or Classification	[19], [98]
Quantum Restricted Boltzmann Machine	Regression or Classification	[99]–[102]

complex. This process requires relying on different quantum models. QC models are based on the items of decomposing computation. Some essential quantum models are shown in Table 5, which are essential in implementation, theoretically.

D. TOOLS USED IN QUANTUM MACHINE LEARNING

In the last decay, most researchers were working on different NISQ devices, and every device is different from its companion. Here are some advantages and challenges of QC in Table 6.

1) QUANTUM ALGORITHMS

Quantum Algorithms (QA) [109], [110] are known as Algorithms to execute on the practical Quantum computational model. The most popular QAs are Shor's Algorithm [26] and Groover's Algorithms [80]. Shor's algorithm is helpful for factorization, and Groover's algorithm for the unstructured database or scrambled data. Shor's and Groover's algorithms are executed exponentially faster than the best-known classical algorithms for factorization and unstructured databases. Some types of algorithms are shown in figure 16.

2) QUANTUM FOURIER TRANSFORM

It is defined by the quantum analog of discrete Fourier transform that can be efficiently executed on a QC using only a polynomial number of quantum gates. Figure 16 and Table 7 show some Quantum Fourier Transform algorithms.

TABLE 6. Quantum computing tools.

Name	Definition	how to use	Advantages	Challenge
Google Quantum AI with Tensor flow [103]	Google has an open environment Cirq, 72 Qubits chip called Bristlecone with tensor flow libraries.	Quantum Gates	Easy to Simulate	Little complex to understand need proper instruction for qubits.
Microsoft Quantum Development Kit [104]	Quantum Computer has its own language called Q sharp (Q#). Having 40 Qubits in the Azure system.	Run-on Azure cloud platform libraries and simulators	High quality of integration through Q# language and created a new language for quantum	Complex to learn the language
IBM Quantum Experience [105]	IBM Qiskit environment allows 127 qubits QC system	Quantum Gates languages: Python, Swift and Java.	Easy to use simulation system	learn Python and docs.
D-Wave [106]	Open-Source Platform called open leap system, which allows the 2000 and 5000 qubits quantum processing unit.	Quadratic Unconstrained Binary Optimization (QUBO) problems, smaller sub-QUBOs.	High-performance computing, good network integrated into the cloud system. Direct programming. Working with thousands of qubits. Quantum Adiabatic.	Complex with QUBO files.
Rigetti Forest [150]	Rigetti Forest have own language called Quil, also work on python. Rigetti forest system allows 128 qubits QC system	a simulation environment called QVM and Forest for simulation and python.	Powerful and simple, and hybrid quantum programs used in games, nucleus	Share Memory Architecture
Quantum Computing Playground [107]	It can efficiently simulate quantum registers up to 22 qubits, runs Grover's and Shor's algorithms, and has a variety of quantum gates built into the scripting language itself.	It runs your configuration on their hardware. 3D Quantum state visualization.	Factorization and efficient	Little Hard to play with gates
Xanadu [108]	Penny Lane & Strawberry Field. Quantum software framework.	Programming can be with C++, Fortran, and Python. Strawberry works on Blackbird Language	Simulation for electromagnetic fields, trapped atoms, harmonic oscillators, Bose-Einstein condensates, phonons, or optomechanical resonators	learn Python and docs.

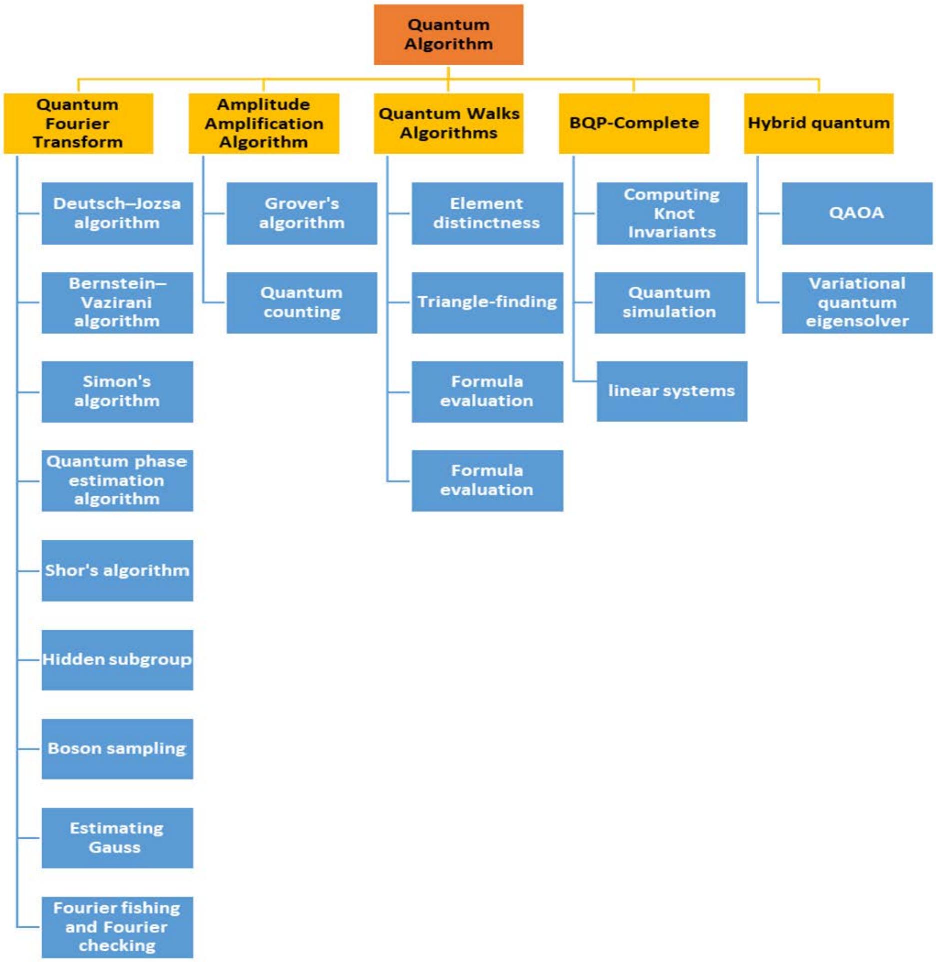

FIGURE 16. Quantum algorithms flowchart [109].

