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Review

Quantum computing meets neural excitability: modeling ion channels and action potentials via membrane biophysics

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Abstract: Understanding neural excitability and action potential generation is a cornerstone of neuroscience, relying on the complex interplay of biophysical mechanisms governed by ion channels in neuronal membranes. Traditional approaches, such as the Hodgkin-Huxley model, have provided a robust framework for simulating these processes using classical computational techniques. However, the advent of quantum computing opens new avenues for exploring neuronal dynamics, particularly due to ion movement's inherently quantum mechanical properties at atomic scales. In this study, I investigated the intersection of quantum computing and membrane biophysics, evaluating how quantum algorithms could revolutionize simulations of ion channel behavior and neuronal signaling. I began by analyzing the limitations of classical methods in handling high-dimensional, nonlinear systems. Next, I introduced key quantum computing principles, including qubits, superposition, and entanglement, and their potential applications in solving molecular dynamics and differential equations relevant to neuronal activity. Despite promising theoretical advantages, practical challenges such as qubit coherence, error rates, and hardware scalability must be addressed before quantum models can outperform classical simulations. I also discussed hybrid classical-quantum approaches as a transitional strategy, leveraging the strengths of both paradigms. By bridging neuroscience, biophysics, and quantum information science, I aimed to stimulate interdisciplinary research toward more efficient and accurate models of neural excitability.

Keywords: quantum computing; neural excitability; ion channel modeling; membrane biophysics; Hodgkin-Huxley model

1. Introduction

Neural excitability, the ability of neurons to generate and propagate electrical signals, is the bedrock of brain function, enabling everything from basic reflexes to complex cognitive processes like memory and decision-making. These electrical impulses, known as action potentials (APs), are the language of the nervous system, enabling neurons to communicate across vast networks. At the heart of this phenomenon lies the intricate dance of ion channels, specialized proteins embedded in neuronal membranes. These channels act as molecular gatekeepers, selectively permitting ions such as sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) to flow in and out of the cell [1]. This ion flux alters the membrane potential, triggering a cascade of depolarization and repolarization that propagates the electrical signal along the neuron [2,3]. Disruptions in this process, as observed in several neurodegenerative diseases, highlight the delicate balance necessary for healthy neural activity. The Hodgkin-Huxley (HH) model, formulated in 1952 through pioneering experiments on squid giant axons, revolutionized neuroscience by mathematically describing how voltage-gated ion conductance generates APs [4]. Using a system of differential equations, the model captures the dynamic interplay of Na^+ and K^+ currents that underlie neuronal firing [5]. Despite its fundamental significance, the HH framework has serious drawbacks since it ignores the quantum mechanical interactions at atomic scales and the stochastic behavior of individual channels, simplifying ion channels as macroscopic conductance [6]. It ignores the stochastic character of ion channel dynamics, which is crucial in tiny neurones like cerebellar granule cells, and instead assumes deterministic channel behaviour [7]. The variety of ionic conductance seen in cortical pyramidal neurones is not captured by their simpler architecture, which has only a small number of ion channel types [8]. Furthermore, it is unable to replicate dendritic processing and spatial signal propagation, which are crucial for hippocampus CA1 neurones, because neurones are modeled as single compartments [9]. Additionally, the model ignores neurotransmitter modulation, such as that affecting the firing modes of thalamic relay neurons, and sets parameters like conductance and reversal potentials [10]. Furthermore, it ignores the metabolic cost of spiking, which is particularly significant in systems with limited energy, such as the retina [11]. Finally, without significant alteration, its usefulness is limited because of its incapacity to replicate complicated behaviors like bursting, which are observed in pre-Bötzinger complex neurons [12]. Classical simulations of large neuronal networks also become computationally prohibitive, often requiring supercomputers to approximate real-time dynamics. Furthermore, the model's inability to resolve molecular details, such as the precise atomic arrangement of ion selectivity filters or the quantum tunneling effects that may influence ion permeation, limits its predictive power for drug design or disease modeling [13].

Emerging quantum technologies offer a transformative path forward. Quantum computing, built on the principles of superposition and entanglement, can process information in fundamentally different ways than classical systems [14]. Quantum bits, or qubits, enable highly parallel computations, making them ideally suited for problems that are intractable on traditional hardware [15]. In neuroscience, algorithms such as the Variational Quantum Eigensolver can model the quantum mechanical behavior of ion channels with subatomic precision [16]. This enables researchers to explore phenomena like ion selectivity and gating at levels of detail that classical simulations cannot achieve; for example, examining how K^+ channels strip ions of their hydration shells and coordinate them via carbonyl oxygen atoms inside the selectivity filter. Beyond molecular modeling, quantum algorithms also offer a powerful way to accelerate the mathematical computations that underpin classical models

of neural dynamics. The Harrow-Hassidim-Lloyd algorithm, for instance, can exponentially speed up the solution of systems of linear equations, potentially enabling real-time simulations of large-scale brain activity [17]. This computational edge could uncover complex neural phenomena, such as circuit-wide synchronization or dynamic encoding strategies in layered cortical networks. Furthermore, quantum-enhanced machine learning could analyze vast neurobiological datasets, ranging from electrophysiological recordings to brain imaging, enabling the discovery of novel disease markers and predictive patterns [18]. Despite these promising capabilities, current quantum systems remain constrained by hardware limitations. Operating in the Noisy Intermediate-Scale Quantum era, present-day quantum computers struggle with limited coherence times, high error rates, and scalability challenges [19]. As a result, the immediate application of quantum tools in neural excitability will likely rely on hybrid quantum-classical models [20]. In these systems, quantum processors would handle tasks that benefit most from quantum speed or precision (e.g., modeling ion permeation or solving core equations), while classical systems manage broader simulation tasks and data interpretation. This cross-disciplinary endeavor also highlights the need for deep collaboration. Progress at this intersection depends on physicists modeling quantum interactions, neuroscientists providing biological context, and computer scientists engineering robust, error-tolerant algorithms. These collaborations are not merely additive; they represent a new paradigm where insights from neuroscience can inform the design of efficient, resilient quantum architectures, and quantum systems can, in turn, illuminate the physical underpinnings of neural function. For example, the brain's energy-efficient and adaptive information processing might inspire novel quantum computing frameworks, while quantum simulations of neural behavior could offer revolutionary advances in drug development or neuromorphic AI [21].

A comprehensive literature review is crucial for consolidating fragmented knowledge and identifying gaps at the intersection of quantum computing and ion channel biophysics. Although there are reviews on quantum computing in biology, few focus on ion channels and their unique role in neuronal excitability, especially in AP generation. This gap obscures opportunities for cross-disciplinary innovation, such as applying quantum simulations to resolve controversies over ion permeation mechanisms or adapting quantum machine learning to predict channelopathies. A systematic review could map existing methodologies, evaluate quantum algorithms' biological relevance, and highlight understudied areas; for instance, how quantum effects in channel proteins influence macroscopic neural rhythms. By synthesizing insights from physics, neuroscience, and computer science, such a review would provide a roadmap for collaborative research, ensuring that quantum advancements are grounded in biological fidelity while steering computational priorities toward pressing neuroscientific challenges.

