Minor Project-ITIT-3203

Quantum-Assisted Multi-modal Fusion for Epilepsy Diagnosis: Integrating MRI, PET, and EEG via Hybrid Quantum-Classical Architectures

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CANDIDATES DECLARATION

We hereby certify that the work, which is being presented in the report, titled **Quantum-assisted multimodal fusion for epilepsy classification**, in partial fulfillment of the requirement for the award of the Degree of **Integrated Postgraduate Masters of Technology in Information Technology** and submitted to the institution is an authentic record of our own work carried out during the period Jan 2025 to Apr 2025 under the supervision of **Prof. Mahua Bhattacharya**. We also cited the references which are used in our project.

Date:

Name: **Signature of the candidate**

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This is to certify that the above statement made by the candidates is correct to the best of my knowledge.

Dated: **Signature of supervisor**

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Abstract

Epilepsy is a complex neurological disorder that affects millions of individuals globally, with accurate diagnosis and subtyping being crucial for effective treatment and management. Conventional diagnostic methods, primarily relying on single-modality imaging and clinical observation, often fail to capture the multifaceted nature of epilepsy, leading to suboptimal outcomes. This research introduces a novel Quantum-Assisted Multimodal Fusion (QMF) framework for epilepsy classification, integrating multiple neuroimaging modalities—MRI, PET, and EEG—using Quantum Machine Learning (QML) techniques. The QMF system leverages Quantum Neural Networks (QNNs) simulated with classical layers to analyze structural and metabolic brain patterns, aiming to enhance diagnostic accuracy and robustness.

The framework consists of a BIDS-compliant preprocessing pipeline, dimensionality reduction via Principal Component Analysis (PCA), and modular quantum modeling stages. Initially, the framework focuses on MRI and MRI-PET data, employing ensemble QNNs for better fusion of complementary modality features. The use of Quantum Variational Circuits (QVCs) for pretraining on healthy controls and Quantum-Classical Fusion Transformers (QCFTs) for modality integration provides enhanced representational capacity and efficient handling of heterogeneous data.

This work paves the way for the integration of EEG data and the deployment of real quantum circuits in future stages. The QMF framework demonstrates potential for handling missing data via a Generative Adversarial Network (GAN)-based approach and offers a scalable solution for personalized, high-fidelity epilepsy diagnostics. This research lays the foundation for the upcoming Bachelor's Thesis Project (BTP), which will further refine the system with real quantum deployment and deeper integration of EEG data for clinical applications.

Contents

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Introduction

1. Introduction

Epilepsy is a complex neurological disorder characterized by recurrent seizures and affects over 50 million people globally [1]. Accurate diagnosis and subtyping are essential for effective treatment planning and surgical intervention. Conventional diagnostic techniques—relying primarily on single-modality imaging or clinical observation—often fail to capture the multifaceted nature of epileptic disorders, leading to delayed or suboptimal therapeutic outcomes. Multimodal neuroimaging, incorporating MRI, PET, and EEG, offers a promising avenue to obtain complementary structural, metabolic, and electrophysiological insights into the epileptic brain [2]. However, integrating heterogeneous data from different modalities poses significant challenges. These include modality-specific noise, sampling rate discrepancies, lack of aligned datasets, and the computational complexity of joint modeling. Traditional machine learning and classical fusion techniques often struggle with such high-dimensional, incomplete, and heterogeneous data [3], thereby motivating the exploration of more sophisticated frameworks. In recent years, Quantum Machine Learning (QML) has emerged as a novel paradigm capable of harnessing quantum properties—such as superposition and entanglement—to represent complex patterns in data [4]. Quantum Neural Networks (QNNs), in particular, have shown potential in encoding intricate correlations across modalities with fewer parameters and enhanced representational capacity compared to classical models [5]. While preliminary QML studies in medical imaging are encouraging, their application in large-scale, multimodal brain data fusion remains underexplored [6]. To address these limitations, we propose a Quantum-Assisted Multimodal Fusion (QMF) framework for epilepsy classification, which combines classical preprocessing pipelines with quantum neural architectures. The QMF system processes and harmonizes MRI, PET, and EEG data using standardized BIDS-compliant workflows, employs Principal Component Analysis (PCA) for dimensionality alignment, and simulates QNNs using classical layers. Two modular pipelines—QNN-MRI and QNN-MRI-PET—are developed and ensembled to leverage complementary modality strengths. This project lays the groundwork for full multimodal integration, with EEG fusion, real quantum circuit deployment, and interpretability modules planned for the next phase

under the Bachelor's Thesis Project (BTP). By bridging classical neuroimaging analytics with emerging quantum computation, this work aims to advance clinically meaningful, high-fidelity diagnostic models for neurological disorders like epilepsy.

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Motivation

In this section, we delve into the underlying reasons that led us to choose this project topic and its relevance within our academic and professional journey.

2.1 Significance of Multimodal Data Fusion in Epilepsy Diagnosis

Epilepsy, a neurological disorder affecting millions worldwide, requires precise diagnostic methods to enable early detection and effective treatment. Traditional diagnostic approaches, which rely on single-modality imaging or clinical observations, often fail to capture the complexity of epileptic disorders. The limitations in diagnosing epilepsy lead to delayed treatments and suboptimal outcomes for patients. Given the diverse nature of the condition, integrating multiple neuroimaging modalities—such as MRI, PET, and EEG—offers significant potential in providing complementary insights into the brain's structure, function, and metabolism. However, this integration poses significant challenges, including the complexity of harmonizing data from different modalities and handling missing or incomplete data. This project is motivated by the need for innovative solutions that can overcome these challenges and enhance diagnostic accuracy.