3) AMPLITUDE AMPLIFICATION

Numerous QAs for ML is founded on the principle of amplitude encoding, which involves associating the amplitude and frequency of a quantum state with the inputs and outputs of computations. Several QML methods in this classification are based on versions of the QA for linear systems of linear

TABLE 7. Quantum Fourier algorithms.

Quantum Fourier Transform Algorithm	Definition
Deutsch–Jozsa algorithm [111]	- Introduces a solution for black-box challenge exponentially faster than any traditional algorithm. - Do not use classical probabilistic to improve speed. - It produces a solution for the constant number problem of queries by using the a small probability of error
Bernstein–Vazirani algorithm [112]	- One of the important algorithms in quantum computation, which Separate the BQP and BPP using Oracle.
Simon's algorithm [113]	- Introduces a solution for black-box challenge exponentially faster than any traditional algorithm. - It includes bounded-error probabilistic algorithms. - It can calculate the average in polynomial time (in n). - One of the important algorithms in the quantum computation for factorization.
Quantum phase estimation algorithm [36]	- The eigenvalue of an eigenvector of a unitary gate presented a quantum status proportional to the eigenvector and access to the gate.
Shor's algorithm [27]	- To introduce a solution for the discrete logarithm and the integer factorization problems in polynomial time. - It is very useful for polynomial time prblems.
Hidden subgroup problem [114]	- It is the most common algorithm used in making a solution in a quantum computer, such as Simon's problem.
Boson sampling problem [115]	- The unitary, which is defined by the evolution of quantum systems based on summation probabilities. - It has conclude a fair sample of the probability distribution. - Boson sampling is useful in photonics (boson is input to boson).
Estimating Gauss sums [116]	- This sum is considered a kind of exponential sum. - The highest rated a classical algorithm uses for evaluating these sums in having time exponentially.
Fourier fishing and Fourier checking [117]	- It is a function of an oracle based on n random Boolean functions. - Solve the BQP in polynomial time.

TABLE 8. Amplitude amplification algorithm.

Amplitude Amplification Algorithm	Definition
Grover's algorithms [118]	- The goal is to search for the unstructured database or an unordered list. - Algorithm use $O\sqrt{N}$ in a quantum system. - For the speedup in the database uses $O\sqrt[3]{N}$.
Quantum Counting	- Presents a solution for a generalization of the search problem by counting the number of marked entries in an unordered list.

TABLE 9. Quantum walks algorithms.

Algorithm Based on Quantum Walks	Definition
Element distinctness	-It is known as an optimal algorithm that targets detecting the list of distinct elements, the challenge is not to search algorithms but has a huge problem.
Triangle-finding angle.	-Targets to deal with graphs include a tri-
Formula evaluation	- It is described by a tree with a gate at each internal node and an input bit at each leaf node as in oracle.
Group commutativity	In black-box problems, there are several group operations should deal with as in oracle (multiplication, inversion, and comparison with identity).

TABLE 10. BQP-complete algorithms.

BQP-Complete Algorithm	Definition
Computing knot invariants	- Which aims to simulate a topological quantum field theory (TQFT) and thereby approximate the Jones polynomial.
Quantum simulation	- Which is based on a simulation that needs exponential time.
Solving linear systems of equations	- HHL algorithm solving a linear system. - System predicates the result of scalar measurement of the solution vector in a linear system.

equations in certain circumstances. The performance of an inversion matrix incorporates physical resources that rise only logarithmically in matrix dimensions. Quantum matrix inversion is worthwhile in ML approaches when the training is reduced to calculate a linear programming problem, such as least-squares linear regression, the least-squares version of support vector machines, and Gaussian processes. The amplitude amplification algorithms are shown in figure 16 and Table 8.

4) QUANTUM WALKS

A quantum walks [119], [120] is defined by the analog of quantum in the traditional random walk. It used probability distribution in some cases. A quantum superposition can describe a quantum walks [122] over states. Quantum walks provide exponential speedups results for several black-box challenges. They rely on polynomial speedups in different problems. In Table 9 and figure 16 introduces the quantum walks algorithms.

5) BQP-COMPLETE

BQP–complete algorithms aim to simulate a topological quantum field and simulation that needs an exponential time [117]. Some of BQP- Complete algorithms are shown in figure 16 and Table 10.

6) HYBRID

Hybrid QA that can integrate quantum situation preparation and evaluation with conventional optimization. The target is to detect ground state eigenvectors and eigenvalue of