2. Neural excitability and membrane biophysics

2.1. Ion channels and action potentials

Ion channels are transmembrane proteins that regulate the selective passage of ions such as Na^+, K^+, and Ca^{2+} across neuronal membranes, establishing electrochemical gradients essential for neural signaling. These gradients, maintained by ion concentration disparities and membrane potential differences, drive the rapid depolarization and repolarization phases of APs, the electrical impulses fundamental to neuronal communication [22]. Voltage-gated ion channels, a major subclass, respond

to shifts in membrane potential by undergoing conformational changes. For example, voltage-gated Na^+ channels activate during depolarization, enabling an inward Na^+ current that amplifies membrane potential reversal, while delayed rectifier K^+ channels open subsequently, restoring the resting potential via outward K^+ flow. Ligand-gated channels, another critical category, open or close in response to neurotransmitter binding (e.g., glutamate or GABA), modulating synaptic transmission and plasticity [23]. Additionally, mechanosensitive and temperature-sensitive channels adjust ion flux in response to physical stimuli or thermal changes, illustrating the diversity of regulatory mechanisms [24]. The precise spatial and temporal coordination of these channels ensures APs propagate unidirectionally along axons, enabling reliable signal transmission. Structurally, ion channels possess selectivity filters, narrow pore regions that discriminate between ions based on size and charge, and gating domains that undergo rearrangements to open or block the pore. Dysregulation of these components, as seen in channelopathies like neurological disorders or cardiac arrhythmias, underscores their physiological significance.

2.2. Foundation of the Hodgkin-Huxley model

The HH model, developed in 1952 through pioneering experiments on squid giant axons, revolutionized neuroscience by mathematically formalizing the ionic mechanisms underlying APs [25]. Using a system of nonlinear differential equations, the model quantifies how voltage-gated Na^+ and K^+ currents drive the depolarization and repolarization phases of neuronal firing. By incorporating variables for channel activation and inactivation gates (e.g., *m*, *h*, and *n*), the HH framework accurately predicts the shape, propagation, and refractory periods of action potentials, cementing its status as a cornerstone of computational neuroscience. The calculation of each ionic current I_{ion} is based on Ohm's law, as conventionally represented by Equation 1.

$$I_{ion} = \bar{g}[m(V_m, t)]^x[h(V_m, t)]^y(V_m - E_{Nernst}) \quad (1)$$

In equation (1), $\bar{g}$ and $E_{Nerrnst}$ represent the maximum conductance and the Nernst potential specific to the ion channel being modeled. The variables *m* and *h* are dimensionless gating parameters that describe activation and inactivation, respectively; they vary with time and membrane voltage. To enhance equation fitting, an additional set of dimensionless variables, *x* and *y*, is introduced. These gating variables are governed by a system of first-order differential equations, by the classical HH formalism [26].

The instantaneous value of the activation variable "m" is computed by the differential equation presented in equation 2.

$$\frac{dm(V_m,t)}{dt} = \frac{m_\infty(V_m) - m(V_m,t)}{\tau_m} \quad (2)$$

In this equation, m_∞ represents the steady-state value, and τ_m denotes the time constant, both of which are functions of voltage and/or ionic concentrations.

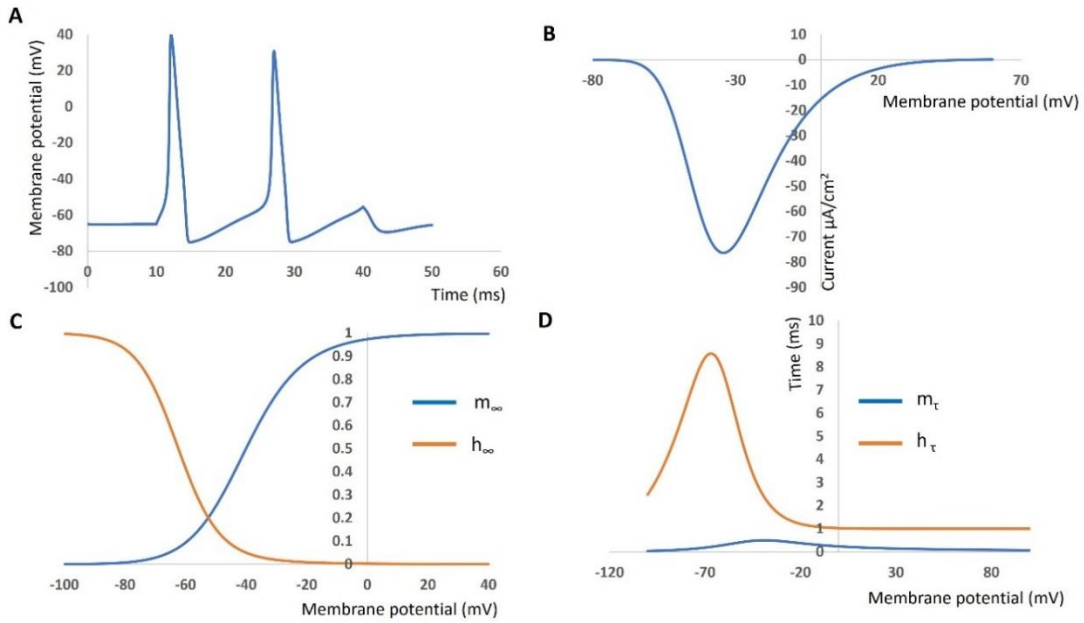

Figure 1. Hodgkin-Huxley-based simulation of action potential generation and sodium channel kinetics. (A) Membrane potential response to repeated depolarizing current stimuli, showing action potential firing. (B) Steady-state sodium current-voltage (I–V) relationship under voltage-clamp conditions. (C) Steady-state activation (m_∞) and inactivation (h_∞) gating variables of the sodium channel as functions of membrane potential. (D) Voltage dependence of the time constants (τ) for activation (m_τ) and inactivation (h_τ) of the sodium channel.