2.2 Relevance to Academic and Professional Development

Our academic background in neuroscience, quantum computing, and machine learning has provided us with the necessary theoretical foundation to explore advanced methods in medical imaging and data fusion. Specifically, our exposure to quantum machine learning (QML) and classical machine learning techniques, coupled with practical experience in handling multimodal data, uniquely positions us to tackle the challenges in epilepsy diagnosis. This project provides an opportunity to apply our knowledge of quantum computing and data fusion in a real-world context, contributing to the growing field of AI-powered biomedical research.

Through our work on Quantum-Assisted Multimodal Fusion (QMF), we aim to de-

velop a robust framework capable of integrating MRI, PET, and EEG data for epilepsy classification. This endeavor allows us to further our understanding of quantum neural networks (QNNs) and how they can be applied to complex medical datasets. By simulating quantum techniques using classical machine learning models, we also bridge the gap between theoretical quantum models and practical applications in clinical diagnostics.

2.3 Envisioned Impact and Contribution

The impact of this project extends beyond our academic growth and development. By proposing a Quantum-Assisted Multimodal Fusion (QMF) framework, we aim to develop an integrated system that can effectively combine heterogeneous neuroimaging data for epilepsy classification. Our work is designed to improve diagnostic accuracy, particularly in cases where traditional methods fall short. Furthermore, the use of quantum computing has the potential to significantly reduce computational complexity, making it possible to analyze high-dimensional, multimodal data more efficiently.

Our framework's ability to handle missing data through a GAN-based mechanism and its modular design offer a flexible and scalable approach to epilepsy classification. As we integrate EEG data and eventually deploy real quantum circuits, the QMF framework has the potential to revolutionize how epilepsy is diagnosed, making it more precise, efficient, and personalized. Additionally, our work lays the groundwork for future research in quantum-classical hybrid models, contributing to the broader effort of advancing quantum computing applications in healthcare.

By leveraging cutting-edge quantum machine learning techniques, this project not only advances the field of epilepsy diagnosis but also positions us at the forefront of the intersection between quantum computing and biomedical science. We are excited to contribute to the development of AI-driven diagnostic tools that will improve patient outcomes and further the integration of quantum technologies into clinical practice.

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Literature Survey

To address these limitations, **Quantum Machine Learning (QML)** has emerged as a promising paradigm for **epilepsy classification**, offering enhanced capabilities for managing complex, high-dimensional data. QML leverages the computational advantages of quantum computing, incorporating quantum neural networks (QNNs) and quantum variational circuits (QVCs), to enhance feature extraction, optimization, and model training. These methods are particularly effective in the context of **multi-modal data fusion**, where traditional classical models face difficulties in capturing the complex interdependencies between modalities.

3.1 Multi-modal Data Fusion for Epilepsy Classification

Multimodal fusion systems combine data from various sources to provide a more comprehensive understanding of the brain's functionality. In the context of epilepsy, integrating **MRI**, **PET**, and **EEG** offers a holistic view of both anatomical and functional changes in the brain. Traditional fusion methods, including **support vector machines (SVMs)**, **random forests**, and **artificial neural networks (ANNs)**, have been widely used for these tasks. However, classical models often face challenges related to data alignment, modality-specific noise, and sparse labeled data. These issues can hinder model generalization and classification performance, particularly in medical datasets, which are often limited in size and complexity. The inability of traditional methods to effectively manage these challenges highlights the need for more robust techniques, such as QML, for improved performance in multimodal epilepsy classification.

3.2 Quantum-Classical Hybrid Models

To capitalize on the strengths of both quantum and classical computing, **hybrid quantum-classical models** have been proposed. These models combine quantum circuits for feature extraction and optimization with classical layers for data processing and decision-making. One notable application of this approach is the use of **Quantum-**

Classical Fusion Transformers (QCFTs) for multi-modal data fusion. QCFTs enable more efficient integration of data from multiple modalities, improving generalization capabilities and better handling of missing data. By incorporating quantum-enhanced feature extraction into the classical decision-making process, hybrid models reduce computational overhead, which is particularly advantageous when working with large-scale neuroimaging datasets. This approach offers a promising solution to the challenges posed by multi-modal fusion in epilepsy classification, where diverse data sources must be efficiently combined.

3.3 Quantum Variational Circuits (QVCs) for Multi-modal Embeddings

Quantum Variational Circuits (QVCs) represent a core component of quantum neural networks, designed to extract quantum-enhanced embeddings from multi-modal data. In the context of the **Quantum-Assisted Multi-modal Fusion (QMF)** framework, QVCs are utilized to transform **MRI**, **PET**, and **EEG** data into a quantum-encoded feature space. This allows for efficient classification and fusion of the diverse data modalities. QVCs have already demonstrated success in various biomedical applications, such as disease classification and predictive modeling. Compared to traditional methods, QVCs offer enhanced accuracy and better interpretability, providing deeper insights into complex medical data [**?**]. These advantages make QVCs a promising tool in the effort to improve epilepsy classification through multi-modal fusion.

3.4 Handling Missing Modalities in Multi-modal Fusion

One of the most significant challenges in multi-modal fusion for epilepsy classification is the presence of missing modalities. In clinical settings, certain data modalities may be unavailable due to technical limitations, patient conditions, or other factors. This can lead to incomplete datasets, which severely affect classification performance.

To address this, **Quantum-Classical Fusion Transformers (QCFTs)**, in combi-

nation with **Generative Adversarial Networks (GANs)**, have been explored as a means to synthesize missing modalities and improve model robustness. This approach has proven particularly effective in real-world epilepsy diagnosis scenarios, where missing data is common. By generating missing modalities, QCFTs and GANs contribute to more resilient models, ensuring that the absence of data does not lead to significant performance degradation.

These strategies are further supported by advances in graph-based and contrastive learning models, which have shown promise in handling incomplete and heterogeneous biomedical datasets. For example, multi-task graph contrastive learning [7] has been used to infer complex biological associations from partially observed data , while graph auto-encoder frameworks have demonstrated effectiveness in reconstructing missing associations in biomedical networks [8].