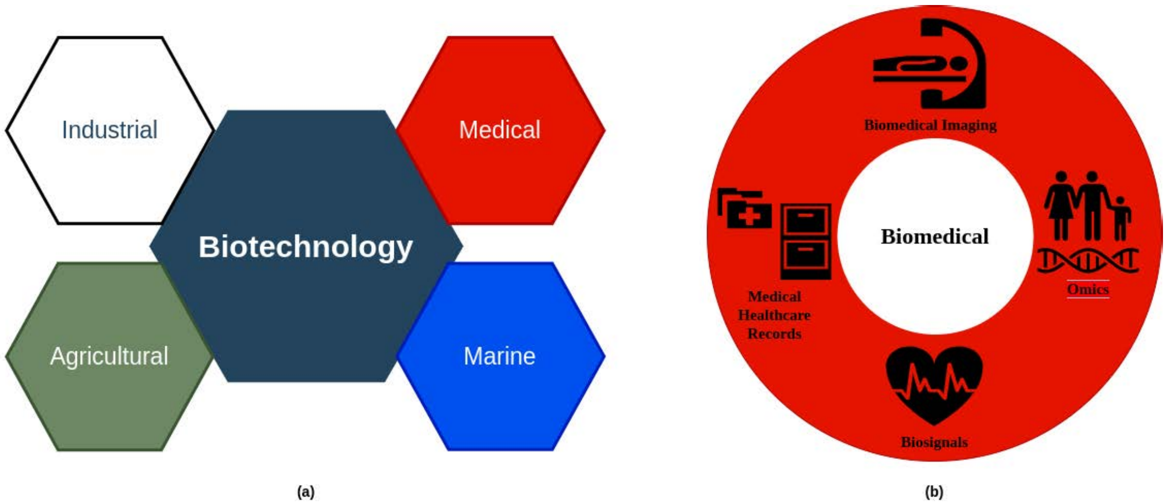

FIGURE 17. (a) Color code fields of Biotechnology and (b) different domains of Biomedical [5], [124].

TABLE 11. Hybrid algorithms.

Hybrid Quantum Algorithm	Definition
QAOA [122]	- A model of quantum annealing targets introducing solutions for graph theory.
Variational quantum eigensolver [123]	- Targets the Reduction of the power anticipation of an ansatz state to discover the ground energy case of a molecule.

Hermitian Operators. The hybrid algorithms are shown in figure 16 and Table 11.

V. QML IN BIOMEDICAL DOMAIN

Biotechnology is the associative discipline of engineering, physics, biology, and chemistry. Biotechnology was discovered by the Hungarian engineer Karl Erkey in 1919 [124]. Biotechnology combines two different entities; the word bio means life, techno means technical, and logy means study. The Organization for Economic Co-operation and Development (OECD) defines biotechnology as applications of scientific and engineering principles to the processing of materials by biological agents to provide goods and services; new biotechnology involves cellular and molecular processes to solve problems or make products'' [125]. Biotechnology is divided into four colors, Red, Blue, White, Green, and other additional colors define the areas, as shown in figure 17a. Our focus is on the red color [126], which is Medical or biomedical engineering. Biomedical plays a vital role in predicting and classifying diseases in healthcare. Moreover, biomedical is divided into four major domains: Omics, biomedical images, BioSignals, and medical healthcare records, as shown in figure 17b. Omics is concerned with bioinformatics, biomedical imaging, which focuses on human diagnostic images, BioSignals involved with human signals, and medical healthcare records, which are concerned with patient's medical records. Using the QML algorithms in biomedical data enhances the prediction and classification of diseases to better future treatments.

A. OMICS

Beginning with genomic sequence, gene expression, and going through protein structure prediction. The bridge between protein and medicine, the early stage of biomedical research, is concerned with all research. The prominent research field where QML plays a crucial part in Omics is rapidly increasing. The subject is commonly referred to as ''omics'' in the current state of the art; the alternative terms are used to call, such as bioinformatics [127] or biomedicine [128]. The word ''omics'' refers to derived data from genetics and (gene/epigene/ meta/ pharmacogen/ multiple) omics [129], with the primary objective of research being to anticipate and prevent disease by including patients in the creation of effective and personalized treatments, such as Gene interaction, protein-DNA interaction. Omics is further broken into two fields: DNA [130] and protein [131]. The most significant aspects of DNA are protein-DNA interactions, gene expression prediction, and genomic sequencing. The categorization of cancer-causing genes in order to identify Cancer early on is still a work in progress. Genomic sequence, protein binding prediction, gene expression, and genomic sequence are QML techniques used to predict phenotypes from the genome. Some of the recently published research studies in the field of Omics and QML are given in Table 12.

In Dabba *et al.* [86] discussed the novel swarm intelligence algorithm was used for binary and multiclassification of Omics (Colon, Leukemia1, Breast, Ovarian, Prostate Tumor, Leukemia2, Small Round Blue Cell Tumors (SRBCT), Brain Tumors1, Brain Tumors2, Lung cancer, 9 Tumors, and 11 Tumors) datasets. The author used the quantum moth fame optimization algorithm (QMFOA) to classify the small

TABLE 12. Published articles in omics.

Year	Authors	country	Methods	Dataset	Type	Results
2021	A Dabba et al [86]	Algeria	For Pre-processing technique, the Feature selection, cross-validation technique, and SVM and Mothflame optimization were used for binary and multiclassification of gene data. In addition, they used the quantum moth flame optimization algorithm.	Binary classification: Colon, Leukemia1, Breast, Ovarian, and Prostate Tumor Multiclass: Leukemia2, Small Round Blue Cell Tumors (SRBCT), Brain_Tumors1, Brain_Tumors2, Lung cancer, 9_Tumors, and 11_Tumors	J	Achieved the Leukemia1 97.2 % Colon 99% Prostate Tumor 96.2% Cns 91.1% Ovarian 99.5% Breast 76% 9_tumors 95% 11_tumors 95.8% Brain Tumor1 95.7% Brain Tumor2 96.9% Leukemia 3 97.8% Lung 98.7% Srbct 96.8% accuracies.
2021	G Sergioli et al [132]	Italy	QML model used as Quantum inspired Machine Learning Helstrom Quantum Classifier along with Pre-processing techniques such as Feature extraction, Normalization, and Scaling for the masking the colonies-background segmentation.	Clonogenic assays, 30 datasets for each of the 6 image features	J	
2021	Richard Y. Li et al [67]	USA	For Pre-processing technique, used Data Normalization,Random cut, PCA for features, and employed on the D'Wave Quantum Ising model.	Omics (Cancer Genome) (Brain, Lung, Breast, Liver, Kidney, Colon & Rectum)	J	Achieved accuracy on Six Cancer 91.22 percent.

gene subsets. In addition, the pre-processing chose the feature selection, and cross-validation techniques were used to classify the Cancer. Quantum-inspired Machine Learning (QiML) was used by Sergioli *et al.* [132] to categorize clonogenic test assessments. The quantum-inspired Helstrom Quantum classifier was employed in the biomedical imaging context of clonogenic test assessment for cell colony segmentation, and the author applied pre-processing techniques such as feature extraction, normalization, and scaling. The QML approach was utilized for binary classification of Omics (cancer, genome, brain, lung, breast, liver, kidney, colon, and rectum) datasets in Li *et al.* [67] discussed. The author employed the Quantum Ising approach to categorize the tiny gene subsets. On the DWave Quantum Ising system [106], data pre-processing, normalization, random cut, and PCA for features selection approaches were also employed in conjunction with the QSVM technique.