With an emphasis on Na^+ channel characteristics, Figure 1 depicts the dynamic behavior of a neuronal cell modeled using the HH formalism. Panel A shows how stepwise current injection causes action potentials (APs) to be generated in a single-compartment model. Membrane potential variations over time demonstrate the neural cell's capacity to reproduce neuronal excitability and firing behavior. The coordinated activation of several voltage-gated ion channels, including as sodium, potassium, calcium, and chloride, which together control the electrical dynamics of the membrane, is what causes the start and advancement of APs. The fidelity of the established ion channel kinetics is reflected in the waveform properties, such as the frequency profile and AP shape. The temporal dynamics of the model under simulated physiological settings are validated by this time-domain response. The sodium (Na^+) channel's current–voltage (I–V) relationship under voltage-clamp conditions is displayed in Panel B, with a noticeable peak inward current at about −30 mV. The voltage-dependent conductance characteristics of the channel are reflected in this steady-state I–V curve, which depicts the relationship between membrane potential and sodium current density. The model's ability to replicate well-known sodium channel behavior is confirmed by the distinctive inward current peak and the reversal potential that follows. This curve enables direct comparison with experimental voltage-clamp recordings and is essential for evaluating channel activation. Panel C shows how the gating variables for activation (m_∞) and inactivation (h_∞) change with membrane voltage. The response of the channel gates to voltage at equilibrium is described by these sigmoidal functions. They are essential for confirming that the model replicates the anticipated steady-state gating kinetics by experimental data and are obtained from the

gating equations. It is crucial to remember that the current is computed at a macroscopic level, reflecting the typical behavior of a sizable ion channel population. Microscopic models, on the other hand, mimic the random opening and closing of individual ion channels. For these sodium ion channel gates, Panel D displays the voltage dependency of the time constants (activation time constant m_τ and inactivation time constant h_τ). This demonstrates how fast the Na^+ channels react to voltage changes, with h_τ being noticeably slower and peaking at about −60 mV. The rate at which the gating variables get closer to their steady-state values is determined by these time constants. This graph, which is frequently directly compared to experimental patch-clamp kinetics, is essential for verifying the channel's dynamic responsiveness to voltage variations.

2.3. Ion channel noise modeling

The random opening and closing of ion channels, known as "ion channel noise", introduces variation in neuronal firing even in the presence of identical circumstances. In both healthy and diseased brain states, this stochastic behavior affects neuronal coding, synaptic integration, and signal dependability, making it experimentally significant. One of the mainstream approaches to modeling ion channel noise in neurons is through stochastic extensions of the classical HH framework and stochastic HH models developed by Fox and Lu [27]. To replicate the intrinsic noise brought about by the random opening and closing of ion channels, which is essential for neuronal excitability and signal propagation, these models adopt probabilistic gating behavior. To mimic ion channel noise, random fluctuations can also be added to ion channel and synaptic conductance. This can be done by adding a Gaussian white noise component to the conductance values or gating variables, which would represent the spontaneous opening and closing of ion channels brought on by random events like heat fluctuations. By altering the synaptic input at random across time, one can introduce noise into synaptic conductance, which can represent variations in neurotransmitter release or receptor binding. The firing patterns of excitable cells, such as neurons or muscle cells, are impacted by these stochastic fluctuations in the ion channels and synaptic conductance, which result in random currents that generate spontaneous variations in membrane potential [28]. This contributes to membrane potential noise. Moreover, because it takes into account the unpredictability seen in actual neurons and synapses under physiological conditions, this noise is crucial for accurately mimicking biological systems. Despite their effectiveness, these classical models have substantial computing difficulties when simulating complex networks over extended periods of time or when the number of ion channels rises. This is because the state space grows exponentially, and high-precision temporal resolution is required.

2.4. Computational challenges in classical simulations

Simulating complex neural systems using classical computational methods presents significant challenges, primarily due to the intensive resources required to solve large networks of nonlinear differential equations. A prime example is the HH model, which, although foundational, exemplifies these limitations. Modeling even a single neuron with this framework necessitates solving multiple coupled equations governing ion currents, membrane potentials, and gating variables. When extended to simulate networks of thousands or millions of neurons, the computational demands scale rapidly, placing heavy strain on memory and processing power [29]. In fine structures, like dendritic spines or thin axons, random fluctuations in ion channel activity can significantly influence signal fidelity and

membrane excitability. These fluctuations can significantly affect neural dynamics, especially in narrow dendrites or during abnormal activity patterns seen in neurological disorders. Capturing such variability typically requires stochastic differential equations or Monte Carlo simulations, both of which dramatically escalate computational complexity due to the need to track individual channel states across time and space [30]. Classical deterministic models based upon the HH equations approximate ion channel behavior using averaged conductance, disregarding the inherent randomness of individual channel gating. This simplification becomes especially problematic in small neuronal structures or pathological conditions such as channelopathies, where stochastic behavior plays a crucial role [31]. The HH framework also lacks molecular detail, omitting crucial aspects like the structural dynamics of ion channels, auxiliary subunit interactions, and conformational changes during gating. These omissions limit its capacity to accurately simulate disorders rooted in specific channel mutations, such as certain epilepsy-related sodium channel variants, or to incorporate modulatory processes like calcium-dependent synaptic plasticity. While enhancements such as stochastic HH models or multi-compartment frameworks aim to improve biological accuracy, they substantially increase computational burden. Accurately modeling processes such as ion selectivity, ligand binding, or conformational transitions often demands molecular dynamics (MD) simulations. These simulations, while detailed, are computationally expensive and typically require compromises in resolution, which can obscure important mechanisms like allosteric effects or quantum phenomena [32]. Real-time network adaptation poses another major challenge. Processes like synaptic plasticity and homeostatic scaling involve dynamic feedback mechanisms that require continuous updates to parameters. Learning rules such as spike-timing-dependent plasticity (STDP) involve iterative synaptic weight modifications across large networks, further amplifying computational load. Traditional computing architectures, constrained by sequential processing and limited memory bandwidth, struggle to handle these adaptive processes efficiently [33].

3. Fundamentals of quantum computing

3.1. Qubits, superpositions, and entanglement

At the heart of quantum computing lies the quantum bit, or qubit, the fundamental unit of quantum information. Unlike classical bits, which exist definitively in one of two states, 0 or 1, a qubit leverages the quantum mechanical principle of superposition, enabling it to exist in a linear combination of both states simultaneously [34]. This capability dramatically expands computational potential, as a system of n qubits can represent 2^n possible states at once, enabling parallel processing of information on a massive scale. Complementing superposition is the phenomenon of entanglement, a uniquely quantum correlation between qubits in which the state of one qubit is intrinsically linked to the state of another, regardless of the physical distance between them [35]. When qubits become entangled, operations performed on one instantaneously influence the others, facilitating complex, non-local information processing that has no classical equivalent [36]. Figure 2 contrasts classical and quantum computing concepts. On the left, a classical bit is shown as being in a definite state, either 0 (blue, up) or 1 (orange, down), with 100% certainty. In the center, a qubit can exist in a superposition, represented by a blend of both 0 and 1 states simultaneously (50% each in this example), mathematically described as $[|0) + |1)]/\sqrt{2}$. On the right, the concept of entanglement is depicted: Two qubits interact so that their states become inseparably linked. The entangled state $[|00) + |11)]/\sqrt{2}$ means that measuring one qubit

instantly determines the state of the other, no matter the distance between them. This figure visually summarizes how quantum information behaves beyond classical logic.

