Artificial Intelligence Review (2025) 58:134
https://doi.org/10.1007/s10462-025-11136-7

Quantum deep learning in neuroinformatics: a systematic review

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Accepted: 6 February 2025 / Published online: 14 February 2025

Abstract
Neuroinformatics involves replicating and detecting intricate brain activities through computational models, where deep learning plays a foundational role. Our systematic review explores quantum deep learning (QDL), an emerging deep learning sub-field, to assess whether quantum-based approaches outperform classical approaches in brain data learning tasks. This review is a pioneering effort to compare these deep learning domains. In addition, we survey neuroinformatics and its various subdomains to understand the current state of the field and where QDL stands relative to recent advancements. Our statistical analysis of tumor classification studies (n = 16) reveals that QDL models achieved a mean accuracy of 0.9701 (95% CI 0.9533–0.9868), slightly outperforming classical models with a mean accuracy of 0.9650 (95% CI 0.9475–0.9825). We observed similar trends across Alzheimer's diagnosis, stroke lesion detection, cognitive state monitoring, and brain age prediction, with QDL demonstrating better performance in metrics such as F1-score, dice coefficient, and RMSE. Our findings, paired with prior documented quantum advantages, highlight QDL's promise in healthcare applications as quantum technology evolves. Our discussion outlines existing research gaps with the intent of encouraging further investigation in this developing field.

Keywords Quantum deep learning · Quantum machine learning · Neuroinformatics · PRISMA · Systematic review

1 Introduction

This systematic review aims to evaluate the efficacy of quantum deep learning (QDL) models in neuroinformatics, specifically as opposed to classical deep learning approaches. Neuroinformatics focuses on neuroscience data and computational frameworks for understanding and mimicking neurological activities and conditions (Nayak et al. 2018; Guillén-Pujadas et al. 2025). On the other hand, QDL, which draws its cues from quantum physics and quantum computing, offers speedups and feature representations that could reshape deep learning and its application (Biamonte 2017; Cerezo et al. 2022). Our study explores

Extended author information available on the last page of the article neuroinformatics from the viewpoint of three data modalities: neuroimaging, electrophysiological signals, and cognitive assessments, and attempts to present QDL's utility in the field.

Neuroinformatics is a multifaceted discipline that seeks to understand the brain's structure, functions, and disorders by integrating concepts and technologies from neuroscience, psychology, cognitive science, data science, and artificial intelligence (AI) (Kasabov 2013). This field involves informatics and data analysis to study the brain's complexities and improve our understanding of neural processes (Dinov 2024). Essentially, neuroinformatics seeks to bridge the gap between the biological mechanisms of the brain and the computational tools that can help us understand it (Ascoli and Halavi 2009). Among its methodologies, deep learning is a key component, excelling in applications such as diagnosing neurological and neurodegenerative diseases (Valliani et al. 2019), brain-computer interfacing (Aggarwal and Chugh 2022), connectomics (Anbarasi et al. 2024), mental health assessments (Su et al. 2020), neurofeedback and rehabilitation therapy (Le Franc 2022), consciousness and awareness modeling (Lee 2022), and neurocognition (Yin 2023). Despite the success of deep learning in this field, there is still room for refinements.

It is no secret that deep learning requires large-scale annotated datasets for optimal outcomes (Sun et al. 2017). However, acquiring such datasets in the biomedical field poses substantial challenges due to the tedious task of data labeling, the scarcity of patients with specific conditions, and the ethical complications involved (Sapoval 2022; Salmi et al. 2024). Even if there is sufficient data, there is still a risk of overfitting, and even minor, undetectable input alterations cause misinterpretation (Chollet 2017). The intricate nature of neurological datasets, which are highly variable and susceptible to noise, further complicates this problem (Wei 2021; Davoudi et al. 2023; Yan et al. 2019; Pedroni et al. 2019).

Deep learning remains an active area of research to address these challenges, with one of its subfields, QDL, being a promising candidate. First, QDL possesses effective generalization properties and robustness against noise (LaRose and Coyle 2020; Cross et al. 2015; Du et al. 2021; Caro 2022; Caro et al. 2021; Gil-Fuster et al. 2024), both essential qualities for working with neuroscience data. Second, quantum advantages in speedups (Huang 2022; Biamonte 2017; Liu et al. 2021b; Saggio 2021; Ciliberto 2018) can help tackle the immense computational demands in brain data analysis. Third, utilizing a vast, high-dimensional quantum space–the Hilbert space–offers a complex yet effective way to represent features (Havlíček 2019; Schuld and Killoran 2019; Goto et al. 2021). This approach can prove critical for uncovering hidden relationships in neurological data. Finally, QDL's effectiveness in handling complex anatomical regions and organs, such as the heart (Zhang et al. 2024; Ovalle-Magallanes et al. 2022), chest (Houssein et al. 2022; Rao et al. 2024), and retina (Toledo-Cortés et al. 2022; Landman et al. 2022), suggests it may also be effective with intricate brain data. Figure 1 illustrates a perspective on QDL's workflow in a neuroinformatic medical setting.

In 2022, Maheshwari et al. explored the adoption of quantum machine learning in diverse areas, such as bioimaging, biosignals, omics, and medical health record data, in their systematic review (Maheshwari et al. 2022). Nevertheless, the review did not cover QDL models that specifically addressed neuroinformatic datasets. Similarly, Rahimi et al. did not report any QDL-related neuro-oncology research in their review (Rahimi and Asadi 2023). A recent systematic review found several articles on QDL in neuroinformatics (Ullah and Garcia-Zapirain 2024). However, there was no discussion of whether these models were

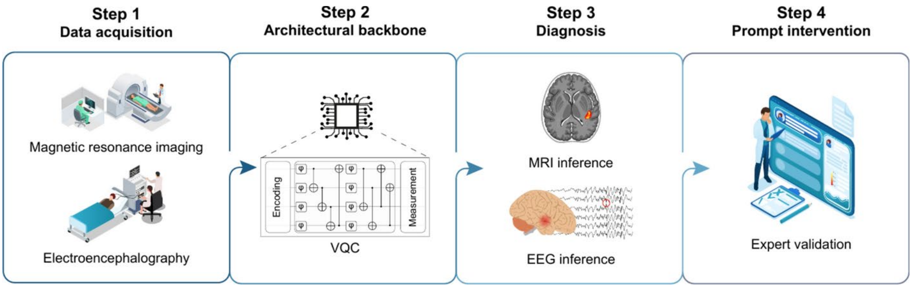

Fig. 1 An example framework of QDL within neuroinformatics. This multimodal framework uses variational quantum circuits (VQC) to generate timely and accurate inferences, which medical professionals subsequently verify. Like classical kernels, the circuits possess learnable parameters that contribute to the analysis

better at diagnostic accuracy (or other performance metrics) than well-known and widely used classical models.