Furthermore, researchers are highly keen on employing quantum approaches in the omics domain. In contrast, various QML models are commonly used to predict and classify omics data.

B. BIOMEDICAL IMAGING

At the same time, QC researchers can overtake the computational power of thousands of supercomputers in terms of swiftly hastening and utilizing the pace of research in medical imaging using QML. Biomedical images are referred to as "medical images." Which may be cytopathology and histopathology [133], ultrasound [134], X-rays [135], CT scans [136], MRIs [137], fNIR [138], and PET images [139].

Human organs are evaluated and investigated in medical imaging using different (medical/clinical/health) imaging techniques. This elicits an accumulation of the examinations expected to be executed. On the other hand, a computer is working at quantum speed, intending to hasten the complex study, which had been making confident progress for the cancer study. The study of cells and tissue is known as cytopathology and histopathology. Diagnosticians often use cytopathology and histopathology for Cancer and some infectious and inflammatory diseases. Cytopathology and histopathology slides for the biopsies are examined under a microscope [87]. Biomedical imaging systems such as CT, MRI, Ultrasound (US), Digital Positron Emission Tomography (PET), X-rays, and histopathology images significantly enhance the classification and prediction of diseases [91]–[93]. Biomedical imaging aims to accurately diagnose the disease, which depends on image acquisition and interpretation of the images. Image acquisition techniques have improved exponentially due to the development of technology lately. Doctors generally perform interpretation of medical imaging, and there may be many differences between interpreters and drowsiness.

In recent pandemics, various QML algorithms have been used on the COVID-19 lungs X-rays images to classify the disease are shown in Table 13. Sengupta and Srivastava [91] presented the QML algorithm, and image processing techniques tend to classify the COVID-19 disease accurately.

TABLE 13. Published articles in biomedical imaging.

Year	Authors	country	Methods	Dataset	Type	Results
2021	K Sengupta et al [91]	India	For the Pre-processing, they employed the state preparation and normalization data techniques and used the QCNN model.	Covid CT scan	J	Achieved accuracy of 95.57 percent for COVID19 data.
2020	E. Acar et al [92]	Turkey	A pre-processing employed the data preparation, BConvLSTMU-Net architecture for lung segmentation, ConvLSTMU-Net architecture and Quantum transfer learning, and ResNet18 implemented on the VQC model.	COVID19 lungs CT Images	J	Achieved accuracies with PennyLane without U = 90.9%, PennyLane with U =100.0%, Qiskit-Noise Simulator = 97.7%, Cirq-Mixed Simulator = 95.65, IBMQx2 = 95.9%, IBMQ-London= 96.6%, and IBMQ-Rome = 96.9%
2020	A.T Jamal et al [87]	United Kingdom	QML algorithms use quantum genetic and quantum support vector machine alongwith Edge Detecting and Entropy -based multilevel thresholding for the breast cancer data.	Breast cancer	J	Detection Image size 150x150 pixels
2020	E. El-Shafeiy et al [81]	Egypt	The QML QNN model, pre-processing techniques such as the Quick Reduction Feature Selection method, and the training QNN model with different nodes.	COVID19	J	The best results were achieved with 30 Nodes QNN model accuracy was 92.334 %
2020	J Amin et al [93]	Pakistan	QML technique: QCNN on the COVID 19 images.	COVID 19 CT scan Images	J	Achieved accuracy of 96 percent.
2017	A. M. Iliyasu et al [140]	Saudi Arabia	For feature selection, geometry, color, and texture of the cervical images and utilizing the quantum-behaved particle swarm optimization with Quantum fuzzy k-nearest neighbors classifier to predicate cervical cancer.	Cervical Cancer	J	Achieved accuracy with Q-fuzzy (k=4) achieved 85 percent.

They implemented the QNN on COVID19 Indian patient x-rays images. Acar and Yilmaz [92] elaborated on the QML algorithm to classify and diagnose COVID 19 patients. They employed the VQC algorithm on different QC such as IBM Qiskit, Google Cirq, and Xanadu Pennylane system, using the COVID 19 patient's images. Amin *et al.* [93] presented the QML algorithm and image processing techniques to classify the COVID disease with high accuracy and precision. This article implemented QNN (3 dense layers, 500 neurons, ReLU activation, and 02 neurons with SoftMax for features mapping) with 4 qubits on Pennylane using COVID 19 Pakistani and Chinese patient's lungs CT images. El-Shafeiy *et al.* [81] presented the QML and image processing techniques to predict the severity of the COVID 19 patients. They employed the quick Reduction Feature Selection (QRFS) method for essential features to enhance the model performance. In addition, they implemented CQNN on COVID 19 patients (1 to 15 days) lymphocytes and blood counts to predict the patient's condition. Finally, the proposed method outperformed its counterparts in terms of effectiveness and high margin of accuracy. Iliyasu and Fatichah *et al.* [140] illustrated quantum hybrid (QH), quantum-behaved particle swarm optimisation (QPSO) techniques for the detection and classification of Cervical Cancer. The QPSO methodology has been used for feature selection after combining the quantum hybrid Quantum-Fuzzy technique on cytopathology cervical Cancer. They concluded that the coordination between QPSO, Fuzzy K-NN, and Q-Fuzzy approaches enhances classification accuracy. The quantum genetic method for edge detection and classification was presented by Jamal *et al.* [87]. The author used the quantum genetic algorithm and SVM on breast cancer pictures to tackle this challenge. The researchers used the quantum genetic algorithm to solve a multi-level thresholding concern premised on Tsallis entropy. The SVM is used to train the model with breast cancer images for edge detection.