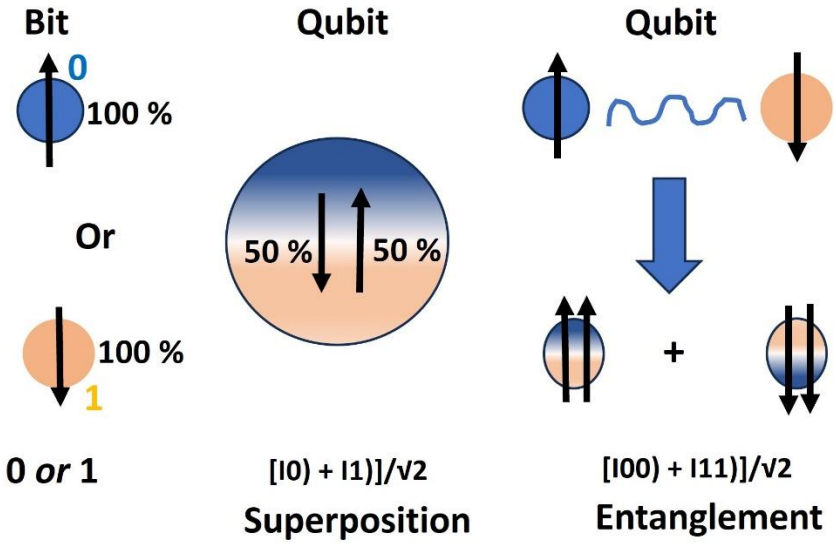

Figure 2. Visual comparison between classical bits and quantum bits (qubits), illustrating the concepts of superposition and entanglement in quantum computing.

3.2. Quantum algorithms: HHL, VQE, and QAOA

Quantum computing's transformative potential in computational biology and neuroscience lies not only in the unique nature of qubits but also in the specialized quantum algorithms developed to leverage their capabilities. Among the most promising of these are the Harrow-Hassidim-Lloyd (HHL) algorithm, the Variational Quantum Eigensolver (VQE), and the Quantum Approximate Optimization Algorithm (QAOA). Each of these algorithms addresses a distinct class of problems with direct relevance to modeling and understanding complex biological systems.

The HHL algorithm, introduced in 2009, was one of the first quantum algorithms to demonstrate an exponential speedup over classical methods for solving certain types of linear systems [37]. Under certain circumstances, this algorithm is a novel quantum method designed to solve linear systems more quickly than conventional classical methods. It uses Quantum Phase Estimation (QPE) to extract eigenvalue information from the system's defining Hermitian matrices. The solution is then encoded in a quantum state that is created by performing a type of quantum inversion using the eigenvalue information. The function of QPE is crucial because it enables the algorithm to identify the spectral characteristics of the matrix, which are necessary for effectively creating the intended output state. Figure 3 outlines a flowchart for a simplified HHL algorithm, which provides a quantum approach for solving linear systems $A|x\rangle = |b\rangle$ with exponential speedup over classical methods.

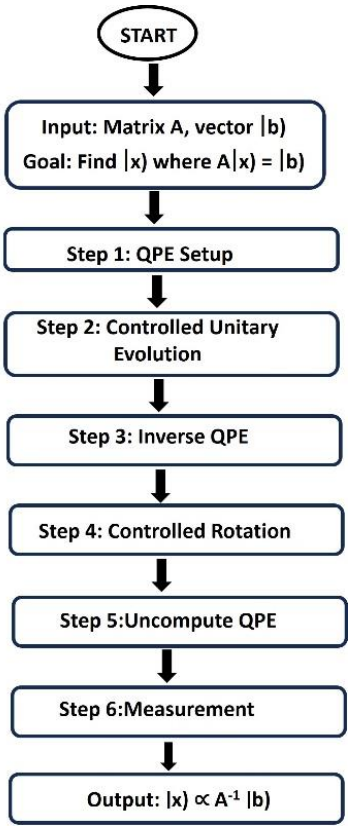

Figure 3. A simplified HHL algorithm flowchart, offering quantum solutions to A|x⟩=|b⟩.

The algorithm (flowchart in Figure 3) begins by taking input matrix A and vector |b⟩, then proceeds through six key steps: First, it establishes quantum phase estimation by preparing ancilla qubits and using Hadamard gates to create superposition states; second, it encodes A's eigenvalues as quantum phases using controlled unitary evolution operators; third, it uses the Quantum Fourier Transform (QFT) to perform inverse quantum phase estimation, extracting eigenvalue estimates from the encoded phases; fourth, it applies controlled rotations that are inversely proportional to eigenvalues, thereby implementing matrix inversion through amplitude amplification; fifth, it uncomputes the quantum phase estimation to disentangle ancilla qubits and eliminate undesired correlations; and sixth, it measures the ancilla qubit and post-selects on |1⟩ to obtain the solution state $|x\rangle \propto A^{-1}|b\rangle$. For sparse linear systems, HHL enables exponential quantum speedup; however, it necessitates post-selection and produces quantum states, which restrict classical extraction, despite its usefulness for quantum machine learning. In neuroscience and systems biology, many computational tasks, from modeling ion channel kinetics to simulating large-scale neural networks, involve solving differential equations that are often represented as large linear systems. HHL offers a potentially revolutionary approach by solving these systems exponentially faster than their classical counterparts under specific conditions. This could dramatically accelerate simulations of brain activity or enable real-time predictions of dynamic biological responses that would otherwise be computationally prohibitive.

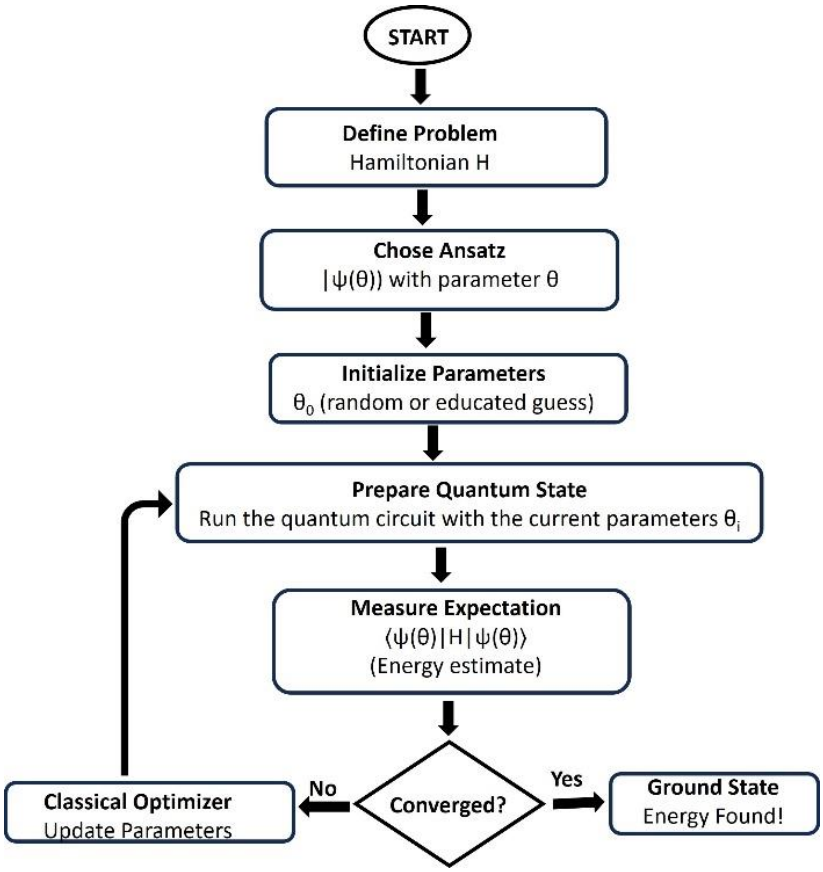

Figure 4. Variational Quantum Eigensolver (VQE) algorithm flowchart.