To the best of our knowledge, no survey or review paper compared the efficacy of QDL algorithms against their classical counterparts despite the need. While QDL holds promise with speedups and parameter efficiency (Liu 2024; Ciliberto 2018), whether QDL can consistently outperform traditional deep learning in practical scenarios is still an open question. It is crucial to assess whether QDL models can meet the demands of modern healthcare, where timely interventions, accurate diagnoses, and precise prognoses are paramount. Moreover, QDL will only live up to its promise with continued improvements. As such, this comparison could spur more focused research efforts, helping to refine existing models or inspire new ones.

In light of this, we conducted a systematic review focusing on the applications of QDL in neuroinformatics while statistically comparing QDL with classical deep learning across a range of data learning tasks like classification, segmentation, and forecasting. For primary outcome analysis, our research question was: "*When considering task-specific performance metrics, how effective are QDL algorithms compared to state-of-the-art classical models in publicly available brain-related datasets*?" Our secondary objective was to explore: "*In what practical ways are quantum circuits and simulators currently applied, and what advantages or limitations exist for their application in the noisy intermediate-scale quantum (NISQ) era?*" The primary contributions of this review are outlined below:

- This is the first study to survey QDL applications in neuroinformatics, focusing on multiple brain-related data modalities.
- Our study is the first to statistically compare the performance of classical and quantum models across diverse datasets and studies, offering a cumulative analysis of their efficacy in data learning tasks.
- This review discusses existing research gaps in depth, examines QDL's practical and technical implications, and offers a forward-looking perspective on future research directions.

2 Overview of quantum deep learning

Quantum theories and algorithms inspire, enhance, or form the foundation of different approaches in QDL. In simpler terms, when a deep learning model with multiple levels or layers of data processing has at least one layer that relies on quantum mechanical concepts, it can be defined as a QDL model. On the contrary, a quantum circuit itself can sometimes emulate a deep neural network, which also falls under the category of QDL. Here, the former represents a hybrid architecture, combining classical and quantum elements, while the latter is purely quantum.

In this section, we will not attempt to discuss every QDL model currently available in the literature. Instead, we will focus on the foundational component of QDL: quantum circuits. We will examine how these circuits function and how they contribute to different quantum neural network architectures. This section aims to help newcomers understand the models presented in our systematic review and provide a strong starting point for exploring other models and architectures.

Qubits form the basis of quantum computing. Conceptually, qubits resemble binary bits, but they differ in that they can exist in a superposition of both $|0\rangle$ and $|1\rangle$ states, enabling parallel computation. In addition to superposition, entanglement allows the manipulation of multiple qubits simultaneously rather than individually. These quantum phenomena provide certain advantages unique to quantum computing over classical approaches, and researchers have been working to integrate them into various algorithms, including those in machine learning and deep learning (Wittek 2014; Nielsen and Chuang 2010; Cerezo et al. 2022).

Quantum circuits serve as frameworks for quantum computation. In these circuits, wires function as qubits, while the gates symbolize operations performed on the corresponding wires. In the context of classical data processing, we can divide quantum circuits into three key stages:

i) Encoding: This phase involves mapping classical information into a quantum feature space and preparing the data for quantum processing. The goal of encoding is to ensure the data is in a specific format suitable for manipulation by quantum operations. The two most common encoding methods are angle encoding and amplitude encoding. Angle encoding represents classical information as angles to the rotational gates applied to wires, initializing each wire in the $|0\rangle$ state. This method requires n qubits to encode n features. On the other hand, amplitude encoding turns classical data into the amplitudes of quantum states. This transformation ensures storing more information in a smaller space since n qubits can hold up to 2^n classical values. Angle encoding is linear, whereas amplitude encoding offers exponential scaling.
ii) Operations: This stage involves manipulating the encoded quantum data through various quantum gates. The choice of gates depends on the specific task at hand. We commonly use the Hadamard gate to create superposition, which places qubits into a state where both $|0\rangle$ and $|1\rangle$ are equally probable, thereby facilitating the simultaneous exploration of multiple possible solutions. Typically, a controlled-NOT gate establishes strong correlations between qubits after a Hadamard gate, creating entanglement between a pair. Entanglement ensures instantaneous discovery of the other state if one of the pair's states is known. We also use phase shift and rotation gates to change or amplify some

computational paths. This alteration can cause constructive or destructive interference, essential for finding patterns and optimizing solutions.

iii) Measurement: The final step involves measuring quantum states to extract classical information. Following the measurement, we observe the qubit states collapsing into classical bits, resulting in 0 or 1. We repeat the process multiple times (known as "shots") to gather sufficient statistics, as quantum measurement is inherently probabilistic. With enough measurements, we can reliably determine the exact or expected outcome of the quantum computation.

Figure 2 demonstrates the versatility of a single quantum circuit in forming various deep learning architectures. Figure 2a depicts a variational quantum circuit (VQC), consisting of unitary blocks that function as deep learning layers and execute quantum operations (Cerezo 2021; Schuld et al. 2020; Skolik et al. 2021; Cong et al. 2019). Due to learnable rotation parameters inside the blocks, researchers often refer to these circuits as parameterized quantum circuits (Benedetti et al. 2019).

In Fig. 2b and Fig. 2c, we show how to integrate the VQC into a hybrid neural network, combining quantum and classical components. Positioning the VQC relative to fully connected layers allows it to function either as a component of an autoencoder (refer to Fig. 2c) or as an artificial neural network (refer to Fig. 2b) (Schmidhuber 2015; Goodfellow et al. 2016). In Fig. 2c, VQC acts as the bottleneck of the autoencoder. In such hybrid models, careful consideration is required to ensure that both quantum and classical layers' output shapes and data types are compatible.