3.5 Self-Supervised Learning and Contrastive Learning

The challenge of sparse labeled data in medical datasets, particularly in the field of epilepsy diagnosis, has led to the development of self-supervised learning (SSL) and **contrastive learning** techniques. These methods enable models to learn useful representations from unlabeled data by creating auxiliary tasks that force the model to extract meaningful features. In the context of epilepsy classification, contrastive learning can be leveraged to improve the generalization of models across different data modalities. Furthermore, quantum-enhanced contrastive learning methods can take advantage of quantum states to create richer and more informative representations. By incorporating quantum-enhanced representations, contrastive learning techniques can improve model performance, particularly in tasks involving complex, multi-modal data.

3.6 Future Directions in Quantum-Assisted Multi-modal Fusion for Epilepsy

While the potential of Quantum Machine Learning (QML) in epilepsy classification is evident, significant challenges remain. Future research will focus on scaling quantum models to handle large, complex datasets, incorporating additional modalities such as genetic and electrophysiological data, and improving the interpretability of quantum models. One promising direction for future work is the exploration of **Quantum Variational Autoencoders (QVAEs)** for generating multi-modal embeddings and handling data sparsity. Additionally, quantum-enhanced methods for data alignment and synchronization between MRI, PET, and EEG modalities will be crucial for improving model accuracy and robustness. By advancing these techniques, QML can offer even greater potential for revolutionizing epilepsy classification and diagnosis.

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Datasets

4.1 Datasets

This study leverages five multimodal datasets comprising MRI, PET-MRI, and EEG modalities. These datasets include both healthy controls and epilepsy patients, enabling robust pretraining and fine-tuning in our quantum-assisted multimodal fusion pipeline. A detailed description of each dataset is provided below.

4.1.1 MRI and PET-MRI Datasets

4.1.1.1 Aerobic Glycolysis Imaging PET-MRI

This dataset includes simultaneous PET-MRI acquisitions from 42 participants (18 healthy controls and 24 patients with suspected epilepsy). PET scans used ^{18}F-FDG to assess glucose metabolism, while MRI sequences include T1-weighted structural scans, arterial spin labeling (ASL), and T2*/T2 mapping. The hybrid design ensures spatial alignment between structural and metabolic information [9].

4.1.1.2 IDEAS Epilepsy MRI Dataset

The Imaging Database for Epilepsy And Surgery (IDEAS) includes MRI data from 442 patients with drug-resistant focal epilepsy. All patients underwent resective surgery, with data including preoperative T1 and FLAIR scans, cortical reconstructions, resection masks, and postoperative outcomes. Detailed clinical annotations (e.g., seizure types, localization, histology) are also available [10].

4.1.2 EEG Datasets

4.1.2.1 SRM Resting-State EEG

The SRM dataset contains resting-state EEG recordings from 111 healthy controls. EEG was recorded using a 64-channel BioSemi ActiveTwo system during 4-minute eyes-closed sessions. The recordings follow the international 10-20 system and are free from task or seizure-related events [11].

4.1.2.2 SeizeIT2 Epileptic EEG Dataset

The SeizeIT2 dataset includes more than 11,000 hours of EEG from patients with focal epilepsy. EEG was recorded via wearable behind-the-ear (bte-EEG) electrodes tailored to individual seizure onset zones. The dataset captures 886 clinically verified seizures, annotated by type (e.g., FA, FIA, FBTC), localization (e.g., temporal, frontal), and hemisphere (left, right, bilateral) [12].

4.1.3 Dataset Summary

Table 4.1: Overview of the datasets used in this study.

Dataset	Modality	Subjects	Condition
PET-MRI (Glycolysis)	PET, MRI	18 + 24	Controls + Patients
IDEAS MRI	MRI	100 + 442	Controls + Patients
SRM EEG	EEG (64-ch)	111	Controls
SeizeIT2	EEG (bte-EEG)	125	Patients

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Methodology

5.1 Methodology

5.1.1 Quantum Machine Learning

The QMF framework incorporates quantum-enhanced learning techniques to improve classification and data fusion performance. We use the **PennyLane** library, which serves as a hybrid quantum-classical machine learning platform. PennyLane integrates seamlessly with classical ML frameworks like PyTorch and TensorFlow and supports a variety of quantum hardware simulators. This allows for the simulation of quantum variational circuits and quantum neural networks (QNNs) within the fusion pipeline.

5.2 System Architecture

The architecture of the proposed Quantum-Assisted Multimodal Fusion (QMF) framework is composed of four interconnected layers:

5.2.1 Data Ingestion Layer

This layer handles the structured import of multimodal neuroimaging and electrophysiological data in BIDS-compliant format:

- **MRI Data:** Acquired from the IDEAS and Aerobic Glycolysis Imaging datasets.
- **PET Data:** Collected in tandem with MRI scans for metabolic-structural co-registration.
- **EEG Data (Future Integration):** Sourced from SeizeIT2 and SRM datasets.

All modalities are organized under a standardized directory structure to enable consistent preprocessing and multimodal alignment.

5.2.2 Preprocessing and Feature Extraction Layer

Each modality undergoes domain-specific preprocessing before feature extraction:

- **MRI/PET:**

  - Skull stripping using ANTsPy and antspynet.
  - Intensity normalization and spatial resampling.
  - PCA-based dimensionality reduction (e.g., to 10 components).
  - Inter-subject and inter-dataset standardization.

- **EEG (Planned Integration):**
  - ICA-based artifact rejection (e.g., eye blinks, muscle artifacts).
  - Extraction of channel-wise quality metrics (variance, entropy, bandpower).
  - Epoching and downsampling for dimensionality compatibility.