In light of the aforementioned articles, it can be concluded that QML models are extensively used in biomedical imaging for prediction and classification tasks. Various authors used different QML techniques for bioimaging datasets, whereas they have achieved outstanding quantum results compared to classical models.

C. BIOSIGNALS

Biosignals play a significant role in the healthcare domain. BioSignal is concerned with electrical signals produced by brain neurons, tissues, and muscles and detected by biomedical sensors [141]. A BioSignal interface is a combination of hardware and software that allows brain activities to be controlled by a computer [142]. The BioSignal system is divided into four major categories: sensors, amplifiers, filters, and control devices. Body interfaces encode, decode, and process biosignals that originate from the body and are facilitated by the machine. Human brain neurons generate signals based on activities that are voluntary and reflex actions. Different methods for signal accretion have lately evolved [5].

TABLE 14. Published articles in BioSignals.

Year	Authors	country	Methods	Dataset	Type	Results
2020	A Seth et al [75]	India	They used the QML techniques such as QCNN, VQC, and QBoost for the ECG signal data.	14 channel ECG signal	J	Achieved accuracy with QCNN 55 percent, VQC 53-55 percent and Qboost 60 percent
2013	V Gandhi et al [82]	UK	Recurrent Quantum Neural Network and Pre-processing techniques used such as Savitzky–Golay Filtration, Feature extraction, and cross-validation for predication of EEG abnormalities.	EEG	J	Achieved accuracy of 66.59 percent.

For biosignals, accretion methods are further divided into invasive and non-invasive. Invasive methods include sensory insertions into the human body, like Electrocorticography ECOG. Non-invasive data collected from the epidermis include electroencephalograms (EEG), magnetoencephalography (MEG), and functions Near-Infrared Spectroscopy (fNIRS). The non-invasive acquired signals from tissues, such as an electrocardiogram ECG, an electrooculogram EOG, and an electroencephalogram EEG. ECG measures the heart's electrical activity and diagnoses coronary artery disease; EOG measures the cornea-retinal of the front and back of the human eye and diagnoses ophthalmological diagnosis and eye movement; and EEG diagnosis of brain-related diseases like Alzheimer's, dementia, and so on. In the study of the movements and ability of muscles, electromyograms (EMG) measure the electrical activity of prosthetic movement and the ability of skeletal muscles. For better accuracy and to avert the disadvantage of each type of signal, such methods are used with a combination of different body signals [5]. Some of the recently published research studies in the field of Biosignals and QML are given in Table 14. In such context, Aishwarya *et al.* [75] explained different QML classifiers by considering the cognitive states of human behavioral outcomes. This system utilized QML algorithms such as VQC, hybrid quantum-classical neural networks, and Quantum annealing Qboost on 14 channel EEG signals, including the pipeline that combined the QML methods to predict future cognitive responses. Gandhi *et al.* [82] elaborated the QML algorithm on the brain-computer interface signals to classify the nonstationary stochastic signal as time-dependent wave packets. The author implemented QRNN on the EEG signals using different noises and filtering methods. The Savitzky–Golay filtered EEG has been compared with QRNN EEG filter signals, significantly improving brain-computer interface performance.

D. MEDICAL HEALTHCARE RECORDS

Medical Healthcare Records (MHRs) are developed to evaluate enormous sizes of medical data in order to enhance healthcare benefits in the medical industry. Disease outbreaks, such as epidemics and pandemics, are studied in connection to human and ecological variables [143]. Clinical test results, radiographic scans, BioSignal, drug history, and treatments are all in MHRs, a viable patient records tool. In order to make better healthcare outcomes, QML is a vital technique to interpret clinical data in the temporal domain. Modeling lifestyle disorders like obesity regarding geographical locations is also part of MHRs. Using social media, where people's lives and social interactions are publicly shared online, it is now possible to track public health risks such as contagious intestinal infections or territorial obesity [5], [144]. Some of the recently published research studies in the field of MHRs and QML are given in Table 15.

Examining such clinical data against temporal dimensions presents an excellent opportunity for QML in healthcare decision-making and creating knowledge-distillation approaches to classifying illnesses. In recently published studies, various authors used different approaches to classify MHRs data. Maheshwari *et al.* [88] highlighted the different QML approaches for binary classification on the diabetes dataset. The author used pre-processing, state preparation, and data encoding approaches on QSVM, VQC, and AEVQC models to improve the model efficiency. They concluded that the classical system exceeded the quantum system by a little margin. With the PIMA diabetes dataset, Gupta *et al.* [95] employed the exploratory data analysis (EDA) and pre-processing technique for data scaling and applied it to the VQC, root mean square propagation (RMSprop), and DL models for classi?cation. They used back-propagation and the VQC approach to assess RMSprop in that research. Sierra-Sosa *et al.* [145] established a pre-processing pipeline approach that employs feature scaling, feature selection, an ellipsoidal coordinate map, and stroke parameters to assess if diabetes is linked to acute illnesses using VQC. They used the two features and three features of diabetic mellitus datasets to investigate the normalized and zero standard deviation, ellipsoidal transform, and Poincare sphere in the domain of VQC. Using the Poincare sphere, they improved precision. The classical and quantum algorithms were used by Maheshwari *et al.* [2] to create a voting model to forecast diabetes with acute illnesses using ensemble techniques and compute the computational time using the DWave System's QPU. In addition, the traditional voting model was compared to the hybrid New Model voting approach in such a study. Both models had almost the same accuracy; however, the new hybrid approach was 55 times faster than the conventional voting model.