Figure 2d presents a hybrid convolutional neural network where the VQC acts as a task-specific head. There is flexibility in designing the base architecture. The baseline may follow a vanilla structure with standard convolution and pooling layers paired with non-linear activations, similar to AlexNet (LeCun et al. 1998; Krizhevsky et al. 2012). Alternatively,

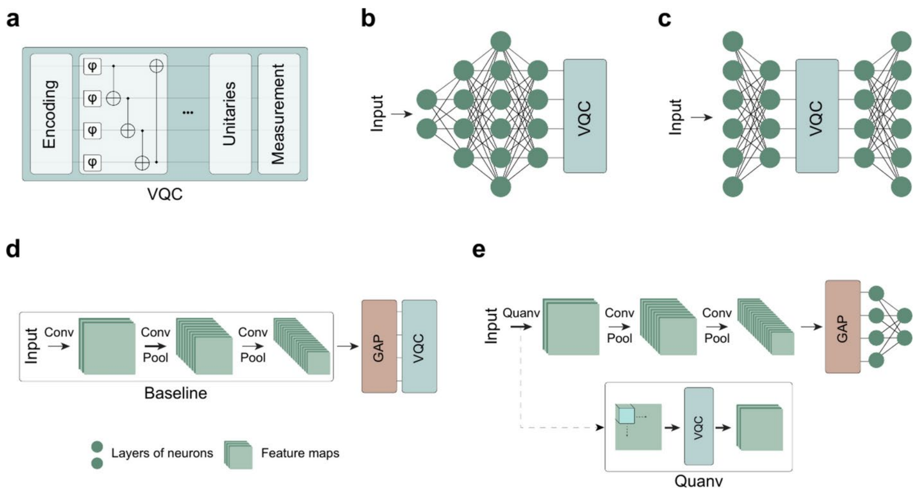

Fig. 2 Overview of various quantum deep learning algorithms using a shared quantum circuit. **a** Variational quantum circuit (VQC). **b** Hybrid quantum-classical neural network with a VQC output layer. **c** Hybrid quantum-classical autoencoder with a VQC bottleneck. **d** Hybrid quantum-classical convolutional neural network with a VQC output layer. **e** Quanvolutional neural network. GAP denotes global average pooling

they may consist of a pre-trained deep learning model, such as ResNet (He et al. 2016), Inception (Szegedy et al. 2015), EfficientNet (Szegedy et al. 2015), DenseNet (Huang et al. 2017), or ViT (Dosovitskiy et al. 2021). Instead of training from scratch, we can also apply transfer learning (Zhuang 2020). In this setup, we can repurpose the learned weights of a pre-trained model for a new task, either by freezing the baseline or fine-tuning it. Transfer learning significantly reduces resource requirements.

Lastly, Fig. 2e showcases a quanvolutional neural network (Henderson et al. 2020). Here, the VQC replaces the usual filters in a convolutional layer, transforming it into a quanvolutional layer. After patch extraction via sliding windows, this layer uses the VQC to generate feature maps from the input patches. The remaining classical layers in the model process these feature maps and draw inferences depending on the task.

3 Methods

3.1 Search strategy and selection criteria

Our systematic review adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Page 2021). The PRISMA checklist is available in Supplementary Material 1. Before the review, we registered the protocol with PROSPERO (CRD42024499193).

Given the lack of QDL studies in prior systematic reviews, we aimed to craft search strings that are maximally inclusive. While retaining the common term "quantum," we incorporated various neural network models into our study, including convolutional and recurrent neural networks, transformers, and multi-layer perceptrons. Concerning neuroinformatics, we targeted three data modalities: neuroimaging, electrophysiological signals, and cognitive assessments, and used relevant terminologies for retrieving articles (refer to Supplementary Material 7). Our thinking behind selecting these modalities stems from the viewpoint of data science, where data can be one-dimensional (such as signals and tabular data) or two-to-three-dimensional (like images), which cover a significant portion of neuroinformatics research (French and Pavlidis 2007).

Due to the multidisciplinary nature of our study scope, we conducted searches across Scopus and the Web of Science Core Collection. Additionally, we explored health-related studies in MEDLINE and Embase while searching computer science studies in the ACM Digital Library. We did not limit the search period or language and conducted the final search on all of the mentioned databases on July 23, 2024. Supplementary Material 7 contains the final search strings for all databases.

NAO conducted the preliminary search, and MAA and MAM validated the final search string. At each stage of the review, NAO and MAA independently assessed the records. Three reviewers (NAO, MAA, and MAM) engaged in discussions to resolve conflicts.

3.2 Data analysis

For this review, we retrieved confusion matrices from studies that compared their QDL models to conventional ones using the same brain-related datasets for the primary outcome. This approach allowed us to compute various classification-related performance metrics, including accuracy, precision, and sensitivity (recall). In cases where confusion matrices were unavailable, we selected the highest reported metrics from each study. We obtained relevant metrics, such as r-squared, dice score, and mean average precision, for non-classification studies like forecasting, segmentation, and object detection. For the secondary outcome, we collected information about quantum simulators or devices, focusing on the number of qubits used and classical-to-quantum data encoding.

Using the MI-CLAIM checklist (Norgeot 2020), we thoroughly assessed the risk of bias for all the included studies (refer to Supplementary Material 2, 3). The checklist promotes explicit clinical impact evaluation and provides a reproducible research strategy to improve transparency and applicability (Norgeot 2020). In addition, we evaluated the certainty of outcomes in the reviewed articles based on the four levels of evidence quality defined by GRADE (refer to Supplementary Material 4, 5) (Balshem et al. 2011). In the reviewed publications, a meta-analysis was inconclusive due to diverse methods and outcome measures, i.e., high study heterogeneity. Multiple studies also did not provide the essential data needed for a meta-analysis. Therefore, we opted for a narrative synthesis approach, following established guidelines (Jones 2022). This review presents a descriptive statistical analysis summarizing QDL's performance in neuroinformatics.

4 Results

Following the search procedure, we exported all returned entries (n = 3510) from five databases and identified 1360 duplicate entries. After screening 2150 non-duplicate records, 93 that met the selection criteria underwent a full-text review. After excluding 64 irrelevant and out-of-scope reports (refer to Supplementary Material 6), we included 29 articles (Amin et al. 2022b; Hasan 2020; Li et al. 2021; Amin 2022a; Chandra et al. 2022; Cattan and Quemy 2023; Kanimozhi et al. 2022; Shahwar 2022; Tantawi et al. 2023; Ajlouni et al. 2023; Liu et al. 2023; Choudhuri and Halder 2023; Felefly 2023; Amin et al. 2023; Dong 2023; Alsharabi et al. 2023; Koike-Akino and Wang 2022; Jeon et al. 2024; Olvera et al. 2024; Lins 2024; Jenber Belay et al. 2024; De and Gupta 2024; Mazher 2024; Roy and Rudra 2024; Singh et al. 2024; Bada et al. 2023; Kim 2023; Ho and Hung 2023; Ahmed et al. 2023) eligible for the systematic review and extracted pertinent data.