Outputs across modalities are temporally and dimensionally aligned to facilitate efficient fusion.

5.2.3 Quantum Neural Network (QNN) Layer

This layer implements modality-specific quantum neural processing:

- **QNN-MRI:** Trained solely on MRI-derived features.
- **QNN-MRI-PET:** Fine-tuned using transfer learning on joint MRI-PET features.

Ensemble Fusion:

- Aggregates predictions from QNN-MRI and QNN-MRI-PET modules to enhance robustness.
- Planned inclusion of EEG outputs via a Quantum-Classical Fusion Transformer (QCFT).

Quantum components are simulated using classical placeholders (e.g., dense layers), with intended future deployment using real quantum circuits (via PennyLane or Qiskit).

5.2.4 Decision and Interpretation Layer

- Final epilepsy classification (Epileptic / Control).
- Planned incorporation of explainability tools (e.g., SHAP, integrated gradients, quantum-aware interpretation).
- Export of class probabilities and intermediate features for downstream analysis or dashboard integration.

5.3 Data Preprocessing

5.3.1 MRI Harmonization

For the harmonization of MRI data across different datasets, the preprocessed outputs of the IDEAS dataset and the Aerobic Glycolysis Imaging PET-MRI dataset were standardized to a uniform format. This was achieved by applying a series of preprocessing steps, ensuring that both datasets were processed in a manner that allows for direct comparison and integration in subsequent analyses. These preprocessing steps included:

- **Skull Stripping:** A robust skull stripping technique was applied to remove non-brain tissue and improve the accuracy of subsequent processing. This step was conducted using the `ANTsPy` library, which includes advanced brain extraction tools for T1-weighted (T1w) images.
- **Bias Field Correction:** The T1w images were subjected to N4ITK bias field correction to correct for intensity inhomogeneity within the images. This ensures more consistent intensity profiles across the dataset.
- **Registration to Standard Template:** To facilitate harmonization, the T1w images were registered to a common standard template (e.g., MNI152) using linear and nonlinear transformations. This step ensured that the MRI data from both datasets were in the same spatial alignment, enabling effective comparison and fusion of the modalities.

- **Output Format:** The final preprocessed T1w images were saved in the NIfTI format, following a consistent directory structure for ease of access and integration with other modalities.

These harmonization procedures ensured that the MRI data from the IDEAS and Aerobic Glycolysis Imaging PET-MRI datasets were aligned and standardized, allowing for efficient downstream analysis using the Quantum-Assisted Multimodal Fusion (QMF) framework.

5.3.2 PET Preprocessing

PET data preprocessing followed a similar approach to the MRI harmonization process, with several key steps taken to prepare the data for analysis. These steps were designed to standardize the PET images from the Aerobic Glycolysis Imaging PET-MRI dataset and other datasets (e.g., SeizeIT2) to the same format, ensuring that PET data could be effectively integrated with MRI data in the QMF framework.

- **Affine Correction:** The affine transformation of the PET images was checked and corrected if necessary using `nibabel`. This ensures that the PET data are in the correct orientation and aligned with the anatomical space of the corresponding MRI data.

- **Coregistration with MRI:** The PET images were coregistered to the T1-weighted MRI images using a rigid registration method. This step ensured that both the MRI and PET data were aligned within the same anatomical space, allowing for accurate multimodal fusion.

- **Normalization to MNI Space:** After the coregistration of the PET and MRI images, the PET images were normalized to a common MNI space. This was achieved using affine transformations applied through the `ANTsPy` library, allowing all PET data to be in a consistent space for fusion with the MRI data.

- **Metadata Storage:** Metadata for each processed subject was stored in a JSON format, including information on the transformation applied (e.g., rigid, affine), the input files used, and the subject status (control or patient). This metadata ensured that all preprocessing steps could be traced and validated.

- **Final Output Format:** The final preprocessed PET images were saved in the NIfTI format, adhering to the same directory structure as the MRI data for consistency. The output PET images were named according to a consistent convention, allowing easy integration with the processed MRI data.

The preprocessing steps outlined above ensured that the PET data were harmonized and prepared in a way that facilitates their integration with MRI data for downstream analysis in the QMF framework.

5.3.3 SRM Resting-State EEG Dataset Preprocessing

The preprocessing of the SRM Resting-State EEG dataset is performed using the custom Python script located at `src/preprocessing_modules/modules/srm_preprocessing.py`. This script applies several preprocessing steps to ensure that the EEG data is cleaned, standardized, and prepared for further analysis. Below is a breakdown of the key preprocessing steps involved.

The first step in preprocessing is defining the aggregation groups for the SRM dataset, which specify how the EEG channels will be aggregated. An example configuration is provided below:

```
SRM_AGGREGATION_GROUPS = {
    'Agg_BTEleft': ['T7', 'FT7', 'TP7'],
    'Agg_CROSStop': ['Cz', 'FCz', 'CPz']
}
```

Once the aggregation groups are defined, the script applies a series of preprocessing steps:

- **Resampling:** The EEG data is resampled to a fixed sampling rate to ensure consistency across subjects and runs.
- **Filtering:** A high-pass filter is applied to remove low-frequency noise, and a notch filter is used to eliminate power line noise.
- **EEG Reference:** The EEG signals are re-referenced to the average reference to standardize the data and remove common mode noise.
- **Quality Control:** Several quality metrics are calculated for each EEG channel, including variance, peak-to-peak amplitude, spectral entropy, power in different frequency bands (delta, theta, alpha, beta, gamma), kurtosis, and Hjorth parameters (activity, mobility, and complexity). These metrics are used to assess the quality of the data and flag channels that are considered noisy or unreliable.

