Computational Sequence-Based Prediction of Creutzfeldt-Jakob Disease (CJD) Using a Nonlinear Synaptic Pruning and Dendritic Integration Spiking Neural Network (NSPDI-SNN) AI Framework

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Creutzfeldt-Jakob Disease (CJD) is a deadly neurodegenerative disease caused by prion proteins (PrPSC), which trigger normal cellular proteins to misfold, resulting in aggregation and neuronal damage. Mutations in the PRNP gene can increase the risk of misfolding, yet testing variant pathogenicity in a lab is difficult given the long incubation times, ethical issues, and prion stability. This project developed and tested an Nonlinear Synaptic Pruning and Dendritic Integration Spiking Neural Network (NSPDI-SNN) AI framework to accurately classify PRNP amino acid sequences as pathogenic or benign, using ESM-2 amino acid sequence embeddings to encapsulate biochemical sequence patterns as inputs. Canonical and variant PRNP sequences were sourced from UniProt and other literature, then embedded using ESM-2, and passed to a neural network combining transformer encoder layers, attention-based pooling, and a biologically inspired NSPDI-SNN framework. The AI processed these embeddings with cross-entropy loss function, decoupled weight decay, AdamW optimization, and a cosine learning rate scheduler, with performance tracked using accuracy metrics and TensorBoard. A learned mean-residue embedding was applied to ensure consistent input shapes. The NSPDI-SNN model accurately classified pathogenic PRNP variants from benign sequences, with visualization methods confirming structured, reproducible differences between sequence types. The model recognized shared patterns across variants accurately rather than memorizing individual mutations. This framework offers a fast, intelligent tool for predicting prion pathogenicity, enabling future integration with structural data and larger variant datasets, and assisting in disease detection and prevention of Creutzfeldt-Jakob Disease.

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