Figure 3a illustrates the entire study selection process. During the title and abstract screening, full-text review, risk of bias and certainty assessment, and data extraction phase, two reviewers (NAO and MAA) independently assessed the reports. Any conflicts were discussed among three reviewers (NAO, MAA, and MAM) until a consensus was reached. In addition, Fig. 3b and c illustrate the continuous trend in research focus, particularly addressing the diverse study objectives and their interconnections. Furthermore, with the increasing accessibility of simulators compared to hardware, a significant portion of the work originates from lower-middle income countries, as indicated in Fig. 4b.

Table 1 describes the characteristics of the reviewed studies that used QDL to handle different neuroimaging modalities. These modalities include structural, functional, and diffusion-weighted magnetic resonance imaging (MRI), computed and positron emission tomography, ultrasound, spectroscopy, etc. However, our review found that all neuroimaging studies (n = 22) only used MRI. In this NISQ era, real hardware resources are not widely accessible, and even the number of feasible simulatable qubits is quite limited. For this rea-

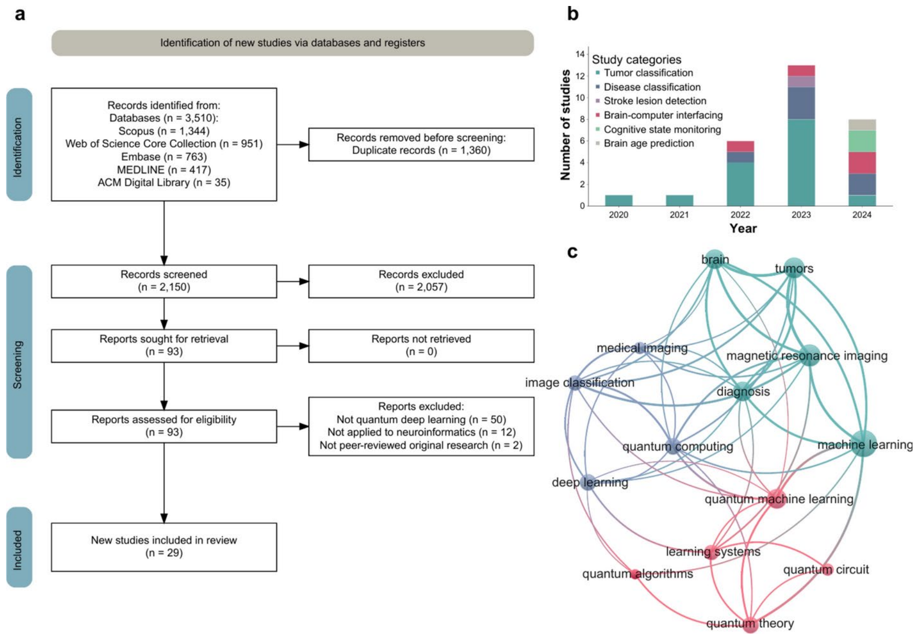

Fig. 3 **a** Study selection using PRISMA. **b** Temporal distribution of study characteristics. Each bar represents the number of studies conducted in a specific year, providing insights into the research priorities. The 2024 data is incomplete because it only includes information until July 23, which was our most recent search date. However, it still offers a valuable understanding of current progress and growth. **c** Keyword co-occurrence network. The network reveals recurring themes and concepts across the reviewed studies, highlighting the interconnectedness of ideas within this field of research

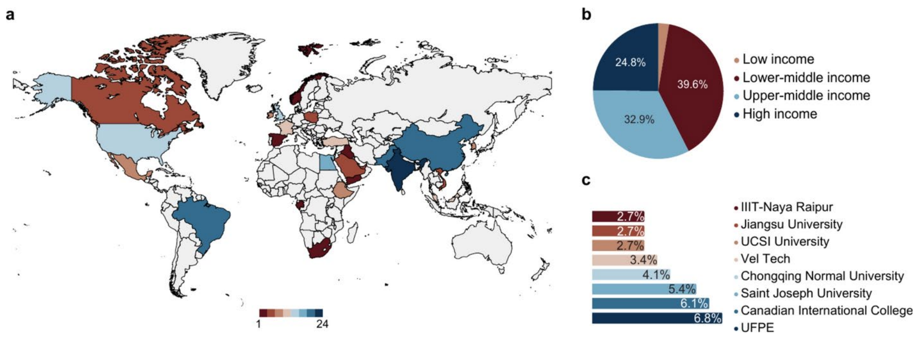

Fig. 4 Bibliometric analysis based on author affiliations. **a** Global distribution of author affiliations, with country-level counts represented by a color gradient. **b** Regional percentage distribution of affiliations based on the World Bank income level. **c** Top 8 institutions contributing the highest percentage of affiliations relative to the total

Table 1 Overview of neuroimaging-based studies

	Target field(s)	Validation	Learning mechanism	Model architecture	Model description
Amin et al. (2022b)	Brain tumors	*k*-fold CV	Supervised	Hybrid	The classifier is a quantum-classical NN consisting of classical linear layers and a quantum layer in the form of a VQC.
Hasan (2020)	Brain tumors	Train/test split	Supervised	Hybrid	In parallel, the authors used quantum calculus-based textural features and deep CNN-based feature maps.
Li et al. (2021)	Brain tumors	Train/test split	Ensemble	Hybrid	Initially, the authors replaced the classification heads of pre-trained ResNet50, VGG16, and AlexNet with a quantum-classical NN and then ensembled them.
Amin (2022a)	Brain tumors	Train/test split	Transfer	Hybrid	For classification, the authors used pre- trained InceptionV3 features to train a VQC.
Chandra et al. (2022)	Brain tumors	Train/test split	Supervised	Hybrid	The authors employed a quantum- classical hybrid structure, feeding classical linear layers with feature maps produced by the quanvolutional layer.
Kanimozhi et al. (2022)	Brain tumors	Train/test split	Transfer	Hybrid	After using ResNet18 to extract features, the authors used a quantum-classical NN with classical linear layers and a VQC.
Shahwar (2022)	Alzheimer's	Train/test split	Transfer	Hybrid	After using ResNet34 to extract features, the authors used a quantum-classical NN with classical linear layers and a VQC.
Tantawi et al. (2023)	Brain tumors	Train/test split	Supervised	Hybrid	The architecture is a classical CNN with a two-qubit VQC as the output layer.
Ajlouni et al. (2023)	Brain tumors	Train/test split	Supervised	Hybrid	In the proposed quantum-classical CNN architecture, a quanvolutional layer precede classical convolutional, pooling, and linear layers.
Liu et al. (2023)	Stroke lesions	Train/test split	Supervised	Hybrid	The authors proposed a quantum mechanics -based bottleneck layer for a typical residual U-net architecture.
Choudhuri and Halder (2023)	Brain tumors	*k*-fold CV	Supervised	Hybrid	The proposed hybrid quantum-classical CNN layout starts off with two successive quanvolutional layers and then transitions to conventional layers.
Felefly (2023)	Brain tumors	Train/test split	Supervised	Pure	The authors extracted radiomic features, reduced their dimensions, and then transferred them to a VQC for classification.