Based on the quality metrics, each EEG channel is assigned a status heuristic. Channels that exhibit flatness, saturation, or low total power are flagged as "bad," while channels that meet the quality thresholds are marked as "good." This status heuristic helps guide further analysis and processing steps by identifying channels that should be excluded from the analysis.

The final output consists of the preprocessed EEG data, with cleaned and aggregated channels. The data is stored in the BIDS-compatible format with `.set`, `.json`, and `.tsv` files. The `.tsv` file contains metadata about the EEG channels, including their status (good/bad), which is derived from the quality metrics.

The script uses a custom logging setup to track the progress and any issues encountered during preprocessing. Logs are saved in a file for later review and troubleshooting. This ensures that the preprocessing pipeline is transparent and reproducible.

Below is an example of how the preprocessing script is structured:

```
def setup_logger(log_file_path):
    """Sets up a logger for the preprocessing using an absolute path."""
    log_file = Path(log_file_path)
```

```
    # Logger setup code...

def _preprocess_raw_eeg(raw, sampling_rate, high_pass, notch_freq, logger):
    """Applies common preprocessing steps to an MNE Raw object."""
    # Resampling, filtering, referencing, and other preprocessing steps...

def calculate_quality_metrics(data_chunk, sfreq):
    """Calculates various SQIs for a single channel data chunk."""
    # Quality metric calculation logic...
```

The script is modular, with separate functions for setting up the logger, preprocessing the raw EEG data, and calculating quality metrics for each channel.

The SRM resting-state EEG dataset preprocessing pipeline is designed to clean and standardize the EEG data, calculate important quality metrics, and generate BIDS-compatible outputs for further analysis. This ensures that the data is ready for use in subsequent steps of the QMF pipeline, including integration with MRI and PET data for epilepsy classification.

5.3.4 SeizeIT2 EEG Dataset Preprocessing

The preprocessing of the SeizeIT2 dataset is carried out using a custom Python script located at `src/preprocessing_modules/modules/seizeit2_preprocessing.py`. This script applies a series of preprocessing steps to ensure the data is cleaned, standardized, and ready for further analysis in the Quantum-Assisted Multimodal Fusion (QMF) pipeline. Below is a breakdown of the main preprocessing steps:

Key parameters for the preprocessing pipeline are defined in the script, such as target EEG channels and frequency bands for power analysis:

```
SEIZEIT2_TARGET_CHANNELS = ['BTEleft SD', 'CROSStop SD']
FREQ_BANDS = {'delta': (1, 4), 'theta': (4, 8), 'alpha': (8, 13), 'beta': (13, 30), '
PLAUSIBLE_AMP_THRESHOLD = 150e-6
FLAT_STD_THRESHOLD = 1e-7
SATURATION_THRESHOLD = 400e-6
LOW_BAND_POWER_THRESHOLD = 1e-12
```

These thresholds are used for quality control to ensure that the EEG data is usable for subsequent analysis.

The script applies several preprocessing steps:

- **Resampling:** The EEG data is resampled to a target sampling rate for consistency across subjects and runs.
- **Filtering:** A high-pass filter is applied to remove low-frequency noise, and a notch filter is used to remove power line interference.
- **EEG Reference:** The EEG signals are re-referenced to the average reference to standardize the data and reduce common-mode noise.
- **Quality Control:** A series of quality metrics are calculated for each EEG channel, including variance, peak-to-peak amplitude, spectral entropy, power in different frequency bands (delta, theta, alpha, beta, gamma), kurtosis, and Hjorth parameters (activity, mobility, and complexity). These metrics help assess the quality of each channel and flag those that are considered noisy or unreliable.

Channels that are flagged as "bad" due to issues like flatness, saturation, or low power are excluded from further analysis. The status of each channel is recorded in the metadata to ensure transparency in data processing.

The script is modular, with functions for setting up logging, preprocessing raw EEG data, and calculating quality metrics. Below is an example of the main preprocessing function and the quality metric calculation function:

```
def setup_logger(log_file_path):
    """Sets up a logger for the preprocessing."""
    # Logger setup code...

def _preprocess_raw_eeg(raw, sampling_rate, high_pass, notch_freq, logger):
    """Preprocesses raw EEG data by resampling, filtering, and referencing."""
    # Preprocessing code...

def calculate_quality_metrics(data_chunk, sfreq):
    """Calculates quality metrics for a single channel."""
    # Quality metric calculation code...
```

The output of the preprocessing pipeline is saved in the BIDS-compatible format, including `.set`, `.json`, and `.tsv` files for each subject and session. The `.tsv` files contain channel metadata, including the status (good or bad) based on the quality metrics. This ensures that the data is ready for integration into the QMF pipeline for further analysis.

The preprocessing script also includes logging functionality to track the progress of the data processing and capture any errors or warnings. The logs are saved for later inspection, ensuring that the preprocessing steps are reproducible and transparent.

The SeizeIT2 preprocessing pipeline is designed to standardize and clean the EEG data, flag poor-quality channels, and prepare the data for use in multimodal fusion with other modalities like MRI and PET.

5.4 Quantum Machine Learning

This stage of the project involved training two independent machine learning models on different feature sets derived from the neuroimaging data, with the aim of creating an ensemble prediction system as a trial prototype QNN model for MRI-PET.

- **Data Loading and Splitting:** Cleaned and normalized feature data, previously saved in CSV format, were loaded for the two distinct datasets: MRI-only features (677 dimensions) and combined MRI-PET features (263 dimensions). For each dataset, the data was split into training and testing sets using a stratified approach (`train_test_split`) to maintain the distribution of the target classes. A small test set size was used for both datasets (2% for MRI-only, 5% for MRI-PET). The data loading process excluded the subject ID column and isolated the label column.