The Variational Quantum Eigensolver (VQE) is a hybrid quantum-classical algorithm designed to estimate the ground-state energy of complex molecular systems [38]. It is particularly well-suited for simulating quantum chemistry problems, such as modeling the behavior of electrons and nuclei within molecules, processes that are central to understanding the biophysics of ion channels, neurotransmitter binding, or protein folding. The approach starts by choosing a parameterized quantum circuit ansatz that can approximate the ground state wavefunction and encoding the problem Hamiltonian. Through an iterative optimisation process, VQE uses current parameter values to prepare quantum states, measures the Hamiltonian's expectation value to estimate the energy of the system, and then uses classical optimisation techniques to modify the circuit parameters in response to the measurement results. Because VQE can operate with shallow circuits and is resistant to quantum noise, it is especially useful for near-term quantum devices. This quantum-classical feedback loop (Figure 4) continues until the energy converges to the ground state value. The algorithm is a fundamental method for quantum chemistry computations, materials science applications, and other issues involving determining the minimum eigenvalues of intricate quantum systems because it can use quantum hardware for state preparation and measurement while using classical computers for parameter optimization. The hybrid quantum-classical workflow of the Variational Quantum Eigen solver algorithm for determining ground state energy is depicted in this flowchart in Figure 4. An iterative optimization loop that alternates between classical parameter optimization (left side, classical processing) and quantum state preparation and measurement (right side, quantum processing) follows the problem specification and ansatz selection steps. The quantum processor prepares parameterized

states $|\psi(\theta)\rangle$ and measures the Hamiltonian expectation value $\langle\psi(\theta)|H|\psi(\theta)\rangle$, while the classical optimizer updates circuit parameters θ based on the measured energies until convergence is achieved. The dashed vertical lines delineate the quantum and classical computational domains, highlighting VQE's hybrid nature that makes it suitable for near-term quantum devices. In neuroscience, VQE can be applied to explore the quantum-level interactions within ion selectivity filters of channels, providing insights into how subatomic forces shape ion flow and influence neural excitability [39]. Unlike purely classical simulations, which often rely on approximations, VQE can capture quantum mechanical properties with higher precision, enabling more accurate representations of molecular behavior.

The Quantum Approximate Optimization Algorithm (QAOA) is designed to tackle combinatorial optimization problems that are widespread in biological modeling and neural network analysis [40]. The QAOA operates through a systematic hybrid quantum-classical approach (shown as a flowchart in Figure 5) that begins by encoding a combinatorial optimization problem (such as MaxCut or the Traveling Salesman Problem) as a cost Hamiltonian H_C, followed by selecting the algorithm depth parameter p that determines the number of alternating quantum circuit layers. After initializing the variational parameters β (mixer angles) and γ (cost angles) for each layer, the algorithm prepares a uniform superposition state $|+\rangle\bigotimes^n$ to ensure equal exploration of all possible solutions. The core quantum circuit execution involves applying p alternating layers of cost unitaries $e^{-i\gamma_i Hc}$ that encode the problem structure and mixer unitaries $e^{-i\beta_i HM}$ that enable transitions between computational basis states. Following quantum state preparation, measurements in the computational basis generate bitstring samples used to compute the cost Hamiltonian expectation value $\langle H_C\rangle$, which is then fed to a classical optimizer that iteratively updates the variational parameters to minimize the cost function until convergence or maximum iterations are reached. Unlike VQE's flexible ansatz design, QAOA employs a structured circuit architecture directly inspired by adiabatic quantum computation principles, making it particularly well-suited for discrete combinatorial optimization problems where the alternating cost-mixer structure can effectively leverage quantum superposition and interference to explore solution landscapes. Tasks such as optimizing synaptic weights in a learning model, identifying minimal energy conformations of biomolecules, or discovering efficient neural circuit topologies often involve navigating vast, multidimensional solution spaces. QAOA combines quantum superposition with classical feedback to search for near-optimal solutions more efficiently than many classical heuristics. Its application in neuroscience could include optimizing model parameters for large-scale brain simulations or solving high-dimensional clustering problems in brain imaging data. Collectively, these quantum algorithms represent a new computational paradigm for biology and neuroscience. HHL offers speed and scalability in systems-level modeling: VQE provides precision in molecular simulations; and QAOA enables efficient exploration of complex optimization landscapes [41]. As quantum hardware evolves, these algorithms will be critical tools in bridging the gap between abstract quantum theory and real-world biomedical applications, empowering researchers to probe the brain's inner workings with unprecedented depth and speed.

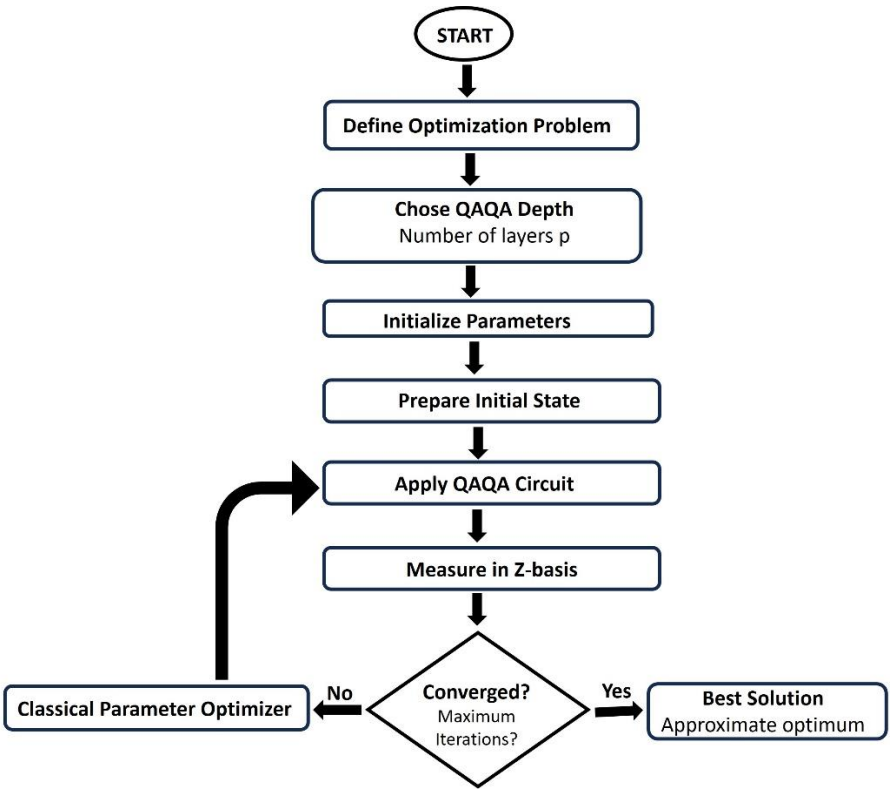

Figure 5. Quantum Approximate Optimization Algorithm (QAOA) flowchart.