Table 1 (continued)

	Target field(s)	Validation	Learning mechanism	Model architecture	Model description
Amin et al. (2023)	Brain tumors	Train/test split	Supervised	Hybrid	In the proposed quantum-classical CNN architecture, a quanvolutional layer precede classical convolutional, pooling, and linear layers.
Dong (2023)	Brain tumors	Stratified *k*-fold CV	Supervised	Hybrid	In the proposed quantum-classical CNN architecture, a quanvolutional layer precede classical convolutional, pooling, and linear layers.
Alsharabi et al. (2023)	Alzheimer's, Parkinson	Train/test split	Transfer	Hybrid	The authors modified pre-trained AlexNet's classifier head with a VQC and linear layers.
Jeon et al. (2024)	Brain aging	Train/test split	Supervised	Pure	To train a VQC, the authors used subcortical and cortical volume parcellation data extracted from images.
Jenber Belay et al. (2024)	Alzheimer's	Train/test split	Ensemble	Hybrid	To extract features for training a quantum SVM model, the authors ensembled pre- trained VGG16 and ResNet50.
Mazher (2024)	Brain tumors, Alzheimer's	DND	Supervised	Hybrid	The authors used a VQC, alongside classical linear layers, in the classification head of a conventional CNN architecture.
Roy and Rudra (2024)	Brain tumors	Train/test split	Supervised	Hybrid	In the proposed quantum-classical CNN architecture, a quanvolutional layer precede classical convolutional, pooling, and linear layers.
Bada et al. (2023)	Brain tumors	Train/test split	Supervised	Hybrid	The authors utilized a quanvolutional layer as a feature extractor and used the features to train a classical NN consisting of linear layers.
Kim (2023)	Alzheimer's	Train/test split	Transfer	Hybrid	The author modified pre-trained ResNet18's classifier head with a VQC and linear layers.
Ahmed et al. (2023)	Brain tumors	DND	Supervised	Hybrid	In the proposed quantum-classical CNN architecture, a quanvolutional layer precede classical convolutional, pooling, and linear layers.

CV cross-validation, *VQC* variational quantum circuit, *CNN* convolutional neural network, *NN* neural network, *SVM* support vector machine *DND* did not disclose

son, researchers frequently employ quantum-classical hybrid methods, with the premise that exploiting both domains and utilizing their synergy can lead to more enhanced and robust deep learning models (Mari et al. 2020). A similar trend is also visible in our review, as out of the 22 neuroimaging-based studies, 20 (90.9%) embraced hybridization.

Table 2 describes the characteristics of the reviewed studies that used QDL to handle different neurophysiological signals, like electroencephalography (EEG) and magnetoencephalography. All such studies (n = 7) used EEG. Unlike neuroimaging-based studies, Table 2 shows a more balanced mix of pure and hybrid models.

4.1 Primary outcome

We included publications that directly compared their proposed QDL model with state-of-the-art classical deep learning models for the primary outcome analysis. Deep learning-related research often comprises several sub-studies with more than one dataset. For clarity, regardless of whether a publication uses one or multiple datasets, we treated each dataset analysis as a separate study, i.e., we treated these sub-studies as individual samples for the statistical analysis.

Table 3 summarizes descriptive statistics for tumor classification studies (n = 16), featuring the mean with a 95% confidence interval (CI) and the median with an interquartile range (IQR). Overall, QDL models slightly outperformed classical ones in terms of both mean and median, but the narrow margin suggests they are comparably effective. For instance, QDL models achieved a mean accuracy of 0.9701 (95% CI 0.9533–0.9868) and a mean F1-score of 0.9784 (95% CI 0.9667–0.9901). In contrast, classical deep learning models achieved a mean accuracy of 0.9650 (95% CI 0.9475–0.9825) and a mean F1-score of 0.9717 (95% CI 0.9614–0.9819). Except for median sensitivity, where classical models are 0.08% better than QDL models, QDL outperforms in all other cases.

Table 2 Overview of neurophysiological signal-based studies

	Target field(s)	Validation	Learning mechanism	Model architecture	Model description
Cattan and Quemy (2023)	BCI	Stratified *k*-fold CV	Supervised	Pure	After extracting features using Riemannian geometry, the authors used a VQC classifier.
Koike-Akino and Wang (2022)	BCI	DND	Supervised	Hybrid	The architecture consists of a VQC feature extractor and an EEGNet-based classifier.
Olvera et al. (2024)	BCI	*k*-fold CV	Supervised	Hybrid	The proposed architecture is a hybrid of temporal convolution, attention mechanism, and a quantum layer in the form of a VQC.
Lins (2024)	Cognitive state	Train/test split	Supervised	Pure	The authors utilized a VQC to handle the manually extracted features.
De and Gupta (2024)	Cognitive state	*k*-fold CV	Supervised	Hybrid	The proposed architecture is a hybrid of convolution, the attention mechanism, and quantum LSTM.
Singh et al. (2024)	BCI	*k*-fold CV	Supervised	Pure	The authors utilized a VQC to handle the manually extracted features.
Ho and Hung (2023)	Alzheimer's	Train/test split	Supervised	Pure	The authors used a VQC classifier.