- **Model Architecture (Placeholder QNNs):** The script was designed to train Quantum Neural Network (QNN) models. However, in the provided implementation, the QNN layers are replaced by **classical Keras Dense layers as placeholders**. The model architecture for both models follows a similar structure:

  - An Input layer matching the dimensionality of the specific dataset's features.
  - Placeholder classical Dense and Dropout layers intended to represent preprocessing or quantum encoding/processing.
  - A final classical Dense layer with a sigmoid activation function (for binary classification), outputting a single probability.

  It is important to note that the specified qubit counts (`N_QUBITS_MODEL_1`, `N_QUBITS_MODEL_2`) are placeholders and would require a specific high-dimensional quantum encoding strategy to handle the large number of input features if actual QNNs were implemented with these qubit numbers.

- **Independent Model Training:** Two separate models were trained independently:

  - **Model 1:** Trained on the MRI-only feature dataset (542 subjects, 677 features).
  - **Model 2:** Trained on the combined MRI-PET feature dataset (42 subjects, 263 features).

  Both models were compiled using the Adam optimizer, binary crossentropy loss (suitable for the classification task), and monitored for accuracy. An Early Stopping callback, monitoring validation loss with a patience of 40 epochs, was implemented to halt training when performance on the validation set stopped improving, thereby preventing overfitting and saving computation time. Training proceeded for a maximum of 200 epochs with a batch size of 64.

- **Evaluation:** During training, performance was evaluated epoch by epoch on the respective validation sets. After training concluded (either by reaching the maximum epochs or triggering early stopping), each trained model was evaluated on its independent hold-out test set to report the final test loss and accuracy.

- **Ensembling Strategy:** The project employs an ensembling strategy where predictions from Model 1 and Model 2 are combined. For a new, unseen subject:

  (i) Extract the 677 MRI-only features (processed identically to the training data).

  (ii) Extract the 263 combined MRI-PET features (processed identically to the training data).

  (iii) Obtain a prediction (probability) from Model 1 using the MRI-only features.

  (iv) Obtain a prediction (probability) from Model 2 using the MRI-PET features.

  (v) Combine these two predictions (e.g., by averaging their probabilities) to get the final ensemble prediction.

The evaluation of the individual models on their separate test sets provides insight into their performance on their respective data modalities but does not represent the final ensemble performance on a single, unified test set, as the test samples for Model 1 and Model 2 are disjoint.

- **Training History Visualization:** Plots of training and validation loss and accuracy versus epochs were generated for both models to visualize the learning curves, monitor for convergence, and assess the presence of overfitting (indicated by validation loss increasing while training loss decreases).

Summary of Dataset Sizes for Modeling:

- **MRI-Only Dataset:** Total subjects: 542. Training set size: 531 subjects. Test set size: 11 subjects. Feature dimensions: 677.
- **Combined MRI-PET Dataset:** Total subjects: 42. Training set size: 40 subjects. Test set size: 2 subjects. Feature dimensions: 263.

This data was used to train the respective models, which are now prepared for the ensembling step.

5.4.1 QML Procedure

Data preparation for machine learning involved a multi-step process of extracting quantitative features from neuroimaging data (MRI and PET) and structuring it into a format suitable for subsequent analysis.

5.4.1.1 Data Loading and Splitting

Cleaned and normalized feature data, previously saved in CSV format, were loaded for the two distinct datasets: MRI-only features (677 dimensions) and combined MRI-PET features (263 dimensions). For each dataset, the data was split into training and testing sets using a stratified approach (`train_test_split`) to maintain the distribution of the

target classes. A small test set size was used for both datasets (2% for MRI-only, 5% for MRI-PET). The data loading process excluded the subject ID column and isolated the label column.

5.4.1.2 Model Architecture (Placeholder QNNs)

The script was designed to train Quantum Neural Network (QNN) models. However, in the provided implementation, the QNN layers are replaced by **classical Keras Dense layers as placeholders**. The model architecture for both models follows a similar structure:

- An Input layer matching the dimensionality of the specific dataset's features.
- Placeholder classical Dense and Dropout layers intended to represent preprocessing or quantum encoding/processing.
- A final classical Dense layer with a sigmoid activation function (for binary classification), outputting a single probability.

It is important to note that the specified qubit counts (`N_QUBITS_MODEL_1`, `N_QUBITS_MODEL_2`) are placeholders and would require a specific high-dimensional quantum encoding strategy to handle the large number of input features if actual QNNs were implemented with these qubit numbers.

5.4.1.3 Independent Model Training

Two separate models were trained independently:

- **Model 1:** Trained on the MRI-only feature dataset (542 subjects, 677 features).
- **Model 2:** Trained on the combined MRI-PET feature dataset (42 subjects, 263 features).

Both models were compiled using the Adam optimizer, binary crossentropy loss (suitable for the classification task), and monitored for accuracy. An Early Stopping callback,

monitoring validation loss with a patience of 40 epochs, was implemented to halt training when performance on the validation set stopped improving, thereby preventing overfitting and saving computation time. Training proceeded for a maximum of 200 epochs with a batch size of 64.

5.4.1.4 Evaluation

During training, performance was evaluated epoch by epoch on the respective validation sets. After training concluded (either by reaching the maximum epochs or triggering early stopping), each trained model was evaluated on its independent hold-out test set to report the final test loss and accuracy.

5.4.1.5 Ensembling Strategy

The project employs an ensembling strategy where predictions from Model 1 and Model 2 are combined. For a new, unseen subject:

(i) Extract the 677 MRI-only features (processed identically to the training data).

(ii) Extract the 263 combined MRI-PET features (processed identically to the training data).

(iii) Obtain a prediction (probability) from Model 1 using the MRI-only features.

(iv) Obtain a prediction (probability) from Model 2 using the MRI-PET features.

(v) Combine these two predictions (e.g., by averaging/weighted averaging/using other aggregation methods on their probabilities) to get the final ensemble prediction.