3.3. Quantum vs. classical computational paradigms

The fundamental difference between classical and quantum computing is how information is represented and processed. Table 1 highlights the fundamental differences between classical and quantum computing, emphasizing their distinctions in data representation, processing power, and underlying computational principles.

Table 1. Key differences between classical and quantum computing, highlighting contrasts in data representation, processing capabilities, and computational principles.

Feature	Classical Computing	Quantum Computing
Basic Unit	Bit	Qubit
State	Either 0 or 1	Superposition of 0 and 1
Information Encoding	Binary digits (0 or 1)	Quantum states (e.g., (
Parallelism	Processes one state at a time	Can process multiple states simultaneously
Entanglement	Not possible	Possible, allows linking of qubit states across space
Data Manipulation	Logic gates (AND, OR, NOT)	Quantum gates (Hadamard, CNOT, etc.)

Continued on next page

Feature	Classical Computing	Quantum Computing
Error Handling	Relatively straightforward with error correction codes	Complex due to decoherence and noise
Execution	Deterministic (same input = same output)	Probabilistic (measurement collapses state to a definite output)
Computational Power	Limited by sequential or parallel processing	Exponential speed-up for certain problems (e.g., factoring, search)
Application Areas	General-purpose (web, apps, databases, etc.)	Cryptography, optimization, quantum simulation, machine learning
Technology Maturity	Fully mature and widely used	Experimental and rapidly developing

Figure 6 illustrates the key differences in execution flow between classical and quantum computing. In classical computing (left), solving a problem involves straightforward steps: Formulating an algorithm, coding it, compiling the code, and executing it to get a binary output (either 0 or 1). On the other hand, quantum computing (right) involves designing a parametric quantum circuit, compiling it for specific quantum hardware, and using a classical optimizer in a loop with quantum circuit execution. The quantum process iterates until convergence is achieved by evaluating cost functions, yielding a probabilistic output. This reflects the fundamental nature of quantum computation, which relies on probabilities and optimization through repeated measurements than single deterministic runs.

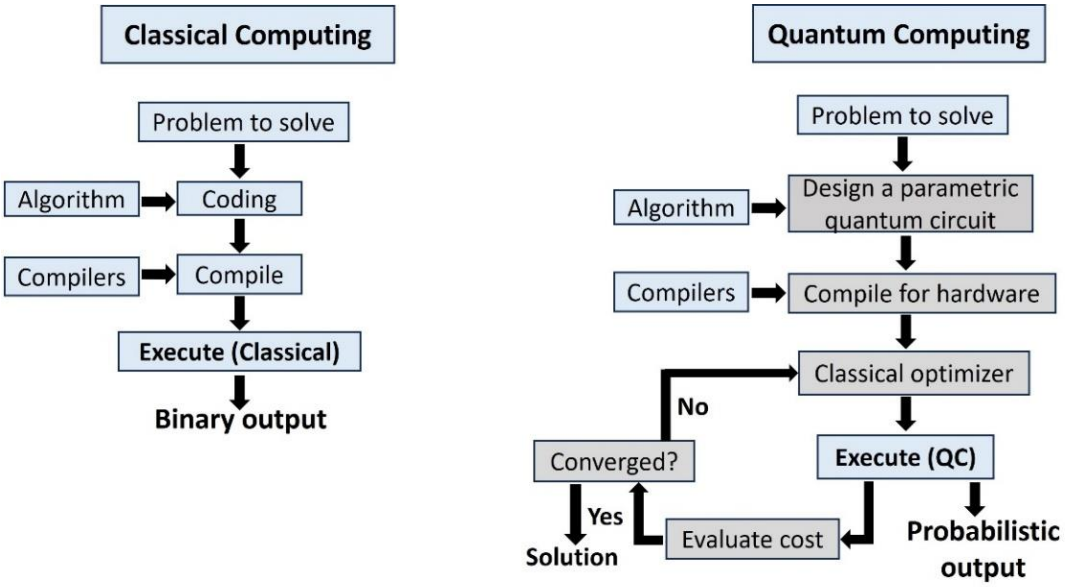

Figure 6. Workflow comparison between classical and quantum computing processes, highlighting the distinct steps and nature of outputs in solving computational problems.

4. Quantum approaches to biophysical modeling

4.1. Ion channel dynamics: Simulating permeation, selectivity, and gating mechanisms

Ion channel function hinges on intricate processes like ion permeation (movement through the pore) and selectivity (discrimination between ion species), which occur at atomic and subatomic scales [42]. These involve electrostatic forces, hydration dynamics, and interactions with the channel's protein structure. While classical MD simulations offer insights, they often approximate quantum effects, such as discrete ion energy levels, electron cloud interactions, and quantum tunneling, leading to gaps in understanding selectivity filter behavior, where ions interact directly with carbonyl oxygens [43]. Quantum computing enables explicit simulation of these quantum interactions. VQE can model ion energy states and spatial configurations in the selectivity filter, incorporating electron correlations, tunneling, and wavefunction overlap. This reveals why channels favor specific ions despite minimal size or charge differences. A key application is ion tunneling, where ions bypass energy barriers via quantum effects, a process classical methods miss but which may influence high-frequency signaling in excitable tissues like the brain or heart. Quantum simulations also clarify how mutations alter selectivity or conductance. For instance, a single amino acid substitution can drastically shift ion preference, an effect classical models struggle to predict. By modeling mutations at the electron orbital level, quantum approaches provide precise functional insights, aiding drug development for neurological, cardiac, or pain disorders by simulating drug-channel quantum interactions for higher specificity. Beyond permeation, channel gating, the opening/closing in response to stimuli like voltage or ligand binding, relies on conformational changes and lipid bilayer interactions [44]. Classical techniques (e.g., patch-clamp, crystallography) overlook quantum fluctuations and atomic-scale dynamics. Quantum computing, via VQE or quantum annealing, maps free energy landscapes of gating transitions, capturing stochastic quantum fluctuations that influence opening timing, especially near physiological thresholds. Quantum models also elucidate lipid-channel interactions, revealing how membrane electrostatics alter the electronic structure of gating residues. This multi-scale approach bridges atomic-level dynamics with cellular function, clarifying channelopathies (diseases from dysfunctional gating) and guiding therapeutics to stabilize specific states or correct aberrant gating. As hardware improves, quantum simulations will become vital for neuroscience and biomedical engineering, offering unparalleled precision in studying ion channels.