CV cross-validation, *VQC* variational quantum circuit, *BCI* brain-computer interfacing, *LSTM* long short-term memory, *DND* did not disclose

Table 3 Outcome measures for tumor classification studies (n = 16)

	Accuracy		F1-score		Precision		Sensitivity	
	Quantum	Classical	Quantum	Classical	Quantum	Classical	Quantum	Classical
Mean (95% CI)	0.9701 (0.9533–0.9868)	0.9650 (0.9475–0.9825)	0.9784 (0.9667–0.9901)	0.9717 (0.9614–0.9819)	0.9791 (0.9669–0.9912)	0 9668 (0 9562–0 9774)	0.9786 (0.9669–0.9902)	0.9769 (0.9628–0.9910)
Median (IQR)	0.9844 (0.9541–0.9915)	0.9804 (0.9442–0.9865)	0.9824 (0.9643–0.9940)	0.9753 (0.9605–0.9836)	0.9813 (0.9647–1)	0.9642 (0.9586–0.9818)	0.9800 (0.9640–1)	0.9808 (0.9600–0.9978)
Sample size	16		14		14		14	

CI confidence interval, *IQR* interquartile range; Unequal sample sizes suggest that certain studies did not provide the metric or offer the required confusion matrices for revisions.

Table 4 Outcome measures for studies other than tumor classification (n = 6)

	Accuracy		F1-score		Precision		Sensitivity	
	Quantum	Classical	Quantum	Classical	Quantum	Classical	Quantum	Classical
Alzheimer's diagnosis	0.8131	0.9762	0.8077	0.955	0.84	0.9525	0.7778	0.9575
Alzheimer's diagnosis	0.9538	0.9523	0.9557	0.955	0.9667	0.96	0.945	0.95
Alzheimer's diagnosis	0.9989	0.993	0.9925	0.995	0.9925	0.995	0.9923	0.995
Drowsiness monitoring	0.986	0.9042	0.9865	0.9351	0.987	0.9203	0.986	0.9505
	Accuracy		AUC		Dice coefficient		ASSD	
	Quantum	Classical	Quantum	Classical	Quantum	Classical	Quantum	Classical
Stroke lesions detection	0.8678	0.8517	0.9086	0.8978	70.98	68.90	8.64	9.13
	R-squared		RMSE		MSE		MAE	
	Quantum	Classical	Quantum	Classical	Quantum	Classical	Quantum	Classical
Brain age prediction	0.425	0.3	4.083	4.28	16.675	18.28	3.302	3.31

RMSE root mean squared error, *MSE* mean squared error, *MAE* mean absolute error, *AUC* area under the curve, *ASSD* average symmetric surface distance

Beyond tumor classification, studies addressed Alzheimer's diagnosis, Parkinson's diagnosis, thrombolysis in cerebral infarction grading, brain age prediction, drowsiness monitoring, motor imagery classification, and more. However, most of these studies did not benchmark their proposed models against established standards. The number of studies that did compare their proposed models with state-of-the-art models was too small to warrant meaningful statistical analysis. In particular, the 95% confidence intervals were very wide. Furthermore, using quartiles provided minimal insights because of the limited data. As a result, we summarized the findings from these investigations in Table 4 instead of a statistical comparison. Table 4 shows an evenly split performance between the two domains in the classification tasks, with QDL outperforming in half of the cases and classical deep learning leading in the others. In contrast, QDL outperforms in both the object detection task with better metric values and the forecasting task with lower error values.

4.2 Secondary outcome

For the secondary outcome analysis, we selectively included publications (n = 26) that adopted a quantum circuit-based approach in their models. We conducted this analysis

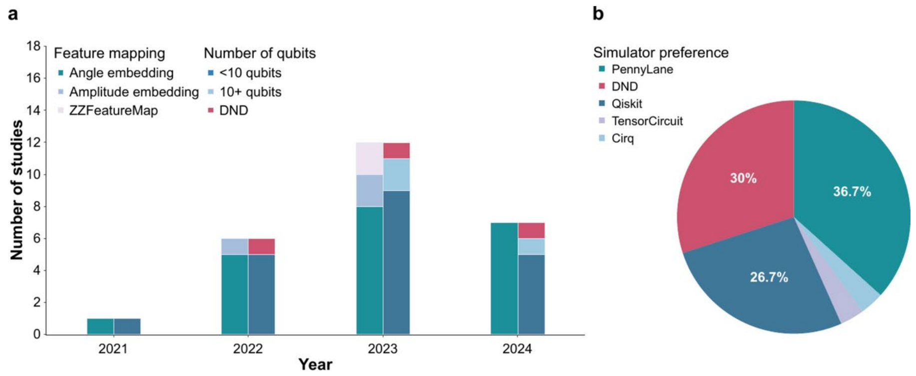

Fig. 5 Outcome measures for studies utilizing quantum circuits (n = 26). **a** Temporal distribution of feature mapping and qubit utilization. **b** Simulator preferences within the reviewed QDL literature. DND is an acronym for 'did not disclose.' This designation indicates that certain studies did not report information regarding the specific quantum simulator or the number of qubits used in their experiments. Note: Some studies validated their models using more than one simulator

to explore how researchers simulate quantum computations in this NISQ era. Figure 5a depicts a timeline showing the progression of qubit usage next to data representation in quantum circuits. In Fig. 5a, it is evident that researchers prefer angle embedding to amplitude embedding. Also, we found that researchers could utilize up to 17 qubits, highlighting the increasing scalability of QDL. Figure 5b portrays the percentage distribution of studies based on the source of simulators used. A total of 70% of the studies specified the simulator they utilized. Within this subset, 36.7% of studies opted for simulators from the PennyLane library (Bergholm et al. 2022), whereas 26.7% chose simulators from IBM's Qiskit library (Aleksandrowicz 2019). 3.33% of the studies use the TensorCircuit (Zhang et al. 2023) and Cirq (Developers 2024) libraries, respectively.

5 Discussion

We systematically reviewed QDL algorithms designed to address neuroinformatics, emphasizing how QDL differs from conventional deep learning. The core findings of our study indicate that QDL models exhibit similar performance, if not a slight advantage over their classical counterparts, across all tasks. The combination of such precision, well-documented speedups (Huang 2022; Biamonte 2017; Liu et al. 2021b; Saggio 2021; Ciliberto 2018), robustness (LaRose and Coyle 2020; Cross et al. 2015; Du et al. 2021), generalization ability (Caro 2022; Caro et al. 2021; Gil-Fuster et al. 2024), and parameter efficiency (Liu 2024; Caro 2022; Cherrat et al. 2024; Kharsa et al. 2023) establishes the potential of QDL. As QDL is still in its earliest phases, it is complicated to assess its practicality in healthcare, considering hardware requirements, noise sensitivity, and computing resources (Cerezo et al. 2022; Peral-García et al. 2024). Still, quantum machine learning (and, by extension, QDL) is a thriving field. As quantum computers continue to advance, we can anticipate the integration of various algorithms into healthcare. However, their application is likely to be limited to specific challenges that require the unique computational power of quantum systems or to address unsolvable problems of traditional computing methods.