To classify diseases, different authors explored the various QML on the publicly available UCI ML repository (skin cancer, breast cancer, lung cancer, diabetes, and liver) datasets.

TABLE 15. Published articles in Medical Healthcare Records.

Year	Authors	country	Methods	Dataset	Type	Results
2021	D Maheshwari et al [88]	Spain	For the Pre-processing employed feature selection to extract 8 distinct features from each dataset and normalize the data, they used the Scalar and Min-Max techniques. For state preparation, they used two encoding techniques such as feature mapping and amplitude encoding, for QSVM and VQC models.	Diabetes Dataset	J	Achieved accuracy for diabetes dataset QSVM = 74.5 percent, VQC= 69 percent, and AEVQC= 74.4 percent.
2021	H Gupta et al [95]	India	For the Pre-processing, they employed Feature Selection along with EDA and shuffles sampling approach to implementing on VQC Model.	PIMA Diabetes	J	Achieved the maximum accuracy of 74 percent for the diabetes dataset
2021	Ishwarya M.S et al [149]	India	For the pre-processing, they used the multi-attribute and multi-agent decision making along with the Ensemble technique to employ on quantum-inspired approach.	PIMA diabetes	J	Achieved the maximum accuracy of 90.5 percent of the diabetes dataset
2021	P. K Guru Diderot et al [148]	India	For Pre-processing, used the Segment the cancer mammogram image features extraction technique and employed on Hybrid Optimally Pruned Wavelet Kernel-based Extreme Learning Machine (HOP-WKELM) model.	Cancer Images	J	Maximum accuracy of 98.8% for cancer data
2021	D Pomarico et al [89]	Italy	The pre-processing technique uses the Feature selection and cross-validation techniques and are employed on the QSVM model.	Breast Cancer	J	Achieved accuracy of 65.8 percent for breast cancer data.
2020	S. Saini et al [90]	India	QML algorithms use quantum support vector machines and VQC for the breast cancer data.	UCI Breast cancer	J	Achieved QSVM accuracy of 85 percent and VQC of 85 percent
2020	S. Chakraborty et al [21]	India	QML technique is used such as hybrid quantum feature selection algorithm (HQFSA) for breast cancer dataset.	UCI Breast cancer	J	Achieved accuracy for Breast cancer 95 percent.
2020	D. Sierra-Sosa et al [145]	USA	They used the ellipsoidal coordinate map, stoke parameters, normalized and zero standard deviation, ellipsoidal transform, and Poincare sphere in the domain for the feature scaling and selection.In addition, they employed the VQC model.	Diabetes	J	The 2 features, 3 features diabetes mellitus dataset. They obtained the 72 percent, using the Poincare sphere
2020	S Jain et al [98]	Canada	They used the QML quantum Boltzmann machine model and feature selection, partition, Normalized, and cross-validation for the lung cancer dataset.	Lung cancer	J	Achieved accuracy of 95.24 percent.
2020	D. Maheshwari et al [2]	Spain	They used the Qboost Quantum Ising model and the voting model to enhance the prediction of diabetes disease.	Diabetes	C	Achieved accuracy of 68.73 percent.
2020	V Iyer et al [96]	India	They used the RBG color on skin cancer images for downsampling and an autoencoder were implemented on the VQC model.	skin cancer	J	Maximum accuracy achieved of 60 percent.
2020	H Yano et al [16]	Japan	A pre-processing technique used State preparation, SDG and Discrete feature mapping for QRAC implemented on the VQC model.	Heart diseases	C	Achieved accuracy with VQC = 66.1 percent and VQC+QRAC = 72.6 percent.
2020	A Bisarya et al [94]	India	The QML QCNN model on cancer data uses state preparation, morphological pattern block, and feature block for classification.	Wisconsin Breast Cancer	J	Maximum accuracy achieved of 98.9 percent.
2019	A. Sagheer et al [20]	Saudi Arabia	The quantum Parallel amplitude estimation and Amplitude amplification were used along with the Autonomous perceptron model (APM) to classify breast cancer.	UCI Breast cancer	J	Achieved accuracy with Breast cancer at 98.8 percent.
2018	R. Narain et al [83]	India	Employed the framingham risk score and QNN model to classify gender-based diabetes.	Cardiovascular dataset	J	Overall achieved an accuracy of 98.57 percent
2018	A Daskin et al [147]	Turkey	To train the Quantum Neural Net, they used the Neural Net, number of layers, Periodic activation function, and backpropagation method.	Cancer	C	With a 0.25 learning rate they achieved 96.9 accuracy
2018	M. Schuld et al [146]	South Africa	The pre-processing used the state preparation and post-processing and employed the VQC model to classify cancer.	UCI cancer	J	Achieved accuracy of 94.8 percent.
2018	G Sergioli et al [49]	Italy	Density pattern of quantum centroid, trace distance between two quantum density operators and implemented on Quantum Nearest Mean Classifier to classify diabetes, cancer, and liver diseases.	UCI Diabetes, Cancer and Liver	J	Achieved accuracy with Diabetes of 68.7 percent, Cancer 93.7 percent, and Liver 59.6 percent.
2017	O P Patel et al [84]	India	The Pre-processing used the Auto-Encoder and employed the QNN model to classify diabetes and liver.	BUPA Liver, PIMA diabetes	J	Achieved accuracy with Liver 95.66 percent and diabetes 92.15 percent.