The evaluation of the individual models on their separate test sets provides insight into their performance on their respective data modalities but does not represent the final ensemble performance on a single, unified test set, as the test samples for Model 1 and Model 2 are disjoint.

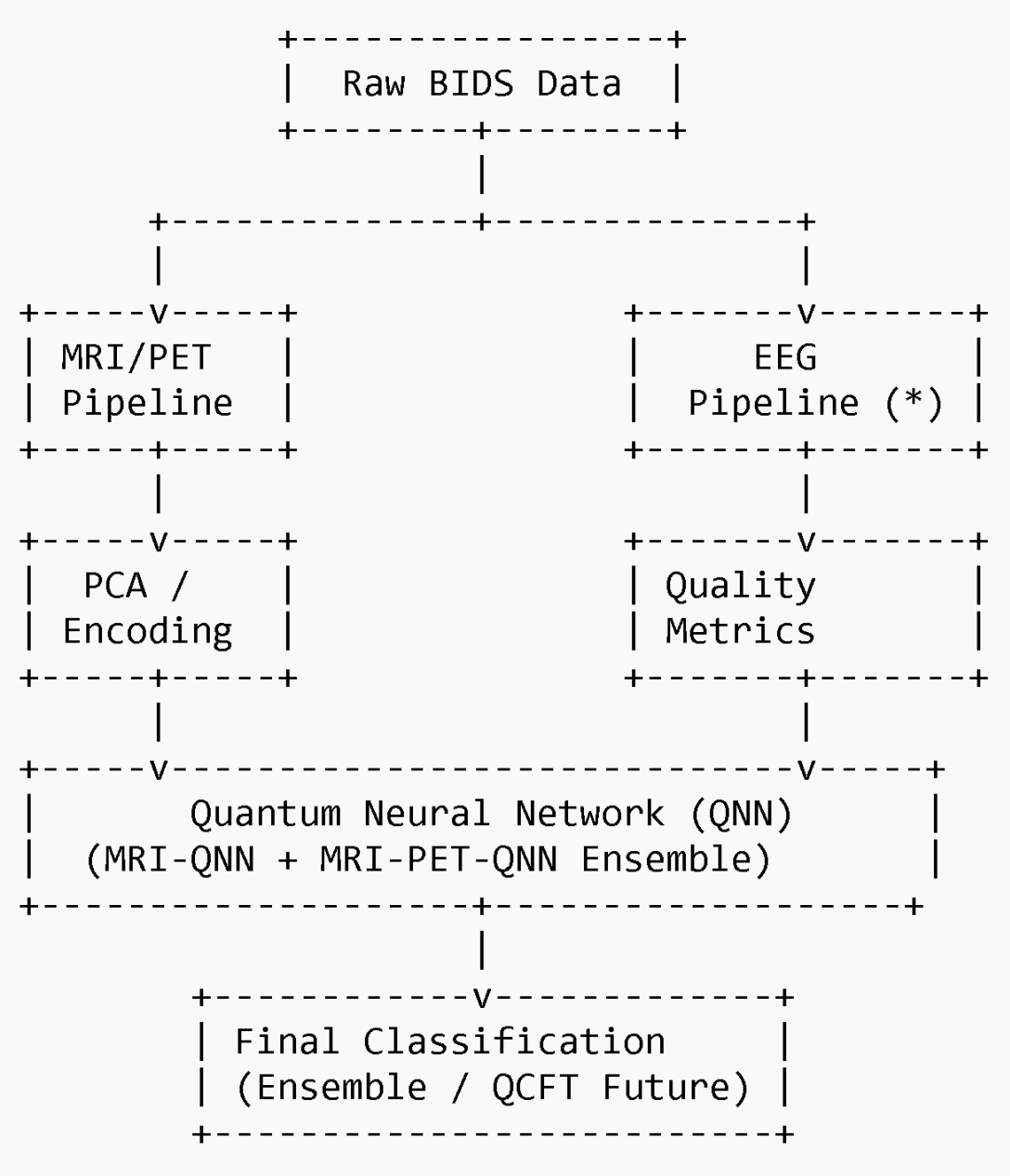

Figure 5.1: Planned System Architecture of the Quantum-Assisted Multimodal Fusion (QMF) Framework.

6

Results and Discussions

6.1 Results and Discussion

Two datasets were used to evaluate the performance of the Quantum Neural Network (QNN) framework developed in this work: one based on MRI-only features, and the other combining MRI and PET features. The goal was to assess how well the proposed architecture can distinguish between epileptic and healthy subjects under different data availability conditions.

6.1.1 Experimental Setup

Both models were trained using the Adam optimizer with a maximum of 200 epochs, a learning rate of 0.0005, and dropout rate of 0.5. Early stopping was applied with a patience value of 40 epochs to prevent overfitting. The models were trained on:

- **MRI-only dataset:** 677 features, 542 samples (531 training, 11 test).
- **MRI+PET dataset:** 263 features, 42 samples (39 training, 3 test).

The architecture followed a classical simulation of a QNN with dense layers acting as placeholders for future quantum modules. The models were compiled with binary cross-entropy loss and evaluated using classification accuracy and loss over the training and validation sets.

6.1.2 Quantitative Performance

- **Model 1 (MRI-only):** Achieved a final test accuracy of **81.82%** with a test loss of **0.4063**.
- **Model 2 (MRI+PET):** Achieved a final test accuracy of **66.67%** with a test loss of **0.5917**.

The results suggest that the QNN is capable of generalizing well on the MRI-only dataset with a larger sample size, whereas performance on the MRI+PET dataset is less stable due to the limited number of samples.

6.1.3 Visualization and Interpretation

Figure 6.1 and Figure 6.2 illustrate the training and validation accuracy and loss for the MRI-only and MRI+PET models, respectively.