5.1 Limitations of the review

Despite our commitment to adhering to the PRISMA guidelines at every stage of our study, it remains a possibility that we overlooked essential reports. Nevertheless, we are confident that the potential oversights will not compromise the review's overall substance and validity. Moreover, as highlighted in Tables 1 and 2, the approaches adopted by the studies were diverse, with diverse target domains. Validation techniques ranged from simple data splitting to more elaborated cross-validation methodologies. While the diversity of approaches reflected the field's richness, this heterogeneous nature posed a challenge in employing a meta-analysis. As a result, a meta-analysis that could have established a robust empirical foundation for QDL was not possible. Finally, this review does not cover molecular-level analyses, such as the protein and gene structures of the human brain, which we plan to address in a future study.

5.2 Limitations of the reviewed articles

Evidence certainty assessments reveal that only a small number of studies (n = 6) provide high certainty evidence, whereas others fall into the low (n = 8) and very low (n = 5) categories. Hence, our confidence in the effect estimate is limited, primarily due to poor methodological descriptions. For example, several studies withheld crucial details like the number of qubits, circuit depths, and simulators. While the former two are essential for reproducible results, understanding the practical realizability of the model requires the latter information. Three studies failed to report the total sample sizes of the datasets considered in their experiments. Moreover, we noticed that some studies did not conduct inferences on unseen data, a critical aspect for assessing the overall generalizability of the proposed models. Furthermore, some studies did not provide specific performance metrics, which led to omitting some data points from our statistical analysis. In light of these limitations, we encourage readers to interpret our findings with due consideration.

5.3 Identified research gaps and pathways

Notwithstanding the above limitations, we aimed to offer a holistic representation of the current progress in this domain. Our goal was not necessarily to establish QDL as the new state-of-the-art; instead, we wanted to highlight the progress in neuroinformatics, show where QDL models currently stand, and explore what might be achievable as we progress toward fault-tolerant quantum computing (FTQC) (Katabarwa et al. 2024). Above all, we have identified research gaps that, once addressed, would benefit neuroinformatics (and healthcare) and facilitate advancements in QDL.

5.3.1 Efficient data encoding

In QDL, the initial step in the processing pipeline–and one of its most critical stages–is data encoding. This step involves transforming classical data into a format suitable for quantum systems. Angle embedding is the most commonly used encoding method due to its minimal complexity. Its primary advantage lies in the straightforward, linear mapping it provides between the input data and the qubits, mirroring the behavior of conventional neural networks. However, as data complexity and size grow, the method becomes inefficient. For example, encoding 256 data points would require a circuit with 256 qubits, which is impractical for even the most advanced supercomputers to simulate, let alone implement in practice in this NISQ era. On the other hand, amplitude embedding offers a more scalable solution. It can encode the same 256 features using just 8 qubits, achieving logarithmic scaling and a more compact representation. Yet, this approach comes with its own challenges, particularly in the setup phase. Issues such as state preparation errors and the significant increase in circuit depth make implementation difficult. As such, we need more efficient encoding schemes. This requirement is even more critical in neuroinformatics, where data types are inherently complex. For example, time-series data, such as EEG, present unique challenges due to properties like autocorrelation and periodicity (Karlsen Kivedal 2024), which demand careful mapping.

5.3.2 Task-specific circuit design

When addressing challenges such as barren plateaus or the vanishing gradient problem (McClean et al. 2018), carefully selecting the circuit architecture is paramount. While many studies rely on pre-existing architectures available in quantum computing libraries, others neglect to detail their choice of ansatz or parameterized circuit, limiting reproducibility and insight. For neuroinformatics tasks, it is crucial to find out if the quantum operations within the ansatz offer any benefits in terms of being more robust, generalized, and regularized. Based on our analysis, we identified two key areas: (i) Researchers must prioritize task-specific architectures, recognizing that no single design guarantees optimal performance. This is crucial given the interplay between barren plateaus, local minima, and the circuit structure. (ii) In the current NISQ era, achieving the appropriate circuit depth is challenging. We need to strike a balance; circuits must remain shallow enough to mitigate computational cost and error propagation while maintaining sufficient expressivity to solve required tasks effectively.

5.3.3 Real-world applicability

Although QDL models hold promise, their practical implementation on real quantum hardware remains challenging due to noise, limited coherence times, and gate fidelity issues. Our review of recent literature and studies suggests that the effectiveness of these models on real hardware still needs to be explored. Therefore, we urge researchers to test their models in practical scenarios. We acknowledge that accessing real quantum hardware can be difficult currently. However, to emulate realistic conditions, high-quality simulators are widely accessible (Altman 2021). For simulation-based approaches, researchers must incorporate noise and errors prevalent in quantum computers. For example, instead of relying on analytical expectation values during measurement, researchers should simulate finite shots to account for the probabilistic nature of quantum operations. Real-life quantum experiments require multiple repetitions to approximate accurate results, reflecting the stochastic behavior in quantum mechanics.

5.3.4 Noise: a disguised blessing

While noise is generally considered detrimental to deep learning due to its impact on training stability, interpretability, and performance, controlled noise injection has proven to aid in regularization and generalization (Lowd and Meek 2005; Qian et al. 2022). In quantum machine learning, the inherent noise of quantum operations (e.g., bit and phase flips, amplitude damping, and stochastic measurements) poses a challenge but may also offer opportunities. Using quantum noise as a regularization mechanism could improve the generalization and robustness of QDL models in a way similar to classical techniques. Additionally, the stochastic nature of quantum systems may internally promote adversarial learning as a natural byproduct of quantum computations. However, in neuroinformatics, such an exploration remains uncharted.

5.3.5 Quantum-aware optimizers

By far, the most prevalent approach in QDL is quantum-classical hybridization. In this approach, neural networks integrate traditional classical layers with quantum layers, such as quanvolution or VQCs. The loss calculation and parameter updates are typically performed on classical computers using well-established optimizers like Adam (Kingma and Ba 2015). However, optimizing the parameters of quantum layers is not straightforward. These parameters operate in the complex, high-dimensional Hilbert space, presenting challenges such as barren plateaus and noise sensitivity. As such, it may be beneficial for optimizers to be quantum-informed–aware of the quantum operations and properties like superposition, entanglement, and interference. Such optimizers could enable more informed gradient updates and mitigate challenges like vanishing or exploding gradients. Above all, quantum-aware optimizers can potentially enhance both convergence speed and model accuracy.