They have adopted different pre-processing techniques to enhance the performance and avoid the complexity of the model. In the QML algorithms QSVM [89], VQC [16], [90], [96], [146], QRAC [16], QCNN [94], QBM [98], APM [20], QNN [83], [84], [147], HQFSA [21], HOP-WKELM [148], and QNMC [49], pre-processing techniques include feature selection and normalization SDG and discrete feature mapping, cross-validation, autoencoder, post-processing, and quantum parallel amplitude estimation and amplification are used. To summarize, QML, like traditional ML, has made significant contributions in the realm of healthcare, particularly in disease segmentation, detection, and healthcare regression issues.

VI. DISCUSSION

This part aims to complete the questionnaires in Table 1, summarize all the data provided in this literature review, and evaluate the possibilities for future medical applications and QML approaches. Based on the statistical data presented in the preceding section, it can be concluded that, based on the number of articles published on a particular theme of the topics. The comprehensive study can be considered the hot topic that has primarily piqued and interest of the scientific community since 2013. Following that, the questions posed at the research commencement will be addressed to grasp the issue and form an opinion correctly. Instantly, it is stated that in the ensuing discussion, several papers will be identified as samples of particular scenarios or criteria from those with the optimum quality score and those that are more illustrative. The general form and substance of the articles have been evaluated and analyzed in Table 1. It stated the importance of the **paper quality** and application in the healthcare domain could be achieved by evaluating the performance and attaining accuracies of the published articles are given in Table 16.

Q1: We evaluate the QML models which are implied in the desired applications. The state-of-the-art methods of general-purpose healthcare are examined and **adapted to the interests** of the patients. This approach is coupled with other technologies to play an essential role in a specific healthcare field [2], [88], [145]. In QML, the results of other methods are compared using well-known metrics [110] and taking into consideration other features of the systems, such as speed or real-time applicability in the form of accuracy. Benchmarks that are freely accessible are compared with the counterpart system's performance. Furthermore, a dataset including omics [9], MHRs [10], Biosignal's [9], and images [8] of the specific use case is developed and compared with other QML systems, which is a perfect way to **evaluate the developed system**. The paper's positive aspect is its replicability; even though a comparison of the produced approach and other QML systems is presented, neither the code nor the datasets are publicly available. Preserving the work privately is understandable because the developed system may have commercial applications in the future. However, the consideration of publicly available public datasets for evaluation could be an interesting approach for the research community to contribute to future aspects.

Q2: QML plays a vital role in healthcare, such as Cancer, COVID-19 detection and Omics, diabetes, heart and liver diseases classifications [2], [49], [84], [86]–[88], [91], [92], [140], [145]. The computers ''understand'' computational input and provide predictable outcomes by utilizing fundamental algorithms. To set the door for a spectrum of uses, including creating clinical care standards and clinical decision assistance. Disease diagnosis and classification, particularly for difficult-to-diagnose disorders, is one of the primary uses of QML in healthcare. For instance, QML can **assist and detect the tumors and malignancies in their early stages, as well as hereditary illnesses, in addition to established diagnostic approaches**. Each successful application is an essential step in the development of QC. One of these applications lies in advancing Machine Learning (QML) techniques, a technology widely used in many healthcare applications motivated by advances in different diseases [151]. QC approaches are developing exponentially, and several industries have significantly seen advancements. However, QC implies and processes the advancement in every point, but it must be evaluated in real-world problems. It could enable QC and QML techniques in the healthcare system to enhance and expedite the computation of the existing ML model, which allows for novel methods to comprehend the disease's complex behavior [2], [145].

Q3: Reviewing and evaluating the articles, QML implies using healthcare data to classify and detect different disease patterns. Different authors used **various QML algorithms** in different aspects of healthcare data. QML algorithms are widely used in healthcare QSVM [88], [89], VQC [16], [88], [90], [96], [145], [146], Qboost [2], [67], QNN [83], [84], [147], QCNN [75], [91], [93], [94], Quantum hybrid models [21], [148], QDNN [23], QBM [19], [98], and so on. Based on application, the authors implied the different healthcare data models. The most commonly used models are QSVM and VQC. Most of the researchers employ earlier proposed by various scholars as to the **foundation of their methods**, transfer learning with public or private datasets, and then apply techniques to increase the efficiency of such systems in certain healthcare domains. From a technical perspective, analysis is followed, and the data shown in Table 4 shows that there is indeed diversity in terms of QML use in the healthcare domain. On the other hand, various studies have discovered that explicitly use general-purpose QML models in a healthcare context, attempting to test the applicability of such methods in those specific applications. Some articles endeavor to revive current systems or frameworks that have demonstrated exemplary performance and practical purpose applications by employing various methodologies aimed at overcoming particular challenges in specific circumstances.

There is a particular adoption in this frame of reference: in QML models, there are two most important things are state preparation techniques [71], [91] and feature map [88], [89], [95], [96], [145], [146], different data encoding methods, such as feature extraction methods [81], [95], [98], [140], [148], and data encoding methods, like basis encoding, amplitude encoding [71], [88], and other encodings. The state preparation method encodes classical data into the quantum state, and the feature map is converted 2D to higher dimensions using Hilbert space [88], [89], [95], [96], [145], [146].

TABLE 16. Content of evaluated considered research articles based on merit points.

