Leveraging the Electrochemical Characteristics of a-Hemolysin Nanopores: Machine Learning & Low-Cost RNA Sequencing for Early Disease Diagnosis in Rural Areas

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In rural areas of the world, such as villages in India & Africa, inhabitants lack access to medical infrastructure. Due to this, early disease diagnosis is not possible, as early symptoms for statistically dominant diseases overlap. Current options for disease diagnosis are not accessible, as they require high upfront costs, areas of use/storage, and maintenance. Whole-transcriptome RNA sequencing is the gold standard for a multi-panel diagnosis for multiple diseases, but it is not possible due to the reasons outlined above. qPCR becomes inefficient and costly as biomarker panels expand. This project proposes a fundamentally different diagnostic paradigm: direct electrical classification of gene signatures without full RNA sequencing. While it has been proven that biological nanopores sustain a measurable ionic current under an applied voltage, experimentation regarding mock “RNA sequencing” has largely focused on reconstructing full nucleotide sequences, resulting in overly complex pipelines that extend beyond the requirements of multi-gene diagnostic classification. A low-cost nanopore system was constructed using a biological nanopore embedded in a lipid bilayer across a dual-reservoir setup with a constant voltage source. Rather than reconstructing nucleotide sequences, the system records ionic current blockade events as molecules interact with the pore. A 30-gene panel, defined through RNA-seq analysis, is selectively enriched using hybrid capture to increase on-target signal and suppress background. Event-level features, including blockade depth and dwell time, define gene-specific electrical “barcodes.” These signals are mapped to gene identities using a 1D convolutional neural network and aggregated into gene abundance vectors for disease classification.

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