4.2. Solving differential equations and accelerating Hodgkin-Huxley simulations

Differential equations, both ordinary (ODEs) and partial (PDEs), form the foundation of many biophysical models, enabling researchers to simulate the evolution of biological systems. A prime example is the HH model, which describes the electrical behavior of neurons through complex systems of differential equations [45]. However, solving these equations, especially when they represent large, nonlinear, or coupled systems, can be computationally intensive, often requiring high-performance computing resources for extended simulations or fine spatial and temporal resolution. Quantum computing presents a promising paradigm shift by offering algorithmic speedups and enhanced scalability for solving differential equations central to neuroscience and systems biology. One key advancement is the HHL algorithm, which can solve certain large systems of linear equations

exponentially faster than classical methods under specific conditions. Since many discretized differential equations reduce to such systems, quantum linear system solvers could significantly accelerate simulations of neural circuits, diffusion processes, or electrophysiological phenomena, particularly when matrices are sparse, a common trait in biological modeling. In the context of the HH model, quantum computing could revolutionize how we simulate ion channel behavior and membrane potentials. Hybrid quantum-classical strategies, where quantum processors manage the computationally intensive subcomponents (such as gating state transitions or conductance updates), while classical systems handle higher-level network dynamics, could yield speed and fidelity improvements [46]. These enhancements are especially valuable for modeling large neuronal networks or for simulating scenarios that require high accuracy, such as action potential dynamics, synaptic integration, or pathological states. Moreover, quantum techniques hold promise for parameter estimation and optimization, two persistent challenges in biophysical modeling [47]. Traditional methods require extensive simulations across vast parameter spaces to fit models to experimental data. Quantum machine learning and optimization algorithms, leveraging superposition and entanglement, can explore these spaces more efficiently, potentially reducing computational cost and iteration count [48]. This could accelerate tasks such as tuning channel conductance, time constants, or reversal potentials in the HH model. While the full potential of quantum computing in this domain is constrained by current hardware limitations, such as qubit count, noise, and error rates, ongoing advances in hybrid quantum-classical systems offer a practical near-term path. These architectures enable researchers to delegate the most demanding numerical tasks to quantum processors while retaining classical control over overall simulation frameworks.

4.3. Large-scale neural network implications

The potential for quantum computing to enhance large-scale neural network simulations is equally exciting. Traditional methods of simulating large neuronal networks, whether through spiking neural networks (SNNs) or compartmental models, are limited by computational resources [49]. The sheer number of neurons and synaptic connections in the brain makes it computationally expensive to simulate networks in real time, especially when considering the complexity of ion channel dynamics and the stochastic nature of neuronal firing. Quantum computing, with its ability to perform parallel computations through quantum superposition and entanglement, offers the potential to solve these computational challenges by processing vast amounts of information simultaneously. For instance, quantum algorithms like the QAOA could be used to simulate complex, large-scale network dynamics and neural synchronization patterns that emerge in conditions such as epilepsy or Parkinson's disease [40]. The enhanced computational power could also be applied to model the plasticity of synapses, which is critical for understanding learning and memory, by simulating the quantum-level interactions between neurotransmitters, receptors, and ion channels. This would enable more accurate models of how neural circuits adapt to stimuli, paving the way for breakthroughs in neuromorphic computing and AI systems designed to emulate brain-like processing. Furthermore, by incorporating quantum methods into neural network simulations, researchers can better understand emergent behaviors in complex neural circuits, such as how synchronized firing patterns across large networks give rise to higher-order cognitive functions like perception, decision-making, and motor control. These insights could also inform the development of quantum-inspired machine learning algorithms that more closely mimic the efficiency and adaptability of biological neural networks, making them particularly suited

for tasks such as pattern recognition and decision-making in AI systems. My discussion will now be grounded in particular neurobiological processes to bolster the physiological significance of brain network modeling based on QAOA. A potential use case is the enhancement of phase synchronisation between remote cortical areas, a phenomenon linked to cognitive function and large-scale brain integration [50]. QAOA can be used to find the best phase relationships that facilitate effective information transfer, such as the theta-gamma coupling seen in the hippocampus and prefrontal cortex during working memory tasks, which can be modeled as a restricted optimisation issue. Beta-band synchronisation is frequently used to facilitate the precise timing between the motor cortex and cerebellum, which is another aspect of motor coordination. To model or optimize these temporal patterns, QAOA could be used to encode them into a cost Hamiltonian that matches coherence metrics reported in experiments [51]. Moreover, Kuramoto oscillator models demonstrate spontaneous synchronization patterns in resting-state networks, such as the default mode network. QAOA may be used to optimize network parameters to match observed synchronisation states, and these models have been demonstrated to replicate empirical fMRI connectivity patterns [52]. While the application of quantum computing to neural network modeling and action potential propagation is in its infancy, the potential to revolutionize our understanding of brain function is immense. As quantum hardware continues to improve, hybrid quantum-classical approaches could become practical tools for simulating large-scale neural networks and unraveling the complex molecular dynamics underlying neural excitability.

5. Challenges and limitations

5.1. NISQ era constraints and error mitigations

Quantum computers today function within the noisy intermediate-scale quantum (NISQ) era, where they are subject to various limitations, primarily related to noise and errors [53]. These devices cannot achieve the fault-tolerant levels of precision required for large-scale quantum computations. The coherence time, or the duration for which qubits maintain their quantum state, remains relatively short, leading to a significant challenge in maintaining the accuracy and stability of computations over time. These inherent constraints necessitate the development and implementation of robust techniques for error mitigation and circuit optimization. Error mitigation methods aim to minimize the impact of noise on quantum computations, enabling more reliable results despite the imperfections in the hardware [54]. This could involve techniques such as error correction codes, which help detect and correct errors during computation, or noise-resilient algorithms designed to work around the limitations of current quantum hardware. One method for mitigating errors is Zero Noise Extrapolation (ZNE), which simulates the dynamics of fragile ion channels by artificially scaling noise in quantum circuits and then extrapolating back to estimate ideal, noise-free outputs [55]. In order to represent stochastic processes like channel gating, it is essential to increase the accuracy of output probabilities through measurement error mitigation techniques such as matrix-free iterative correction [56]. Adaptive Neural Network Quantum Error Mitigation (ANN-QEM) is another technique that uses machine learning to dynamically fix noise effects in simulations of quantum biology [57]. When it comes to circuit design, hardware-aware compilation aligns circuit structure with particular quantum devices to lower error rates [58], while gate count and depth reduction minimize decoherence in order to simulate rapid neural events such as spike-timing-dependent plasticity [59]. Finally, AI-powered optimisation based on

reinforcement learning reconfigures quantum circuits for reduced noise and increased efficiency, which is advantageous for scaling up to network-level models of brain activity [59]. Additionally, circuit optimization plays a crucial role in reducing the number of gates and simplifying quantum circuits. By optimizing circuits, it becomes possible to reduce the chances of errors occurring due to gate operations, thus enhancing the overall performance of quantum algorithms. Together, error mitigation and circuit optimization are pivotal to advancing practical applications of quantum computing, enabling quantum systems to be used effectively within the constraints of the NISQ era.