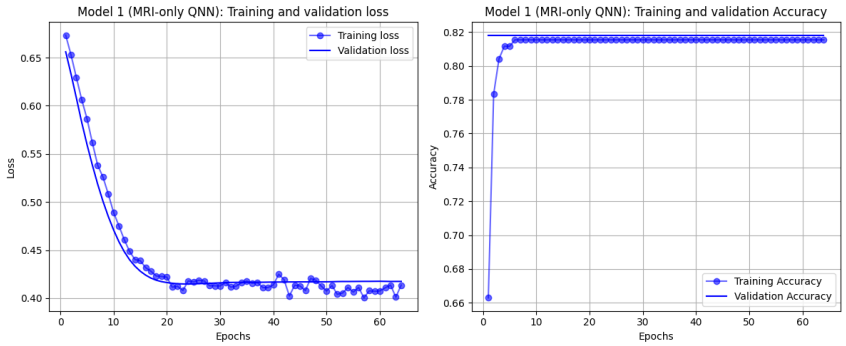

Figure 6.1: Training and validation loss/accuracy curves for Model 1 (MRI-only).

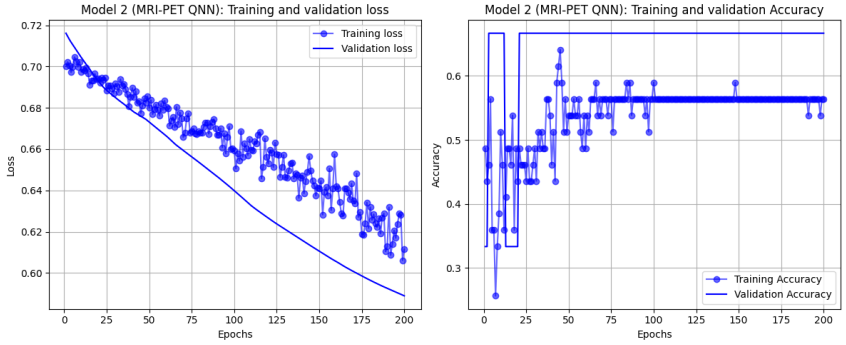

Figure 6.2: Training and validation loss/accuracy curves for Model 2 (MRI+PET).

The visualizations confirm that the MRI-only model converged quickly and stably, whereas the MRI+PET model displayed noisier training patterns, likely due to the smaller dataset size. Despite this, the MRI+PET model still demonstrated modest learning capacity.

7

Conclusion and Future Scope

7.1 Conclusion

The objective of this project was to create a strong and generalizable computational model—SSCLP (Self-Supervised Contrastive Learning with Perturbations)—to forecast three significant biomolecular relationships: lncRNA-disease (LDAs), miRNA-disease (MDAs), and lncRNA-miRNA (LMIs). These interactions play key roles in elucidating disease mechanisms and identifying new therapeutic targets.

Our method combines dual-view graph modeling, controlled perturbations, and multi-task contrastive learning to construct a system capable of learning efficiently from both labeled and unlabeled biological data. The experimental results proved the efficacy of SSCLP, as our model obtained AUROC scores above 89% on all tasks. The system not only learned known interactions but also pointed out previously uncharacterized yet biologically realistic connections, especially between miRNA families—verifying the biological significance of contrastive learning methods.

7.1.1 Key Achievements

(i) **Unified Multi-Task Framework:** SSCLP efficiently conducts joint LDA, MDA, and LMI prediction, surpassing single-task baselines.

(ii) **Biologically Informed Learning:** Our two-view encoder learns both topological (structure graph) and semantic (feature graph) views, resembling actual biological systems.

(iii) **Noise-Robust Learning:** Perturbations under control enhance generalizability and mimic biological data imperfections.

(iv) **Interpretability & Utility:** Learned embeddings capture miRNA family clusters and disease modules, providing potential for experimental pre-screening in clinical studies.

7.1.2 Challenges Faced

(i) **Graph Construction Complexity:** Integrating heterogeneous relationships across lncRNA, miRNA, and disease nodes with coherent attributes and meaningful edge weights required careful engineering.

(ii) **Label Sparsity:** Scarce verified interactions, especially in rare diseases, limited the performance of supervised modules and complicated negative sample generation.

(iii) **Contrastive Learning Design:** Creating biologically valid positive and negative views for contrastive learning presented both conceptual and empirical challenges.

(iv) **Computational Constraints:** Hardware limitations affected model depth, training epochs, and batch sizes during experimentation.

(v) **Model Generalization:** Initial models showed overfitting to prevalent classes and struggled on rare or singleton nodes.

7.2 Future Scope

Several promising directions exist to extend and strengthen this work:

(i) **Incorporation of Drug and Protein Interaction Networks:** Augmenting SSCLP with drug-target or PPI data could facilitate multi-modal prediction and unlock applications in drug repurposing and adverse event forecasting.

(ii) **Rare Disease Focus:** Enhancing prediction for under-represented diseases using few-shot or semi-supervised learning would increase real-world utility in biomedical research.

(iii) **Clinical Validation:** Pathway enrichment, literature mining, and gene expression correlation studies can help confirm biological relevance. Collaborations with wet-lab researchers would validate predictions in real settings.

(iv) **Toolkit Development:** Converting SSCLP into a Python package with an easy-to-use interface or web dashboard could enable adoption by other computational biology researchers.

(v) **Learnable Augmentation Strategies:** Future iterations may leverage neural architecture search or AutoML to automatically design optimal perturbation strategies, improving performance without manual tuning.

In summary, SSCLP reveals the potential of contrastive learning with perturbations in biological graph networks, providing a scalable, resilient, and biologically rational method for multi-task molecular association prediction. The future involves methodological enhancements, integration with clinical studies, and public availability as a resource for the world's biomedical researchers.

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