5.3.6 Ablation studies

In deep learning, an ablation study involves systematically removing parts of a neural network to determine which components are most influential in achieving the desired performance. Simply put, this debugging tool helps identify and eliminate unnecessary complexity, leading to lighter, more interpretable models. For pure quantum neural networks like VQCs, researchers must explain how certain unitary operations or a group of unitary layers inside the circuit affect the whole network. In hybrid quantum-classical models, it is crucial for researchers to rationalize placing a quantum layer at any specific position among classical layers and to explore the quantum layer's performance with positional shifts. By providing these justifications while conducting ablation studies, quantum models can become less enigmatic and more user-friendly.

5.3.7 Shortcomings of quantum convolution

Quantum convolution is gaining popularity in computer vision, with two main variants discussed in the literature: circuit-based and kernel-based. The circuit-based approach reimagines a convolutional neural network as a VQC, where quantum operations emulate traditional convolution and pooling layers (Cong et al. 2019). In contrast, kernel-based quantum convolution, often referred to as “quanvolution," employs a VQC as a convolutional filter or kernel (Henderson et al. 2020). Both methods face significant scalability challenges. For example, in the circuit-based approach, flattening high-resolution images with multiple channels for input into the circuit is infeasible in this NISQ era. The quanvolution method attempts to address this by processing image patches individually. However, it, too, has several limitations, such as a lack of flexibility in choosing kernel sizes, generating a fixed and limited number of feature maps, and an inability to handle data with arbitrary dimensions–tasks that classical convolution performs seamlessly. These shortcomings highlight the need for a substantial overhaul in designing and implementing quantum convolution techniques.

5.3.8 Interpretability

The importance of explainable AI (XAI) (Minh et al. 2022), particularly in biomedical applications, cannot be overstated. Incorporating XAI is crucial for achieving high interpretability, which can help reduce skepticism among clinical professionals regarding model outcomes. XAI approaches can shed light on how quantum features and enhancements contribute to a model’s ability to identify clinically relevant patterns. These approaches not only clarify the internal workings of these models or layers but also assess the role of different quantum unitaries in inferencing. As such, prioritizing interpretability in designing and evaluating QDL systems is essential for building trust in healthcare and neuroinformatics applications. However, the use of such methods in QDL has been very limited.

5.3.9 Domain diversity

Neuroinformatics is an expansive and multifaceted field with numerous application areas. However, QDL in neuroinformatics has been limited and focused, primarily exploring a few areas, like tumor classification with MRI. We encourage researchers to broaden the scope of QDL’s application. This could involve integrating diverse neuroinformatic modalities, such as neuropsychological assessments (Vieira et al. 2022) related to perception, attention, and memory, where QDL’s potential remains largely unexplored. Moreover, QDL remains uncharted in areas like connectomics (Anbarasi et al. 2024), a key domain in neuroinformatics. In addition to traditional supervised learning, there is potential for using reinforcement learning (François-Lavet 2018), which can capture how the brain adapts to changes in the environment, and self-supervised learning (Liu 2021a), which can make models more robust and generalizable. Also, with recent advancements in generative AI (GenAI) (Sengar et al. 2024), it is important to explore tasks like image reconstruction, cross-modality synthesis, and disease progression modeling, all of which can help us better understand how the brain works.

5.4 Concluding remarks

To wrap up our review, we offer a set of both short-term and future-oriented recommendations for advancing QDL in neuroinformatics.

5.4.1 Immediate actions

- Model validation: Any model must be validated with real hardware or, at the very least, a realistic simulator to ensure its practical viability.
- NISQ vs efficiency: We must account for NISQ-related constraints and focus on building efficient models accordingly.
- Resources for newcomers: There is a strong need for more open-source codes and tutorials that facilitate learning and experimentation to support newcomers.
- Interdisciplinary collaboration: Quantum physicists, computer scientists, and neuroscientists must collaborate across disciplines to fully realize the potential of QDL in neuroinformatics.
- Reporting standards: We strongly encourage researchers to adopt transparent and reproducible reporting practices while maintaining ethical and privacy considerations when handling sensitive medical data.

5.4.2 Long-term plans

- Policies and Resources: As interest in quantum machine learning grows, we need clear guidelines and tools for infrastructure, training, and legal concerns.
- Pure Models: While hybrid models are effective given current quantum computing challenges, the transition to FTQC will necessitate purely quantum models to achieve the true "quantum advantage."
- Exploring New Areas: We must expand QDL into new fields related to neuroimaging, neurophysiological signals, and neuropsychological assessments. Relevant resources include HCP (Van Essen 2013), the ABCD study (Casey 2018), UK Biobank (Miller 2016), OpenNeuro (Markiewicz 2021), PREDICT (Cavanagh et al. 2017), NEMAR (Delorme et al. 2022), Physionet (Goldberger 2000), and the TUH-EEG corpus (Obeid and Picone 2016).
- Diverse Learning Strategies: Effective QDL requires integrating strategies like semi-supervised (Yang et al. 2022), self-supervised (Liu 2021a), reinforcement (François-Lavet 2018), and few-shot learning (Wang et al. 2020).
- Integration with Advanced Computing: Investigating how QDL can merge with paradigms like neuromorphic (Marković et al. 2020) and neuro-symbolic (Sheth et al. 2023) systems may advance neuroinformatics.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10462-025-11136-7.

Author contributions Nabil Anan Orka: Conceptualization, Methodology, Software, Formal Analysis, Investigation, Writing– Original Draft, Visualization. Md Abdul Awal: Software, Supervision, Investigation, Writing– Review & Editing. Pietro Liò: Validation, Writing– Review & Editing. Ganna Pogrebna: Resources, Writing– Review & Editing. Allen G. Ross: Validation, Investigation, Writing– Review & Editing. Mohammad Ali Moni: Conceptualization, Validation, Resources, Writing– Review & Editing, Supervision.

Funding Open Access funding enabled and organized by CAUL and its Member Institutions
This work was funded by a grant from the Commonwealth of Australia, represented by the Department of Health (Grant Activity 4-DGEJZ1O/4-CW7UT14).

Data availability All relevant data are within the paper and its Supplementary Materials file.

Code availability Not applicable.

Materials availability Not applicable.

Declarations

Conflict of interest The authors declare no Conflict of interest.

Ethical approval Not applicable.

Consent to participant Not applicable.

Consent for publication Not applicable.

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