5.2. Scalability and integration with classical systems

As the development of scalable and fault-tolerant quantum hardware remains a significant challenge, hybrid quantum-classical models have emerged as one of the most promising approaches to leveraging the potential of quantum computing in the near term. These hybrid models combine the strengths of classical computing with the unique capabilities of quantum systems, enabling more practical applications even while quantum hardware is in its infancy. In such hybrid models, quantum processors are typically used to perform specific tasks that are particularly well-suited for quantum speedups, such as optimization or simulation problems, while classical systems handle the more routine or computationally intensive parts of the process [46]. This division of labor enables the two systems to complement each other, balancing the advantages of quantum computation with the robustness and reliability of classical computing. However, achieving seamless integration between quantum and classical components remains an area of active research. One of the major challenges is ensuring smooth communication between the two systems, as the quantum processor must be able to exchange data with classical systems without introducing significant overhead or delays [60]. Furthermore, the partitioning of tasks between quantum and classical systems must be done efficiently to maximize the performance of both components, which requires sophisticated algorithms and protocols. Overall, while fault-tolerant quantum hardware is under development, the hybrid quantum-classical approach represents a practical pathway forward. It offers a way to begin solving real-world problems with quantum resources while continuing to push the boundaries of research needed for full quantum scalability and integration [61].

6. Prospects in quantum computing for neuroscience

As quantum computing continues to evolve, its application in neuroscience is becoming increasingly feasible. Future advancements will rely heavily on three critical areas: Hybrid quantum-classical algorithms, improvements in quantum hardware and error correction, and thoughtful consideration of ethical and practical implications.

6.1. The hybrid quantum-classical algorithm

Given the present constraints in quantum hardware, hybrid quantum-classical algorithms provide a practical and innovative framework for utilising the advantages of both quantum and classical computing. Computational tasks in these systems are split between quantum and classical components based on their capacities **[55]**. Data pre-processing, feature extraction, and initial model training are examples of steady, low-complexity activities that are handled by classical processors, whereas

subtasks that capitalize on quantum mechanical advantages are handled by quantum processors. The hybrid model can be divided into the following sub-modules to offer a more practical and implementable framework for next neuroscience research:

- **Data Preprocessing and Feature Extraction** *(Classical)*: Raw brain imaging or electrophysiological data can be filtered, normalized, and segmented using classical methods due to their robustness and efficiency.
- **Dimensionality Reduction** *(Quantum)*: Quantum Principal Component Analysis (qPCA) or Quantum Singular Value Decomposition (QSVD) could be used to reduce high-dimensional datasets, such as fMRI or EEG recordings, more efficiently than classical counterparts.
- **Model Optimization** *(Quantum)*: Quantum Approximate Optimization Algorithm (QAOA) and Variational Quantum Eigensolver (VQE) can be integrated to optimize complex neural models or synaptic weight configurations within deep learning architectures.
- **Pattern Recognition and Classification** *(Hybrid)*: Classical neural networks or support vector machines can be paired with quantum classifiers or quantum-enhanced kernels to detect neurological patterns, such as seizure prediction or early Alzheimer's diagnosis.
- **Simulation of Neural Dynamics** *(Quantum)*: Quantum simulation methods can replicate non-linear and high-dimensional dynamics of neural circuits, offering new insights into brain behavior and cognitive modeling.

Researchers can create neuroscience applications that are both practical with existing quantum devices and scalable as hardware advances, thanks to this modular divide, which also indicates where quantum advantage is most likely to appear. Therefore, hybrid algorithms provide a strategic basis for applied quantum neuroscience, enabling significant advancements in the present while laying the groundwork for a future that is entirely quantum.

6.2. Advances in hardware and error correction

The potential of quantum computing is closely tied to progress in hardware development and error mitigation. Quantum processors are highly sensitive to environmental disturbances, making stability and error correction critical [62]. Current systems rely on cryogenic environments to maintain the fragile quantum states of qubits, and ongoing improvements in cryogenic technology are supporting the development of more powerful, reliable processors. Innovations such as topological qubits are also promising; these qubits are inherently more stable and resistant to error due to the unique properties of topological matter, potentially reducing the need for complex correction schemes. In parallel, quantum error correction techniques, like surface codes and cat codes, are being refined to identify and fix errors during computation [63]. Together, these advancements will improve the reliability and scalability of quantum systems, enabling their use in complex neuroscience applications such as neural network modeling, biochemical pathway analysis, and simulations of brain function at the molecular level.

6.3. Ethical and practical considerations

As quantum technologies begin to intersect with cognitive and behavioral research, new ethical and practical concerns emerge. One major issue is privacy. Quantum systems could process and

interpret vast quantities of sensitive neural or behavioral data, raising the risk of misuse [64]. Clear guidelines are essential to ensure that this information is handled responsibly and ethically. Another concern involves the implications of predictive quantum models on concepts like free will and personal agency. If these models can anticipate or influence decisions and behaviors, they challenge existing ideas about autonomy and accountability. Furthermore, the complexity and opacity of quantum models make it difficult to guarantee fairness and transparency. Without robust oversight, there is a risk that such technologies could reinforce biases or exacerbate inequalities. Moving forward, the development of quantum applications in neuroscience must be guided by ethical frameworks that prioritize human rights, data protection, and societal well-being.

7. Conclusions

The convergence of neural dynamics with quantum computing signifies a paradigm shift in our capacity to simulate and comprehend the complex behavior of the brain. While the fundamentals of classical techniques have been established, they frequently encounter computational constraints when attempting to capture real-time whole-brain activity or simulate biological processes at the molecular level. A paradigm shift in computing is brought about by quantum computing, which can represent intricate, probabilistic systems. From quantum effects in ion channels to large-scale network oscillations, quantum-enhanced models can fill important gaps by incorporating the multiscale character of biological systems. In addition to speeding up solutions to classical models like the Hodgkin-Huxley equations, quantum algorithms, for instance, may simulate ion permeation and voltage gating at atomic resolution, providing fresh insights into how dynamics at the micro level translate to macroscopic brain rhythms. Existing hybrid quantum-classical models are promising for tackling important subproblems like conductance tuning and ion selectivity.

Going forward, the use of these techniques will be broadened by further developments in quantum hardware, especially in the areas of error correction and qubit coherence, which may make it possible to simulate diseased channel behaviors or conduct quantum-informed drug screening. However, in order to fully realize this paradigm's potential, interdisciplinary cooperation and technological advancement are also necessary. For this to be successful, biologists, computational neuroscientists, and quantum physicists must work together to create scalable, physiologically accurate tools. Deeper understanding of cognition and consciousness as well as precision diagnostics and neuromorphic computing could be made possible by this intersection of neuroscience and quantum technology. Redefining our understanding of, and ability to interact with, the human brain may result from the integration of biological complexity and quantum theory.

Use of generative-AI tools declaration

The authors declare that Artificial Intelligence (AI) tools were not used in the creation of this article, except for grammar checking.

Conflict of interest

The authors declare no conflict of interest.

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