		Content of paper					Additional Quality Measures					
Sr No	Reference	1	2	3	4	5	6	7	8	9	10	Merit points	Quality
1	D. Maheswari et al [88]	1	1	2	1	1	1	0	0.5	1.0	0.5	9.0	High Impact factor
2	H.Gupta et al [95]	1	1	2	1	1	0	0	0.5	1.0	0.5	9.0	High Impact factor
3	Ishwarya M.S et al [149]	1	1	2	0.5	0	0	0	0.5	1.5	0.5	8.0	Impact factor
4	K.Sengupta et al [91]	1	1	2	0.5	0	1	0	0.5	1.5	0.5	8.0	Impact factor
5	A.Dabba et al [86]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	8.5	Impact factor
6	P. K Guru Diderot et al [148]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	9.0	High Impact factor
7	D.Pomarico et al [89]	1	1	2	0.5	1	1	0	0.5	0.5	0.5	8.0	Impact factor
8	G.Sergioli et al [132]	1	1	2	0.5	1	1	0	0.5	0	0.5	7.5	Low Impact Factor
9	Richard Y. Li et al [67]	1	1	2	1	1	1	0	0.5	1.5	0.5	9.5	High Impact factor
10	A.T Jamal et al [87]	1	1	2	0.5	1	1	0	0.5	0	0.5	7.5	Low Impact Factor
11	S.Saini et al [90]	1	1	2	0.5	1	0	0	0.5	1.0	0.5	7.5	Low Impact Factor
12	S.Chakraborty et al [21]	1	1	2	1	1	0	0	0.5	1.5	0.5	9.0	High Impact factor
13	D.Sierra-Sosa et al [69]	1	1	2	1	1	1	0	0.5	1.0	0.5	9.0	High Impact factor
14	S.Jain et al [98]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	9.0	High Impact factor
15	D.Maheshwari et al [2]	1	1	2	1	1	1	0	0.5	0.5	0.5	8.5	Impact factor
16	A.Seth et al [75]	1	1	2	0.5	1	1	0	0.5	0	0.5	8.5	Impact factor
17	A.Bisarya et al [94]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	9.0	High Impact factor
18	H Yano et al [16]	1	1	2	0.5	1	1	0	0.5	1.0	0.5	8.5	Impact factor
19	E.Acar et al [92]	1	1	2	0.5	0	1	0	0.5	1.5	0.5	8.0	Impact factor
20	E. El-Shafeiy et al [81]	1	1	2	0.5	0	1	0	0.5	1.5	0.5	8.0	Impact factor
21	J.Amin et al [93]	1	1	2	0.5	0	1	0	0.5	1.5	0.5	8.0	Impact factor
22	V.Iyer et al [96]	1	1	0	0.5	1	1	0	0.5	0	0.5	5.5	Low Impact Factor
23	A.Sagheer et al [20]	1	1	2	0.5	1	0	0	0.5	1.5	0.5	8.0	Impact factor
24	R.Narain et al [83]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	9.0	High Impact factor
25	A. Daskin et al [147]	1	1	2	0.5	1	1	0	0.5	1.5	0.5	9.0	High Impact factor
26	M.Schuld et al [146]	1	1	2	1	1	0	0	0.5	1.5	0.5	7.5	Low Impact Factor
27	G.Sergioli et al [49]	1	1	2	0.5	1	0	0	0.5	1.5	0.5	8.0	Impact factor
28	A M. Iliyasu et al [140]	1	1	2	0.5	1	1	0	0.5	1.0	0.5	7.5	Low Impact Factor
29	V.Gandhi et al [82]	1	1	2	0.5	1	1	0	0.5	0.5	0.5	8.0	Impact factor
30	OP.Patel et al [84]	1	1	2	0.5	0	0	0	0.5	1.5	0	6.0	Low Impact

Q4: Yes, QML models are also tested on all types of datasets, whether publicly available [20], [49], [84], [94]–[96], [120], [146], [147] or private [67], [75], [82], [86]–[88], [98], [120], [132], [145]. On the one hand, numerous authors produced their own datasets for system development and testing using manual annotations or other ground truth predication. Which certainly did not publish in the public domain. Conversely, most researchers developed and released datasets to benefit the scientific community. The most **common QC system** used by the scientific community, such as DWave systems quantum annealing [106], IBM Qiskit [105], and Google Cirq adiabatic system [103] for the QSVM, VQC, QNN, QDNN, RQN, QHM, and so on.

Q5: We have achieved the reliability and validity of research work by analyzing the multiple states of the art using different techniques. We considered 30 articles from different sources of databases. The reliability of the work has been obtained by analyzing these articles through **quality matrices**, as shown in Table 2. The Quality metrics describe the complete information of the previous state of the arts. i.e., the paper's content and additional quality measurement as shown in Table 16. In the content of this article, we deeply evaluated the manuscript's key points, such as the comprehensive overview of the background problem, literature review, evaluation of the system, execution of QML classifier, enhance the system predication, impartial discussion, and limitation of the study. In addition, we analyze the research dataset, availability of code, and research novelty.

Furthermore, the **reliability of work** is obtained by clustering the different healthcare domains such as Omics, biomedical imaging, Biosignal's, and medical healthcare records.

VII. CONCLUSION

This manuscript elaborates on the systematic review to identify, evaluate, and analyze the quantum machine learning algorithms in the healthcare domain: All of the articles in this field of study were assessed impartially. As a result, we discovered 3149 publications from 5 different databases throughout the selection process of papers published between 2013 and 2021. By eliminating repetitions and using alternative criteria and quality evaluations, we were able to minimize the number of articles. 30 publications were chosen as the most relevant for this study. During the literature review, we find the different QML designs and implementations. However, the primary trend of the QML algorithm was QNN, which were VQC, QDNN, RQNN, and QHM, along with different standardization of data encoding techniques for the classification of images and UCI well-known datasets such as Cancer, diabetes, liver, heart, and lungs. Several findings might be drawn on various parts of the reviewed material during the literature review. To begin with, as a definitive consensus, there is a dearth of articles on the particular topic of QML applied to the healthcare domain. Even though hundreds of publications can be retrieved by utilizing relevant search phrases, only several other attendant articles are available. The limits of noisy intermediate-scale quantum devices, the restricted number of quantum bits, and the limited size of sample data were all noted by the majority of writers in their research papers.

Future approaches to QML algorithms open up endless possibilities for researchers. A large number of quantum bits and a vast amount of data will contribute to enhancing and developing quantum technology. Explore diverse data encoding methods in order to apply QML to human healthcare problems.

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